Primary Prevention of Cardiovascular Disease

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LEARNING OBJECTIVES

1. Assess cardiovascular risk in the patient without previously diagnosed atherosclerotic cardiovascular disease (ASCVD).
2. Evaluate novel risk markers and cardiovascular screening tools in determining ASCVD risk.
3. Construct an evidence-based plan for therapeutic lifestyle change that incorporates nutrition, physical activity, and individual patient characteristics.
4. Assess the appropriateness of aspirin and statin therapy to lower ASCVD risk based on individual patient characteristics.
5. Justify the role of the pharmacist in primary prevention of cardiovascular disease.

ABBREVIATIONS IN THIS CHAPTER

ABI	Ankle-brachial index
ASCVD	Atherosclerotic cardiovascular disease
CAC	Coronary artery calcium
CIMT	Carotid intima-media thickness
hs-CRP	High sensitivity C-reactive protein

Table of other common abbreviations.

INTRODUCTION

Atherosclerotic cardiovascular disease (ASCVD) remains the leading cause of death in the United States (Benjamin 2017). Currently, one in three Americans have at least one type of ASCVD, with projections estimating that almost half of the U.S. population will have some form of ASCVD by 2030 (Benjamin 2017). Secondary prevention strategies to reduce ASCVD risk in patients with established disease are more clearly defined and viewed as less controversial than those for primary prevention, defined as asymptomatic individuals without established, or known, disease. Primary prevention strategies can significantly reduce ASCVD risk if certain healthy behaviors are adopted early and continued throughout the lifespan to avoid developing established ASCVD risk factors, such as high blood pressure and hyperlipidemia. In 2011, the American Heart Association set a goal to reduce deaths from ASCVD by 20% before the year 2020 (Lloyd-Jones 2010). To achieve this goal, a conceptual model of prevention named "Life's Simple 7" was developed to promote healthy behaviors. These metrics include smoking, body mass index, physical activity, healthy diet pattern, total cholesterol, blood pressure, and glucose. This approach provides guidance for individuals but also informs health promotion strategies at the population level. Clinical pharmacists, especially those in ambulatory care and community settings, can play a major role in helping to identify and improve modifiable risk factors (e.g., high blood pressure). This chapter focuses on risk factor assessment and therapeutic strategies that have been shown to be effective at primary prevention of ASCVD.

APPROACHES TO RISK ASSESSMENT

The terms *primary prevention* and *secondary prevention* suggest a dichotomous relationship; however, this assertion is inaccurate. Each patient likely lands on a spectrum of risk determined by a wide range of factors. Initial strategies to evaluate ASCVD risk relied on absolute presence or absence of independent risk factors (Box 1-1). Epidemiologic studies support the hypothesis that these risk factors do not equally contribute to ASCVD risk; instead, they are each affected by the presence of other health determinants.

Established ASCVD Risk Factors

Age, Sex, Race/Ethnicity

The prevalence of cardiovascular disease increases with age in both men and women (Benjamin 2017). Almost 70% of adults between the ages of 60 and 79 years have evidence of cardiovascular disease as indicated by either coronary heart disease, heart failure, stroke, or hypertension. Cardiovascular disease death is more common in men than women overall (age-adjusted death rates were 266.1 for men and 182.1 for women), but tends to be higher among non-Hispanic African American women than non-Hispanic African American men. Moreover, the age-adjusted death rates for coronary heart disease tend to be higher among non-Hispanic African American women compared with non-Hispanic white or Hispanic women.

Family History

Family history of cardiovascular disease in first-degree relatives tends to be associated with future risk. First-degree relatives share about half of their genetic variation with each other, and they also likely share negative lifestyle behaviors that contribute to similar phenotypic expression. Family history of one or both parents having a myocardial infarction increases the risk of myocardial infarction, especially if the event occurred before age 50 years. Paternal history of premature myocardial infarction (before age 50 results in a 2-fold increase of heart attack in men and increases the risk by 70% in women (Benjamin 2017). Using the Framingham Heart Study data for validation, most ASCVD risk factors are considered to have at least moderate heritability; however, most risk calculators do not account for family history.

Hypertension

Hypertension increases the risk for heart disease in a log-linear fashion. Adults with hypertension develop ASCVD five years earlier than their normotensive peers whose life expectancy is 5 years longer. Each systolic blood pressure rise of 20 mm Hg, and 10 mm Hg rise in diastolic blood pressure, is associated with a doubling in the risk of death from stroke, heart disease or other vascular disease. Hypertension affects more men than women up to age 64 years, but the percentage of women with

Box 1-1. Major Risk Factors for ASCVD

- Age (men ≥45 years; women ≥55 years)
- Family history of early CHD
  Age <55 years in male first-degree relative
  Age <65 years in female first-degree relative
- Current cigarette smoking
- High blood pressure (≥140/≥90 mm Hg or on blood pressure medication)
- Low HDL
  Men <40 mg/dL
  Women <50 mg/dL

CHD = coronary heart disease; HDL = high-density lipoprotein cholesterol.

Information from: Jacobson TA, Ito MK, Maki KC, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 1—executive summary. J Clin Lipidol 2014;8:473-88.

BASELINE KNOWLEDGE STATEMENTS

Readers of this chapter are presumed to be familiar with the following:

- General knowledge of the pathophysiology that leads to the development of atherosclerotic cardiovascular disease (ASCVD)
- Drug knowledge of pharmacological strategies (i.e., aspirin, statins) used for primary prevention of ASCVD.
- Current clinical practice guidelines for the management of hyperlipidemia, diabetes, and hypertension.

Table of common laboratory reference values.

ADDITIONAL READINGS

The following free resources have additional background information on this topic:

- 2013 ACC/AHA Cardiovascular Risk Guideline. Circulation 2014;129(suppl 2):S49-73.
- 2013 ACC/AHA Blood Cholesterol Guideline. 2014;63:2889-934.
- 2016 USPSTF Recommendation Statement on Aspirin
- 2016 USPSTF Recommendation Statement on Statin Use for the Primary Prevention of Cardiovascular Disease in Adults
- American College of Cardiology Mobile Apps
  - ASCVD Risk Estimator Plus
  - Guideline Clinical App
  - LDL Manager
  - Statin Intolerance App

hypertension is higher for those older than age 65. Despite improved awareness campaigns about the risk of hypertension, about 15.9% of adults in the United States with hypertension remain unaware of their disease. The prevalence of hypertension among patients age 60 years and older is 67.2%, whereas only 11% of children and adolescents between ages 8 and 17 years have high or borderline high blood pressure. Additionally, the prevalence of hypertension among non-Hispanic African Americans is 45% for men and 46.3% for women, the highest among all other ethnic groups at all ages. Even more concerning is control rates among hypertensive U.S. adults continue to hover around 50% (Benjamin 2017).

Hyperlipidemia

Deposition of cholesterol carried by apolipoprotein B-containing lipoproteins into the endothelial lining of arteries is the root cause of atherosclerosis. Long-term exposure to even moderately elevated levels of LDL and non-HDL is an essential component of most clinical ASCVD events. About 11.9% of adults age 20 years and older have total cholesterol levels ≥240 mg/dL, and higher rates of hyperlipidemia are observed in non-Hispanic whites (12.5%) and Hispanic (13.1%) adults. The overall prevalence of abnormal lipid levels requiring treatment based on the 2013 ACC/AHA Blood Cholesterol Guideline could result in more than 45 million middle-aged Americans without ASCVD being recommended to start statin therapy (Stone 2014). Although low levels of HDL are not considered a target of therapy due to the lack of proven benefit with interventions that raise HDL, low HDL is associated with increased ASCVD risk and is a major risk factor for ASCVD (Jacobson 2014).

Diabetes

Diabetes is a major risk factor for ASCVD, affecting 23.4 million diagnosed adults and 7.6 million adults who are undiagnosed. The risk of ASCVD increases with increasing duration of diabetes; for every decade with diabetes, the relative risk of coronary heart disease is 1.38 times higher and the risk of coronary heart disease death is 1.86 times higher (Benjamin 2017). The increasing prevalence of diabetes results in an increasing rate of ASCVD that is also influenced by body habitus. Based on data from the Framingham Heart Study over 30 years, the incidence of ASCVD among normal-weight women with diabetes was 54.8% compared with 78.8% among obese women. Men with diabetes display a similar ASCVD trend, with 78.6% incidence of ASCVD in normal-weight men and 86.9% in obese men. Among people older than 65 years with diabetes, 68% of deaths are attributable to heart disease and 16% are due to stroke. In general, heart disease deaths are 2 to 4 times as likely among people with diabetes compared with those without diabetes.

Tobacco Use

Almost one-third of ASCVD deaths in adults older than age 35 years are attributable to smoking or secondhand smoke exposure (Benjamin 2017). Tobacco smoking is the leading cause of preventable deaths worldwide. Men who smoke die 13.2 years earlier than nonsmokers; women smokers die 14.5 years earlier than their nonsmoking peers. In general, the mortality rate in the United States is 3 times higher for smokers than for those who never smoked. A particularly concerning observation is that ASCVD risk dramatically increases with low levels of cigarette exposure, including secondhand smoke. Among adults older than age 18 years, the prevalence of smoking is higher in those with physical disability and psychiatric illness. Smoking is also inversely associated with family income; the rate of smoking for adults living below the federal poverty line is 26.3% compared with 15.2% for those living at or above poverty level. Smoking rates are highest among non-Hispanic Indian or Alaskan Native males (25.6%), followed by non-Hispanic African American males (20.9%), Hispanic males (14.3%), and non-Hispanic Asian males (13.4%). The highest regional prevalence of cigarette smoking in the United States occurs in the Midwest (23.7%), while individual states with the highest prevalence include: West Virginia (26.7%), Kentucky (26.2%), Arkansas (24.7%), and Tennessee (24.2%). Fortunately, the age-adjusted rate of smoking has declined significantly since publication of the U.S. Surgeon General's report in 1965 (51% to 16.7% for men; 34% to 13.7% for women), suggesting that public health measures implemented during that period have been successful (Benjamin 2017).

Quitting smoking is extremely difficult: Almost seven in ten smokers want to quit smoking, and more than four in ten attempted to quit in the past year. Although decreasing smoking is a proven quit method, even a few cigarettes per day convey substantial ASCVD risk. Quitting smoking at any age decreases the mortality risk from smoking-related diseases. Stopping smoking dramatically decreases ASCVD risk after just 1 year; stroke risk decreases to that of nonsmokers between 2 to 5 years after quitting; overall ASCVD risk decreases to that of nonsmokers after about 10 years of cessation (Benjamin 2017).

Tools to Estimate ASCVD Risk

Several tools are available to estimate ASCVD risk in adults between ages 20 and 79 years. These tools are intended to more accurately define ASCVD risk for treatment-naive patients who lack evidence of established ASCVD (Table 1-1).

Framingham Risk Calculator

The Framingham Risk Calculator was the first risk scoring system to be adopted as part of a national guideline. The Third National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP-III) Guidelines recommended using the Framingham Risk Calculator in patients without ASCVD (or a risk equivalent) and two or more traditional risk factors (Grundy 2002). Patients with a 10-year risk score of more than 20% for death or definite myocardial infarction were determined to be at high cardiovascular risk. Use of

Table 1-1. Characteristics of ASCVD Risk Score

Risk Calculator	Endorsement	Outcome
Framingham Risk Calculator	ATP III (2001) and NLA (2014)	10-year risk of definite MI or death
Pooled Cohort Equation Risk Calculator	ACC/AHA (2013)	10-year and lifetime ASCVD risk (coronary death or nonfatal myocardial infarction, or fatal or nonfatal stroke)
Reynolds Risk Score (2008)	Not included in national guidelines	10-year, 20-year and 30-year risk of MI, stroke or revascularization
Million Hearts Longitudinal ASCVD Risk Assessment Tool (2017)	Not included in national guidelines	10-year ASCVD risk *and* projects changes in risk expected with therapy initiation

ACC/AHA = American College of Cardiology/American Heart Association; ASCVD = atherosclerotic cardiovascular disease; ATP = Adult Treatment Panel; MI = myocardial infarction; NLA = National Lipid Association.

hard cardiovascular end points in this risk score increases its reliability but limits its ability to predict other heart-related outcomes of interest to patients. Also, the predominantly white population in the Framingham database limits its application to other ethnic groups. Revision of the Framingham risk score in 2008 increased the number of inputs to include diabetes and mapped the outcomes to include stroke, stroke death, and heart failure.

Reynolds Risk Score

The Reynolds Risk Score sought to improve upon the Framingham Calculator by adding family history and high-sensitivity C-reactive protein (hs-CRP). The final equations were validated in women using data from the Nurses' Health Study in 2007 and in men from the Physicians' Health Study in 2008. A comparison of the ATP-III and Framingham Scores found that the Reynolds Risk Score better predicted cardiovascular events in white and African American women (Cook 2012). Whereas the ATP-III and Framingham scores tended to overpredict cardiovascular risk in women, the Reynolds Risk Score was better calibrated in a population that excluded diabetes. This calculator is not endorsed by any guideline or organization, but provides an additional tool to educate patients and determine treatment course.

Pooled Cohort Equation

The Pooled Cohort equation was created and included in the 2013 American College of Cardiology/American Heart Association (ACC/AHA) Cardiovascular Risk Guideline (Goff 2013). This equation sought to expand the population reach from Framingham to include African American patients to better represent the U.S. population. It also broadened the outcomes of interest to include fatal or nonfatal stroke. Despite these improvements, the equation lacks specificity for certain ethnicities. For comparison with non-Hispanic white adults, the equation tends to overestimate 10-year risk of ASCVD events in Hispanic Americans and Asian Americans, but underestimates risk in the American Indian population. Until an algorithm is sufficiently validated in these populations, providers are encouraged to use the current equation and consider secondary risk factors.

Million Hearts Longitudinal ASCVD Risk Assessment Tool

The Million Hearts Longitudinal ASCVD Risk Assessment Tool fills a gap left out from the other risk estimators (Lloyd-Jones 2017). Because the online tools provide a single estimate of risk, they are often used with patients to aid in shared decision-making. However, previous tools were not developed to accurately predict the effects of implementing cardiovascular prevention strategies in a specific patient. For example, simply changing a patient from "smoker" to "nonsmoker" in the Pooled Cohort equation does not accurately predict the true response. The Million Hearts Tool builds on the benefits of a single risk estimate by mapping the effects of initiating and adherence to "ABCs" (aspirin therapy in appropriate patients, blood pressure control, cholesterol management, and smoking cessation) therapies.

Although the various estimators for ASCVD risk are useful, they are limited by the population characteristics from which they were validated. For specific patients, the predictive value of the algorithm depends on how closely the patient fits the inclusion and exclusion criteria of the validation studies. The most practical solution to avoid inappropriate risk classification is to consistently begin ASCVD risk assessment with the presence or absence of traditional risk factors before assigning a 10-year risk estimation. For younger patients (between ages 20 and 39 years) or those at low 10-year risk (less than 7.5% for adults between ages 40 and 59 years) using the Pooled Cohort equation, providers may consider lifetime or 30-year risk to better inform patient treatment decisions. For example, a lifetime ASCVD risk >50% may be useful to motivate a young patient to engage in lifestyle interventions. Providers should also consider the results from multiple risk

estimators in those primary prevention patients when treatment decisions are not clear. Finally, the risks, benefits, and cost of treatment should be carefully discussed with patients before determining a therapy plan.

Other Cardiovascular Risk Markers

Although traditional risk factors for ASCVD are often the focus of risk assessment, it is well established that other risk factors should be considered when evaluating individual ASCVD risk. These include blood and urine markers (e.g., hs-CRP and albuminuria), measures of subclinical disease (e.g., coronary artery calcium [CAC]), and family history. The 2013 ACC/AHA Cardiovascular Risk Guideline was cautious to avoid widely recommending these additional risk markers due to limited randomized controlled trial evidence, evaluation of their cost-effectiveness, and potential for harm (Goff 2017). With that said, the Guideline Work Group did recommend (based on expert opinion) that knowledge of family history of premature ASCVD, hs-CRP, CAC, and/or Ankle-brachial index (ABI) may be useful when a risk-based decision is unclear (Table 1-2).

Family History as an Independent Risk Marker

Although family history of ASCVD has long been recognized as a major risk factor, there are limitations to incorporating it into 10-year risk assessment tools. The Cooper Center Longitudinal Study evaluated the long-term risk (more than 10 years) of family history in 49,255 men and demonstrated that those with a family history of premature (defined as younger than age 50 years) ASCVD had a 50% higher lifetime risk of ASCVD and mortality than those without a family history of ASCVD (Bachmann 2012). Interestingly, family history of ASCVD contributes only modestly to short-term risk (less than 10 years), and thus, has been omitted from most risk prediction tools used to estimate short-term risk.

The significance of family history as a risk factor depends greatly on the age at which the family member was diagnosed with ASCVD. As such, clinicians should focus on identifying patients with a family history of premature ASCVD. Although cutoffs for age of presentation and definitions for relatives vary, the generally accepted definition of *premature family history* is younger than age 55 years for a first-degree male relative and younger than age 65 years for a first-degree female relative. A first-degree relative includes an individual's biological parents, siblings, and offspring. A major limitation of family history is the reliance on the patient's knowledge of their personal family history, which may be inaccurate, or unknown, such as in the case of a patient who was adopted. Additionally, the presence of additional modifiable risk factors or lifestyle habits, such as tobacco use or sedentary lifestyle, may differ between members of a family and influence their ASCVD risk.

Table 1-2. Recommended Thresholds for Revising Individual ASCVD Risk

Risk Marker	Threshold to Revise Risk Assessment
Family history of premature ASCVD	1st-degree male relative age <55 years[a] 1st-degree female relative age <65 years[a]
hs-CRP	≥2 mg/L
CAC Score	≥300 Agatston units or >75th percentile for age, sex, and ethnicity[b]
ABI	<0.9

[a]1st-degree relative: biological parents, siblings, and children

[b]www.mesa-nhlbi.org/CACReference.aspx

ABI = ankle-brachial index; ASCVD = atherosclerotic cardiovascular disease; CAC = coronary artery calcium; hs-CRP = high-sensitivity C-reactive protein.

High-Sensitivity C-Reactive Protein

Vascular inflammation plays a significant role in the development and progression of atherosclerosis. The most commonly used biomarker of vascular inflammation is hs-CRP, a downstream acute-phase protein produced by the liver in the presence of inflammation in the body. Although nonspecific, elevated hs-CRP is a strong predictor of ASCVD risk in healthy individuals and those with stable coronary heart disease (Ridker 2008). Furthermore, high levels of hs-CRP (>10 mg/L) are often associated with acute illnesses (e.g., infection) and autoimmune disorders (e.g., rheumatoid arthritis), whereas moderately elevated levels of hs-CRP (1–10 mg/L) is more indicative of chronic vascular inflammation. As such, an hs-CRP of ≥2 mg/L is often the threshold for which an upward adjustment in an individual's ASCVD risk is suggested.

The clinical utility of hs-CRP was evaluated in the JUPITER study, which randomized almost 18,000 subjects to rosuvastatin 20 mg/day or placebo (Ridker 2008). Enrolled subjects had low or normal levels of LDL (median 108 mg/dL) but an elevated hs-CRP of ≥2 mg/L (median 4.2 mg/L). The study was stopped early after a median follow-up of 1.9 years due to an observed 44% relative risk reduction in the primary end point of a first major cardiovascular event or death in the rosuvastatin group. The early stopping of JUPITER may have led to an overestimation of benefit; it is important to note that JUPITER only enrolled patients with elevated hs-CRP levels. Recently, the HOPE-3 trial found that rosuvastatin 10 mg/day reduced the co-primary outcome (death from cardiovascular disease, nonfatal myocardial infarction, or nonfatal stroke) by 24% regardless of whether baseline hs-CRP was elevated (Yusuf 2016). Additionally, two Mendelian analyses found hs-CRP has no causal role of in the development of atherosclerosis and coronary heart disease (Elliot 2009; Zacho 2008). These

data suggest hs-CRP may be a poor risk discriminator in intermediate-risk patients and is not a reliable target of therapy. It is, however, a reliable biomarker of inflammation that remains useful in assessing the need for statin therapy in select intermediate-risk patients. Recent efforts have shifted to a focus on investigating the upstream interleukin-1 signaling pathway as a potential causal pathway and therapeutic target (Ridker 2016).

Coronary Artery Calcium Score

Atherosclerotic calcification coincides with the formation of fatty streaks in the coronary arteries and is a well-established independent risk factor for ASCVD (Goff 2013). With the discovery of radiography in the 20th century, calcium was the only recognizable feature found during radiographic imaging of the heart due to its large density. Calcium is deposited in atherosclerotic coronary arteries, similar to the mechanism for increased bone formation and remodeling, yet the precise sequence of events causing this phenomenon remains unclear. Nevertheless, the detection of calcium in coronary arteries is an effective biomarker for diseased arteries. Improvements in computed tomography technology have made it possible to measure CAC in a relatively quick and noninvasive manner.

Whereas the primary use of CAC testing is to determine if an individual's ASCVD risk should be adjusted upward, one study has suggested that CAC testing could be used to "de-risk" patients. An analysis of the MESA study found that about 50% of individuals with a 10-year ASCVD risk score between 7.5% and 20% could be "de-risked" if their CAC score was zero (Blaha 2016). Such an approach may also be cost effective by reducing the number of individuals on statin therapy and the occurrence of statin-related adverse effects. It is also true that CAC testing may be useful to reclassify a perceived low-risk patient as being at higher risk in some cases. Based on this evidence, it is reasonable to consider CAC testing in patients whose 10-year ASCVD risk is less than 5% to help inform clinical decision-making (Pender 2016).

The 2013 ACC/AHA Cardiovascular Risk Guideline determined that CAC testing was likely the most useful approach to improve risk assessment in individuals deemed to be at intermediate risk after using traditional risk assessment approaches. Concerns regarding the cost-effectiveness and potential for radiation exposure have limited its widespread use and led to a Class IIb recommendation.

Ankle-Brachial Index

The ABI is the ratio of the systolic blood pressure at the ankle and brachial artery and is primarily indicated to screen symptomatic patients for peripheral artery disease. Additionally, there has been considerable interest in evaluating the use of ABI to serve as a general marker of atherosclerosis at other sites because it is non-invasive. Evidence suggests that adding the ABI to the traditional Framingham Risk Score leads to reclassification of risk for some patients; however, it remains unknown if this reclassification is appropriate and actually improves clinical outcomes (Fowkes 2008). In 2013, the U.S. Preventive Services Task Force found insufficient evidence to support widespread use of ABI to screen asymptomatic patients for peripheral artery disease or other forms of ASCVD (Moyer 2013). Additional concerns about the reliability of ABI are the lack of clear standards for measuring and interpreting ABI and the variation in the procedures used by the examiner to perform the test (e.g., patient's positioning, cuff size used for the arm and ankle).

Carotid Intima-Media Thickness

Carotid intima-media thickness (CIMT) can be measured using non-invasive imaging, which captures ultrasound images of both the right and left carotid arteries. These images are used to measure the distance between the lumen-intima interface and the media-adventitia interface. The wide availability, safety, and reproducibility have created significant interest in CIMT as a surrogate marker of atherosclerosis. A meta-analysis of adding a one-time CIMT measurement to the Framingham Risk Score found only small improvement in 10-year risk prediction with limited clinical significance (Den Ruijter 2012). Another meta-analysis evaluated the benefit of serial CIMT measurements (defined as ≥2) and found no association between CIMT progression and ASCVD risk (Lorenz 2012). As such, the 2013 ACC/AHA Cardiovascular Risk Guideline does not recommend CIMT for routine measurement in clinical practice, citing the lack of evidence to support a discernable benefit.

Albuminuria

Albuminuria, defined as increased urinary excretion of albumin ≥30 mg/day, is an early marker of kidney disease and associated with an increased risk of ASCVD in patients with and without diabetes. Traditional risk factors and risk factors associated with chronic kidney disease (e.g., albuminuria) both contribute to the excessively high ASCVD risk observed in patients with chronic kidney disease. The mechanism by which albuminuria increases ASCVD risk remains unclear, but one hypothesis is that albuminuria may be an early indicator of endothelial dysfunction (Cosson 2006). Screening for albuminuria is most often performed by obtaining a random spot urine collection to determine the urinary albumin-to-creatinine ratio instead of timed or 24-hour collections because of the additional burden on the patient and lack of additional accuracy. Several observed increases in urinary albumin excretion over a period of months is needed to confirm albuminuria because urinary albumin excretion varies for biological reasons and in the setting of fever, infection, elevated blood pressure, and exercise. Currently, only patients with diabetes are recommended to have routine annual screenings for albuminuria; widespread screening in patients with hypertension, but without diabetes, provides little value and may not be cost-effective (ADA 2017;

Patient Care Scenario

A 41-year-old non-Hispanic African American man presents for evaluation of his ASCVD risk. His mother is still living, and his father died from a myocardial infarction at age 52 years. This patient has hypertension for which he takes hydrochlorothiazide but no other prescription medications. He works as an accountant, does not smoke, and "tries to exercise when he has time." His vital signs and laboratory findings are as follows: blood pressure 138/86 mm Hg; weight 102.5 kg [226 lb]; body mass index 38.9 kg/m^2; total cholesterol 231 mg/dL; triglyceride 120 mg/dL; HDL 61 mg/dL; LDL 146 mg/dL; urine albumin/creatinine 33 mg/g; hs-CRP 3.4 mg/L; and CAC 476 Agatston units. In addition, his Pooled Cohort 10-year ASCVD risk is 6.2%, and lifetime ASCVD risk is 50%. Reynolds Risk Score 10-year at age 45 years = 5%, age 55 = 11%, age 65 = 21%.

Evaluate the ASCVD risk for this patient and determine the next steps to decrease his risk.

ANSWER

Cardiovascular risk is higher in African American patients than non-Hispanic white adults. This patient has two major ASCVD risk factors (family history and hypertension). The next step is to estimate his ASCVD risk using the Pooled Cohort Calculator. Due to his young age, his 10-year ASCVD risk falls below the 7.5% threshold to consider statin therapy; however, his lifetime risk is 50%, which is considered high. To further evaluate his risk, an hs-CRP was drawn. The hs-CRP (3.4 mg/L) of greater than 22 mg/L indicates a higher ASCVD risk than the Pooled Cohort Calculation. When included in the Reynolds Risk Score, the hs-CRP with the family history of this patient describes an exponential rise in ASCVD risk as the patient ages. The CAC score (476 Agatston units) of >300 Agatston units also suggests a higher ASCVD risk and complements the risk imparted by his family history.

This patient is at higher ASCVD risk than calculated by Pooled Cohort equation and would benefit from intensification of therapeutic lifestyle changes and initiation of a Mediterranean or DASH diet. Due to the calculated ASCVD risk and presence of additional risk markers (e.g., hs-CRP, CAC score), he would likely benefit from initiation of a high intensity statin, such as atorvastatin 40–80 mg/day or rosuvastatin 20–40 mg/day.

1. Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart disease and stroke statistics–2017 update: a report from the American Heart Association. Circulation 2017 Mar 7;135:e146-603.
2. Goff DC Jr, Lloyd-Jones DM, Bennett G, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014 Jul 1;63:2935-59.
3. Stone NJ, Robinson J, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults. J Am Coll Cardiol 2014;63:2889-934.

Boulware 2003). As such, the 2013 ACC/AHA Cardiovascular Risk Guideline made no recommendation for or against albuminuria screening.

Other Conditions Associated with High Risk of ASCVD

It is well acknowledged that individuals with certain comorbid conditions are at particularly high risk of ASCVD compared with that of the general population (Jacobson 2015). These conditions include HIV and rheumatologic and other inflammatory conditions. However, individuals with these conditions are poorly represented in randomized controlled trials, limiting our understanding of how to treat these patients and apply national guidelines to these patients. The 2013 ACC/AHA Cardiovascular Risk Guideline does not include recommendations for these high-risk groups. Similarly, the 2013 ACC/AHA Blood Cholesterol Guideline only recommends clinical judgment regarding the use of statins in those with HIV or with rheumatologic or other inflammatory conditions. However, the National Lipid Association Recommendations for Patient-Centered Management of Dyslipidemia: Part 2 offers clinicians specific guidance on approaches to risk assessment and prevention strategies in patients with rheumatoid arthritis and HIV (Jacobson 2015).

Human Immunodeficiency Virus

With the advent of antiretroviral therapies, individuals with HIV effectively have similar life spans to that of the general population. HIV is associated with an increased risk of ASCVD, especially in untreated individuals, even after adjusting for traditional risk factors. Metabolic abnormalities are common in those treated with antiretroviral therapy, including hypertriglyceridemia, insulin resistance, and lipodystrophy. Novel antiretroviral therapies are not as strongly associated with metabolic adverse effects. Regardless, continuous antiretroviral therapy is highly recommended as HIV-infected individuals on antiretroviral therapies are at lower risk of ASCVD. Controlling modifiable risk factors, such as dyslipidemia, is also important. Risk assessment in individuals with HIV is challenging because they are often not represented in cohort studies used to develop risk assessment tools. The National Lipid Association does, however, suggest counting HIV as a risk factor when assessing ASCVD risk and determining appropriate treatment goals for dyslipidemia. Statin therapy should be considered in these individuals but

drug–drug interactions with antiretroviral therapies must be considered when selecting statin therapy (Jacobson 2015, Wiggins 2017). Atorvastatin, pitavastatin, pravastatin, and rosuvastatin are reasonable choices for most patients on antiretroviral therapy; ultimately however statin selection will depend on an individual patient's antiretroviral treatment regimen.

Rheumatoid Arthritis

The systemic inflammation associated with rheumatoid arthritis affects not only joints but the vasculature as well. Unsurprisingly, the ASCVD risk in patients with RA is 1.5–2.0 times higher than the general population, and ASCVD is the leading cause of death in these patients (Jacobson 2015). The chronic inflammation associated with rheumatoid arthritis may accelerate the development of atherosclerosis, particularly in patients with other uncontrolled ASCVD risk factors. Risk assessment in rheumatoid arthritis patients is challenging, and none of the known risk assessment tools have been proven to be very useful in this patient population. To complicate matters, LDL levels may be falsely low during an acute flare and may require repeating the lipid panel when the patient is more stable to accurately assess ASCVD risk. Furthermore, certain rheumatoid arthritis therapies (e.g., tofacitinib, tocilizumab) actually increase LDL levels by 15%–20% and require lipid monitoring 4-8 weeks after initiation. Based on limited evidence to suggest otherwise, the National Lipid Association recommends the same treatment goals and statins as first-line therapy for lowering ASCVD risk in patients with rheumatoid arthritis as the general population.

PRIMARY PREVENTION STRATEGIES

Whereas performing risk assessments to increase individual awareness of ASCVD risk is the first step in providing comprehensive cardiovascular risk reduction, this process also informs patients regarding the benefits and risks of interventions shown to reduce ASCVD risk. The cornerstone of any primary prevention strategy is lifestyle management, which includes following a healthy eating pattern, engaging in regular physical activity, maintaining a healthy weight, and avoiding tobacco products. Additionally, certain pharmacological interventions, including aspirin and statins, have indications for primary prevention and are considered in select patient groups based on their ASCVD risk.

Lifestyle Management

It is well established that maintaining a healthy weight, following a healthy dietary pattern, exercising regularly, and not using tobacco products markedly reduces ASCVD risk. Adherence to such a lifestyle has also been shown to offset genetic factors associated with increased ASCVD risk (Khera 2016). Khera and colleagues evaluated individuals from several population cohort studies by using a polygenic risk score of DNA polymorphism and adherence to four lifestyle factors: no cigarette smoking, no obesity, physical activity, and a healthy diet. Among participants at high genetic risk, adherence to three of the four lifestyle factors was associated with a 46% reduction in coronary events. Thus, lifestyle interventions are of major importance for all patients, including individuals predisposed to ASCVD because of family history. It is beyond the scope of this chapter to extensively review the intricacies of lifestyle management. Instead, we will highlight key lifestyle management recommendations that are essential to the primary prevention of cardiovascular disease.

Heart Healthy Dietary Patterns

Dietary patterns are often measured by their impact on surrogate markers, such as weight or blood pressure, but modern nutritional science has shifted in recent years to focus more on the impact that certain dietary patterns have on cardiovascular and metabolic health outcomes (Mozaffarian 2016). Despite the popularization of isolated nutrient-specific diets, such as the low-fat and low-carbohydrate diets, the clinical benefit of these diets on cardiovascular disease is sparse. In fact, the 2015 Dietary Guidelines Advisory Committee determined that low-fat diets have no effect on cardiovascular disease. Contrarily, the Mediterranean and DASH diets, both of which emphasize fruits, vegetables, and healthy fats (e.g., fish, nuts), are the most well studied dietary patterns that have been shown to not only improve surrogate markers (e.g., blood pressure, insulin resistance), but also clinical outcomes (Mozaffarian 2016). The PREDIMED study was a randomized trial that assigned participants at high cardiovascular risk to a Mediterranean diet supplemented with extra-virgin olive oil, a Mediterranean diet supplemented with mixed nuts, or a control group (low-fat diet) (Estruch 2013). Of note, none of the study participants were advised to restrict calories. The trial was stopped after median follow-up of 4.8 years due to a significant 30% reduction in the primary end point of major cardiovascular events (i.e., myocardial infarction, stroke, or death from cardiovascular causes) for those assigned to either of the Mediterranean diets versus the control group. It is important to note that this reduction was driven primarily by the significant reduction in stroke, although favorable trends were observed for the other secondary end points. A key limitation of PREDIMED is its limited external validity because 97% of the participants were White Europeans, which does not represent other important racial/ethnic groups. Nevertheless, PREDIMED was the first study to demonstrate the benefit of a Mediterranean diet supplemented with added "healthy" fats in the primary prevention of cardiovascular disease.

Physical Activity Behaviors

Physical activity is protective against cardiovascular disease, reduces cardiovascular morbidity and mortality, and reduces the risk of developing key risk factors (e.g., hypertension, obesity) that can lead to, or accelerate, atherosclerosis.

Contrarily, sedentary lifestyle rivals smoking as one of the leading preventable causes of death. Despite the preventive and therapeutic benefit of physical activity, only half of Americans are sufficiently physically active (Centers for Disease Control and Prevention [CDC] 2017. The American Heart Association and American College of Sports Medicine currently recommend 30 minutes or more of moderate-intensity physical activity 5 days per week, 25 minutes of vigorous aerobic activity 3 days per week, or a combination of the two, plus resistance training 2 to 3 days per week (Garber 2011). Before recommending patients increase their physical activity by beginning a new exercise program, it is important to ensure sedentary individuals have a comprehensive evaluation.

Aspirin

The use of aspirin to reduce the risk of cardiovascular disease has been widely studied. Aspirin has been used to prevent myocardial infarction and stroke since the 1960s (Capodanno 2016). Low-dose aspirin (75–100 mg/day) inhibits platelet activation and aggregation by selectively inhibiting cyclooxygenase 1 (COX-1), while not inducing COX-2 mediated adverse effects on blood pressure, renal function, or drug–drug interactions with certain antihypertensive therapies (e.g., diuretics, angiotensin-converting enzyme inhibitors). Inactivation of COX-1 does, however, increase the risk of upper gastrointestinal bleeding by impairing prostacyclin-mediated cytoprotection in the gastrointestinal mucosa, whereas the bleeding risks associated with aspirin are dose-dependent and less likely to occur with the low-doses used for the prevention of ASCVD. Aspirin resistance, defined as the failure of aspirin to completely inactivate COX-1, is another potential limitation of aspirin. However, the available data are highly variable due to the assays used to assess COX-1 activity. As such, this phenomenon is thought to be virtually nonexistent and may be mostly likely due to poor adherence to aspirin therapy (Capodanno 2016).

Although the net benefit of aspirin is well established in patients with established ASCVD, it remains unclear if aspirin provides a net benefit in the majority of the primary prevention population. Despite numerous studies, significant research gaps remain, including limited to no evidence in certain populations based on age, race/ethnicity, duration of aspirin use, and a true understanding of the bleeding risks. These knowledge gaps have led to the development of a risk-based approach to inform the clinician and patient in their decision regarding the use of aspirin for primary prevention of ASCVD. In 2016, the U.S. Preventive Services Task Force updated their recommendations on the use of aspirin for the prevention of cardiovascular disease and colorectal cancer (Table 1-3) and advised clinicians to consider the patient's age, 10-year ASCVD risk, life expectancy, and willingness to take aspirin for at least 10 years (Bibbins-Domingo 2016a). The U.S. Preventive Services Task Force also concluded that there was insufficient evidence to recommend aspirin for individuals age younger than 50 years and older than 70 years. Similarly, the American Diabetes Association now recommends aspirin (75–162 mg/day) only for individuals with type 1 or 2 diabetes who are at least age 50 years, have additional cardiovascular risk factors (e.g., family history, hypertension, smoking), and are not at increased risk of bleeding, whereas previous guidelines recommended more widespread use of aspirin in the diabetes population (ADA 2017). Several ongoing randomized clinical trials evaluating the benefits and risks of aspirin in primary prevention populations are expected to be completed in the next few years and will improve our understanding of which individuals should receive aspirin (Capodanno 2016).

Table 1-3. U.S. Preventive Services Task Force Aspirin Recommendations

Age (years)	[a]10-year ASCVD Risk	Duration of Use	Recommendation and Evidence Grade
< 50	Insufficient evidence to recommend		
50–59	≥10%	≥10 years	Recommended
60–69	≥10%	≥10 years	Recommended
>70	Insufficient evidence to recommend		

B = USPSTF recommends the service. There is high certainty the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.

C = USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.

[a]American College of Cardiology. ASCVD Risk Estimator Plus [homepage on the Internet].

Statins

While the benefit of lowering blood cholesterol for the primary prevention of ASCVD was first established with clofibrate in 1978, subsequent primary prevention studies with statins have also demonstrated their effectiveness in reducing cardiovascular events and mortality (Oliver 1978; Pender 2016). Despite many unanswered questions and concerns about the use of statins for the primary prevention of ASCVD, recent guidelines have recommended more widespread use of statins in this population. Furthermore, the recent HOPE-3 trial, which randomized intermediate-risk individuals to either rosuvastatin 10 mg/day or placebo, demonstrated a significant reduction in cardiovascular events in the rosuvastatin group without significant adverse effects (Yusuf 2016). It is important to note that 100 people would need to be treated with rosuvastatin for 5 years to prevent one event. Although, HOPE-3 did not enroll patients from centers in the United States, future guidelines may still recommend greater utilization of statin therapy for primary prevention.

Predicting ASCVD risk in individuals without established ASCVD or other significant risk factors (e.g., diabetes) is an imperfect science, yet is the primary mechanism by which clinicians and patients determine if statin therapy is an appropriate intervention. Additionally, data are limited to support the use of statins for primary prevention in select patient groups, such as individuals age younger than 40 or older than 75 years, women, and certain racial/ethnic groups (Stone 2014). Some clinicians, and many patients, have concerns over the potential short- and long-term risks with statin therapy (e.g., myalgias, new-onset diabetes), which have been highly publicized. It is beyond the scope of this chapter to discuss each of these controversies in great detail; therefore the following sections provide a summation of the various guidelines and their key differences as it relates to the use of statins for the primary prevention of cardiovascular disease.

2013 ACC/AHA Blood Cholesterol Guideline

The 2013 ACC/AHA Blood Cholesterol Guideline resulted in a significant shift in how, and when, statins are used in clinical practice (Stone 2014). Guideline authors only utilized randomized controlled trial evidence, which resulted in a more simplified approach to determining which individuals should receive statin therapy. The guideline authors found no evidence in favor of, or against, the use of treatment goals for LDL or non-HDL, which led to the replacement of the traditional LDL treatment goal approach with an ASCVD risk-based approach. The guidelines recommend fixed-doses of statins for four statin benefit groups, which includes individuals who meet any of the following criteria: clinical ASCVD, LDL ≥190 mg/dL, diabetes (ages 40 to 75 years), or 10-year ASCVD risk ≥7.5% (ages 40 to 75 years). High-intensity statins that lower LDL by ≥50% are recommended in higher risk groups, whereas moderate-intensity statins that lower LDL by 30%–50% are recommended for moderate risk patients or those unable to tolerate high-intensity statins. Given their lack of use in clinical trials, low-intensity statins have limited use and are only recommended in patients unable to tolerate moderate-intensity statins.

National Lipid Association Recommendations

In contrast to the 2013 ACC/AHA Blood Cholesterol Guideline, the National Lipid Association released their own patient-centered recommendations, which advocate for treatment goals (LDL and non-HDL) and a traditional approach to risk assessment (Table 1-4) (Jacobson 2014). The writing committee also developed these recommendations based on a broader view of the literature, including not only randomized controlled trials, but also pooled analyses from multiple clinical trials, epidemiological and genetic studies, and metabolic and mechanistic studies. Essentially, the National Lipid Association recommendations are useful to fill in gaps that exist in the 2013 ACC/AHA Blood Cholesterol Guideline. Examples include how to address patients who are statin intolerant, those with high triglycerides, and appropriate use of combination lipid-lowering therapy. In addition, an expert consensus decision pathway on the role of non-statin therapies was recently published by the American College of Cardiology (Lloyd-Jones 2016).

Table 1-4. National Lipid Association Risk Assessment and Treatment Goals

Risk Category	Criteria	Treatment Goal LDL (non-HDL) mg/dL
Low	• 0-1 major risk factors[a] • Consider other risk indicators[b]	<130 (<100)
Moderate	• 2 major risk factors • Consider calculating risk score • Consider other risk indicators	<130 (<100)
High	• ≥3 major risk factors • Diabetes with ≤1 risk factor but without end-organ damage • Chronic kidney disease (Stage 3B or 4) • LDL ≥190 mg/dL • 10-year risk ≥10% (Framingham) or ≥15% (ACC/AHA Risk Calculator)	<130 (<100)
Very High	• ASCVD • Diabetes with ≥2 other major risk factors or signs of end-organ damage	<100 (<70)

[a]See Box 1-1.

[b]See Table 1-2, plus metabolic syndrome, LDL ≥160 mg/dL, lipoprotein(a) ≥50 mg/dL, urine albumin/creatinine ratio ≥30 mg/g.

ASCVD = atherosclerotic cardiovascular disease; LDL = low-density lipoprotein cholesterol; non-HDL = non-high-density lipoprotein cholesterol.

Information from: Jacobson TA, Ito MK, Maki KC, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: Part 1—executive summary. J Clin Lipidol 2014;8:473-88.

U.S. Preventive Services Task Force Recommendations

Recommendations by the U.S. Preventive Services Task Force on statin use for the primary prevention of ASCVD were updated in 2016 (Bibbins-Domingo 2016b). Despite similarities between these recommendations and the 2013 ACC/AHA Blood Cholesterol Guideline, there are important differences.

Although a 10-year ASCVD risk greater than or equal to 7.5% was defined as the point at which a statin should be considered (Grade C), a higher grade recommendation (Grade B) was assigned to individuals whose 10-year ASCVD risk was greater than or equal to 10%. This approach was due, in part, to concern over the precision of the Pooled Cohort equation and its reliance on age as the major determinant of risk. Furthermore, the association between higher-intensity statins and increased risk of new-onset diabetes, as well as limited efficacy data with high-intensity statins for primary prevention, resulted in the recommendation that only low to moderate-intensity statins be considered. The U.S. Preventive Services Task Force also found no evidence that lipid panel screening in individuals between ages 21 and 39 years had any impact on short- and long-term cardiovascular outcomes; and evidence insufficient to support the routine use of statins in those older than age 75 years.

Omega-3 Fatty Acids

Almost 20 million adults take "fish oil" supplements, making it the most commonly used dietary supplement in the United States (Clarke 2015). The cardioprotective effects of omega-3 fatty acids are associated specifically with eicosapentaenoic acid (EPA), and to a lesser extent, docosahexaenoic acid (DHA), which are found in oils from fish and other marine life. Although some OTC dietary supplements contain higher amounts of EPA and DHA, the average capsule contains only 180 mg of EPA and 120 mg of DHA (Siscovick 2017), which is well below the 1 g/day and 4 g/day doses associated with cardioprotective and triglyceride-lowering benefits, respectively. As such, several prescription preparations containing either EPA + DHA, or EPA only, are currently available; however, these products are solely indicated for treating hypertriglyceridemia (≥500 mg/dL) and not for the prevention of cardiovascular disease. Although evidence suggests omega-3 fatty acids may reduce ASCVD risk in the secondary prevention population, no randomized controlled trials have specifically evaluated the role of omega-3 fatty acids for the primary prevention of ASCVD. Consequently, the 2017 AHA Scientific Advisory was unable to provide a recommendation on the use of omega-3 fatty acids for primary prevention.

ROLE OF THE CLINICAL PHARMACIST

Clinical pharmacists provide a variety of services for patients with cardiovascular disease including complex medication management, transitions of care, and education (Dunn 2015). Several literature reviews and meta-analyses found that clinical pharmacists improved control of blood pressure, lipids and glycemic control with no evidence of harm (Dunn 2015). The specific roles extend from inpatient to outpatient settings and depend on state regulations and reimbursement structure.

Currently, 48 states authorize some form of pharmacist–physician–patient collaborative practice agreements, the most progressive of which allow pharmacists to provide independent direct medication management (McBane 2015). Federal pharmacists have provided cognitive medication management services for more than 40 years. Evaluation of a Kaiser Permanente of Colorado collaborative practice model found it significantly reduced all-cause and coronary heart disease mortality after following patients with ASCVD for 3 years. The success of this model, which included nurses and pharmacists in collaboration with physicians, was related to improved monitoring and management of diseases that increase ASCVD risk (i.e., hypertension, hyperlipidemia, diabetes, tobacco abuse). Application of this success to the Million Hearts campaign suggest that pharmacist roles may include direct management of cardiovascular risk factors, monitoring and encouragement of medication adherence, patient education, and provider support.

Key elements of successful collaborative practice agreements include alignment of incentives among stakeholders, improvement of outcomes, and controlling costs (CDC 2013). Implicit in this recommendation is recognition of compensation as a significant barrier to expansion of clinical pharmacy services to prevent cardiovascular disease. Although clinical pharmacists currently employ various compensation strategies, substantive change depends on recognition by the Centers for Medicare and Medicaid Services of the pharmacist's contribution to the patient care team. Even without formal recognition by CMS, health system participation in a merit-based incentive payment system will likely increase pharmacist roles.

Life's Simple 7

As described earlier, "Life's Simple 7" represents a framework to promote healthy lifestyle choices to improve cardiovascular health. This framework may be useful for clinical pharmacists who provide comprehensive cardiovascular risk reduction as a means to educate and monitor their patient's overall cardiovascular health. Ideal cardiovascular health is defined by absence of clinical ASCVD combined with optimal levels of all 7 metrics (Table 1-5). Children tend to achieve optimal levels more frequently than adults, with the exception of diet and physical activity in which more adults achieve optimal levels. Neither age group achieves optimal levels for all 7 metrics. Among adults, 3% achieve 0 of 7 ideal metrics and 15% achieve only 1 of 7, which is much worse achievement than children age 12 to 19 years, 41% of whom have at least 5 metrics at ideal levels. As discussed earlier, successful achievement of ideal cardiovascular health falls along age, gender, and ethnic lines. African American and Hispanic adults tend to have fewer metrics at ideal levels than other races. About 60% of adults older than age 60 have less than 2 metrics at ideals levels, and males have fewer ideal metrics than females at all ages. Southern states tended to have lower percentages of adults at ideal health and higher percentages of

Table 1-5. Definition of Poor, Intermediate, and Ideal Cardiovascular Health for Adults

	Poor	Intermediate	Ideal
Current smoking	Yes	Former ≥12 mo	Never or quit >12 mo
BMI	≥30 kg/m^2	25–29.9 kg/m^2	<25 kg/m^2
Physical activity	None	• 1–149 min/wk moderate or • 1–74 min/wk vigorous or • 1–149 min/wk moderate + vigorous	• >150 min/wk moderate or • ≥75 min/wk vigorous or • ≥150 min/wk moderate + vigorous
Healthy diet (AHA diet score)	<2 (0–39)	2–3 (40–79)	4–5 (80–100)
Total cholesterol (mg/dL)	≥240	200–239 or treated to goal	<200
Blood pressure (mm Hg)	SBP ≥140 or DBP ≥90	SBP 120–139 or DBP 80–89 or treated to goal	SBP <120 and DBP <80
Fasting plasma glucose (mg/dL)	≥126	100–125 or treated to goal	<100

BMI = body mass index; DBP = diastolic blood pressure; SBP = systolic blood pressure.

Information from: Lloyd-Jones DM, Hong Y, Labarthe D, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction. The American Heart Association's strategic impact goal through 2020 and beyond. Circulation 2010;135:586-613.

adults at poor cardiovascular health. By using the My Life Check tool, patients can identify successes and areas of improvement.

This tool helps patients focus on those areas most likely to impact their cardiovascular health and provides common ground for provider–patient discussions. However, beyond identification of poor, intermediate, and ideal, the tool does not establish an overall sense of risk or help prioritize interventions. For example, although smoking is an independent risk factor for ASCVD, it disproportionately amplifies the risk imparted by other traditional risk factors (i.e., plasma lipid levels, uncontrolled hypertension, diabetes). Because traditional risk factors are not equally weighted, a series of tools are available to more accurately assess individual ASCVD risk. Finally, although this tool identifies potential areas for improvement, it should not be confused with nationally recognized targets of drug therapy for specific patient groups.

Practice Points

Cardiovascular disease remains the number one cause of death in the United States and warrants a team-based approach to ensure earlier identification and better control of modifiable risk factors. Our understanding of how to appropriately assess individual cardiovascular risk is improving, but will always have limitations. As a result, appropriate use of primary prevention strategies, lifestyle and pharmacological, continue to evolve.

- **Traditional risk factors remain highly prevalent among the U.S. population and continue to drive individual ASCVD risk. Management of modifiable risk factors (e.g., smoking, hypertension, weight) however, management remains poorly controlled. Clinical pharmacists can play a significant role in helping identify and control certain risk factors.**
- **Risk assessment tools have improved, but should remain as initial steps toward a provider–patient discussion about individual risk and what prevention strategies may be most appropriate for them. Clinical pharmacists should be comfortable using these tools and interpreting and explaining the results to patients.**
- **Certain conditions (e.g., HIV, rheumatoid arthritis) beyond those normally considered when assessing individual ASCVD risk should be accounted for in all patients undergoing comprehensive cardiovascular risk evaluation. Both HIV and rheumatoid arthritis increase ASCVD risk and may require an adjustment in counting risk factors.**
- **Premature family history, ABI, hs-CRP, and CAC are reasonable options to further risk stratify patients lacking traditional risk factors. Clinical pharmacists should be familiar with these tests and remember to thoroughly assess a patient's family history when determining ASCVD risk.**
- **Lifestyle management remains the most important strategy to reduce ASCVD risk. Clinical pharmacists should be familiar with updated evidence-based recommendations on nutrition and physical activity, and serve as a resource for their patients.**
- **Evidence supporting the benefit of aspirin therapy for primary prevention remains limited in certain groups and a better understanding of the potential bleeding risks is needed. Clinical pharmacists should be able to explain the risk to benefit profile of aspirin therapy in select patient groups.**
- **Various guidelines differ in their recommendations regarding the use of statin therapy for primary prevention, but evidence is growing to support more widespread use of statins in asymptomatic individuals at increased risk of ASCVD.**

CONCLUSION

The global burden of cardiovascular disease reinforces the need for increased efforts from all healthcare professionals to provide comprehensive cardiovascular risk reduction. Pharmacists in ambulatory care clinical settings are uniquely positioned to work collaboratively with patients and other healthcare professionals to provide preventive education and clinical services. Early screening for cardiovascular risk factors and global risk estimation are important approaches to increase patient awareness of modifiable factors that may reduce their ASCVD risk. No intervention is more important than lifestyle management, which requires a greater commitment from the healthcare community to ensure patients have the necessary knowledge, access, and resources to adopt healthier lifestyle behaviors. In addition to lifestyle management, aspirin and statin therapy should also be considered for much of the adult population. However, significant knowledge gaps remain regarding the appropriate use of these agents and their risk to benefit ratio. The clinical pharmacist can engage in multiple aspects of primary prevention strategies, including patient education, lifestyle and wellness coaching, and identification and management of individuals who may benefit from aspirin and/or statin therapy.

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Self-Assessment Questions

1. A 56-year-old man without history of an atherosclerotic cardiovascular disease (ASCVD) event presents to the pharmacist clinic for evaluation of his cardiovascular risk. Which one of the following most suggests that this patient is at high ASCVD risk?

   A. High sensitivity C-reactive protein (hs-CRP) 1.2 mg/L
   B. Coronary artery calcium (CAC) score 175 Agatston units
   C. Ankle-brachial index (ABI) 0.7
   D. Father with high cholesterol

2. You have been asked to target a patient population that would most benefit from a new therapy to reduce cardiovascular disease death. Which patient population would potentially benefit the most from your intervention?

   A. Non-Hispanic African American women
   B. Non-Hispanic white women
   C. Non-Hispanic African American men
   D. Hispanic women

3. Which of the following patients is most at risk of hypertension?

   A. 30-year-old non-Hispanic African American man
   B. 45-year-old Hispanic woman
   C. 50-year-old non-Hispanic white man
   D. 65-year-old non-Hispanic African American woman

4. Which of the following smoking behaviors most increases cardiovascular disease risk?

   A. Daily exposure to electronic cigarettes
   B. Daily exposure to secondhand cigarette smoking
   C. 5-year history of 2 packs per day with 10 years of cessation
   D. 15-year history of one pack per day with 5 years of cessation

5. Which of the following ASCVD risk calculators would be most appropriate for a 46-year-old non-Hispanic African American woman with a high sensitivity C-reactive protein (hs-CRP) of 2 mg/dL?

   A. Reynolds Risk Score
   B. ATP-III Framingham Risk Calculator
   C. Pooled Cohort Equation Risk Calculator
   D. Million Hearts Longitudinal ASCVD Risk Assessment Tool

6. A 56-year-old uninsured woman with hypertension, dyslipidemia, and history of tobacco abuse is overwhelmed with her health problems. She states that she wants to change her lifestyle but is uncertain where to start. Which of the following ASCVD risk calculators would be most appropriate to predict the success of evidence-based interventions?

   A. Reynolds Risk Score
   B. ATP-III Framingham Risk Calculator
   C. Pooled Cohort Equation Risk Calculator
   D. Million Hearts Longitudinal ASCVD Risk Assessment Tool

7. A 55-year-old non-Hispanic white man presents to clinic for evaluation of his ASCVD risk following a recent hospitalization for pneumonia. He does not smoke and has no family history of premature heart disease. The following measurements are obtained: blood pressure is 144/92 mm Hg; total cholesterol 200 mg/dL; HDL 34 mg/dL; fasting glucose 98 mg/dL; and high sensitivity C-reactive protein (hs-CRP) 14 mg/L. Which one of the following best interprets this patient's hs-CRP level?

   A. hs-CRP indicates cardiovascular disease (CVD) risk is low
   B. hs-CRP indicates CVD risk is very high
   C. hs-CRP is due to noncardiac causes
   D. hs-CRP is within the normal range

8. A physician consults the clinical pharmacist about a primary prevention patient with a Pooled Cohort Equation Risk Score of 7.4%. Which of the following secondary risk factors is the most useful to aid in the decision to start a statin?

   A. Urine albumin/creatinine ratio
   B. Ankle-brachial index (ABI)
   C. Carotid intima-media thickness (CIMT)
   D. High-sensitivity C-reactive protein (hs-CRP)

Questions 9 and 10 pertain to the following case.

M.L. is a 56-year-old non-Hispanic white woman with rheumatoid arthritis (RA) and hypertension presents for atherosclerotic cardiovascular disease (ASCVD) risk evaluation. Her home drugs include methotrexate, tocilizumab, and lisinopril. M.L. does not smoke but reports that her mother died of a heart attack at age 60 years. The following measurements are obtained at the event: blood pressure is 134/82 mm Hg; total cholesterol 254 mg/dL; triglyceride 188 mg/dL; HDL 44 mg/dL; LDL 172 mg/dL; and fasting glucose 112 mg/dL. Pooled Cohort 10-year ASCVD risk = 5%; lifetime ASCVD risk = 50%.

9. Which of the following is best to recommend for M.L.?

   A. Vigorous aerobic activity at least 150 minutes per week
   B. Rosuvastatin 20 mg/day
   C. Simvastatin 20 mg/day

D. Continue current lifestyle behaviors

10. Which of the following best describes the effect of tocilizumab on the lipid profile in patients like M.L.?

    A. Falsely lowers LDL
    B. Falsely raises LDL
    C. Raises LDL
    D. Has no effect

Questions 11–13 pertain to the following case.

K.T. is a 48-year-old non-Hispanic white woman who presents for evaluation. She does not take any medications and has no history of heart disease. K.T. works as an administrative assistant and does not have a regular exercise program. Her blood pressure is 120/76 mm Hg and her atherosclerotic cardiovascular disease (ASCVD) risk is 5%.

11. Which one of the following is best to recommend to improve K.T.'s cardiovascular risk?

    A. DASH diet
    B. Low-fat diet
    C. Low-carbohydrate diet
    D. Mediterranean diet

12. Which of the following exercise recommendations would best help K.T. prevent a cardiovascular event?

    A. 60 minutes of low-intensity aerobic activity 5 days per week
    B. 30 minutes of moderate-intensity aerobic activity 3 days per week
    C. 25 minutes of vigorous aerobic activity 3 days per week
    D. Resistance training 2 to 3 days per week

13. Three years later, K.T. is now age 51 years with type 2 diabetes and hypertension. According to the American Diabetes Association, which of the following is best to recommend regarding aspirin therapy for K.T.?

    A. 81 mg/day
    B. 202 mg/day
    C. 325 mg/day
    D. No aspirin

Questions 14 and 15 pertain to the following case.

R.W., a 56-year-old non-Hispanic Native American man with type 2 diabetes and hypertension, presents for ASCVD risk evaluation. His home drugs include metformin, lisinopril, and hydrochlorothiazide. R.W. does not smoke and reports that his father died of a heart attack at age 47 years. The following measurements are obtained at the visit: blood pressure 146/92 mm Hg; total cholesterol 235 mg/dL; triglyceride 248 mg/dL; HDL 38 mg/dL; LDL 148 mg/dL; fasting glucose 168 mg/dL; and urine albumin/creatinine 126 mg/g. Pooled Cohort 10-year ASCVD risk = 24.1%; lifetime ASCVD risk = 69%.

14. Which of the following is the best assessment of Pooled Cohort ASCVD Risk Equation in R.W.?

    A. ASCVD risk is overestimated.
    B. ASCVD risk is underestimated.
    C. Lifetime ASCVD risk is not appropriate due to age.
    D. Lifetime ASCVD risk is not appropriate due to ethnicity.

15. Which of the following is the most appropriate treatment plan for R.W.?

    A. Atorvastatin 40 mg/day
    B. Fluvastatin 40 mg/day
    C. Simvastatin 40 mg/day
    D. Pravastatin 40 mg/day