AHA Scientific Statement

Secondary Prevention of Atherosclerotic Cardiovascular Disease in Older Adults
A Scientific Statement From the American Heart Association

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Since the initial scientific statement on Secondary Prevention of Coronary Heart Disease (CHD) in the Elderly was published in 2002,[1] several trends have continued that make an update highly appropriate. First, the graying of the US population and those of other industrialized countries has progressed unabated because more adults are surviving into their senior years. The number of Americans aged ≥75 years was estimated at 18.6 million in 2010, representing ≈6% of the population,[2] and it is expected to double by 2050. The population aged ≥85 years is growing the most rapidly, with numbers expected to reach 19.5 million by 2040. In 2008, 67% of the 811 940 cardiovascular deaths in the United States occurred in people aged ≥75 years.[3] In parallel to this increase in the older adult demographic, the number of Americans with CHD has increased to an estimated 16.3 million, more than half of whom are >65 years of age.[3] Similarly, 7 million have had a stroke, the incidence of which approximately doubles with successive age decades after 45 to 54 years.[3] Peripheral artery disease (PAD) affects 8 to 10 million Americans, the majority of whom are >65 years of age. Between 2015 and 2030, annual US costs related to atherosclerotic cardiovascular disease (ASCVD) are projected to increase from $84.8 billion to $202 billion.[3] Moreover, given that ASCVD often undermines functional capacity and independence and increases reliance on long-term care, indirect expenses related to ASCVD are also expected to increase. Thus, the need for effective secondary prevention measures in the older adult population with known ASCVD has never been greater.

Notably, the 2011 American Heart Association (AHA)/American College of Cardiology Foundation (ACCF) updated guidelines for secondary prevention of CHD broadened its title to *Secondary Prevention and Risk Reduction Therapy for Patients With Coronary and Other Atherosclerotic Vascular Disease*.[5] The expanded title acknowledges that the benefits of CHD risk reduction extend to atherosclerotic vascular disease throughout the body. Given that CHD, and PAD, atherosclerotic aortic disease, and ischemic stroke, as well, all increase with advancing age,[2] the mandate for secondary risk reduction among older adults has also expanded.

Over the decade since the original scientific statement was published, there has been an explosion of randomized controlled trials (RCTs) addressing secondary prevention of ASCVD, especially with regard to the treatment of hypertension, hyperlipidemia, diabetes mellitus, and antithrombotic therapy. Such trials have included increasing numbers of older adults, although still well below their proportion in the population with ASCVD, and with especially few patients aged ≥80 years. As a consequence, the generalizability of the studies' conclusions to typical older patients is tenuous, and, despite the ever-increasing number of published guidelines for management of ASCVD and its risk factors, a large proportion of ostensibly eligible older patients are not receiving evidence-based therapies in clinical practice.[6]

Given these relevant trends in ASCVD prevalence and management, the current update is intended to clarify the benefits and risks of secondary prevention interventions in older adults, and to stimulate an increased application of proven secondary prevention therapies to the expanding population of older patients with CHD and the broader spectrum of atherosclerotic vascular diseases. Specific focus will center on the utility of secondary prevention in the context of age-related physiological changes and comorbidities that often complicate the care of patients of advanced age. Although the term older in this document refers to individuals aged ≥65 years, the emphasis (where the data are available) is on those aged ≥75 years, in whom these age-associated challenges are most pronounced.[1]

The major goals for secondary ASCVD prevention in older patients, and in younger patients, as well, are to prevent or delay the progression of disease that results in major clinical events such as myocardial infarction (MI), stroke, or critical limb ischemia. By preventing these events, not only is longevity likely to increase, but quality of life (QOL) is likely to improve, and yearly healthcare costs are likely to decrease. Secondary prevention of ASCVD also enhances the potential of seniors to perform activities of daily living and thereby maintain their independence.

Nonetheless, secondary prevention goals in older patients with ASCVD must also incorporate consideration of the greater iatrogenic risks of the therapies themselves in older adults. Comorbidities, polypharmacy, socioeconomic stresses, and cognitive limitations frequently confound secondary prevention considerations. Thus, instruments to better delineate the relative risks and benefits of specific therapies in older patients are needed.

Overview of CHD in Older Adults

Age-related endothelial dysfunction, inflammation, and vascular stiffness, in combination with the increasing prevalence and duration of traditional cardiovascular risk factors, lead to a progressive rise in the incidence and prevalence of CHD with increasing age in both men and women.[3] Autopsy studies indicate that obstructive CHD is present in ≈50% of older women and 70% to 80% of older men.[1] In addition, older CHD patients tend to have more extensive coronary atherosclerosis with a higher prevalence of previous MI, multivessel disease, and significant obstruction of the left main coronary artery than younger patients.[1] Thus, although people ≥75 years of age account for only 6% of the US population, 35% to 40% of

incident MIs and up to 60% of deaths attributable to MI occur in this age group.[7] Because they have a longer life expectancy than men, women aged ≥65 years account for approximately half of all hospitalizations for MI and CHD. CHD is by far the leading cause of cardiovascular death in older adults,[3] and CHD-related complications, including heart failure and heart rhythm disorders, are a major source of chronic disability, loss of independence, and impaired QOL. Moreover, because atherosclerosis is a systemic process, older patients with CHD often have concomitant PAD and cerebrovascular disease that further compromise functional capacity and contribute to diminished QOL.[8]

Clinical Manifestations

Although chest pain or discomfort is considered the hallmark of symptomatic CHD, the prevalence of chest discomfort as the presenting manifestation of CHD declines significantly with age in both men and women.[9] Diminished activity levels may forestall the development of exertional angina until disease severity is far advanced. In addition, exertional dyspnea, which may represent an angina equivalent, could be secondary to deconditioning, pulmonary disease, heart failure, or a host of other conditions rather than CHD. Furthermore, the increasing prevalence of cognitive impairment and dementia with advancing age may make it difficult or impossible to obtain a reliable history, thus contributing to diagnostic uncertainty.

The diagnosis of an acute MI is also confounded by advanced age. In the National Registry of Myocardial Infarction, for example, 77% of patients <65 years of age hospitalized with an acute coronary syndrome (ACS) presented with chest pain in comparison with only 40% of patients ≥85 years of age.[10] Conversely, older CHD patients were substantially more likely to present with atypical symptoms, including dyspnea (49%), diaphoresis (26%), nausea and vomiting (24%), and syncope (19%). Whereas women have sometimes been reported to experience more atypical symptoms than men, Canto et al[11] recently demonstrated that such sex differences in presentation narrow markedly with age, essentially disappearing by 75 years. The high prevalence of atypical or nonspecific symptoms contributes to the rising proportion of MIs that are clinically silent or unrecognized at older age, from ≈25% in younger patients to up to 60% in patients >85 years of age.[10]

Age-related alterations in left ventricular diastolic function (impaired relaxation and increased myocardial stiffness) coupled with increased impedance to left ventricular ejection attributable to increased arterial stiffness and impaired contractile reserve predispose older patients to develop heart failure in the setting of acute or chronic myocardial ischemia.[12] Thus, the proportion of ACS patients presenting with heart failure increases from <20% in patients <65 years of age to >40% in patients ≥85 years of age.[10,13] Cardiogenic shock is also 2- to 4-fold more common in older ACS patients. In turn, the higher prevalence of heart failure and shock portend a less favorable prognosis in older patients after MI, and case-fatality rates following ACS increase exponentially with age.[10,14]

Taken together, the above factors often lead to delayed presentation and diagnosis of both acute and chronic CHD in older patients.[10,13] Despite these difficulties, and as discussed

in the ensuing sections of this document, existing evidence strongly supports the value of secondary preventive measures in most community-dwelling older patients with established CHD. It is therefore incumbent on the clinician to maintain a high index of suspicion for CHD in patients of advanced age, and to implement appropriate diagnostic and therapeutic strategies in accordance with existing guidelines and individual patient circumstances and preferences.

Prognosis

In both clinical trials and observational studies, increasing age is a powerful predictor of both short-term and long-term mortality following acute MI. Median survival following a first MI decreases from 17.0 years and 13.3 years in men and women 55 to 64 years of age, respectively, to 3.2 years in both men and women ≥75 years of age.[3,10,13] In the Global Registry for Acute Coronary Events, hospital mortality was 6-fold higher in patients ≥85 years of age in comparison with those <65 years of age, and 30-day mortality was >7-fold higher (Figure).[10]

In addition to higher mortality, older patients are at increased risk for hemorrhagic complications, stroke, reinfarction, and readmission following an incident coronary event.[3,10,13] Among patients ≥65 years of age with a first MI, 21% of white men and women, 33% of black men, and 26% of black women will experience a recurrent MI or fatal CHD event within 5 years.[3] Over this 5-year time frame, heart failure will develop in 19% of white men, 31% of black men, 23% of white women, and 24% of black women ≥65 years of age; a stroke will occur in 5%, 9%, 8%, and 10% of these respective groups.[3] The exceptionally high rate of adverse outcomes in older patients with CHD provides further support for the role of secondary prevention in this population.

Several pharmacological agents have shown efficacy in reducing the high residual morbidity and mortality in older adults with known CHD. The 2011 AHA/ACCF Secondary Prevention Update recommends that all patients without contraindications should receive a β-blocker after an MI or ACS.[5] In older patients with cardiac conduction disorders, claudication, or obstructive lung disease, β-blockers should be started at low doses and uptitrated slowly. Angiotensin-converting enzyme (ACE) inhibitors should be used in all CHD patients with left ventricular ejection fraction of <40% unless contraindicated; in patients intolerant of ACE inhibitors, an angiotensin receptor blocker should be substituted.[5] Antiplatelet drugs, including aspirin 75 to 162 mg daily is

recommended in all CHD patients unless contraindicated. In patients receiving anticoagulation for atrial fibrillation, prosthetic heart valve, left ventricular thrombus, or venous thromboembolic disease, the aspirin dose should be 75 to 81 mg. Clopidogrel 75 mg daily is recommended for patients with aspirin intolerance or allergy. For patients receiving a bare metal or drug-eluting stent, clopidogrel or another P2Y12 receptor antagonist should be given for at least 12 months.[5] The lowering of low-density lipoprotein cholesterol with statins has shown benefit in patients up to the early 80s, as will be discussed subsequently.

Despite the class 1 indications for these pharmacological therapies for patients with established CHD, they are underused, especially in older adults. Such underuse extends to nonpharmacological therapies as well, most notably cardiac rehabilitation. Underuse of specific proven secondary prevention therapies will be covered in greater detail later in this document.

Cerebrovascular Disease and Stroke in Older Adults

An estimated 7 million adults have had a stroke, the prevalence of which increases from 2% in people aged 40 to 59 years to nearly 15% in those aged >80 years.[3] Of the 610 000 first and 185 000 recurrent strokes that occur annually, 87% are ischemic in origin, usually attributable to the disruption of advanced atherosclerotic plaque.[3] The mean age of those dying of a stroke is 79.6 years, and ≈60% are women.[3] The 1-month case-fatality rate from ischemic stroke in Medicare beneficiaries is 8%. However, residual disability rates are much higher. In ischemic stroke survivors >65 years of age from the Framingham Heart Study, 50% had residual hemiparesis, 30% could not walk without assistance, and 26% were institutionalized.[15] Thus, the medical and societal costs of stroke in older adults are very high.

In addition to age per se, the classic atherosclerotic risk factors for CHD—hypertension, dyslipidemia, diabetes mellitus, and smoking—also increase the risk of ischemic stroke. Control of hypertension and hyperlipidemia have shown strong and consistent reduction in new and recurrent stroke risk in numerous clinical trials of older adults, although the data in people aged >80 years are limited. Smoking cessation has similar benefits in reducing stroke risk; within 5 years of smoking cessation, the risk of stroke declines to that of people who never smoked.[16] Antiplatelet drugs reduce the risk of recurrent stroke, and nonfatal MI and vascular death, as well,
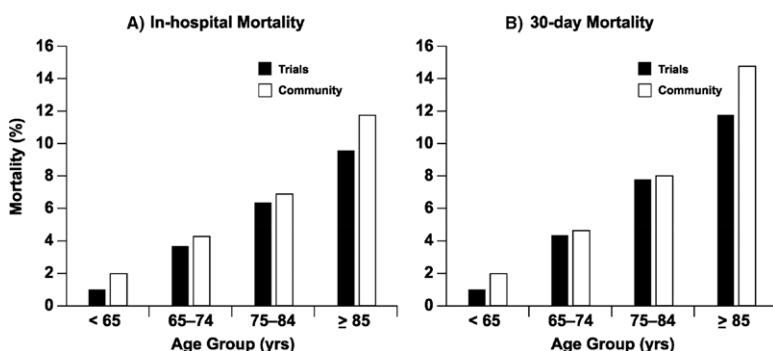
Figure. Trial and community-based assessments of in-hospital (**A**) and 30-day (**B**) mortality relative to age stratifications. Acute coronary syndrome mortality increases relative to age. Moreover the progressive increase in death with advancing age is greater in community populations than in clinical trials. In addition to greater intrinsic cardiac instability, coexisting conditions such as chronic obstructive pulmonary disease, renal failure, and cerebrovascular disease lead to higher morbidity and mortality over time. Reprinted from Alexander et al[10] with permission. © 2007, American Heart Association, Inc.

in stroke survivors. In patients with >50% stenosis of the internal carotid artery, carotid endarterectomy or stenting reduces stroke risk; the greatest benefits accrue in patients with a 70% to 99% stenosis. In the CREST trial there was no overall difference between carotid endarterectomy and stenting on cardiovascular events, but carotid endarterectomy was superior to stenting in reducing stroke risk in patients >70 years of age.[17]

PAD in Older Adults

Atherosclerotic PAD affects an estimated 8 to 10 million Americans, with a marked increased prevalence with age.[18,19] In the Rotterdam study, PAD was present in 10% of subjects 55 to 59 years of age, increasing to nearly 60% in those ≥85 years.[19] Among older people with PAD, 30% to 50% are asymptomatic, and only 5% to 19% have classic claudication.[18,19] The high proportion of asymptomatic older PAD patients parallels that for asymptomatic CHD and probably relates in part to the low physical activity levels in this population. Furthermore, given the diffuse nature of ASCVD, and that risk factors for PAD closely parallel those for coronary and cerebrovascular disease, many older adults with PAD have coexistent disease in these vascular beds. For example, among 1802 people aged 60 to 90 years residing in a chronic care facility, 79% of patients with PAD also had clinical CHD and a previous stroke.[8] Smoking and diabetes mellitus are particularly potent risk factors for PAD in older as in younger adults.

The ankle-brachial index (ABI) is the best screening test for PAD because of its simplicity, wide availability, low risk, and low cost. An ABI <0.9 suggests PAD with a sensitivity of 79% to 95% and a specificity of ≥95%.[18] However, an ABI >1.3 is more common in older than in younger PAD patients because of calcified, noncompressible arteries. Greater reduction in ABI is associated with both a higher prevalence of claudication symptoms and risk for critical limb ischemia. Among 6880 older patients in the primary care setting, low ABI was a strong and graded independent predictor of mortality and was the best predictor of death, stroke, or MI.[20] Given the high prevalence of asymptomatic PAD in older adults, those with claudication or atypical leg symptoms, and those with known CHD or previous stroke, as well, should undergo ABI testing.

The goals of PAD treatment include the relief of symptoms and improvement of function in symptomatic older adults and the reduction of the high risk for atherothrombotic events. Supervised walking programs are particularly effective in reducing ischemic leg symptoms and increasing walking distance.[21] Smoking cessation may also reduce claudication and future cardiovascular events, as well. Aggressive treatment of dyslipidemia and hypertension, and antiplatelet drugs have all been shown to improve the prognosis of older PAD patients.[18] Limb revascularization is usually reserved for patients with refractory symptoms or critical limb ischemia.

Atherosclerotic Risk Factors in Older Patients With ASCVD

Atherosclerotic risk factors are highly prevalent among older men and women with ASCVD. In a recent analysis of the Get With The Guidelines and National Cardiovascular Disease Registry databases,[10] 76% of women and 68% of men (average age, 74 years [range, 61–83 years]) presenting with a non-ST elevation MI had hypertension, 36% and 32% of women and men, respectively, had diabetes mellitus, 20% and 30% were current or recent smokers, and 49% and 53% had dyslipidemia. Obesity and physical inactivity among older adults were also common. Moreover, risk factors often occurred in clusters and in association with a substantial comorbidity burden. As discussed above, atherosclerotic risk factors are also highly prevalent in seniors with an ischemic stroke and PAD. The remainder of this document will discuss the management of these risk factors and other secondary prevention strategies in older adults with ASCVD.

Obesity in Older People

The absolute number and proportion of older people with obesity has increased dramatically over the past 2 decades. Recent estimates from the National Health and Nutrition Examination Survey suggest that 35% of noninstitutionalized women and 40% of men 65 to 74 years of age are obese, as defined by a body mass index (BMI) ≥30 kg/m^2— indicating ≈40 or more extra pounds; comparable numbers in those ≥75 years of age are 27% of women and 26% of men.[3] These percentages increased 30% to 40% in older women and 67% to 100% on older men between the 1988–1994 and 2007–2008 surveys. Approximately another 33% are overweight (BMI 25–30 kg/m^2, or 10–30 extra pounds).[3] Thus, nearly two-thirds of seniors are overweight or obese, closely paralleling these rates in the general population.

There are several contributors to high rates of obesity among older people. Metabolic rate declines with age, such that older people require fewer calories to support their energy needs than they did when they were younger. Changing life-long dietary habits is difficult. Combined with age-related declines in daily physical activity, these habits can lead to even more rapid weight gain in the later decades of life. People who have struggled with overweight/obesity their entire life often find it more difficult to lose weight when they are older because of their lower metabolic rate and physical limitations that restrict their ability to exercise.

Although both obesity and ASCVD are highly prevalent among seniors, there are considerably fewer data specifically in the older population regarding the relationship between obesity and ASCVD than in younger, middle-aged patients. Obesity increases the risk for multiple atherosclerotic risk factors, including hypertension, hyperlipidemia, and diabetes mellitus.[3] Obesity also appears to be a significant independent risk factor for nonfatal ASCVD outcomes.

An observational study of nearly 1 million individuals showed that overweight and obesity were associated with mildly increased total mortality over a 12-year follow-up.[22] However, the risk ratio decreased with advancing age and became 1.0 (no increased risk) at age ≥85 years. Nevertheless, the mortality risk attributable to obesity was much higher in older people because of their higher overall mortality. The effect of obesity on cardiovascular mortality is more questionable.[23] Furthermore, the effect of weight loss interventions on achieving long-term weight reduction in older adults as in younger people has been modest.[4]

In a systematic review of reported cohort studies across a broad age range, obese patients with CHD did not have increased total or cardiovascular mortality.[23] Even patients with severe obesity (BMI >35) did not have increased total mortality, but they did have the highest risk for cardiovascular mortality. The better outcomes for cardiovascular and total mortality seen in the overweight and mildly obese could not be explained by adjustment for known confounding factors.[23] The authors speculated that this may have been attributable to the inability of BMI to differentiate between body fat and lean mass. However, the few observational studies using more accurate methods to measure fat mass have noted similar results.

Weight reduction interventions have shown significant reductions in hypertension, including older adults. The TONE study showed that dietary weight reduction was equally effective in reducing blood pressure as sodium restriction, and both were additive.[24] Weight reduction also improves insulin sensitivity and glucose control, but has inconsistent effects on hyperlipidemia. In a meta-analysis of 7 intervention trials of long-term weight loss using diet, physical activity, or both in obese older (>60 years of age) adults, average weight loss was significant but relatively modest (3.0 kg) at 1 year.[25] Total, high, and low-density lipoprotein cholesterol and triglycerides were unchanged. In a single study, recurrent hypertension and cardiovascular events were reduced. The authors concluded that, although modest weight reductions were achieved, there was lack of high-quality evidence to support the efficacy of weight loss programs on atherosclerotic risk factors or events in older people.

The first long-term follow-up mortality data from randomized, intentional weight loss intervention trials in adults ≥65 years of age were recently published. In patients with osteoarthritis, the initial 18-month dietary intervention showed an average 4.8 kg of weight loss and improved physical function.[26] At 7-year follow-up, there was a nonsignificant trend toward improved survival in the group randomly assigned to weight loss, even in those who had regained weight after the intervention.[27] In the second trial, older adults with mild hypertension showed no long-term difference in total mortality in the weight loss group in comparison with the non–weight loss group.[28] In both studies, physical function improved with no deleterious effect of weight loss. Other studies have also shown improved physical function and QOL following intentional weight loss in older people.[29] This is highly relevant, because physical function and freedom from physical disability are unquestionably influenced by obesity, and both impact QOL.[30,31] These outcomes are often particularly important in older people, in whom mortality should not be seen as the sole definitive end point.

Even with the best methods, it is often difficult to discern the impact of fitness versus fatness on outcomes, because both are interrelated.[32] Indeed, dietary interventions are synergistic with exercise interventions for weight loss, and many older adults find it difficult to achieve significant weight loss without increasing physical activity. Furthermore, as discussed elsewhere in this document, exercise can have other general health benefits for older people.

A frequently unrecognized consequence of dietary weight loss, especially in older women, is that skeletal muscle, which is critical for physical function, is lost along with adipose tissue,[33] likely accelerating age-related loss of skeletal muscle mass.[34] Exercise, particularly strength training, may help retain skeletal muscle and function during caloric restriction. Dietary protein supplements have had mixed results in older adults.[35]

Unfortunately, the majority of individuals who attempt to lose weight do not achieve significant weight loss. Furthermore, most of those who achieve significant weight loss do not sustain it. Because there is potential for harm, weight loss interventions in older adults should include attention to muscle preservation and specific strategies for long-term weight maintenance. Few data are available in this regard, and focused studies are needed.

Many routinely prescribed medications in older adults such as hypoglycemic drugs, antidepressants, and steroids, can compound tendencies for weight gain and muscle atrophy. Efforts should be made to minimize weight gain in seniors when these medications are initiated.

Hypertension

Hypertension is extremely common among older men and women, with prevalence rates of ≈70% in adults ≥75 years of age,[36,37] and with a lifetime risk in the Framingham study of 90%.[3] Hypertension is more common in older women than men and in non-Hispanic blacks than other ethnic cohorts. Among older adults, hypertension is the most prevalent modifiable cardiovascular risk factor with the greatest population-attributable risk for CHD, cerebrovascular disease, and PAD. More than 70% of older adults with incident MI, stroke, acute aortic syndromes, and heart failure have preexisting hypertension. Hypertension is the most common antecedent of heart failure, particularly in the setting of a preserved ejection fraction and chronic kidney disease.[3]

Aging is associated with a progressive increase in central conduit artery stiffness (eg, aorta and great vessels), which is in part related to increased collagen cross-linking and the concomitant degradation of elastin fibers.[12,37] This age-related arterial stiffening is exacerbated by a sedentary lifestyle and high-salt diets, and the atherosclerosis-associated accumulation of arterial calcium with advancing age, as well. Accordingly, systolic blood pressure (BP) progressively rises and diastolic BP plateaus in late middle age (eg, ≈50–59 years of age) and declines slightly thereafter, resulting in a widened pulse pressure with age.[12,37] As a result, after 70 years of age, isolated systolic hypertension accounts for >90% of all patients with hypertension.[38] The prevalence of isolated systolic hypertension is higher in women than in men, but the proportion of hypertension attributable to isolated systolic hypertension in older adults is similar across racial and ethnic groups.[3] Over the past few decades, several epidemiological studies have provided compelling evidence that systolic or pulse pressure were independent predictors for CHD events,[39–41] and clinical trials have shown the benefits of treatment.[42,43]

Although older patients with hypertension are more likely to be aware of their condition and receiving treatment than middle-aged patients,[3,36] BP control is poorer in older adults, especially after 75 years of age.[37,44] This is related to many factors including a lingering misperception that hypertension is an

adaptive physiological phenomenon in very old adults required to ensure organ perfusion. The latter theory was disproven by the landmark HYVET Trial among 3845 patients ≥80 years of age with systolic BP ≥160 mm Hg, who demonstrated a 39% significant decrease in fatal stroke, 21% significant decrease in all-cause mortality, and 64% significant decrease in heart failure with more versus less aggressive BP control over 1.8 years of mean follow-up.[45] The higher prevalence of hypertension in older women, whose BP is more difficult to control than that of older men,[36] may contribute to overall patterns of poor BP control among seniors. Concomitant age-related changes in the kidney increase in salt and water retention, further contributing to high BP among older adults. Furthermore, most older patients require ≥2 agents to achieve satisfactory BP control, essentially multiplying the potential for side effects and reduced adherence. Similarly, increased use of nonsteroidal anti-inflammatory agents and other medications among older adults also commonly raises BP levels, further undermining BP control. Dietary indiscretion is also more common, because sodium restriction is harder to maintain amid greater reliance on processed foods, especially for older patients whose mobility and finances are constrained. Age-related changes in taste also contribute to the tendency of many older adults to add salt as a means to bolster the flavor and appeal of their food.[46]

Hypertension Management

Nonpharmacological approaches to management of hypertension are always recommended as initial therapy, especially in older adults, in whom the benefits of such approaches can either avoid or reduce the need for pharmacological therapy and their potential for adverse effects, biochemical changes, and high costs. For milder hypertension, lifestyle modifications may be the only treatment needed; such interventions (eg, reduction in excess body weight, mental stress and intake of sodium and alcohol, smoking cessation, adoption of the Dietary Approaches to Stop Hypertension [DASH] eating plan [a diet rich in fruits, vegetables, and low-fat dairy products and low in saturated and total fat]), and increased physical activity, as well, all may lead to a reduction in the number and dose of antihypertensive drugs.[12,24,37] The declines in BP with both weight reduction and sodium restriction are usually larger in older than in younger adults.[24,37] However, data in patients >75 years are minimal. The generally recommended BP goal in patients with hypertension is <140/90 mm Hg, both in primary and secondary prevention. However, this target for older hypertensive patients is based on expert opinion rather than on data from RCTs. The recent AHA/ACCF expert consensus document on hypertension in older adults recommends that "achieved systolic blood pressure of <140 mm Hg is an appropriate goal for most patients <79 years of age; for those >80 years of age, 140 to 145 mm Hg, if tolerated, can be acceptable."[37]

Excessive lowering of diastolic BP should be avoided in older patients with CHD to prevent deleterious reductions in coronary blood flow. Although not a universal finding, some studies have found higher CHD rates when diastolic BP is reduced to <70 to 75 mm Hg.[37] Five major classes of antihypertensive drugs: diuretics, β-adrenergic blockers, ACE

inhibitors, angiotensin receptor blockers, and calcium channel blockers, have been shown in clinical trials to reduce cardiovascular events in older adults.[37,47,48] In approximately two-thirds of seniors with hypertension, ≥2 drugs will be required to achieve target BP levels. Given the age-related changes in absorption, distribution, metabolism, and excretion of pharmacological agents, the initiation of antihypertensive drugs in older adults should generally be at the lowest doses with gradual increments as tolerated.

Although relying on multiple medications to control BP adds some iatrogenic risk for an adverse reaction, combination drug therapy provides increased efficacy from additive and synergistic drug effects. With combination therapy, lower individual drug dosages are often sufficient, minimizing dose-dependent side effects and typically achieving longer duration of action and additive target organ protection.[37,49] The choice of specific agents is dictated by efficacy, tolerability, presence of specific comorbidities (Table 1), and cost. For more detailed guidelines of hypertension management in secondary prevention, recently published Consensus/Expert Statement[37] and JNC VII[48] should be consulted.

Lipids

The cumulative effects of comorbidities (eg, cancer, malnutrition, and chronic inflammation) in older adults are often associated with reduced total serum cholesterol (TC), such that the U-shaped association between TC level and mortality becomes more prominent after the seventh decade.[1,49] This observation has challenged the rationale for lipid-lowering therapy in older adults. Although TC and low-density lipoprotein cholesterol (LDL-C) decline after the seventh decade, LDL-C remains strongly associated with CHD events in older adults.[51,52]

Lipid-lowering therapy is an important component of secondary prevention of ASCVD in older patients. Multiple RCTs prospectively substantiating statin efficacy for secondary ASCVD prevention have included some older patients (mainly 65–75 years of age). These trials show that relative risk reduction (RRR) is similar in older and younger patients (Table 2). The absolute risk reduction for death and recurrent ASCVD events in these trials was up to 2-fold higher in older versus younger patients because of the higher baseline risk in seniors.[61,62] Accordingly, the number needed to treat with statins to prevent ASCVD events and death is much lower in older than in younger patients.

More recent trials have also demonstrated benefits of LDL-C–lowering therapy in older cohorts. The MRC/BHF Heart Protection Study (HPS) stratified >20 000 subjects by age decade (53% of subjects ≥65 and 28% ≥70 years) and reported significant RRRs with simvastatin versus placebo in all-cause mortality (13%), vascular death (18%), and stroke (25%).[56] First major vascular event RRR with simvastatin (24%) was similar across all age strata (<65, 65–69, ≥70 years). The HPS was novel in that the pretreatment LDL-C was relatively low, supporting the concept for more aggressive LDL lipid-lowering therapy for secondary ASCVD prevention than the ATP III Guidelines had endorsed.[63] Pravastatin in elderly individuals at risk of vascular disease (PROSPER), the first RCT specifically designed to exam the efficacy and safety of statins for ASCVD prevention in older patients

Table 1. Selection of Antihypertensive Therapy for Older Adults Based on Comorbidities

Compelling Indication	Initial Therapeutic Choice
Heart failure	Thiazide, β-blocker, ACE inhibitor, angiotensin receptor antagonist, calcium channel blocker, aldosterone antagonist
Previous myocardial infarction	β-Blocker, ACE inhibitor, aldosterone antagonist, angiotensin receptor antagonist
CHD or high-risk CVD	Thiazide, β-blocker, ACE inhibitor, calcium channel blocker
Angina pectoris	β-Blocker, calcium channel blocker
Aortopathy/aortic aneurysm	β-Blocker, angiotensin receptor antagonist, ACE inhibitor, thiazide, calcium channel blocker
Diabetes mellitus	ACE inhibitor, angiotensin receptor antagonist, calcium channel blocker, thiazide, β-blocker
Chronic kidney disease	ACE inhibitor, angiotensin receptor antagonist
Recurrent stroke prevention	Thiazide, ACE inhibitor, angiotensin receptor antagonist, calcium channel blocker
Early dementia	Blood pressure control

Most patients will require combination therapy. ACE indicates angiotensin-converting enzyme; CHD, coronary heart disease; and CVD, cardiovascular disease.
Adapted from Aronow et al[37] with permission. © 2011, American Heart Association, Inc.

(aged 70–82 years at baseline), showed a significant 22% pravastatin-related RRR in combined CHD death+MI+stroke in the 43% of the sample with known cardiovascular disease.[57] Pravastatin or Atorvastatin Evaluation and Infection Therapy–Thrombolysis in Myocardial Infarction 22 (PROVE IT–TIMI 22) extended the concept of LDL-lowering benefit by assessing greater versus lesser intensity LDL-C lowering during or just after hospitalization for an acute MI. A subgroup analysis of PROVE-IT patients ≥70 years of age showed a 40% RRR in CHD death or MI at 30 days and a 40% RRR in CHD death in those taking high-dose atorvastatin versus 40 mg of pravastatin.[58]

Other recent clinical trials have examined the efficacy of more intensive lipid-lowering regimens in older adults with chronic ASCVD. In the Treating New Targets (TNT) trial, the efficacy of high- versus low-dose atorvastatin on risk reduction was compared. In a subgroup aged 65 to 75 years, a significant 19% RRR in the composite primary end point (CHD death, all-cause mortality, and CHD death/MI/cardiac arrest/stroke) was seen in the high-dose versus the low-dose arm.[59] The Study Assessing Goals in the Elderly (SAGE) demonstrated a nonsignificant 29% RRR in CHD events but a 67% RRR in all-cause mortality (*P*=0.01) in 893 seniors 65 to 85 years of age randomly assigned to 80 mg of atorvastatin in comparison with 40 mg of pravastatin.[60] Although compelling, these trials had several limitations: fixed statin doses were tested in lieu of specific LDL-C levels such that none systematically achieved LDL-C levels <70 mg/dL. Also, none of these trials enrolled adults aged >85 years or older patients with extensive comorbidities.

Meta-analyses have also demonstrated the benefits of statin therapy in older patients.[61,62] In a meta-analysis of 19 569 older CHD patients (aged 65–82 years) from 9 secondary statin RCTs, Afilalo et al[61] demonstrated statin-related RRR in all-cause mortality (22%), CHD mortality (30%), nonfatal MI (26%), need for revascularization (30%), and stroke (25%), with number needed to treat=28 to save 1 life. The Cholesterol Treatment Trialists' meta-analysis of 26 RCTs (N=170 000) showed 22% RRR of major vascular events in patients 66 to 75 years of age and 16% RRR in those ≥75 years of age, with age-related increasing absolute risk reduction.[62] Such data from RCTs and meta-analyses underlie the 2011 AHA/ACCF Secondary CHD Prevention Guidelines that endorse aggressive LDL-lowering therapy <100 mg/dL) with an optional target of <70 mg/dL in very-high-risk patients.[5]

Statins also reduced the risk of incident stroke in older patients with ASCVD in RCTs, leading to 25% stroke RRR in a recent meta-analysis.[61] A secondary analysis of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) study showed a nonsignificant 10% RRR in fatal or nonfatal stroke over 5 years with atorvastatin 80 mg in comparison with placebo in 2249 patients ≥65 years of age with a previous stroke or transient ischemic attack, but without CHD, in comparison with a significant 26% RRR in younger patients.[64] However, there was no statistically significant age interaction. Older patients with PAD also benefit from cholesterol-lowering therapy. A study of 69 PAD patients aged 60 to 85 years showed significantly improved treadmill-walking time before the onset of claudication, with 24% and 42% increases 6 and 12 months after statin initiation, respectively.[65]

Despite observational studies suggesting that statin therapy reduces the risk and progression of dementia, RCTs (HPS, PROSPER) do not support this premise.[56,57] In contrast, case series suggest that statins may worsen cognitive function and memory loss, a concern that has prompted a new advisory labeling, although this too has not been demonstrated in a RCT.[66]

Overall evidence supporting lipid-lowering medication for secondary CHD prevention is credible through ≈85 years of age. Secondary prevention guidelines advise lipid-lowering therapy regardless of age in the majority of older patients with ASCVD unless issues of frailty, comorbidity, and polypharmacy confound management. Despite this mandate, statins are notoriously underprescribed and underdosed in this cohort despite their higher risk of recurrent events.[6,67,68] Only 24% of patients ≥65 years of age and 15% of those ≥80 years of age were receiving a statin at discharge after an MI in 1 analysis of 23 013 Medicare beneficiaries based on a 1998 to 2001 data set.[68] Ongoing adherence to lipid-lowering drugs is particularly low in older patients.[69] Several factors seem to determine this treatment–risk paradox, including the lack of knowledge of statin efficacy and absolute risk reduction, fear of adverse events, polypharmacy (both in regard to costs and cumulative side effects), and the perception that benefits diminish in the context of reduced life expectancy and mounting comorbidities.[6,69]

Table 2.   Statin Trials for Secondary Prevention in Older Adults

Trial (ref)	Intervention	Age Subgroup (n)	All-Cause Death RRR%/ARR%	CHD Death RRR%/ARR%	CHD Events RRR%/ARR%	Stroke RRR%/ARR%	Comment
4S[53]	S20-40 vs PL	65–70 (1021)	34/6.2*	43/6.0	34/13.3 33/7.1†	NR	↓CV admissions by 21%
LIPID[54]	P40 vs PL	65–75 (3514)	21/4.5	24/2.9*	26/3.3	12/1.3	
CARE[55]	P40 vs PL	65–75 (1283)	NR	45/4.5	32/9* 39/6.7‡	40/2.9	32% RRR/5.2% ARR for PCI/CABG
HPS[56]	S40 vs PL	70–80 (5806)	NR	NR	18/5.1‡	NR	9.2% ARR in primary end point in patients 75–80 y (n=1263)
PROSPER[57]	P40 vs PL	70–82 (5804)	NS	24/0.9	19/2.1‡	NS	25% ↑ cancer risk with P40
PROVE-IT TIMI 22[58]	A80 vs P40	≥70 (634)	NR	NR	40/8 LDL-C < 70 vs LDL-C ≥70 mg/dL (in death/MI/UAP*)	NR	AE rate similar to young
TNT[59]	A80 vs A10	65–75 (3809)	NS	NS	19/2.3* (A80 vs A10)	21/0.9-NS	↑LFTs w A80 vs A10
SAGE[60]	A80 vs P40	65–85 (893)	67/2.7	67/0.9 based on 8 deaths	29/3.1‡ (P=0.11)	Too few to compare	↑LFTs w A80 vs P40
Meta-analysis[61]		65–82 (19 569)	22/3.1*	30/2.6	17/2.1‡ 26/2.3 NFMI	25/1.7	30%↓PCI/CABG

A indicates atorvastatin; AE, adverse events; ARR, absolute risk reduction; CABG, coronary artery bypass grafting; CARE, The Cholesterol and Recurrent Events; CHD, coronary heart disease; CV, cardiovascular; HPS, Heart Protection Study; LDL-C, low-density lipoprotein cholesterol; LIPID, Long-Term Intervention with Pravastatin in Ischaemic Disease; LFTs, liver function tests; MI, myocardial infarction; NFMI, nonfatal myocardial infarction; NR, not reported; NS, not significant; P, pravastatin; PCI, percutaneous coronary intervention; PL, placebo; PROSPER, PROspective Study of Pravastatin in the Elderly at Risk; PROVE IT–TIMI 22, Pravastatin or Atorvastatin Evaluation and Infection Therapy–Thrombolysis in Myocardial Infarction 22; S, simvastatin; w, with; RRR, relative risk reduction; SAGE, Study Assessing Goals in the Elderly; TNT, Treating New Targets; and UAP, unstable angina.

*Primary end point.

†NFMI.

‡Death or NFMI.

Despite concerns over statin-related adverse events in older patients, pooled analyses of many large clinical trials show no significant difference in adverse events in older versus younger patients.[61,62,70] Dyspepsia is the most commonly reported side effect. However, few, if any, of these trials included patients >80 years of age at baseline or patients with frailty or other significant comorbidities.[70] In contrast, several recent aggressive lipid-lowering trials (TNT, SAGE, PROVE-IT TIMI 22) have revealed a higher incidence of abnormal liver function tests with high-dose statins in older adults.[58–60] However, in TNT, liver function tests increased similarly to statin dose in older and younger patients.[59] Statins also cause a spectrum of muscle concerns that are more common among older adults, ranging from myalgias without creatine phosphokinase elevation to fulminant rhabdomyolysis. Included in this spectrum are neuropathies, balance problems, and extremity weakness, which, along with myalgias, are common and often debilitating, particularly for a population inherently prone to frailty and diminished QOL.[71]

Adding to management challenges, older patients and their families may be less likely to articulate pertinent concerns, assuming that such symptoms are related to arthritis or aging itself. Although the etiology of statin-related muscular and neurological concerns is unclear, it is often dose-related and certain risks have been identified: female sex, small stature/low BMI, concomitant fibrates and drugs using the cytochrome P450 enzyme pathway, use during surgery, decreased hepatic or renal function, fatty liver disease, hypothyroidism, diabetes mellitus, and heavy use of alcohol all increase statin-related adverse events.[71,72]

Lipid Management

Although clinical practice, in general, is to administer statin therapy for older patients with ASCVD, just as for younger adults, decisions whether or not to prescribe a statin to an older patient mandate careful assessment of life expectancy, goals of therapy, time-to-treatment benefit, and comorbidities, as well, that could potentially complicate statin therapy.[69] Life expectancy may be estimated by using an appropriate multimorbid tool,[73] rather than actuarial data. Patients with conditions that severely compromise life expectancy or QOL (certain cancers, severe dementia, severe frailty) may not be suitable candidates for statins. Nonetheless, a patient may place more emphasis on statin-related stroke risk reduction or preventing worsening claudication despite the negligible benefit on longevity. Important considerations include RCT data that indicate a 1- and 3-year lag time until benefit is demonstrable for CHD and stroke, respectively.[61,62]

A lipid profile should be obtained on all older patients with ASCVD who are deemed candidates for lipid-lowering therapy.[5,63] The goal LDL-C level for most older as in younger patients is <100 mg/dL, but a relative decrease of 30% to 40% from the baseline LDL-C may provide greater risk

reduction, given other factors that can also affect the baseline TC.[5,50,51,63] In very-high-risk older patients, a target LDL-C of <70 mg/dL is considered optional, but this target should be approached with caution, given the increased adverse event risk with higher statin doses.[63,70] The non–high-density lipoprotein cholesterol (HDL-C) (LDL-C+very low density lipoprotein) target should be <130 mg/dL in patients with tri-glyceride ≥200 mg/dL.

Statins remain the first-line therapy for secondary ASCVD prevention in seniors and should be initiated at the lowest dose and judiciously titrated as tolerated to achieve a 30% to 40% reduction in LDL-C. Although statins remain rela-tively safe drugs in older adults, very advanced age, female sex, small body size, fatty liver disease, and multisystem dis-ease may predispose to adverse events. In addition, lipophilic statins, such as lovastatin, simvastatin, and atorvastatin, are metabolized via the cytochrome P450 system, increasing the likelihood of interactions with other drugs metabolized by this pathway.[70]

Nonstatin lipid-altering agents may be helpful adjuvant or alternative therapy, although specific evidence support-ing their use in older patients is sparse or lacking. Fibrates (gemfibrozil, fenofibrates) are effective in lowering triglyc-eride and LDL-C and raising HDL-C, but a recent meta-analysis of 5 fibrate trials (n=21 065) does not support their primary use for ASCVD risk reduction; however, older patients were not adequately represented in these studies.[74] Although fibrates in combination with a statin are particu-larly appealing for those with elevated triglycerides, the combination is associated with elevated risk of myopathy (gemfibrozil>fenofibrate), and extreme caution is warranted, particularly in seniors.[5,63]

Nicotinic acid, when added cautiously to statins, may fur-ther reduce LDL-C and triglycerides and raise HDL-C, but the negative results of AIM-HIGH have dampened enthusiasm for its use.[75] Outcome evidence is lacking to support the use of bile acid sequestrants (cholestyramine, colestipol, and cole-sevelam) to reduce ASCVD risk in older patients, especially given the potential for drug–drug interactions and a high rate of gastrointestinal adverse events.

The cholesterol absorption inhibitor, ezetimibe, appears safe in older patients and effective at lowering LDL-C when added to statin therapy, but hard ASCVD outcome data are not available.[76] The use of herbals and nutraceuticals to lower sec-ondary ASCVD risk has not been supported by clinical trials, and their common use in older patients may lead to significant interactions with prescription drugs.

Although evidence supports statins as the most efficacious lipid-lowering strategy to prevent recurrent ASCVD events (class I), increased physical activity and a step II AHA diet are considered fundamental at any age, despite limited data in seniors.[5,61] The ingestion of plant sterols and stanols, and soluble fiber, as well, may play an additive role to diet in low-ering TC and LDL-C. Patients aged ≥75 years who completed a phase II cardiac rehabilitation program had a significant decline in TC, LDL-C, and depression score, and an increase in HDL-C and QOL, as well.[77]

Lipid-lowering therapy should be carefully and continu-ously monitored with respect to treatment goals, medication interactions, life expectancy, and comorbidities.[69] Patients aged ≥80 years remain at highest risk for incident and recur-rent cardiovascular events and experience worst outcomes; thus, future studies should clarify the efficacy and safety of lipid-lowering therapy among the oldest old, including those with multimorbidities, frailty, and polypharmacy and possibly those living in assisted living and nursing homes. Finally, it remains important to develop better risk assess-ment tools to predict relevant outcomes in older adults (eg, stroke, functionality/independence, and QOL) that can be used to gauge the rationale for and efficacy of lipid-low-ering therapy.

Diabetes Mellitus

Advancing age is associated with both increased insulin resistance and impaired insulin secretion.[78] The insulin resistance of aging results from decreased sensitivity to insulin at the level of target tissues, particularly skeletal muscle, and is associated with greater visceral adiposity and an overall higher ratio of fat-to-lean body mass. Impaired insulin secretion, on the other hand, has been attributed to inappropriately low pancreatic β-cell function in older adults.[79] The coupling of insulin resistance with impaired insulin secretion in aging contributes to greater glucose intolerance. Accordingly, the incidence and prevalence of type 2 diabetes mellitus, and that for ASCVD, as well, pro-gressively rise with age, such that ≈15% of people aged ≥65 years have diagnosed diabetes mellitus and another 7% have undiagnosed diabetes mellitus. Approximately 30% of older adults with diabetes mellitus have concomitant CHD, double the prevalence of nondiabetic age peers.[80] The diag-nosis and management of diabetes mellitus in older adults with ASCVD present unique challenges. Diabetes mellitus tends to be underdiagnosed in older adults, who can often present with nonclassical and nonspecific symptoms. Thus, routine screening for diabetes mellitus is strongly recom-mended for all older adults, particularly those with diag-nosed ASCVD.[81] Older individuals with diabetes mellitus experience excess morbidity and mortality in comparison with those without diabetes mellitus, even in the absence of cardiovascular disease.[82] Consequently, older adults with both diabetes mellitus and ASCVD are at especially high risk for adverse macrovascular and microvascular outcomes in addition to functional disability and geriatric syndromes (eg, cognitive impairment, depression, urinary incontinence, falls, and chronic pain).[83] Because of the fre-quency of comorbidities and complications, as well, older adults with prevalent diabetes mellitus and ASCVD com-prise an extremely heterogeneous population, ranging from relatively fit individuals living independently in the com-munity to frail individuals with multiple comorbidities and living in nursing homes. Thus, the management of diabetes mellitus in this population must be specifically tailored for each individual.

Diabetes Mellitus Management

The primary goals of care for all patients with diabetes mel-litus include managing hyperglycemia and reducing the risk

of adverse clinical outcomes. However, a critically important additional goal in the seniors is the prevention of hypoglycemia.[81,84] Because patient unawareness of hypoglycemia is common, even in functionally independent older adults,[85] glucose management should include fingersticks after exercise and missed meals. Given the challenges related to managing diabetes mellitus in older adults, diabetes mellitus care should be coordinated with the patient's primary provider and endocrinologist.

Therapeutic interventions for diabetes mellitus should begin with lifestyle modification. For older adults with obesity, weight loss can reduce insulin resistance[86] and improve glycemic control.[86–88] Dietary interventions focused on optimizing macronutrient content in addition to overall calorie count can also improve glycemic control in older adults, independent of weight change.[81] Thus, a medical nutrition evaluation is recommended for all older adults with diabetes mellitus. Current guidelines additionally recommend regular aerobic and resistance exercise, which has been shown to lower hemoglobin A1c by 0.5% to 1.0%.[87] Structured exercise training has also been shown to improve insulin sensitivity in older adults, even without changes in body weight or fat mass.[88] Although physical activity for many older adults is limited by health status and comorbidities, any exercises that help to improve aerobic capacity and preserve and increase muscle mass are likely to be beneficial.

Notwithstanding the benefits of lifestyle interventions, the majority of older patients with diabetes mellitus will require medications to achieve optimal glycemic control. Large clinical trials have investigated the effects of intensive versus standard glycemic control on adverse outcomes. Despite a possible reduction in microvascular outcomes,[89] these trials have consistently observed either no effect on or even increased mortality in older patients receiving intensive glycemic therapy.[89–91] Therefore, glycemic targets for older adults should be determined based on individual risk status. Whereas an hemoglobin A1c target of <7% may be appropriate for adults aged <65 years or very healthy older adults, a less intensive target hemoglobin A1c of 7% to 7.9% is recommended for most older adults, particularly those with longstanding diabetes mellitus and chronic comorbidities including ASCVD.[92] Even higher targets may be considered for older patients with frailty, increased risk for hypoglycemia, and short life expectancy.[93]

The selection of pharmacological therapy should be based on the presence or absence of comorbidities that can impact drug metabolism and tolerability (eg, renal impairment, heart failure, and liver disease). Because polypharmacy is common in older patients with both ASCVD and diabetes mellitus, attention to possible drug–drug interactions is also required. In general, glucose-lowering medications should be started at the lowest dose and uptitrated slowly. Metformin is favored as a first-line therapy, given its low risk for hypoglycemia and other adverse effects. Additional options considered safer for older adults include the short-acting sulfonylurea, glipizide, and the short-acting insulin secretagogue, repaglinide.[94] In cases where insulin therapy is needed, ultra long-acting basal and very short-acting prandial insulins are strongly preferred over intermediate-acting insulin formulations. When glycemic goals are not being met for any older patient, however,

the clinical assessment should include a careful evaluation for possible contributors to nonadherence. Although glycemic control is important, greater cardiovascular risk reduction in diabetes mellitus may be achieved from the control of concurrent risk factors such as hypertension and dyslipidemia.[95]

Tobacco

Cigarette smoking remains the leading preventable cause of death worldwide; a large proportion of these deaths are attributable to ASCVD. Tobacco smoking has multiple deleterious effects that include increased generation of free radicals, reduced nitric oxide bioavailability, enhanced leukocyte and platelet activation, and prothrombotic alterations in coagulation factors.[96] Clinical and laboratory manifestations of tobacco smoking include increases in heart rate, inflammatory markers, and plasma catecholamines, and reduced flow-mediated arterial dilation and HDL-C. The cumulative effects of these smoking-induced changes is a proatherogenic, prothrombotic, and vasoconstrictive environment that further increases the older ASCVD patient's already elevated risk status.

In 2008, 9.8% of men and 8.5% of women ≥65 years of age were current smokers, representing rates less than half those of younger adults; another 54.3% of men and 28.9% of women ≥65 years of age were former smokers.[3] Although some older smokers may have genetic protection from the noxious effects of tobacco to account for their longevity, multiple studies over the past 3 decades have demonstrated that continued smoking increases the rate for recurrent coronary and vascular events in both younger and older patients with known ASCVD, and reduced cardiovascular event rates, as well, among those who quit smoking. A meta-analysis of 20 studies demonstrated a 36% lower crude mortality risk and 32% lower rate of nonfatal MI among patients with CHD who quit smoking in comparison with those who continued to smoke.[97] A recent meta-analysis of 17 general population studies in >1.2 million people ≥60 years of age from 7 countries showed a dose-dependent increase in all-cause mortality rates in current smokers, with a mean relative mortality of 1.83 in comparison with never smokers; in former smokers, the mortality risk was attenuated to 1.34. The benefits of smoking cessation were seen even in people ≥80 years of age.[98] Data from the Coronary Artery Surgery Study (CASS) registry showed a reduction in MI and death in former smokers aged ≥70, similar to that in younger patients with CHD.[99] In an ongoing registry of patients with CHD, the mortality rate was markedly lower in recent quitters than in persistent smokers.[100] Furthermore, sudden cardiac death risk was also lower in quitters than in continual smokers among 3122 coronary patients (mean age, 60 years) in the Bezafibrate Infarction Prevention Trial over a mean 8.2-year follow-up.[101] As noted earlier, smoking cessation also reduces the risk of new or recurrent stroke[16,100] and improves claudication symptoms in PAD patients.[18] Aside from the cardiovascular benefits of smoking cessation, the age-associated decline in pulmonary function is accelerated in smokers, and this accelerated decline is attenuated or abolished by smoking cessation.[102]

Given the strong and consistent published findings supporting the morbidity and mortality benefits from smoking cessation in both older and younger patients with ASCVD, the AHA/ACCF Secondary Prevention guidelines list

smoking cessation as a class IA recommendation.[5] In the Get With the Guidelines CAD program, a similar increase in composite adherence to 6 quality measures, which included smoking cessation, was observed in patients ≥75 years of age as in younger individuals between 2002 and 2007.[103] Despite these encouraging findings, the success rates for smoking cessation remain modest. Patient counseling combined with pharmacological therapies such as nicotine replacement and psychotropic medications can improve cessation rates by 2- to 3-fold over nonaided cessation attempts. However, data on smoking cessation success rates in very old adults are extremely limited.

Psychosocial Issues in Secondary Prevention

Epidemiological Evidence

Personality Factors
Although the type A behavior pattern was originally touted as a risk factor for CHD that was comparable to such traditional risk factors, hostility is now recognized as the toxic component of the type A personality, in both healthy adults and cardiac populations.[104] However, older adults have remained largely excluded from these analyses, and, even among younger adults, effect sizes of hostility on CHD development have been modest.

Depression
Over the past 2 decades, clinical depression has emerged as an important psychosocial risk factor that is common in cardiac patients and is associated with increased adverse events. Major depressive disorder or elevated depressive symptoms in various CHD populations (ie, post-MI, coronary artery bypass grafting [CABG], heart failure, stable angina) are associated with 2 to 4 times the risk for all-cause mortality in comparison with nondepressed individuals.[105–107] Older depressed post-MI patients may have up to 4 times the risk of dying 4 months after hospital discharge.[107] A scientific panel commissioned by the AHA concluded that depression should be routinely assessed and treated when indicated in patients with CHD.[108]

Anxiety
The prevalence rates of moderate to severe anxiety among hospitalized MI patients has been reported to be as high as ≥40%, and 15% to 20% of patients still report anxiety 1 year after hospital discharge. In a study of 516 older CHD patients (mean age, 68 years), the age-adjusted hazard ratio for anxiety was 1.97 (95% confidence interval, 1.03–3.78; P=0.04) for nonfatal MI or death.[109] Older participants tended to report lower anxiety levels, although age did not appear to moderate the relationship between anxiety and increased risk of death or a cardiac event.

Stress
Stressful life events and emotional distress can trigger fatal cardiovascular events. In the international INTERHEART study of 15 152 individuals with their first MI (median age, 59 years) and 14 820 age- and sex-matched healthy individuals without CHD, stress was assessed by 4 questions about stress at work, home, finances, and major life events.[110] Patients with CHD reported higher levels of stress in all categories and also were more depressed. The composite stress index had an odds ratio of 2.67 for fatal CHD, which was comparable to the traditional CHD risk factors. Although smoking, dyslipidemia, hypertension, and diabetes mellitus had a greater relative risk in younger patients with acute MI than in older patients, age did not moderate the adverse prognostic value of stress.

Socioeconomic Status and Social Support
Low socioeconomic status is a significant independent contributor to increased cardiovascular risk in healthy people and to poor prognosis in CHD patients. Williams et al[111] found that the 5-year mortality rate of CHD patients with incomes <$10 000/year was 1.9 times higher than that among patients with incomes >$40 000/year. This effect was independent of social isolation and disease severity. In a study of 194 older post-MI patients, Berkman et al[112] reported that the presence of emotional support before the MI was the most powerful and significant predictor of survival after the MI. At 1-year follow-up, 55% of patients without support had died in comparison with only 27% with ≥2 sources of support.

Consequences of CHD
Acute MI and other clinical manifestations of CHD have a profound effect on psychosocial functioning, QOL, and activities of daily living. There are data suggesting that age may moderate the relationship between CHD and psychological well-being. In a prospective cohort of 2498 survivors of acute MI, patients 65 to 74 years of age had higher late mortality but reported fewer symptoms and better health-related QOL at 1 year in comparison with younger patients, independent of baseline angina, QOL, and other clinical and demographic variables.[113]

Dementia
Surveys indicate that, with the exception of cancer, older Americans fear developing dementia more than they do any other major illness, including ASCVD. Dementia affects almost 10% of adults >65 years of age, and up to 50% of adults aged ≥85.[114] More than twice as many are affected with significant cognitive impairment, but without meeting diagnostic criteria for dementia. Epidemiological data demonstrate that cardiovascular disease also increases the risk of cognitive decline and Alzheimer's disease. For example, in the Rotterdam study,[115] cognitive function was lower among those with a history of stroke, electrocardiographic evidence of MI, PAD, or plaques in the internal carotid arteries. The high rate of cognitive impairment among older adults with CHD has important implications for disease management, including issues of medication adherence.

Psychosocial Management

Psychological Treatments
Despite the substantial epidemiological evidence for a stress-CHD relationship, the health benefit of reducing stress in CHD patients is not well-established. To our knowledge, no studies have examined the effects of stress reduction specifically in older CHD patients on clinical outcomes; thus, such benefits must be inferred from studies of middle-aged CHD patients.

A Cochrane meta-analysis of 36 trials examined the effects of RCTs of psychological interventions in 12 841 CHD

patients.[116] Approximately half of these studies were stress management interventions, and the quality of studies was generally poor. Results showed no differences between groups in cardiac mortality or revascularization, and only a small reduction in nonfatal reinfarction.[113] Surprisingly, psychological outcomes were reported in relatively few trials, with little attention to age as a potential moderator.

Depression has been the primary target of several recent psychological and pharmacological RCTs in coronary patients. In the Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) trial, post-MI patients with an average age of 61 years, who were depressed or who had low social support, were randomly assigned to receive either usual care or a 6-month cognitive behavioral therapy intervention. The trial showed greater improvements in psychosocial outcomes, such as reduced depression and increased social support, in the treatment group than in controls, but no improvement in event-free survival.[117]

Pharmacological Treatments

The SADHART trial was a randomized, double-blind, placebo-controlled, 24-week trial of sertraline versus placebo for major depressive disorder among patients hospitalized for acute MI.[118] Improvements in depressive symptoms were comparable in participants treated with sertraline and placebo, but patients with more severe depression benefitted more from sertraline. The study was a safety trial and was not powered to examine clinical outcomes.

Alternative Approaches

Aerobic exercise has been studied as a treatment for depression. A Cochrane review found a large, clinically meaningful improvement associated with exercise in comparison with controls (standardized mean difference = −0.82 (95% confidence interval, −1.12 to −0.51). When analyses were limited to trials using the most rigorous methodologies, only a moderate antidepressant effect of exercise was noted.[119] Studies of middle-aged and older adults showed that exercise was comparable to antidepressant medication in reducing depressive symptoms,[120] but the impact of exercise on clinical outcomes was not assessed.

Comorbidities

Overall, secondary prevention of ASCVD risk factors for older adults entails a trade-off between the benefits and risks of treatment. The trials that served as the basis of secondary prevention guidelines typically excluded older adults (especially those ≥85 years of age) or included only exceptional seniors who had few of the comorbidities typical of community-dwelling seniors.[121] Therefore, although there is a conceptual rationale to assume that favorable benefit-to-risk ratios of most medical therapies extend to very old adults, corroborating data are limited.

The potential for substantial risk reduction for older patients receiving secondary prevention therapy is counterbalanced by the potential for increased risks from therapy as well. Risks accrue from the medications themselves, particularly from aging changes in drug distribution and metabolism, and multiple comorbidities may further compound medication risks.[122,123] Intrinsic medication risks escalate amid age-related

changes in physiology such that cardiac reserve, hemodynamics, balance, hemostasis, renal function, and cognition are all more tenuous. Examples of age-related medication hazards include increased hemorrhagic risks from thienopyridenes, greater chronotropic incompetence from β-blockers, increased falls and syncope from nitrates and ACE inhibitors, and increased myalgias or confusion from statins.[122] Thus, many secondary prevention medications or procedures are more likely to induce greater iatrogenic sequelae in an older than in a younger cardiac patient because of age-associated changes in metabolism and physiology.[10,121,122]

Therapeutic risks associated with standard secondary prevention medications are also exacerbated by the presence of age-associated comorbidities.[10,121,122] Antiplatelet agents are, for example, more likely to precipitate bleeding in the context of arteriovenous malformations, gastritis, hemorrhoids, and atrial fibrillation (ie, using concomitant vitamin K antagonists or direct thrombin inhibitors). The rationale to implement secondary prevention strategies for ASCVD is counterbalanced by their potential to aggravate noncardiac conditions.

Common iatrogenic effects of medications among older cardiac patients are listed in Table 3. β-Blockers, for example, are more likely to precipitate bronchospasm in patients with chronic obstructive lung disease, and heart block, as well, in those with conduction system disease, and exercise intolerance in those with chronotropic incompetence.[122] Nitrates are more likely to precipitate falls in those with orthostatic or postprandial hypotension.

Polypharmacy is an overlapping source of risk; most older patients with ASCVD are taking numerous medications for multiple cardiac and noncardiac conditions. Not only are the salutary effects of a multipill regimen for a frail elderly patient unclear, but medication costs, adherence, and drug–patient/drug–drug interactions become substantial concerns.[122] High age-related use of over-the-counter medications (eg, nonsteroidal anti-inflammatory agents and dietary supplements) adds to these risks, potentially exacerbating risks of bleeding, renal insufficiency, and fluid retention. Likewise, the tendency of many providers to routinely prescribe pain and sleeping medications to their older patients can aggravate hazards, because they increase the potential for confusion, somnolence, and impaired self-care. Nonspecific medication side effects such as confusion, weakness, and changes in mood, appetite, and sleep are all widespread in older cardiac patients, especially in association with hospitalizations, procedures, and other transitions of care that often disrupt clinical stability.[123] Thus, even when conceptual value for a particular medication is strong, benefits are less clear in a multiple-pill regimen.

Aging is also associated with sensory impairments (hearing, vision) and limitations in cognition that can diminish adherence to both medications and lifestyle interventions. Access to caregivers is often more limited, hindering assessments and monitoring; arthritis, parkinsonism, cardiovascular disease, or functional impairments often undercut physical activity goals; financial constraints and altered taste may frustrate dietary recommendations; limited finances may also discourage use of vital ancillary services.

The net effect of this inherent complexity of managing older patients with ASCVD is that use of evidence-based

Table 3.   Common Iatrogenic Effects of Secondary Prevention Medications in Older Patients With ASCVD

Medication Class	Medication	General Side Effects in Older Cardiac Patients	Medication-Medication Side Effects	Comorbid Disease–Medication Interactions
Anti-ischemics and antihypertensives	β-Blockers	• Confusion, fatigue, dizziness, bronchospasm, conduction block, chronotropic incompetence, claudication, depression, cold sensitivity, incontinence • Hypoglycemia • Increased system absorption in body fat, with delayed metabolism	• Calcium channel blockers: conduction disease and chronotropic incompetence • Sulfonylureas: hypoglycemia	• COPD: bronchospasm • Depression or anxiety: ↑fatigue and depression • PAD: claudication • Raynaud syndrome: ↑symptoms • CHF: acute decompensation • Conduction disease: bradycardia, heart block
	ACE inhibitors	• Falls, dizziness, hypotension (orthostatic, postprandial), hyperkalemia, fatigue, azotemia, cough	• Diuretics (and other antihypertensives): ↑susceptibility to hypotension • NSAIDs: ↑susceptibility to renal failure	• CKD: hyperkalemia and ↑renal failure
	Nitrates	• Dizziness, hypotension, syncope, headache	• Diuretics: hypotension and low cardiac output • Phosphodiesterase inhibitors: severe hypotension • Alcohol: hypotension	• Aortic stenosis: hypotension
	Diuretics	• Urinary frequency and incontinence, electrolyte abnormalities (eg, hypokalemia, hyponatremia, hypomagnesium), hyperglycemia, hyperuricemia, dehydration, muscle cramps	• ACE inhibitors and other diuretics: hypotension	• CKD: ↑renal failure • Diabetes mellitus: ↑hyperglycemia • Incontinence: ↑incontinence
	Calcium channel blockers	• Dizziness, flushing, and peripheral edema (dihydropyridines), constipation (verapamil)	• β-Blockers: conduction disease and chronotropic incompetence	• CHF: decompensation • Conduction disease: bradycardia, heart block
Antiplatelet	Aspirin	• GI bleeding, dyspepsia, tinnitus, skin reactions	• Warfarin, direct thrombin inhibitors, or thienopyridine: ↑bleeding	• GI bleeding history, hypertension: ↑bleeding risks
	Thienopyridines	• GI bleeding, bruising, rash	• Warfarin and ASA: ↑bleeding.	• GI bleeding history, anticipated surgery: ↑bleeding risks
Cholesterol reduction	Statins	• Myalgias, confusion, renal insufficiency, liver toxicity	• Meds metabolized by the cytochrome P450 system (fibrates, amiodarone, erythromycin, diltiazem, azole antifungals): ↑statin levels and ↑levels of the other meds • Grapefruit juice: ↑statin levels (via cytochrome P450 mechanism) • Fibric acids: myopathy (gemfibrazole>fenofibrate)	• Hypothyroidism, CKD, diabetes mellitus: ↑susceptibility to statin-induced myopathy
	Fibric acids	• Nausea, liver toxicity, gallstones	• Statins: myopathy • Warfarin: ↑warfarin levels	• CKD: ↑renal failure

ACE, angiotensin-converting enzyme; ASA, acetylsalicylic acid; ASCVD, atherosclerotic cardiovascular disease; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; GI, gastrointestinal; Meds, medications; NSAID, nonsteroidal anti-inflammatory drug; and PAD, peripheral artery disease.

medications remains lower than recommended by guide-lines, although rates have significantly improved in recent years.[10,13,124] In a cohort of MI survivors aged ≥65 (73% women) discharged in 2004, 61% filled prescriptions for statins, 80% for β-blockers, and 58% for ACE inhibitors or angiotensin receptor blockers within 90 days of discharge. However, only ≈35% of patients in this cohort filled prescriptions for all 3 drug classes, and black patients were less likely

to fill such prescriptions than their white counterparts.[124] Older women with ASCVD are also less likely to receive aspirin in the acute and chronic settings. In an analysis of the Global Registry for Acute Coronary Events with data collection from 1999 to 2007, women with ACS aged 65 to 74, 75 to 84, and ≥85 years were 14%, 32%, and 54% less likely to receive aspirin during their hospitalization than men <65 years of age.[125] Data from the 2000 to 2002 Medical Expenditure Panel

Surveys showed significantly lower rates of chronic aspirin use among older individuals and women with a history of CHD even after adjustment for contraindications against aspirin use, which were more frequent among women than men.[126]

Lifestyle Therapy of ASCVD

General Dietary Guidelines

Although calorie and sodium restriction have already been discussed in relation to obesity and hypertension, broader dietary principles require a brief discussion. Diet is an important component for optimizing both general and cardiovascular health in older adults, but it frequently receives inadequate attention. Both cardiologists and primary care providers should assess the dietary habits of their older patients, provide general dietary advice, and refer them for more detailed dietary counseling if significant dietary deficiencies or malnutrition are suspected.

Undernutrition is a major concern among seniors because of a complex combination of medical and socioeconomic factors. An estimated 5% to 10% of community-dwelling adults >70 years of age are undernourished; this proportion rises to 30% to 65% among institutionalized elderly patients.[127] Protein intake should in general be at least 0.8 g/kg body weight unless severe renal insufficiency is present.[128]

The Mediterranean diet, consisting of large proportions of fruits and vegetables, whole grains, fish, and nuts, and low levels of saturated fats, has consistently demonstrated favorable effects on cardiovascular risk factors and outcomes in older adults.[129,130] Flavonoids, found primarily in fruits and vegetables, nuts, cocoa, tea, and wine, promote antioxidant and anti-inflammatory properties. In a study of 98 000 adults with an initial mean age of 70 years who were then followed over 7 years, flavonoids were associated with lower risk of cardiovascular death.[131] Adequate dietary fiber intake is generally beneficial in maintaining optimal bowel function, which is often impaired in older adults secondary to the effects of age, medications, and inactivity.

Deficiencies of vitamins and minerals are common among the older adults because of inadequate dietary intake, reduced absorption, or disease/medication-specific factors; a daily multivitamin can reduce the risk of such deficiencies. Vitamin D deficiency has been increasingly identified among older adults because of inadequate sun exposure and a reduced capacity for synthesis in the skin.[132–134] Recent studies have identified vitamin D deficiency as an independent risk factor for cardiovascular mortality in older adults.[126,127] Several clinical trials of vitamin D supplementation in older adults with ASCVD are ongoing. Although omega-3 fatty acid supplementation has been shown to reduce cardiovascular events in some studies, a recent randomized trial in patients 60 to 80 years of age with a previous MI showed no significant effects on new major cardiovascular events.[135] There is little evidence to suggest a benefit from B vitamin supplementation in preventing cardiovascular disease in seniors.[136]

Physical Inactivity in Older Adults

The role of physical inactivity as a risk factor for chronic diseases, including hypertension, CHD, stroke and PAD, type 2 diabetes mellitus, depression, osteoporosis, and certain cancers, is well established.[137,138] The seminal work of Morris et al[139] established a significant association between physical inactivity and ASCVD disease risk 6 decades ago. Physical inactivity is also associated with increased cardiovascular mortality.[140]

The health consequences and financial and societal costs of physical inactivity are especially relevant to older adults, because much of age-related ASCVD pathophysiology and morbidity is compounded by the biological and clinical repercussions of a sedentary lifestyle. For older adults, physical inactivity also leads to diminished functional health, an increased risk of falling, worsened psychological status, and decreased cognitive function. Furthermore, the increased prevalence of inactivity with aging constitutes perhaps the most common modifiable cardiovascular risk factor in older adults after hypertension. Survey data from 2008 indicate that only 18% of people ≥75 years of age reported regular moderate or vigorous physical activity.[3] Furthermore, only 14% of men and 8% of women ≥65 years of age reported participating in aerobic and muscle-strengthening activities that met the 2008 Federal physical activity guidelines.[141,142] Patel and colleagues[143] recently found increased total mortality and especially cardiovascular mortality in older men and women who sat >6 hours a day in comparison with those sitting only 3 hours a day.

Research has clearly demonstrated that reducing physical inactivity dramatically improves health status. This holds true across age, sex, race, and ethnicity.[140,141] The benefits of moving from a physically inactive to a more active lifestyle are attributed to the strong influence that increased energy expenditure has on physiological functioning and psychological risk factors.[141] Regular physical activity positively influences CHD risk factors, including serum lipids, blood pressure, insulin sensitivity, body weight, and bone density, muscular strength, functional capacity, and cognitive and psychological functioning, as well, which are key elements of health and well-being in older adults.[140,141] Given the overwhelming evidence that physical inactivity is harmful for older adults, moving from the couch to the sidewalk or gym has become a major goal of federal, state, and professional health organizations, clinicians, and the public.[144]

In both observational studies and RCTs, older adults with ASCVD have experienced benefits from undertaking an exercise program, including reductions in morbidity and mortality, less functional decline, less mobility disability, reduced recurrent cardiovascular events, and an increase in active life expectancy.[144] Even modest amounts of physical activity have been associated with reduced cardiovascular risk in older adults. For example, men 71 to 93 years of age in the Honolulu Heart Program who walked >1.5 miles/day experienced half the risk for new CHD than men who walked <0.25 miles/day over 2 to 4 years of follow-up[145]; risk of incident dementia was similarly reduced.[146] Even in frail older adults, regular physical activity has resulted in substantial physical, cognitive, and psychological benefit.[147] In such individuals, achievable goals for increasing physical activity include regular leisure activities such as walking, gardening, and housekeeping.

Exercise Training and Prescription

The prescription of exercise for increasing physical activity and fitness for older patients with ASCVD is an essential component of secondary prevention.[5] Numerous studies have demonstrated that improvements in exercise capacity, lipids, and mental health are similar in older versus younger patients with ASCVD.[148–150] Among seniors, exercise training is also associated with the prevention of falls, reduced ambulation limitations attributable to comorbidities, and improved cognition.[148–151] Methods for prescribing exercise generally do not require major modification for older patients.[152,153] The most important considerations include creating an exercise program that is achievable and avoids injury or exacerbation of known musculoskeletal disorders. In addition, the absolute starting work intensities will generally be lower than in younger patients, with smaller increments over time. The exercise prescription should define individual patient guidelines for activity while allowing for, and encouraging, variation in the exercise regimen. The exercise program should also promote all aspects of physical conditioning, including aerobic capacity, muscular strength and endurance, balance, and flexibility to achieve the greatest benefit to functional capacity, QOL, and cardiovascular disease risk.[152,153]

Initiating and reinforcing physical activity requires clinicians to strongly and repeatedly encourage participation, while carefully considering the appropriate and individualized recommendations for the exercise prescription. Consideration of the differences in needs between women and men, occupational and leisure activities, activities of daily living, and diversity of activities are all relevant. Modification of the components of the exercise prescription should be considered for older patients, particularly those ≥75 years of age and those with significant comorbidities that limit mobility (eg, arthritis, pulmonary disease, and PAD).[153] Increasing caloric expenditure for overweight and obese patients and enhancement of functional mobility should be emphasized, and participation in activities that increase socialization with others, as well, which may combat feelings of isolation and depression. Increasing frequency and duration of exercise sessions should supersede the increases in intensity to reduce the potential for overuse injuries.

Patients with ASCVD generally benefit from a symptom-limited exercise test before initiating an exercise program. An exercise test helps to ascertain the safety of exercise by assessing for severe ECG ischemia or cardiac arrhythmias that would contraindicate exercise training or require additional therapeutic interventions before starting exercise training.[154] It also helps clarify the baseline fitness level, pertinent symptoms, and an appropriate starting exercise workload, as well. However for patients who do not undergo exercise testing, and particularly for those with known ASCVD who do not plan to exercise in a supervised medial program such as cardiac rehabilitation, initiating only low-intensity activity should be the alternative training standard, with instructions to report symptoms such as chest pain or shortness of breath to their physician.

Accumulating evidence suggests that the extent of exercise benefits may increase in proportion to the intensity of exercise training. Reports in patients with established heart disease, including 1 study of patients with a mean age of 75 years, suggest that a high-intensity aerobic interval training can elicit greater improvement in exercise capacity than continuous exercise at a lower intensity.[155] In general, high-intensity aerobic interval training entails short periods of higher-intensity exercise alternating with longer periods at lower exercise intensity, a training pattern that has been demonstrated to achieve higher training effects than continuous training, with preserved safety. Details regarding the specific intensities and duration of the training regimen must be tailored relative to each individual's baseline capacities and circumstances. Despite such encouraging data, high-intensity aerobic interval training is more complex than continuous training, necessitating more supervision for implementation and safety. Larger studies are needed to more definitively establish the efficacy and safety of high-intensity interval training in broader populations of older patients.

Strength training for older patients as a component of the overall exercise prescription, and balance and flexibility training, as well, should improve neuromuscular function, muscular strength, and endurance. Such training is essential in improving the responses to the various physical demands of daily living and to occupational and recreational activities, as well,[148,152] and to moderate the effects of sarcopenia, particularly in those struggling with disease and trying to lose weight. Furthermore, this training is likely to improve self-esteem and functional independence, both critical issues among seniors.

Cardiac Rehabilitation

Cardiac rehabilitation (CR) constitutes structured exercise training integrated with broader secondary prevention reinforcements. Studies show that older patients with CHD benefit greatly from CR,[148–150,153] improving from the individualized prescription, and its close supervision and support, as well. Among 601 099 Medicare beneficiaries, those who participated in supervised CR experienced 21% to 34% lower mortality than nonusers over the subsequent 5 years, independent of other risk factors.[156] Furthermore, patients who attended at least 25 of the 36 CR sessions were 19% less likely to die than those who attended fewer sessions.

CR Referral, Participation, and Adherence

Despite the clear benefits of CR in the older adults with ASCVD (Table 4), the vast majority of older patients do not participate because of a variety of factors: lack of referral, patient-related factors, or societal and economic barriers. The cumulative effect of the these factors is abysmally poor CR use rates among the older adults. Overall CR participation in Medicare recipients is ≈12%; within this population, older individuals, women, and nonwhites were less likely to receive CR.[157] Thus, men and women aged 75 to 84 years were only 87% and 69%, respectively, as likely to receive CR as men aged 65 to 74 years. Sex-related differences in referral increased with age. Whites were 33% more likely to receive CR than nonwhites after the adjustment for age and sex. Both CABG surgery and percutaneous coronary intervention (PCI) during the index hospitalization were strong predictors of higher CR use,[157] but this may reflect an implicit preselection

Table 4.   Benefits of Cardiac Rehabilitation for Older Adults

Cardiac Rehabilitation Effects	Clinical Implication
Exercise training CV effects	
Increased functional capacity (10%–60%) with decrease myocardial work (10%–25%) at standardized work with 12 weeks of exercise training posthospitalization.	• Improved CV health, both in terms of plaque stability and CV work efficiency • Enhanced ability to perform ADLs and prolonged independence with aging
Training effect from improved skeletal muscle work capacity, although exercise may also improve health of the vasculature, autonomic balance, and cardiac performance.	Peripheral physiology is an important part of CV health
Absolute levels of functional gain are less in elderly than in younger cohorts, particularly for those patients ≥75 years of age.[4–6]	
Extended periods of training result in further modest gains.	Lifelong training is a worthwhile goal
Improved heart rate recovery	Decreased susceptibility to arrhythmia
Exercise training non-CV effects	
Enhanced quality of life	Improved self-efficacy and self-worth
Reduced depression	Improved quality of life
Decreased BMI and body fat	Improved metabolism and decreased inflammation, increased joint stability
Improved lipid profiles	Decreased CV events and mortality
Cardiac rehabilitation effects on diet and lifestyle	
Comprehensive assessment and management in relation to diet, medications, exercise that can compensate/reinforce compliance, monitor for iatrogenesis, and monitor/compensate for possible cognitive deficiencies.	Appropriate care for a population with predictable polypharmacy, multimorbidity, frailty, cognitive limitations, and atypical symptoms.

ADL indicates activity of daily living; BMI, body mass index; and CV, cardiovascular.

in respect to which senior patients are referred for revascularization in the first place.

Physician referral is a key determinant of CR enrollment; failure to refer is probably the major contributor to the underrepresentation of older adults, especially those ≥75 years of age in secondary CHD prevention programs.[153] Analyses of system-level factors that appear to impact CR referral and use include the degree of automation and physician assertiveness around securing CR referrals and the level of integration of CR within the hospital setting and physician community. In many cases, this is already evident in cardiothoracic surgical programs that routinely refer to cardiac rehabilitation as part of postoperative management. Automated referrals of all eligible patients, in combination with a discussion between the patient and a nurse or physiotherapist, can achieve more than a doubling of CR participation rates.[158]

Older patients may also be reluctant to enter a structured exercise program, which may be novel to them or, in some instances, includes activities in which they have never participated or, at a minimum, not for many years. Low functional capacity, multiple comorbidities, and chronic deconditioning may also deter patients from participating in CR programs.[149] Recent data suggest that current smoking, a BMI ≥30 kg/m², diabetes mellitus, and cognitive dysfunction are associated with failure to enroll in outpatient CR in this age group.[159] In addition, patients may often have logistical or personal barriers to attending CR, including the lack of transportation or the need to care for a sick spouse. Nonetheless, CR staff must recognize the importance of encouraging and supporting these patients by any available means, given the convincing data suggesting that older patients, including those with significant medical comorbidities or other barriers to participation, benefit substantially from CR participation.[149] Providing

the opportunity for the patient and family to participate in the design of the intervention, underscoring the importance of specific interests and concerns, and overcoming potential limitations to participation are essential to long-term adherence.

The financial commitment of CR program entry is another potential deterrent to CR participation by older adults. For eligible patients aged ≥65 years, Medicare Part B reimburses for CR services in all states.[160] However, individuals without supplemental insurance or Medicaid may still be responsible for 20% of the overall payment. For private insurance, copayments for each CR visit can also be problematic. Patients without insurance or who are underinsured may qualify for financial waivers in some cases, dependent on institutional policy. Program staff can be a valuable resource for facilitating participation and various appeal processes related to insurance coverage. Lower-cost options such as home-based or community center programs should be strongly considered to help overcome these financial barriers.

Coronary Revascularization

Revascularization procedures for ACS in older adults are discussed in separate AHA Scientific Statements.[10,13] However, it is important to highlight the benefit of revascularization in chronic CHD, both as a means to treat symptoms, and, in certain situations (multivessel disease, certain coronary lesions, large ischemic burden, left ventricular systolic dysfunction), to improve survival. Both CABG and PCI have been increasingly used in older patients, with about two-thirds of all PCIs being performed in patients ≥60 years of age and 11% in those ≥80 years of age.[161] Relevant outcomes in this age group include general well-being, functional status, QOL, and mortality, as well.

Older patients tend to have more calcified, tortuous, and multivessel coronary disease, and their peripheral vessels are

also more often abnormal. The incidence of PAD approaches 25% in octogenarians. These factors can make both PCI and CABG more challenging and lead to suboptimal results or complications with either procedure.

Percutaneous Coronary Intervention

Despite the challenges noted above, procedural success for PCI typically exceeds 90% in older patients, and patient outcomes have also been improving. In an analysis of the National Cardiovascular Disease Registry Cath PCI Registry Database, in-hospital mortality for patients aged >80 years undergoing elective PCI declined from >3.5% to 3% between 2001 and 2006.[161] However, nonmortal complications of PCI, including vascular and bleeding problems, are more frequent in older adults, particularly in very advanced age. Whether the use of radial artery for access may reduce complications in older adults, who may have upper extremity arterial disease, is uncertain.

The Trial of Invasive versus Medical therapy in Elderly patients (TIME) Trial randomly assigned older patients (mean age, 80 years) with refractory angina to invasive versus medical therapy; 74% of the invasive group underwent revascularization (73% PCI and 27% CABG).[162] There was a reduction in major adverse cardiac events in the invasive arm, primarily attributable to a decreased rate of rehospitalization for ACS. QOL, angina severity, and health status were also better in the intervention group, and these differences persisted at 4 years.[162]

In patients with stable angina, the COURAGE trial showed that the addition of PCI (only 15% drug-eluting stents) to optimal medical therapy did not reduce the rate of death, nonfatal MI, or hospitalization for ACS; results were similar for the 39% of patients who were >65 years of age.[163] Patients in the PCI group, however, did undergo fewer subsequent revascularization procedures during follow-up. They also had improved health status and QOL measures in the first 2 years than the medical therapy group had. These differences were more pronounced in those with more severe angina.[163]

Thus, although a reduction in symptoms and antianginal medications and greater QOL may initially accompany PCI, the greater potential for complications in older patients with other comorbid conditions must be considered. Thus, the decision whether to perform PCI in an older patient must be individualized.

Coronary Artery Bypass Grafting

Patients with left main, multivessel disease, those with depressed left ventricular systolic function, and those with diabetes mellitus have traditionally been referred for CABG, based on RCT data. Older patients are at higher risk of morbidity and mortality after CABG. Postoperative complications such as prolonged intubation, inotropic dependence, intraaortic balloon pump placement, atrial fibrillation, bleeding, renal failure, infection, and delirium are more common with increasing age. Those at increased risk include patients with renal dysfunction and patients undergoing more complex or emergency procedures. Outcomes have been improving, however. In an analysis of CABG in octogenarians between 1990

and 2005, in-hospital mortality fell from 7.1% to 3.2%, and postoperative complications also fell significantly.[164]

Modern series have suggested a rate of CABG-associated stroke of ≈3% with advancing age associated with increased risk.[164] Risks of cognitive changes secondary to CABG remain controversial, but a prominent study in the *New England Journal of Medicine* reported 53% of CABG patients with neurocognitive testing abnormalities at discharge, and 42% with persistent/worsening neurocognitive abnormalities at 5 years.[165] Increasing age, diabetes mellitus, extent of atherosclerosis, and lower educational status, and operative events such as hypotension and hypoxia, as well, are risk factors. The wide reported range of cognitive dysfunction is attributable to variable definitions, testing times, and modalities. Studies performed several weeks after surgery typically show lower rates of impairment.

PCI versus CABG

Because of the potential complications of CABG in older patients, and the greater prevalence of left main and multivessel coronary disease in these patients, a comparison of PCI and surgical revascularization is relevant. The BARI trial, which compared CABG with PCI in the early 1990s, showed an advantage of CABG for MI-free survival in patients with diabetes mellitus and multivessel CHD, regardless of age.[166] However, PCI in that study did not include stenting, and adjuvant therapy for PCI has also evolved since that time. A modern meta-analysis that included 66 studies of octogenarians undergoing PCI or CABG showed similar 30-day and 1-year mortality for the 2 strategies.[167] Another meta-analysis of 10 trials of CABG versus PCI showed no difference in mortality at 6 years, although the data suggested an advantage for CABG with increasing age.[168] However, the number of patients >75 years of age was very limited. In addition, fewer than half of the studies included PCI with bare metal stents, and none included drug-eluting stents. A recent observational study of nearly 190 000 patients nonemergently revascularized for multivessel coronary disease found a survival advantage for CABG over PCI; 78% of the PCI group received drug-eluting stents.[169] The decision to pursue coronary revascularization in an older adult must be individualized, taking into account the possibility that this may provide greater reduction in symptoms, improved QOL, and increased function over medical therapy, at least in the short term. CABG should be considered for standard indications, regardless of age, but the increased risk of periprocedural complications, including neurocognitive dysfunction, should be factored into decision making. Whether the use of drug-eluting stents in multivessel or left main CHD provides an appropriate alternative to CABG is uncertain, particularly in this population.

Implantable Cardioverter-Defibrillator Therapy

Indications for implantable cardioverter defibrillator (ICD) therapy for sudden cardiac death (SCD) prevention have been published with comprehensive reviews of clinical evidence in the 2 most recent guideline statements.[170,171] These guidelines were developed from pivotal trials that generally enrolled

younger patient cohorts relative to those typically observed in the clinical setting. This section will critically appraise the current recommendations and level of evidence for primary and secondary SCD prevention in the older adult with CHD. Primary prevention of SCD refers to the use of ICDs in individuals who are at risk for, but have not yet had, an episode of sustained ventricular tachycardia, ventricular fibrillation, or resuscitated cardiac arrest. Secondary prevention refers to the prevention of SCD in those patients who have survived a previous sudden cardiac arrest or sustained ventricular tachycardia.

ICD Therapy: Randomized Clinical Trials of Secondary Prevention

Prospective, randomized, multicenter trials have demonstrated that ICD therapy is effective for secondary prevention of SCD by improving overall survival in selected populations.[172–174] The Antiarrhythmics Versus Implantable Defibrillator (AVID),[172] Canadian Implantable Defibrillator Study (CIDS),[173] and Cardiac Arrest Study Hamburg (CASH)[174] provided evidence for the current secondary SCD prevention recommendations. The mean ages were 65±10 years, 64±10 years, and 58±11 years in AVID, CIDS, and CASH, respectively. The AVID trial demonstrated significant survival improvement from ICD therapy in comparison with antiarrhythmic drug therapy. Survival benefit was not observed in patients with an ejection fracton >35%. The CIDS and CASH trials enrolled a smaller number of patients and showed nonsignificant trends toward improved survival. In a meta-analysis of these 3 trials, the mean survival benefit was 4.4 months longer in the ICD cohorts than in those receiving medical therapy.[175] Concerns of antiarrhythmic drug–mediated adverse effects and the low use of β-blocker therapy in the drug-treated control group may have potentially overestimated the modest benefit of ICD therapy. In another meta-analysis of the 1866 patients from these 3 secondary prevention trials, ICD therapy significantly reduced all-cause and arrhythmic death in the 86.5% of patients <75 years of age, but not in the 252 patients ≥75 years of age.[176] Although advanced age alone should not be the determinant to withhold ICD therapy in older patients with a history of malignant arrhythmias, the limited data available suggest that ICD therapy may not afford survival benefits similar to those observed in younger patients.[176,177]

ICD Therapy: Randomized Clinical Trials of Primary Prevention

Randomized trials have established that ICD therapy is effective for the primary prevention of SCD in selected populations with CHD and reduced left ventricular ejection fraction.[178–182] The mean or median age of patients in these trials ranged from 60 to 67 years. The MADIT I,[178] CABG-Patch,[179] and DINAMIT[181] trials excluded patients >80 years of age. The 2006 guidelines indicate that the primary prevention of SCD in seniors does not differ from that in the general population, but the authors qualified the recommendation by stating "very elderly patients with multiple comorbidities and limited life expectancy may not be appropriate candidates for ICD therapy even if they meet the standard criteria."[170] The 2008 guidelines further emphasized that "all primary SCD prevention ICD recommendations apply only to patients who are receiving optimal medical therapy and have reasonable expectation of survival with good functional capacity for more than one year."[171] When evaluating seniors for ICD therapy, the clinical assessment that life expectancy is at least 1 year is particularly relevant, considering that the survival benefit does not become apparent until 1 to 2 years after ICD implantation, and the median survival for octogenarians with heart failure is ≈2 years.[183] Among the 4915 patients from 4 randomized trials included in a recent meta-analysis, 579 (11.8%) were ≥75 years of age.[184] The ICD was found to be efficacious in reducing all-cause mortality in this selected older patient population (hazard ratio, 0.73; *P*=0.03).

Registries of ICD Therapy

Older patients constitute a large and rapidly growing segment of cardiac patients. Comprehensive registry databases, although not suitable for the assessment of comparative effectiveness, are excellent sources for the general trend of day-to-day clinical practice. The National Cardiovascular Disease Registry National ICD Registry is the sole repository for ICD data for Medicare beneficiaries.[185] Although initially intended for the Medicare population, ≈90% of all ICD implants performed in the United States are reported to the registry. According to the 2009 data, >550 000 patients had been entered into the registry since 2006. The mean age was 68.1±12.8 years. Of the total, 29.6% were 70 to 79 years of age; 12.4% were octogenarians. The Advancements in ICD Therapy (ACT) Registry is a prospective 2-year study of new ICD implants from a single manufacturer[186] and includes 4566 patients from 264 centers in 38 states in the United States. Of the total, 29.0% were 70 to 79 years of age; 12.0% were octogenarians. The PREMIER Perspective Comprehensive Database includes data from several hundred hospitals and healthcare systems.[187] Among 26 887 PREMIER patients who received an implantable cardiac device for heart failure from 2004 to 2005, 93.3% received ICD with or without cardiac resynchronization therapy. The median age was 70.0 years, and 17.5% were ≥80 years. Overall, registry data show that age is a strong predictor of survival. Mortality rates at 2 years follow-up were 8.0%, 15.0%, and 17.8% in patients aged 60 to 69 years, 70 to 79 years, and ≥80 years, respectively.[186]

In contrast to consistent survival benefits of ICD in younger patients, benefits in adults aged 75 to 80 years are less clear. Projections of SCD prevention in older adults, extrapolated from younger patients studied in randomized trials, are not straightforward. The combination of advanced age and age-associated medical comorbidities increase risks of noncardiac mortality and morbidity, which can diminish or even abolish the beneficial effects of ICD in the prevention of SCD in many senior patients. Furthermore, increased depression and reduced QOL can result in many ICD recipients through inappropriate discharges and the apprehension that may occur, especially in those who are predisposed to such emotional flux.[188] Similar ICD-related emotional distress may also extend to ICD patients' families.[188] Such stresses and potential clinical implications (eg, depression, anxiety, and potentially even changes in cognition) merit greater study in relation to advanced age and cumulative infirmity.

For older patients with ICDs who may be facing subsequent end-of-life circumstances and decisions, open and early communication between the physician and the patient regarding withholding or withdrawing ICD therapy are recommended. Such decisions are increasingly relevant in this rapidly expanding segment of our population.[189]

Final Considerations for Secondary Prevention of ASCVD in Older Adults

Given the greater attributable risk associated with ASCVD in older adults in relation to morbidity, mortality, and decreased QOL, physical function, and personal independence, as well, beside higher healthcare costs, older patients are particularly likely to benefit from secondary prevention strategies. Nonetheless, risks attributable to these therapies also increase for seniors in comparison with the younger populations on which evidence-based secondary prevention standards were based. Secondary prevention pharmacological, invasive, and lifestyle interventions are all technically feasible in older and younger adults with ASCVD, as well, but their risk-to-benefit ratios vary significantly. Whereas some subsets of very old CHD patients will likely experience disproportionate benefit, with secondary therapy moderating greater likelihood of clinical decrements, others experience disproportionate iatrogenesis and the perception of unwanted therapeutic burden.

Further research is necessary to clarify which senior patients with ASCVD are likely to derive the most benefit from secondary prevention therapy. Pertinent risk assessment must be improved to address the concept of hazard among older adults in the context of age-related multimorbidity, polypharmacy, and altered lifestyle. Implications of costs, logistics, and the overall management complexity are also pertinent, particularly in relation to each patient's circumstances. Improved health literacy among seniors and their families is also pertinent, because expectations must correspond realistically to the advantages, burdens, and limitations of care. This also implies a need for effective communication amid complicating dynamics of cognitive, visual and hearing impairments of old age. In addition to ascertaining whether or not secondary prevention measures yield overall favorable risk-to-benefit balance, it is incumbent on providers to ascertain whether their use is consistent with each older patient's goals and perceived QOL.

Further research is needed to clarify the medication regimens, lifestyle modifications, and revascularization/ICD strategies that yield the greatest benefit/risk in this rapidly expanding age group. It is therefore essential to include older and very elderly patients in pertinent clinical trials, expand comprehensive national registries pertaining to medication, devices, and procedures, develop educational programs designed specifically for older patients and their families, and refine the assessment of age- and sex-specific benefit-to-risk ratios for older patients with ASCVD with respect to short- and long-term morbidity and mortality, QOL, function, independence, cost efficacy, and other relevant measures.

Disclosures

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(Continued)

Writing Group Disclosures, *Continued*

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
Karen Alexander	Duke University	None	None	None	None	None	None	None
Deborah Chyun	New York University	None	None	None	None	None	None	None
Nanette K. Wenger	Emory University	Abbott†; Gilead Sciences†; Merck*; NHLBI†; Pfizer*	None	None	None	None	Abbott*; Amgen*; AstraZeneca*; Gilead Sciences†; Janssen Pharmaceuticals*; Merck*; Pfizer*	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

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Secondary Prevention of Atherosclerotic Cardiovascular Disease in Older Adults: A Scientific Statement From the American Heart Association

Jerome L. Fleg, Daniel E. Forman, Kathy Berra, Vera Bittner, James A. Blumenthal, Michael A. Chen, Susan Cheng, Dalane W. Kitzman, Mathew S. Maurer, Michael W. Rich, Win-Kuang Shen, Mark A. Williams and Susan J. Zieman
on behalf of the American Heart Association Committees on Older Populations and Exercise Cardiac Rehabilitation and Prevention of the Council on Clinical Cardiology, Council on Cardiovascular and Stroke Nursing, Council on Lifestyle and Cardiometabolic Health

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AHA Scientific Statement

Executive Summary: Secondary Prevention of Atherosclerotic Cardiovascular Disease in Older Adults
A Scientific Statement From the American Heart Association

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Although this document provides considerable data in support of secondary prevention in older patients with atherosclerotic cardiovascular disease, the evidence is infrequently stratified by age or by the physiological and psychosocial complexities associated with aging. Therefore, the implementation of secondary prevention principles first requires reflection regarding each patient's broader health/psychosocial circumstances. The benefit of lifestyle modifications (tobacco cessation, weight loss, diet changes, and exercise) must be counterbalanced by clinical context, allowing for the potential that a patient may prefer to continue in a pattern that they feel provides greater satisfaction despite untreated, modifiable cardiovascular risks. Similarly, the benefits of medications and procedures must be counterbalanced by considering the therapeutic burden, ie, allowing for the fact that polypharmacy, iatrogenesis, cost, and other implicit trade-offs may sometimes seem to supersede benefits. Such predictable equipoise mandates that patients be involved with secondary prevention decisions; improved health literacy among seniors is a key aspect of effective care. It is incumbent on providers to inform older patients with atherosclerotic cardiovascular disease regarding the benefits and risks of secondary prevention, a priority that may be challenging amid the dynamic cognitive, auditory, and visual changes of old age.

Secondary prevention lifestyle changes to increase longevity often seem inappropriate in the context of advanced age, but their utility to improve function, quality of life, and independence is often clear-cut. For example, although the mortality benefit of intentional weight loss is uncertain, improved glucose control, arthritic pain, mobility, dyspnea, and other end points are likely. Likewise, exercise training may not have intense appeal as a means to prolong life for someone who is older and deconditioned, but it may be much more compelling as a reliable means to foster independence, greater quality of life, and personal choice. Similarly, many octogenarians may be reluctant to discontinue tobacco for assumed mortality benefits, especially for seniors who associate tobacco with comfort and pleasure. However, tobacco cessation may be appealing if and when it is presented as an option to reduce claudication and to improve exercise capacity.

Therefore, secondary prevention lifestyle changes should be actively considered for every community-dwelling older patient with atherosclerotic cardiovascular disease. Tobacco cessation use stands out as the risk factor most likely to reduce mortality, and exercise training (including aerobics, strength, balance, and flexibility) as the one most likely to reinforce a broader spectrum of qualitative benefits (including improved function, mood, and blood pressure control). Weight loss and diet control (glucose, salt, and caloric moderation) are similarly important. Ideally, providers should have teaching tools that provide information to patients clearly, including mode (eg, large font and audio) and language commensurate with their physical and learning capacities. Despite its unequivocal utility in older adults, cardiac rehabilitation remains an underused resource for improving lifestyle habits and the cardiovascular risk profile in this age group.

Pharmacological and procedural secondary prevention options remain equally important in older cardiac patients. Extended life expectancy and improved quality of life reinforce the rationale for revascularization and device therapy. Even octogenarians and nonagenarians may derive added years of life from implanted defibrillators and possibly coronary

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revascularization. Even more compelling is the potential for improved quality of life, with reduced pain, reduced reliance on medications, and greater function/independence.

Data demonstrating life prolongation and reduced cardiovascular morbidity are relatively clear-cut for statins and antihypertensives through the early 80s. Although the utility beyond these years is less certain, it remains eminently logical to consider these medications in those seniors who have experienced a cardiovascular event, ie, who are thereby at greatest risk for repeat events and related disease progression. Nonetheless, such inferred benefits progressively diminish in patients who are more frail or who have other health liabilities that detract from potential benefits of these medications (eg, patients with severe dementia or another life-threatening disease). Depression and mood instability are common and often insidious among adults struggling with disease, loss, and decline, and mandate appropriate therapy.

The inherent ambiguity between primary and secondary prevention among adults >75 years of age is also important to highlight. Eventually, most seniors develop atherosclerosis as a function of age itself, especially in context of the lifestyle patterns in the United States and Western cultures. Therefore, the most important secondary prevention is ultimately primary prevention; lifelong lifestyle and medical care oriented to minimizing cardiovascular risks, and promoting physical, mental, and emotional well-being provide the best foundation for moderating disease in old age.

References

References are available in the full text of this guideline: http://circ.ahajournals. org/lookup/doi/10.1161/01.cir.0000436752.99896.22.