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INSTRUCTIONS

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pharmacy PRACTICE + BUSINESS

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Cardiovascular care in atherosclerotic cardiovascular disease

by Sheri L. Koshman, BScPharm, PharmD, ACPR, FCSHP

Learning objectives

After completing this lesson, the pharmacy technician participant will be able to:

1. Define atherosclerotic cardiovascular disease (ASCVD)
2. List common risk factors associated with ASCVD
3. Describe healthy behaviours that are used to prevent and treat ASCVD
4. Describe pharmacotherapy used in the prevention and treatment of ASCVD
5. Recognize the role of the pharmacy technician in identifying patients at risk of ASCVD events

Introduction

What is atherosclerotic cardiovascular disease (ASCVD)?

Cardiovascular disease (CVD) is one of the leading causes of morbidity and mortality in Canada.[1] It is a group of disorders that affects the heart or blood vessels.[2] One of the most common disorders in this group is atherosclerotic cardiovascular disease (ASCVD). This condition is characterized by a buildup of plaques

(called atherosclerosis) in the medium and large arteries. These plaques can form in a number of different vascular beds, including the heart, brain, extremities (most commonly the legs), and the kidneys (Table 1). These plaques or "fatty deposits" contain cholesterol and a number of other substances, such as calcium, that form deposits in the artery wall. They can grow and cause the lumen of the artery to narrow, which leads to reduced blood flow over time. Plaques can also become unstable and rupture, causing a blood clot to form and abrupt loss of blood flow.

TABLE 1 - Common areas for ASCVD

Area of the body	Medical term	Examples of conditions caused by ASCVD
Heart	Coronary artery disease (CAD)	Stable angina, myocardial infarction (heart attack), acute coronary syndrome (ACS)
Brain	Cerebrovascular disease	Transient ischemic attack (TIA), stroke, carotid artery disease
Lower Extremities	Peripheral artery disease (PAD) Abdominal aortic aneurysm	Intermittent claudication, amputation
Kidney	Chronic kidney disease (CKD)*	Renal failure, dialysis

*There are many different causes of chronic kidney disease

Who is at risk of ASCVD?

It is generally thought that ASCVD is largely preventable. It starts developing slowly in the first decade of life and rapidly accelerates with age. A number of factors have been identified as being associated with a higher risk of developing ASCVD.[3] Major risk factors can be divided into things that can be modified and things that cannot (i.e., are non-modifiable) to reduce the risk of ASCVD events (Table 2). Other emerging risk factors that are believed to increase the risk of ASCVD include, but are not limited to, ethnicity (e.g., First Nations, South Asian), inflammatory conditions, metabolic syndrome, HIV, chronic kidney disease (CKD), and socioeconomic determinants.[4]

TABLE 2 - Risk factors for ASCVD

Modifiable	Non-modifiable
Tobacco dependence/smoking	Age (males ≥ 45 and females ≥ 55)
Hypertension	Male sex
Dyslipidemia	Family history of premature CVD (first-degree relative; male ≤ 55 and female ≤ 65)
Diabetes	
Obesity	
Lack of physical activity	
Diet	

TABLE 3 - Parameters used to screen for risk factors

Risk factor	Screening parameter
Obesity	Height, weight, body mass index (BMI), waist circumference
Tobacco dependence/smoking	Tobacco use status
Hypertension	Blood pressure; measurement using electronic (oscillometric) upper arm devices is preferred
Diabetes	Hemoglobin A1C or fasting blood glucose (lab tests)
Dyslipidemia	Non-fasting lipid panel (lab test)
Physical activity	Physical activity status
Diet	Diet status

Risk factor identification and management are important in both preventing and treating ASCVD. A number of parameters, in addition to doing a patient history, can be used to assess for risk factors (Table 3). Screening for most risk factors typically starts in adulthood; however, screening for diabetes and dyslipidemia is recommended in those greater than 40 years old if there are no other high-risk features before this age (e.g., multiple risk factors). Risk factor screening should take place at least every five years and more often as the situation dictates (e.g., change in risk factor status, multiple risk factors).[5]

A number of scoring tools are available to help quantify cardiovascular (CV) risk for individual patients. The most commonly used tool in Canada is the Framingham Risk Score (https://ccs.ca/app/uploads/2020/12/FRS_eng_2017_fnl_greyscale.pdf).[4] This tool provides an estimate of what an individual's risk of having a CV event is in the next 10 years, using their own parameters (age, lipids, blood pressure, smoking status). Possible CV events include myocardial infarction, CV death, cerebrovascular disease, angina, resuscitated cardiac arrest, heart failure, peripheral artery disease, and revascularization (coronary bypass or coronary stent insertion). Scoring on this tool helps to identify patients at low (0%–9%), intermediate (10%–19%) or high risk (> 20%) of developing a CV event within the next 10 years, which in turn, helps identify those who are in need of more intensive prevention and treatment strategies. This tool is only used in patients who do not have ASCVD (primary prevention), diabetes or CKD, as those with ASCVD, diabetes, or CKD are automatically considered high risk. This tool can also be used as a teaching aid to help patients better understand their own risk.

Management of ASCVD

Management of ASCVD can be split into

two categories: prevention and treatment. Primary prevention of ASCVD refers to the implementation of strategies prior to developing clinically evident CV disease (no signs or symptoms of CV disease, with the aim to prevent disease). Secondary prevention of ASCVD refers to the implementation of strategies in those who already have CV disease (signs and symptoms of CV disease, with the aim to prevent disease progression and poor outcomes). The goals of therapy in primary and secondary prevention differ (Table 4); however, identification and management of risk factors for ASCVD are the cornerstones of both. Management involves both nonpharmacologic and pharmacologic strategies.

TABLE 4 - Goals of therapy

Prevention	Presence of disease	Goals of therapy
Primary prevention	Disease not present	Prevent ASCVD and related events
Secondary prevention	Disease present	Treat ASCVD and prevent progression and ASCVD events

Nonpharmacologic management

Nonpharmacologic management consists of strategies to promote and achieve healthy behaviours. These are often used in combination, as they are interrelated, to improve outcomes related to ASCVD and common risk factors. These strategies are used in both primary and secondary prevention and are typically the backbone of treatment, with or without pharmacotherapy (Table 5).[5-13]

Pharmacologic management

Primary prevention

Pharmacological management in primary prevention typically focuses on risk factors associated with ASCVD, since the disease has not manifested yet.

Acetylsalicylic acid (ASA)

Historically, the use of low-dose ASA (80–325 mg daily) was considered for primary prevention in those deemed at high risk of CV events. However, recent evidence has led to a new recommendation to avoid the routine use of ASA in primary prevention.[14-21] ASA works by preventing platelets from clotting via inhibiting the production of thromboxane A2, a prostaglandin. This action is helpful in the case of a heart attack or stroke when a blood clot forms causing ischemia (lack of oxygen to the area), but is also harmful in the case of bleeding when

TABLE 5 - Non-pharmacologic management options

Risk factor	Recommendation	Impact of intervention on ASCVD
Diet	• Maintain a healthy body weight (see below for parameters) with moderate caloric intake. A number of dietary patterns may reduce ASCVD risk including: - Mediterranean dietary pattern - Portfolio dietary pattern - DASH dietary pattern - Low glycemic load or low glycemic index dietary pattern - Vegetarian patterns - Dietary patterns high in: · Nuts (≥ 30 g/day) · Legumes (≥ 4 servings/week · Olive oil (≥ 60 mL/day) · Fruits and vegetables (≥ 5 servings/day) · Total fibre (≥ 30 g/day) and whole grains (≥ 3 servings/day)	• Reduced cardiovascular events overall (Mediterranean diet) • Reduced blood pressure (DASH diet) • Reduced risk of diabetes/better control of diabetes (low glycemic load or glycemic index diet) • Reduced cholesterol • Reduced weight
Sodium (salt intake)	• Reduce sodium intake toward 2 g/day	• Reduced blood pressure
Alcohol	• Limit alcohol intake to a maximum of ≤ 2 standard drinks per day, or ≤ 14 standard drinks per week for men and ≤ 9 standard drinks per week for women. • One standard drink contains 13.6 g alcohol (e.g., 45 mL spirits, 150 mL table wine, 360 mL beer)	• Reduced blood pressure • Reduced weight • Reduced triglycerides (a type of lipid)
Physical Activity	• At least 150 minutes of moderate to vigorous aerobic physical activity per week, in bouts of 10 minutes or more. • Adding muscle- and bone-strengthening activities, using major muscle groups, twice weekly is also beneficial	• Increased cardiovascular fitness • Reduced weight • Reduced blood pressure
Body habitus/ weight	• Achieve and maintain a healthy body weight (BMI of 18.5–24.9 kg/m^2). • Achieve a waist circumference of < 102 cm for men and < 88 cm for women.	• Reduced weight • Reduced blood pressure • Reduced risk of diabetes/better control of diabetes • Reduced lipids
Smoking	• Stop using tobacco and minimize exposure to second-hand smoke; this includes use of smoked cannabis. • Nonpharmacologic therapies may include behaviour support.	• Reduced cardiovascular events overall

TABLE 6 - Risk factors for bleeding

Risk factors for bleeding
- History of GI bleeding
- Peptic ulcers
- Bleeding at other (non-GI) sites
- Age > 70 years
- Chronic kidney disease
- Uncontrolled hypertension
- Concurrent use of NSAIDs, anticoagulants, corticosteroids, or anticoagulants
- Low platelets
- Coagulation disorders

TABLE 7 - Indications for HMG-CoA reductase inhibitors in primary prevention of ASCVD

Statin-indicated condition	• Most patients with diabetes (Age ≥ 40; Age ≥ 30 + ≥ 15-year duration of diabetes, microvascular disease) • Chronic kidney disease • LDL-C ≥ 5 mmol/L (or genetic dyslipidemia)
*Low risk (< 10%)	• LDL-C ≥ 5 mmol/L (or genetic dyslipidemia)
*Intermediate risk (11%–19%)	• LDL-C ≥ 3.5 mmol/L • Men ≥ 50 year and women ≥ 60 year + risk factor (low HDL-C ["good cholesterol"], impaired fasting glucose, high waist circumference, smoker or hypertension)
*High risk (≥ 20%)	• All patients

*Risk determined by the Framingham Risk Score; HDL-C–high-density lipoprotein cholesterol.

platelets are needed to stop the bleeding. ASA also decreases the protective prostaglandins in the lining of the stomach and therefore increases the risk of ulcers and gastrointestinal (GI) bleeding. Recent evidence has called into question the benefit (preventing CV events) to risk (bleeding) ratio of ASA in primary prevention. While there is a small benefit, there is also a small risk of bleeding which is thought to cancel out the small benefit in most people, especially in those at higher risk of bleeding (Table 6). Although ASA should now generally be avoided for primary prevention, it may still be considered in some individuals at very high risk of CV events who are not at high risk of bleeding.

In contrast, low-dose ASA should be considered for all patients who already have ASCVD (i.e., for secondary prevention) as the benefits are felt to outweigh the risks because their risk of having a CV event is higher than those without known ASCVD.

HMG-CoA reductase inhibitors (statins)

Statins are often use in the setting of primary prevention and have been proven to decrease CV events.[22] Statins work by inhibiting the HMG-CoA reductase enzyme in the liver, which decreases cholesterol production. It mainly reduces low-density lipoprotein cholesterol (LDL-C), but other types of lipoproteins are also lowered. It is thought that LDL-C is one of the main components of atherosclerotic plaques and it is sometimes called "bad cholesterol." Additionally, statins increase the number of LDL-C receptors on the liver, which helps to clear LDL-C from the body. They are also thought to have anti-inflammatory properties and help "stabilize" existing plaques, making them less likely to rupture and cause heart attacks or strokes.

In terms of treatment, statins can be used in the context of a "statin-indicated condition" or if the patient's risk of CV events is deemed high enough to derive significant benefit based on their cholesterol level (Table 7).[4]

In contrast, all secondary prevention patients should be on statin therapy regardless of cholesterol levels, as they are at very high risk of further CV events and disease progression.

Nutritional supplements

Nutritional supplements in primary or secondary prevention have not been proven to decrease CV events. Studies evaluating the use of fish oils, omega-3 and omega-6 fatty acids, multivitamins, vitamin D, antioxidant supplements (e.g., selenium, beta-carotene, vitamins A, C, and E), Homocysteine-lowering vitamins (e.g., vitamin B6 and B12, folic acid) have either not shown any benefit in reducing CV events or have shown inconclusive results.[23-29]

Secondary prevention

In secondary prevention, patients are at much higher risk of experiencing CV events and therefore treatment strategies are intensified. While ASCVD can occur in multiple vascular beds, the general approach to treatment is similar regardless of the underlying CV condition and despite differences in specific CV outcomes with each strategy.

In addition to risk factor management, there are two general approaches to pharmacotherapy in secondary prevention: prevention of blood clot formation and prevention of disease progression (Table 8). The majority of these approaches require lifelong pharmacotherapy.

Prevention of blood clots

Antiplatelet agents:

Most commonly, low-dose ASA is used as a single antiplatelet agent in secondary prevention to prevent blood clots. However, in some scenarios, a second antiplatelet agent such a clopidogrel or ticagrelor may also be used.[30, 31] Both of these agents inhibit the P2Y12 receptor on the platelet to prevent platelet aggregation or clotting. When used in combination with ASA, synergistic effects occur by inhibiting platelets in two different ways. This strategy has been shown to further decrease the risk in CV events in certain scenarios including during and immediately after a heart attack, in a patient in which a coronary stent has been placed, and after an acute stroke/transient ischemic attack (TIA). This dual antiplatelet strategy also increases the risk of bleeding and may be selectively used in some patient populations. Generally, some type of antiplatelet therapy is required lifelong, however, dual antiplatelet strategies may be variable in duration (months to years to lifelong).

Antithrombotic agents:

More recently, a "dual pathway" strategy to prevent blood clots had been introduced. This strategy uses low-dose ASA to target platelets and low-dose rivaroxaban (2.5 mg BID), a direct oral anticoagulant (DOAC) to target thrombin, another pathway responsible for blood clotting. This strategy may be used in high-risk patients (e.g., patients with multiple CV events, patients with ASCVD in

TABLE 8 - Summary of medications used in secondary prevention

Class of medications	Examples of common agents* (Brand names)	How it may help patients	Common adverse effects
Antiplatelet agents	Acetylsalicylic acid/ASA (Aspirin®)	Prevent blood clots Prevent CV events	Bleeding GI discomfort
	Clopidogrel (Plavix®)	Prevent blood clots Prevent CV events	Bleeding
	Ticagrelor (Brillinta®)	Prevent blood clots Prevent CV events	Bleeding Shortness of breath
Anticoagulant agents	Rivaroxaban (Xarelto®)	Prevent blood clots Prevent CV events	Bleeding
HMG-CoA reductase inhibitors (statins)	Atorvastatin (Lipitor®) Rosuvastatin (Crestor®)	Prevent disease progression Prevent CV events	Muscle discomfort GI discomfort
Ezetimibe	Ezetimibe (Ezetrol®)	Prevent disease progression	GI discomfort
PCSK-9 inhibitors	Alirocumab (Praluent®), evolocumab (Repatha®)	Prevent disease progression Prevent CV events	Injection site discomfort
Icosapent ethyl	Icosapent ethyl (Vascepa®)	Prevent disease progression Prevent CV events	GI discomfort
Angiotensin converting enzyme inhibitors (ACEIs)	Ramipril (Altace®) Perindopril (Coversyl®) Enalapril (Vasotec®) Lisinopril (Prinivil®)	Prevent disease progression Prevent CV events	Dizziness/low blood pressure Cough High potassium Kidney dysfunction Angioedema (swelling of mouth, face, or neck) – uncommon, but life-threatening
Angiotensin receptor blockers (ARBs)	Candesartan (Atacand®) Irbesartan (Avapro®) Telmisartan (Micardis®) Valsartan (Diovan®) Losartan (Cozaar®)	Prevent disease progression Prevent CV events	Dizziness/low blood pressure High potassium Kidney dysfunction

*This list is not exhaustive and is meant to illustrate common agents used in practice.

multiple vascular beds) and has been shown to decrease CV events.[32] Like a dual antiplatelet strategy, the dual pathway strategy strategy also increases the risk of bleeding and therefore is used selectively.

Prevention of disease progression

Prevention of disease progression in ASCVD is aimed at preventing further plaque development and stabilizing plaques that have already developed to prevent rupture and clot formation. Currently little evidence supports plaque regression or reversing plaque with existing therapies, but this is evolving with new lipid-lowering agents under study.

Lipid-lowering agents:

The strategy of lipid or cholesterol lowering is typically intensified in patients with ASCVD or who have had a recent CV event. For every 1 mmol/L of LDL-C reduction, there is roughly a 20% reduction in CV events and therefore it is generally felt that "lower is better."[33] Guidelines have also changed to advocate for lower lipid levels that have been shown to improve CV outcomes.[4] Typically this strategy includes high doses of statins and add-on therapy with either ezetimibe, a PCSK-9 inhibitor (alirocumab, evolocumab) or icosapent ethyl.

Ezetimibe

Ezetimibe inhibits the absorption of dietary and bile sources of cholesterol from the small intestine. In patients who have recently suffered a heart attack, ezetimibe added to a statin further lowers cholesterol levels and further reduces CV events compared to a statin alone.[34] Ezetimibe is sometimes used as a single agent in patients who cannot tolerate statin therapy, or as an add-on therapy in patients who have not reached their target lipid levels.

PCSK-9 inhibitors

PCSK-9 inhibitors are monoclonal antibodies that inhibit the PCSK-9 protein, which is responsible for the breakdown of LDL-C receptors in the liver. Inhibiting this protein increases the number of LDL-C receptors, which in turn clears more LDL-C from the blood and lowers LDL-C levels dramatically. These agents have also been shown to decrease CV events in high-risk patients with ASCVD when combined with statins.[35, 36] Because these agents are very costly and must be given by injection, their use is limited to select high-risk groups.

Icosapent ethyl (IPE)

IPE is a highly purified type of omega-3 fatty acid. It is unclear what its exact mechanism of action is, but it may include anti-inflammatory and plaque stabilization properties. Use of IPE plus statins has been shown to improve CV events in patients with or at high risk of ASCVD who also have elevated triglycerides.[37]

Vascular protection: ACEIs/ARBs

Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are thought to provide "vascular protection" or protect the arteries in a number of ways, including causing vasodilation, improving blood vessel wall function, and slowing atherosclerosis. They are commonly used to treat hypertension and heart failure and to prevent worsening kidney function in patients with chronic kidney disease. Many of these conditions overlap with ASCVD and therefore most patients will be on one of these agents. They have been proven to decrease CV events in patients at high risk or with ASCVD independent of blood pressure lowering.[38]

The role of the pharmacy technician

Collaboration among pharmacy team members is essential for both screening and treating patients with or at risk of ASCVD. Pharmacy technicians can play an active role with these patients to help prevent disease and improve outcomes in a variety of ways including:

- Reinforce healthy behaviours messaging. Ensure educational materials are available to support healthy behaviours and risk factor modification.
- When filling prescriptions, monitor refill intervals (e.g., irregular fills) and refer to the pharmacist if non-adherence is suspected. Ensure that there is a good selection of adherence tools (e.g., pill boxes, alarms, etc.) to help patients organize their medications.
- Be well versed in a selection of monitoring tools, such as weigh scales, blood pressure monitors, and blood glucose monitors, to support patient self-management of risk factors.
- Organize and participate in screening clinics to help identify patients at risk of ASCVD.
- Identify patients who are currently smokers and refer those who indicate a willingness to quit to the pharmacist for further counselling. Ensure there is a good selection of smoking cessation educational materials and aids available.
- Identify patients who use the in-pharmacy blood pressure monitor and inquire about their results. Refer those who have elevated readings to the pharmacist for further evaluation. Ensure the availability of approved monitors.

Conclusion

Cardiovascular disease, including ASCVD, is common and largely preventable. Screening and identifying those at high risk of developing disease is a great opportunity for the pharmacy team to improve outcomes, while working in one of the most accessible healthcare settings. As frontline healthcare workers, pharmacy technicians can help to proactively identify these at-risk patients. In those with established ASCVD or at high risk, pharmacy technicians can support patients with educational materials and self-monitoring devises and by monitoring adherence. Pharmacy technicians are uniquely positioned to engage in the spectrum of ASCVD care.

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QUESTIONS

Please select the best answer for each question and answer online at eCortex.ca for instant results.

1. Atherosclerosis typically develops in small arteries.
a) True
b) False

2. Atherosclerosis is typically found in the following vascular beds:
a) Heart
b) Brain
c) Lower extremities
d) All of the above

3. All of the following risk factors are modifiable except:
a) Hypertension
b) Male sex
c) Dyslipidemia
d) Obesity

4. Premature family history of ASCVD includes a first degree relative with the first event in males < 55 year or females < 65 years old.
a) True
b) False

5. In the average adult, how often should screening for ASCVD occur at least?
a) Every year
b) Every two years
c) Every five years
d) Every 10 years

6. What parameters can be used to screen for obesity?
a) Clothing size
b) Body mass index
c) Waist circumference
d) Lipid panel
e) b and c

7. The Framingham Risk Score (FRS) is an objective tool to assess CV risk in patients without:
a) Diabetes
b) A history of heart attack
c) CKD
d) A history of stroke
e) All the above

8. Secondary prevention of ASCVD is a term used to describe interventions aimed at preventing disease when disease is not present.
a) True
b) False

9. It is recommended that patients exercise at moderate to vigorous intensity for how long?
a) 60 minutes per day
b) 150 minutes per week
c) 30 minutes per day
d) 300 minutes per week

10. ASA should be considered in all patients for primary prevention of ASCVD.
a) True
b) False

11. Statin indicated conditions include the following, except:
a) High triglycerides
b) Diabetes
c) Chronic kidney disease
d) Genetic dyslipidemia

12. The following supplement has been shown to improve CV outcomes in primary prevention:
a) Fish oils
b) Multivitamins
c) Vitamin D
d) Vitamin E
e) None of the above

13. The dual pathway approach to treating ASCVD includes:
a) Two antiplatelet agents
b) One antiplatelet agent and an oral anticoagulant
c) Two lipid-lowering agents

14. The following agents fall into the lipid-lowering category:
a) Ticagrelor
b) Rivaroxaban
c) PCSK-9 inhibitors
d) Statins
e) c and d

15. Which of the following side effects are not associated with ARB therapy?
a) Dizziness/low blood pressure
b) Cough
c) High potassium
d) Kidney dysfunction

TECH talk CE

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Cardiovascular care in Atherosclerotic Cardiovascular Disease

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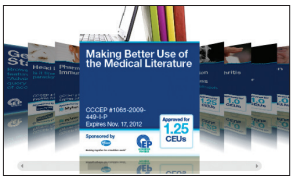

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