# CME Secondary Prevention in Coronary Artery Disease

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*Secondary prevention has been shown to decrease coronary artery disease morbidity and mortality by 20–25%. Exercise, smoking cessation, and management of dyslipidemia, hypertension, diabetes, and obesity, along with psychological therapies, are typical elements of secondary prevention programs offered by a multidisciplinary clinical team often including physicians, nurses, pharmacists, exercise physiologists, registered dieticians, and psychologists. Special considerations for older adults in a secondary prevention setting in reference to medications, exercise, diet, smoking cessation, and hypertension are addressed. Current practice guidelines and clinical trials are presented, along with practical tools for the primary care physician treating the older coronary artery disease patient.*

***Key words:*** *multidisciplinary, cardiac rehabilitation, coronary artery disease, secondary prevention*

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## Introduction

Older adults with coronary artery disease (CAD) represent a unique patient group as the manifestation of CAD is not solely represented by the disease but is also influenced by the physiologic effects of aging.

Traditional components of secondary prevention programs include exercise, smoking cessation, and management of cardiac risk factors, along with psychological interventions typically introduced in a cardiac rehabilitation (CR) setting.[1] The most powerful predictor of participation in CR is the strength of the primary care physician's referral.[1] Comprehensive CR after a major coronary event can decrease CAD morbidity and mortality by 20–25%.[2,3] Studies demonstrate an improvement in risk factors among older CR patients, highlighting it as an effective and appropriate means of treatment.[3]

The management of dyslipidemia, diabetes, and obesity has recently been reviewed in this journal.[4,5,6] Consequently, unique considerations for secondary prevention in the older adult will be discussed in reference to medications, exercise, diet, smoking cessation, and hypertension.

## Medications

Medications reduce cardiovascular morbidity and mortality in secondary prevention of CAD. Selected evidence supporting the use of acetylsalicylic acid (ASA), beta-blockers, angiotensin-converting enzyme inhibitors (ACEI), and statins in older adults is presented in Table 1. An illustration of the mechanism of action of statins and ACEIs is presented in Figure 1. Although the benefit appears to be similar, if not greater, than for younger individuals, these therapies are underused in older patients.

### Acetylsalicylic Acid

Daily ASA (75–325 mg) is recommended post–coronary event (Table 1). Low-dose ASA is preferred; it is as effective as a medium dose and is associated with less bleeding, especially when used with clopidogrel.

Side effects, especially bleeding, may deter the use of ASA. Risk factors for gastrointestinal bleeding include age greater than 75, a history of peptic ulcer disease, and concomitant medications (nonsteroidal anti-inflammatory agents, warfarin, clopidogrel, and corticosteroids).[13] A proton pump inhibitor may be warranted in these situations.

Clinicians must weigh the risks and benefits when considering initiation of ASA in older adults.

### Beta-Blockers

Beta-blockers are recommended following a coronary event and should be continued for at least two years. Consideration to stop beta-blockers may include low-risk patients (normal ejection fraction, no angina, and negative stress test).

Contraindications to starting a beta-blocker include overt heart failure, second or third degree heart block, severe sinus bradycardia, and hypotension. Cautious use with monitoring for adverse effects is recommended in patients with asthma, chronic obstructive pulmonary disease, diabetes, and peripheral vascular disease. Adverse effects include hypotension, bradycardia, fatigue, reduced sexual activity, and nightmares. Initial doses should be low with gradual titration to minimize side effects in older adults.

## Statins

Patients with low-density lipoprotein cholesterol (LDL-C) >2.6 mmol/L should be considered for statin therapy. Statins should be initiated at moderate doses to achieve target LDL-C <2.5 mmol/L and a ratio of total cholesterol to high-density lipoprotein cholesterol (HDL-C) <4 mmol/L.

Nonspecific muscle aches or joint pains, which may be accompanied by creatine kinase elevation, may occur with the use of a statin. Risk factors for myopathy include multisystem disease, small body frame, and combined use of fibrates, macrolides, and azole antifungals.[14] Hydrophilic statins (e.g., pravastatin) and lower doses may reduce this likelihood. Grapefruit and its juice inhibit statin metabolism, increasing the potential for side effects (exceptions include rosuvastatin, pravastatin, and fluvastatin).[15]

## Angiotensin-Converting Enzyme Inhibitors

Patients should receive an ACEI post-coronary event, partic-

**Table 1:** Selected Evidence for Medications Used in Secondary Prevention

| STUDY | PATIENT POPULATION | INTERVENTION | EFFECT |
|---|---|---|---|
| **Acetylsalicylic Acid** | | | |
| Antiplatelet Trialists Collaboration[7] | Vascular disease or high risk patients | ASA 75–325 mg daily and other antiplatelets | **Nonfatal MI, nonfatal strokes or vascular death**<br>19% RRR (age ≥65) vs. 23% RRR (age <65); P< 0.001 |
| **Beta-blockers** | | | |
| Pooled analysis[8] | Post-MI | Various beta-blockers vs. placebo | **Mortality**<br>40% RRR (age 65–75) vs. 28% RRR (age <65); P< 0.001 |
| **ACE inhibitors** | | | |
| AIRE[9] | Post-MI and clinical evidence of HF<br>Mean age 65 | Ramipril 5 mg b.i.d. vs. placebo | **Mortality**<br>36% RRR; P<0.05<br>(age >65) |
| EUROPA[10] | CAD (prior MI, coronary revascularization, >70% narrowing of major artery)<br>Mean age 60 | Perindopril 8 mg daily vs. placebo | **Death from CHD, nonfatal MI or cardiac arrest**<br>17% RRR; P<0.05<br>(age >65) |
| **Statins** | | | |
| HPS[11] | High-risk individuals (CAD or DM or HTN) with TC >3.5 mmol/L<br>46% over age 65 | Simvastatin 40 mg daily vs. placebo | **Major coronary events, strokes or revascularization**<br>23% RRR (age 65–69)<br>18% RRR (age ≥70) |
| PROSPER[12] | History of or risk factors for vascular disease between 70–82 years; TC 4–9 mmol/L TG <6 mmol/L<br>Mean age 75 | Pravastatin 40 mg daily vs. placebo | **Death from CHD, nonfatal MI and fatal and nonfatal stroke**<br>20% RRR; P<0.05 |

RRR=relative risk reduction; MI=myocardial infarction; HF=heart failure; CAD=coronary artery disease; DM=diabetes mellitus; HTN=hypertension; TC=total cholesterol; TG=triglycerides; CHD=coronary heart disease; ACE=angiotensin-converting enzyme; ASA=acetylsalicylic acid

ularly those with left ventricular dysfunction (ejection fraction <40%). The Heart Outcomes Prevention Evaluation (HOPE) and European Trial on Reduction of Cardiac Events with Perindopril in Stable Coronary Artery Disease (EUROPA) trials demonstrated benefit in those with high-risk and stable CAD, respectively.[16,10]

Adverse effects include cough, hypotension, and dizziness. ACEIs can be initiated at low doses for older patients, particularly in those prone to orthostatic hypotension. Dose titration can be performed every four to six weeks. Monitoring of serum creatinine and potassium is recommended one to two weeks after dose initiation or change, as renal dysfunction may occur. An increase in serum creatinine <30% from baseline is considered acceptable.[17] Caution should be used when an ACEI is added to existing medications that may affect the renin-angiotensin system (e.g., spironolactone).

### Adherence

Older adults inappropriately use medications in 16–73% of cases, often leading to poor clinical outcomes.[18] Barriers to adherence in seniors include complicated drug regimens and inappropriate drug prescribing, multiple health care providers, medication side effects, health beliefs, lack of social support, cognitive impairment, and depressed mood.[19]

Older patients may have chronic conditions, posing significant adherence challenges. Stage modeling may help identify how ready seniors are to implement changes in their health risk behaviours and to tailor interventions accordingly (Table 2). The transtheoretical model has been applied to older adults in a variety of settings.[20,21] One can also gauge adherence in the office by asking, "Have you missed any pills in the last week?" Self-reported omission of any medication has been shown to correlate with an adherence rate of less than 60%.[22] Patients who miss appointments and who are uninformed about their medications are also more likely to be noncompliant.

Interventions that may improve adherence include simplifying regimens (once daily dosing, "forgiving" agents with longer half-lives), a properly loaded pill box, written instructions, and tailoring regimens to activities of daily living.[23,19]

## Exercise and the Older Adult

Maximal oxygen consumption, an index of cardiovascular function, decreases 5–15% per decade after the age of 25.[24] Although the physiologic effects of aging are inevitable, the rate and magnitude of decline may be modified by and even reversed with an exercise intervention.

**Table 2:** Transtheoretical Model: Stages of Change

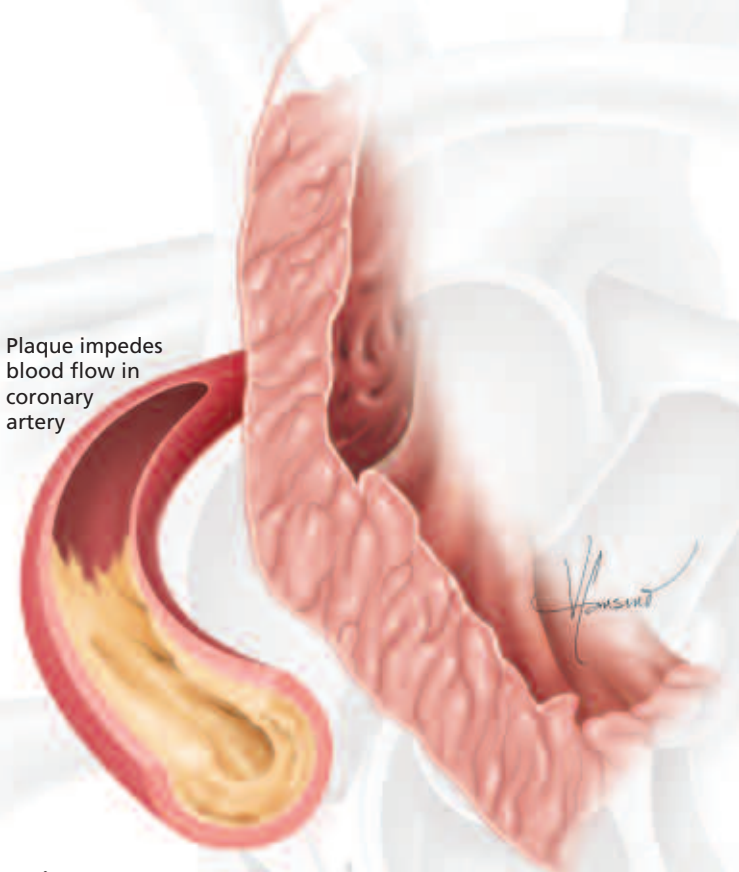
| STAGE OF CHANGE | DEFINITION | PATIENT STATUS | HEALTH TEAM INTERVENTION |
|---|---|---|---|
| Precontemplation | Patient does not plan to change behaviour within next six months | Un- or underinformed about importance of behaviour change; may be discouraged with past change efforts; unlikely to initiate discussion of risk behaviours | Discuss patient concerns regarding CAD; provide brief information while avoiding scare tactics; emphasize that change is patient's decision |
| Contemplation | Patient intends to change behaviour within next six months | Aware of pros and cons of behaviour change, but ambivalence remains | "Decisional balance" exercise: discuss both pros and cons of behaviour change; convey empathy |
| Preparation | Patient intends to take action within next month | Has likely undertaken/experienced significant action/event in past year; has plan of action (e.g., spoken to physician, joined fitness club) | Provide specific information for change; discuss strategies that worked in past; encourage social support; discuss stimulus control and environmental triggers; select change date |
| Action | Patient has made behaviour change within past six months | Meets specific criteria of behaviour change (e.g., exercising total of 200 minutes/week, complete smoking cessation) | Support and encourage change; encourage behaviour rewards; identify triggers for relapse |
| Maintenance | Patient has maintained behaviour change for over six months | More confident; less tempted to relapse | Support and encourage maintenance; express understanding and support in the event of relapse |

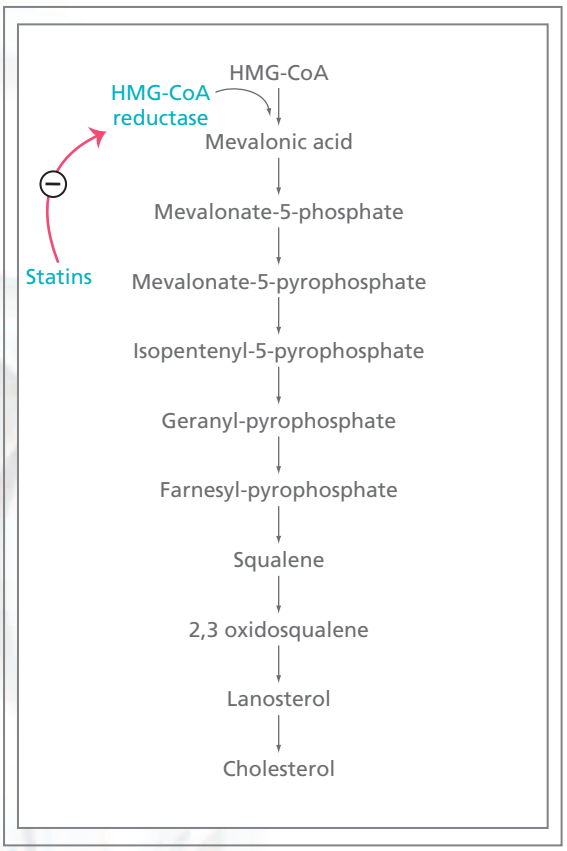
Source: Adapted from Prochaska JO, et al., 1994.[20]

Figure 1:

## Secondary Prevention of Coronary Artery Disease

### Statins and Angiotensin-Converting Enzyme Inhibitors

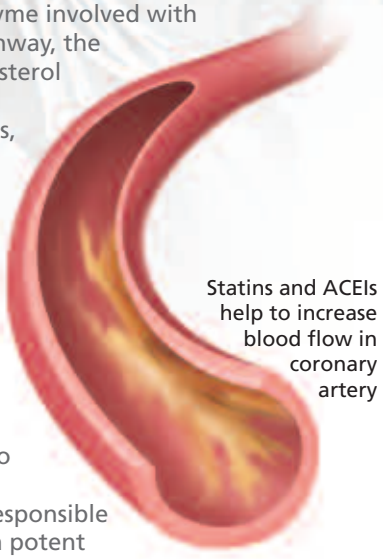



Site of action of Statins

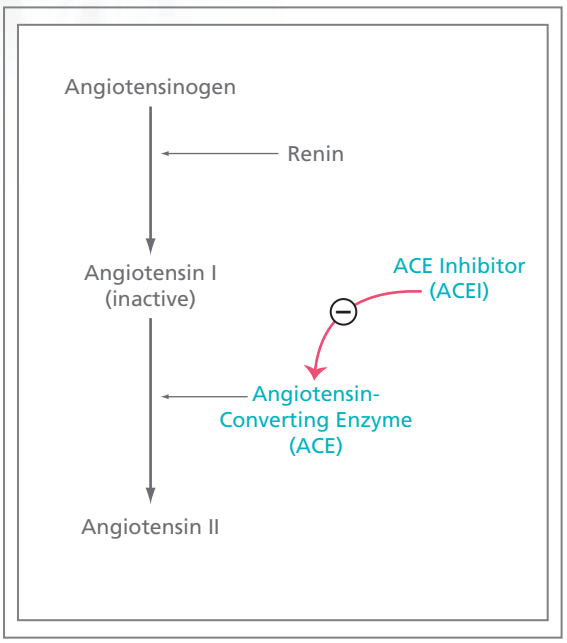
### statins

Statins act by competitively inhibiting HMG-CoA reductase, an enzyme involved with the HMG-CoA reductase pathway, the metabolic pathway for cholesterol synthesis. By reducing intracellular cholesterol levels, statins cause liver cells to upregulate the expression of the LDL receptor, leading to increased clearance of LDL cholesterol from the bloodstream.




### ACE inhibitors

Angiotensin-converting enzyme (ACE) catalyses the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor. ACE is also responsible for inactivating bradykinin, a potent vasodilator. Inhibition of ACE through the action of ACE inhibitors (ACEIs), results in decreased formation of angiotensin II and decreased inhibition of bradykinin. Therefore, ACEIs have an overall vasodilation effect on the coronary arteries.




Site of action of ACE inhibitors

**Table 3:** Major Contraindications to Exercise Participation and Testing

| ABSOLUTE | RELATIVE |
|---|---|
| Recent ECG changes | Cardiomyopathy |
| Recent MI | Valvular heart disease |
| Third-degree heart block | Complex ventricular ectopy |
| Acute CHF | |
| Uncontrolled hypertension | |
| Uncontrolled metabolic disease | |

Note: this list is not all encompassing. For a more complete list refer to the ACSM's Guidelines for Exercise Testing and Prescription, 7th ed.[26]

## Preparatory Screening

Before starting an exercise program, older adults should undergo a physical examination and history targeting the identification of cardiac risk factors, exertional signs and symptoms, and physical limitations.[25] Potential contraindications to exercise testing and training are shown in Table 3.

Older adults can safely begin moderate exercise training with gradual progression under the guidance of an exercise professional or physician with minimal risk of complications. Exercise stress testing is recommended for sedentary older adults who plan to initiate vigorous activity.[26]

## Exercise Prescription

A comprehensive review on exercise among older adults was recently published by the American College of Sports Medicine.[24] Due to its powerful impact on CAD risk, cardiovascular training will be the focus here. Effective cardiovascular training should take into consideration the frequency, intensity, time, and type of exercise as detailed below.

Cardiovascular exercise should be performed on most days of the week (no fewer than four days/week with nonexercising days spread out).[26] The majority of older adults are inactive; therefore, it is important to suggest they start out slowly and increase gradually to decrease injury risk and improve adherence.

Moderate intensity exercise on most days each week is required for the greatest health benefits.[26] The moderate intensity activity should allow patients to comfortably carry on a conversation ("talk test"). The use of heart rate for intensity measurement is complicated by patients' ability to monitor it and the usage of beta-blockers; therefore, the Borg Scales of Perceived Exertion may be useful.[27] Generally, exercise rated as 11–13 (6–20 scale) or 3–4 (0–10 scale) correspond to moderate intensity.

Improved health is achieved with 30–60 minutes of continuous activity at moderate intensity on most days a week.[26] To begin, exercise can be broken down into shorter time intervals (e.g., three bouts of 10 minutes). To avoid injury and ensure safety, older adults should concentrate on increasing duration rather than intensity.

Exercises should be continuous and rhythmic, utilizing a large muscle mass (e.g., walking, dancing, swimming, and cycling).[26] Aquatic exercises may prove useful in individuals with musculoskeletal injury/pain. Group activities (e.g., CR) provide continued guidance and reinforcement, which may improve adherence. Resistance training (which should be guided by an exercise professional in older adults) offsets the loss in muscle mass and strength associated with aging and may prevent falls.

## Diet

Long-term reductions in serum cholesterol levels are not facilitated by brief dietary interventions utilizing simplified advice.[28] Studies have demonstrated that increased time spent with a dietician positively correlates with reductions in cholesterol levels, and the magnitude of LDL-C reduction is significantly higher with four visits than with two.[29,30] Taking the time to review and implement healthy diets can have a positive impact on older adults. For example, in the HALE (Healthy Ageing: a Longitudinal study in Europe) project, a Mediterranean diet, moderate to high physical activity levels, and nonsmoking were associated with lower mortality rates from CAD and cerebrovascular disease among individuals 70–90 years of age.[31,32]

Dietary modifications are difficult to implement as they involve altering existing behaviours, and food is often loaded with socio-cultural meaning. Furthermore, healthy eating is perceived as being more costly than fast food. Several techniques may improve outcomes and adherence, such as the use of a plate model[33] (which demonstrates a balanced meal),

**Table 4:** Impact of Lifestyle Therapies on Blood Pressure

| INTERVENTION | SBP/DBP(mmHg) |
|---|---|
| Sodium restriction (<100mmol/day) | –5.8 / –2.5 |
| Weight loss: for every 4.5kg lost | –7.2 / –5.9 |
| Alcohol intake (<2.7 drinks/day) | –4.6 / –2.3 |
| 30–60 min. of moderate intensity, dynamic exercise three times/week | –7.4 / –5.8 |
| DASH diet<br>Emphasis on fruits, vegetables, low-fat dairy products, and reduced saturated fat and cholesterol | –11.4 / –5.5 |

Source: Adapted from the 2005 Canadian Hypertension Education Program Recommendations.[40]

a shopping guide, nutrition labeling education,[34] and setting specific and realistic goals.

## Smoking Cessation

Smoking is an important modifiable risk factor for CVD, doubling the risk of heart attacks in older adults.[35] Moreover, cessation has immediate and long-term benefits; in patients with CAD, it may be associated with a 36% risk reduction in all-cause mortality.[36]

Patients who are most addicted (e.g., time from waking to first cigarette is <30 minutes) are least likely to quit and will need counselling and pharmacotherapeutic interventions. First-line strategies include brief counselling by a physician, nicotine replacement therapy, and the antidepressant bupropion combined with counselling, all of which may double smoking cessation rates.[36,37] Pharmacotherapies in older patients require close monitoring, as they may lead to side effects (e.g., dry mouth and insomnia). However, transdermal nicotine, initiated at least two weeks after an acute event, has been proven safe in patients with CAD.[38]

## Hypertension

A recent article in this journal reviewed the relevant evidence for the prevalence, consequences, targets, and treatment of hypertension in older adults.[39] We would like to emphasize that ACE inhibitors and beta-blockers should be the first-line agents for treatment of hypertension in patients with CAD. One must also recognize that older patients may be more prone to side effects associated with antihypertensive agents (e.g., orthostatic hypotension, incontinence, electrolyte abnormalities, and renal insufficiency).

Blood pressure is also lowered with lifestyle modifications, as shown in Table 4, further supporting the importance of a multidisciplinary approach to treatment. For example, the DASH (Dietary Approaches to Stop Hypertension) diet, which shares many characteristics with the Mediterranean diet, has a positive effect on both systolic and diastolic blood pressure.[41]

## Conclusion

Emerging evidence supports the implementation of secondary prevention programs involving a multidisciplinary team including physicians, nurses, pharmacists, exercise physiologists, registered dieticians, and psychologists for the comprehensive treatment of the older CAD patient.[1,3] The most powerful predictor of participation in CR is the strength of the primary care physician's referral, and physicians are encouraged to refer CAD patients irrespective of their age as participation has clear and lasting benefit.[1] Tailoring treatment for patients is an integral part of CR programs, often improving adherence to prescribed therapies targeting medications, exercise, diet, smoking cessation, and hypertension, thereby improving outcomes.[2] ◆

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