

Beyond the Numbers

A Pharmacist's Guide to Practical Dyslipidemia Management

Presented by: Michael Boivin
2025-02-13.



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Disclosures

- Presenter's Name: Michael Boivin
- I have the following relationships with commercial interests:
 - Advisory Board/Speakers Bureau: Novo-Nordisk, Emergent BioSolutions, Pfizer, Novavax, GSK, Bavarian Nordic, AbbvieFunding
 - Speaker/Consulting Fees: Teva, Pfizer, Novo Nordisk, mdBriefcase, Kenvue, Abbvie, Astra Zeneca, Boehringer Ingelheim, Moderna, Canopy, Valneva, Abbott Diabetes, GSK

Learning Objectives

Upon completion of this learning activity, participants will be better able to:

1. Apply current Canadian Cardiovascular Society (CCS) screening recommendations to identify patients requiring dyslipidemia assessment.
2. Evaluate patients' cardiovascular risk using the Framingham Risk Score and develop evidence-based treatment plans incorporating both lifestyle modifications and pharmacological interventions.
3. Implement an approach to manage statin intolerance and determine appropriate criteria for initiating add-on therapies in patients not reaching targets on maximally tolerated statin therapy
4. Design holistic cardiovascular risk reduction strategies that integrate dyslipidemia management with other modifiable risk factors.

Really? Dyslipidemia...

adf



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CCS 2021 Dyslipidemia Guidelines

Canadian Journal of Cardiology 37 (2021) 1129–1150

Society Guidelines

2021 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in Adults

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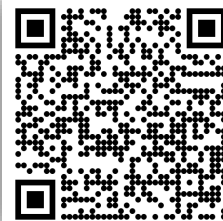
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[https://onlinecjc.ca/article/S0828-282X\(21\)00165-3/fulltext](https://onlinecjc.ca/article/S0828-282X(21)00165-3/fulltext)



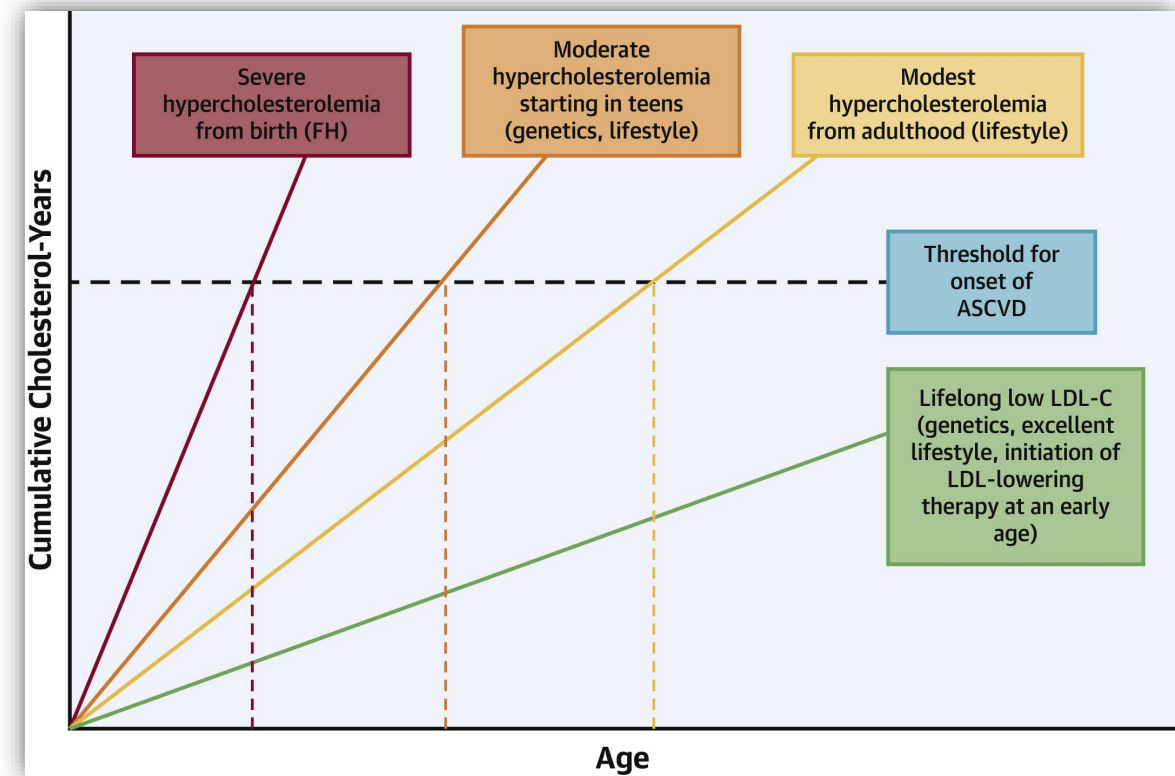
<https://ccs.ca/wp-content/uploads/2022/07/2022-Lipids-Gui-PG-EN.pdf>



Early Intervention Impacts CV Risk

- The longer the patient's LDL-C is elevated the higher the risk
 - Think of cholesterol-years as pack-years for smoking
- Every 1 mmol/L decrease in LDL-C:
 - 26% reduction in the risk of vascular event in primary prevention
 - 20% reduction of risk in secondary prevention
- Fundamentally, the better we can manage dyslipidemia, the better we can improve CV risk for our patients

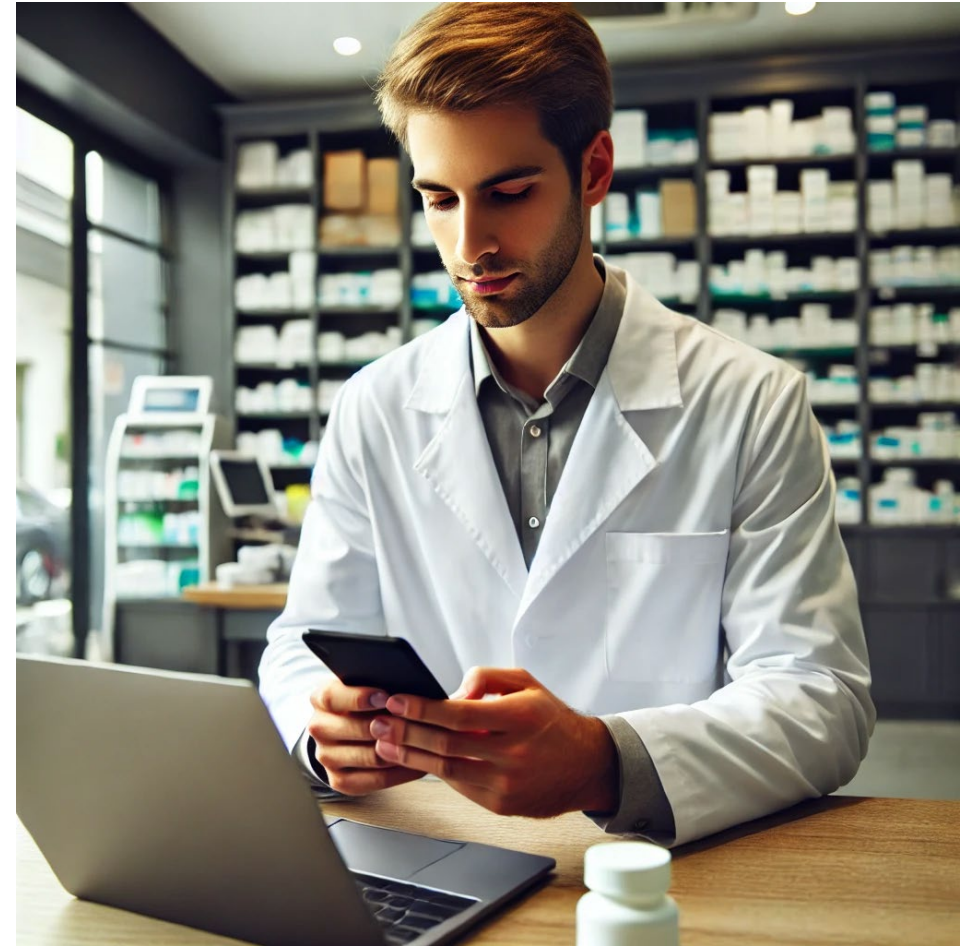
“Cholesterol-Years” and ASCVD



Interactive Question 1

What is the estimated percentage of Canadian Adults ≥ 40 years presenting in primary care have dyslipidemia?

- a) 10%
- b) 25%
- c) 37%
- d) 50%



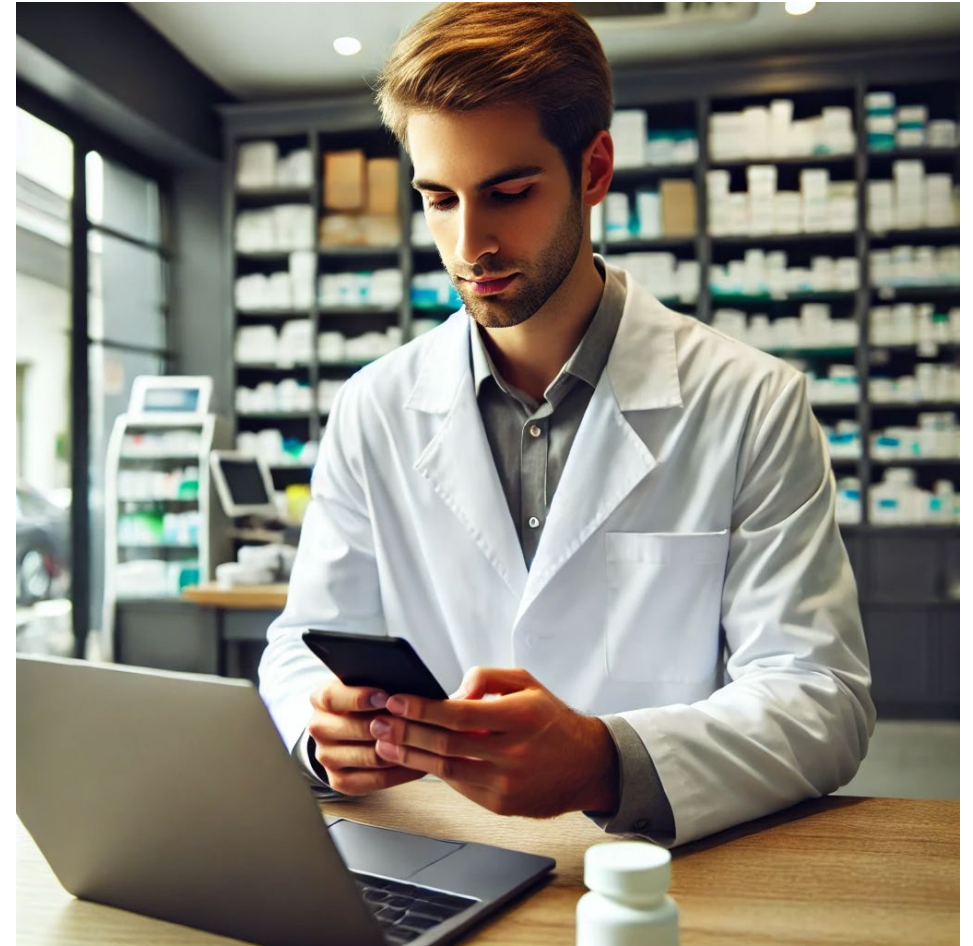
Answer Interactive Question 1

What is the estimated percentage of Canadian Adults ≥ 40 years presenting in primary care have dyslipidemia?

- a) 10%
- b) 25%
- c) 37%
- d) **50%**

Only **42.8%** were taking lipid lowering therapy (LLT)

Only **65% of high-risk** patients were taking LLT



Dyslipidemia is a Key Modifiable Risk Factor for ASCVD

- Diseases of the heart
 - 2nd leading cause of death after malignancy in 2023
 - 1 Canadian died of heart disease every 10 minutes in 2023
- Managing cardiovascular risk can help to lower morbidity and mortality
 - Dyslipidemia
 - Lowering LDL-C will lower the risk of ASCVD
 - “How low can you go?” – even with an LDL-C < 1.4 mmol/L there is a reduction in CVD risk
 - Hypertension
 - Obesity
 - Smoking cessation
 - Behaviour modification (e.g. nutrition and physical activity)



Our Scope is Evolving to Allow Better Care for People with Dyslipidemia

- Pharmacists are playing an increasingly important role in chronic disease management
 - Remember that it is estimated that 20% to 25% of Canadians do not have a primary care clinician
- Scope that can address the needs of people with dyslipidemia:
 - Laboratory monitoring
 - Adaptations
 - Independent prescribing
- **What I am going to do is give you a highly interactive program to test you on the components on the CCS guidelines to show what you can do for your patients.**



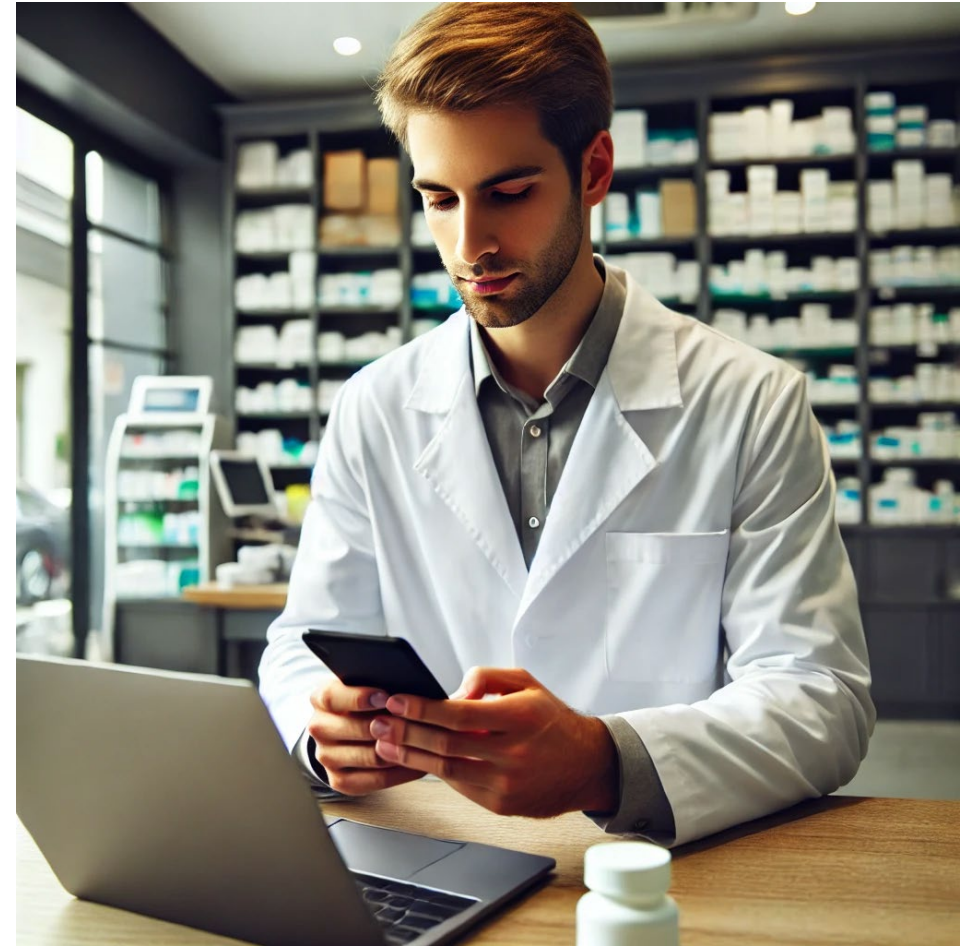
Section 1 – Screening



Interactive Question 2

According to the CCS guidelines, which of these patients should be screened for dyslipidemia? (Select all that apply)

- a) A 28-year-old person who smokes ½ a pack per day
- b) A 45-year-old with a BMI of 25 kg/m² and is a triathlete
- c) A 30-year-old male with a mother who had an MI at the age of 68 years
- d) A 22-year-old with rheumatoid arthritis



Dyslipidemia Screening Recommendations

WHO TO SCREEN

**Men ≥ 40 years of age;
women ≥ 40 years of age
(or postmenopausal)**

Consider earlier in ethnic groups at increased risk such as South Asian or Indigenous individuals

All patients with any of the following conditions regardless of age:

- Clinical evidence of atherosclerosis
- Abdominal aortic aneurysm
- Diabetes mellitus
- Arterial hypertension
- Current cigarette smoking
- Stigmata of dyslipidemia (corneal arcus, xanthelasma or xanthoma)
- Family history of premature CVD*
- Family history of dyslipidemia
- Chronic kidney disease**
- Obesity (BMI ≥ 30 kg/m²)
- Inflammatory diseases (RA, SLE, PsA, AS, IBD)
- HIV infection
- Erectile dysfunction
- Chronic obstructive pulmonary disease
- History of hypertensive disorder of pregnancy

*Men younger than 55 years of age and women younger than 65 years of age in first degree relatives.

**Chronic Kidney Disease = eGFR ≤ 60 mL/min/1.73 m² or ACR ≥ 3 mg/mmol for at least 3 months duration.

ACR = albumin-to-creatinine ratio; AS = ankylosing spondylitis; BMI = body mass index; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; eGFR = estimated glomerular filtration rate; IBD = inflammatory bowel disease; PsA = psoriatic arthritis; RA = rheumatoid arthritis; SLE, systemic lupus erythematosus.

- Remember, everyone at 40 years of age
- When a person has other CV risk factors:
 - Screen **regardless** of age
- **Practice Tip:**
 - If you are screening for dyslipidemia, consider also screening for type 2 diabetes, kidney disease, and assess the person's blood pressure

Interactive Question 3

You have a patient in practice who is 42 years of age and has never been screened for dyslipidemia before. According to the 2021 CCS guidelines, what should a pharmacist order on the lab requisition? (select all that apply)

- a) Standard lipid profile (total cholesterol, LDL-C, HDL-C, non-HDL-C and triglycerides)
- b) Triglycerides
- c) Fasting plasma glucose or A1C
- d) eGFR
- e) Lipoprotein(a)



The Screening List for People at Risk

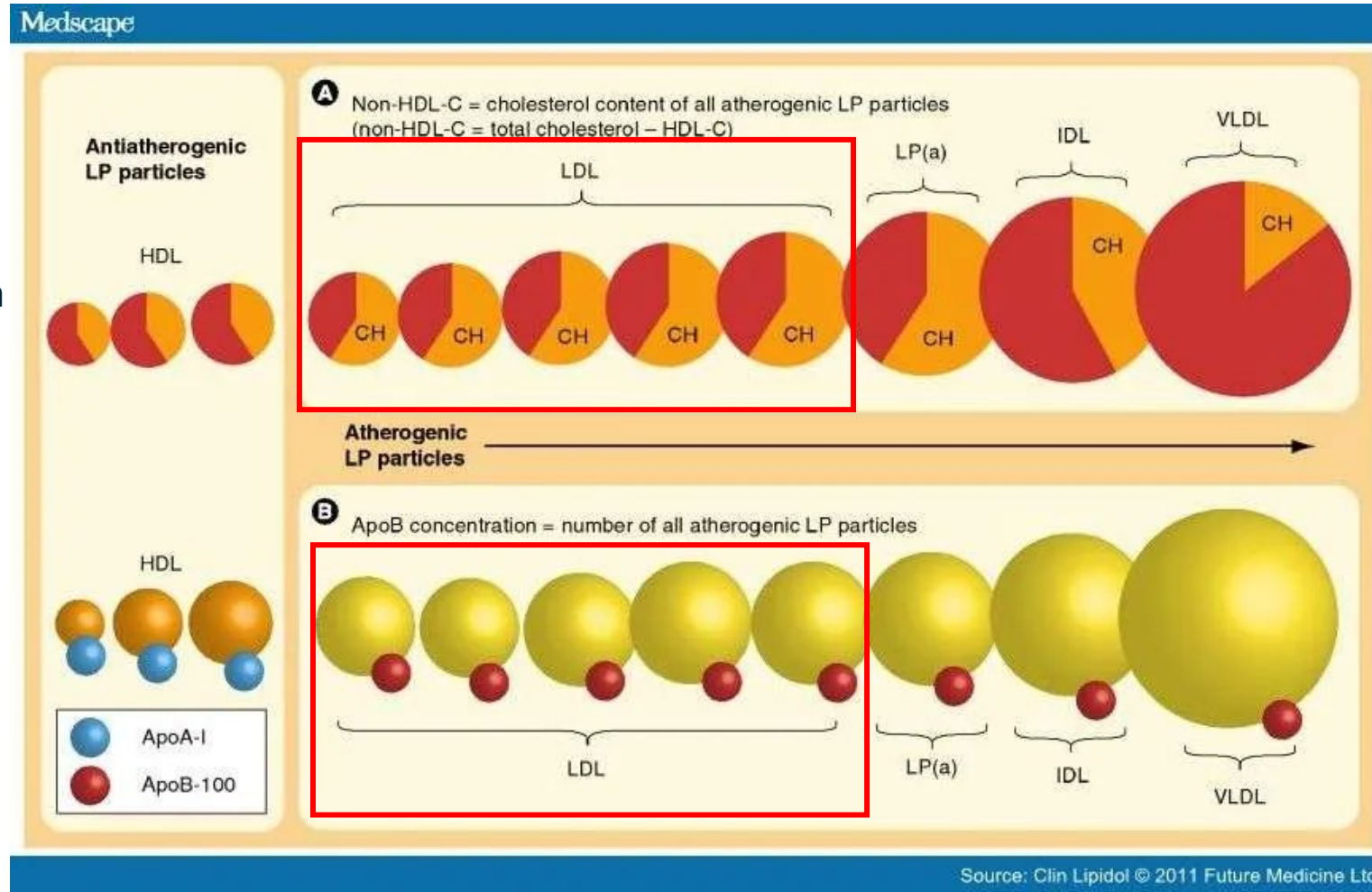
- Key tips:
 - Non-fasting is recommended, unless the patient's TG levels are lower than 4.5 mmol/L
 - Non-HDL-C or ApoB are preferred over LDL-C for interpreting lipid results (especially if TG > 1.5 mmol/L)
 - Lipoprotein(a) is recommended to be assessed only once in a lifetime at it does not normally change over time
 - Marker of CV risk vs. currently being a therapeutic target

CCS Screening Recommendations for Dyslipidemia

For all:	Optional:
<ul style="list-style-type: none">• Standard lipid profile: TC, LDL-C, HDL-C, non-HDL-C,• TG• FPG or A1C• eGFR• Lipoprotein(a)—once in patient's lifetime, with initial screening	<ul style="list-style-type: none">• ApoB• Urine ACR (if eGFR < 60 mL/min, hypertension or diabetes)

Why non-HDL-C and ApoB?

- LDL-C does not capture the full level of atherogenic lipid particles
- Use of non-HDL-C or ApoB:
 - If TG > 1.5 mmol/L - Some cholesterol in LDL-C is replaced by TG, which promotes production of more atherogenic small dense LDL particles
- Non-HDL-C is preferred as it is no additional cost:
 - Total cholesterol – HDL-C



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- Wilson DP, Jacobson TA, Jones PH, et al. Use of Lipoprotein(a) in clinical practice: a biomarker whose time has come. A scientific statement from the National Lipid Association. *J Clin Lipidol* 2019;13:374-92.



Section 2 – Determining who requires treatment



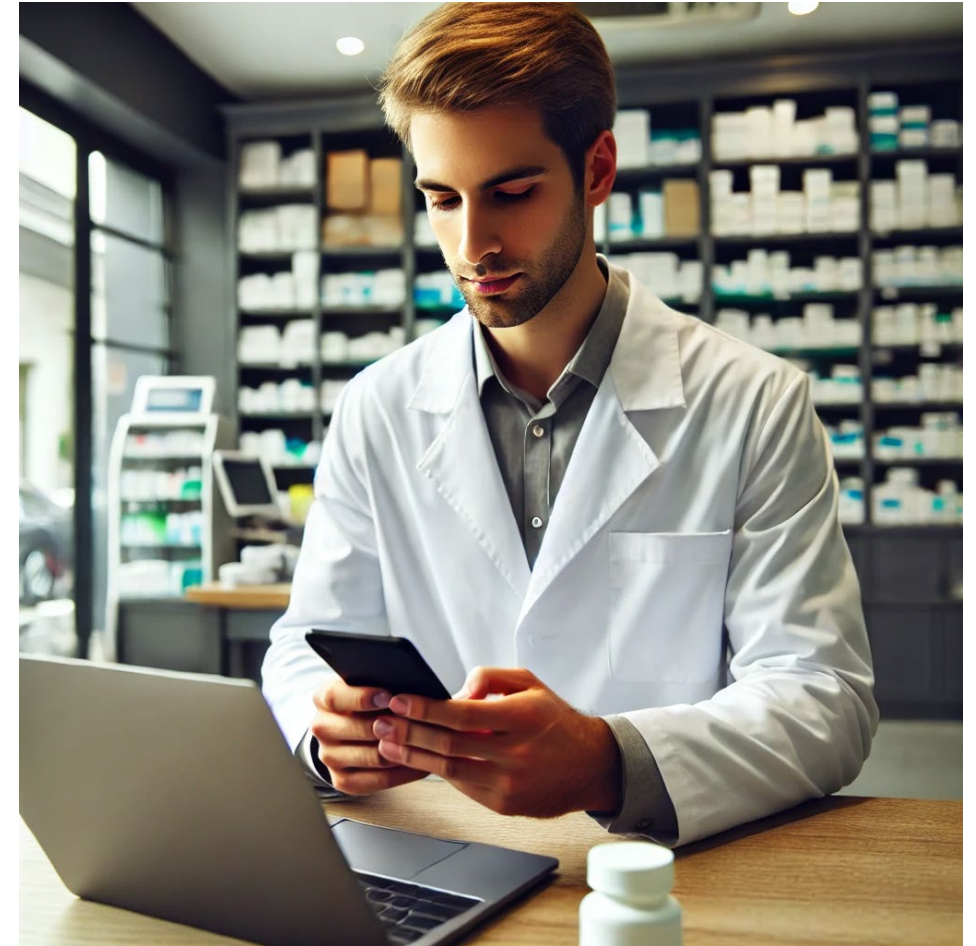
Interactive question 4

A pharmacist is screening a 54-year-old male for dyslipidemia. The labs came back today, and the results are:

- HDL-C = 0.9 mmol/L, Total Cholesterol = 4.5 mmol/L, TG = 2.0 mmol/L, LDL-C = 2.7 mmol/L
- His blood pressure in the pharmacy is 142/86 mmHg
- Non-smoker, no medication, no diabetes or history of premature CVD

What do you perceive as his risk?

- a) Low
- b) Intermediate
- c) High
- d) Very high



Framingham Risk Score and Heart Age

- This patient has an intermediate CV risk score (10-19.9%)
- FRS should be calculated (not guessed) for primary prevention patients 40 – 75 years without statin-indicated conditions
- **Practice tip:**
 - Heart age is a helpful tool for educating patients about their CV risk

FRS Calculator

Age years

Sex

HDL-C mmol/L

Total-C mmol/L

Systolic BP mmHg

BP Treated

Smoker

Diabetes

Fam Hx. of premature CVD

Calculate

10-Year CVD Risk **15.6 % (Intermediate-Risk)**

Heart Age **64**

Risk Level†	Initiate Statin Treatment if:	Consider Add-on Therapy or Treatment Intensification
High FRS ≥ 20%	Consider treatment in all (Strong, High)	If LDL-C ≥ 2 mmol/L or Non-HDL-C > 2.6 mmol/L or ApoB ≥ 0.80 g/L on maximally tolerated statin dose
Intermediate FRS 10-19%	If LDL-C ≥ 3.5 mmol/L or (Strong, Moderate) If LDL-C < 3.5 mmol/L initiate if: • non-HDL-C ≥ 4.3 mmol/L or • ApoB ≥ 1.05 g/L or (Strong, Moderate) • Men ≥ 50 yrs and women ≥ 60 yrs with 1 additional risk factor: low HDL-C, impaired fasting glucose, high waist circumference, smoker, or hypertension, or with the presence of other risk modifiers: hsCRP ≥ 2 mg/L, CAC > 0 AU, family history of premature CAD, Lp(a) ≥ 100 mol/L (≥ 50 mg/dL)	If LDL-C ≥ 2 mmol/L or Non-HDL-C > 2.6 mmol/L or ApoB ≥ 0.80 g/L on maximally tolerated statin dose
Low FRS < 10%	Statins generally not indicated	N/A

Statin-Indicated Conditions** (Consider treatment in all; Strong, High)

LDL-C ≥ 5 mmol/L **or** non-HDL-C ≥ 5.8 mmol/L **or** ApoB ≥ 1.45 g/L (FH or genetic dyslipidemia)

Most patients with diabetes:
• Age ≥ 40 yrs old **or** Age ≥ 30 yrs & DM x ≥ 15 yrs duration **or** Microvascular disease

Chronic Kidney Disease:
• Age ≥ 50 yrs & eGFR < 60 mL/min/1.73 m² **or** ACR > 3 mg/mmol

Atherosclerotic Cardiovascular Disease (ASCVD):
• Myocardial infarction (MI), acute coronary syndrome (ACS), **or**
• Stable angina, documented coronary artery disease (CAD) using angiography, **or**
• Stroke, TIA, documented carotid disease, **or**
• Peripheral arterial disease, claudication, and/or ankle-brachial index (ABI) < 0.9, **or**
• Abdominal aortic aneurysm (AAA) – abdominal aorta > 3.0 cm or previous aneurysm surgery

If LDL-C ≥ 2.5 mmol/L **or** < 50% reduction, **or** non-HDL-C ≥ 3.2 mmol/L **or** ApoB ≥ 0.85 g/L

If LDL-C ≥ 2.0 mmol/L **or** non-HDL-C ≥ 2.6 mmol/L **or** ApoB ≥ 0.80 g/L on maximally tolerated statin dose

If LDL-C ≥ 1.8 mmol/L **or** non-HDL-C ≥ 2.4 mmol/L **or** ApoB ≥ 0.70 g/L on maximally tolerated statin dose

** Statin-indicated condition refers to any condition for which pharmacotherapy with statins is indicated, and consists of all documented ASCVD conditions, as well as other high-risk primary prevention conditions in the absence of ASCVD.

What Does a 15.6% Score Mean to a Patient

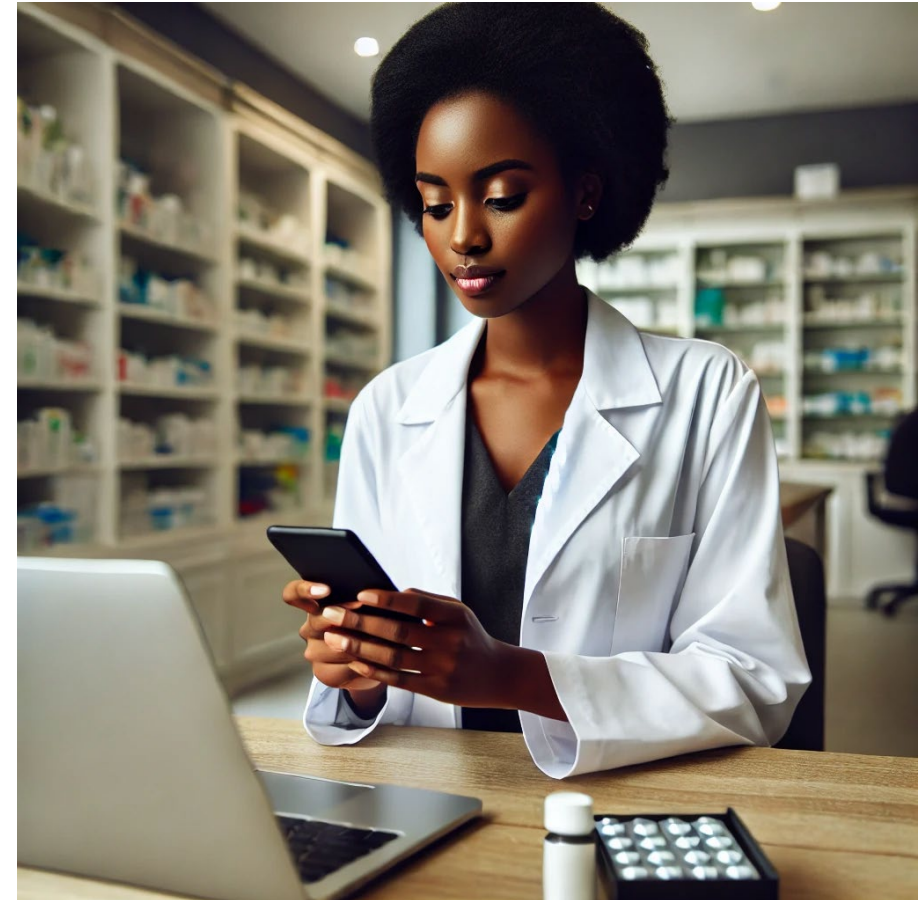
- **Start with a simple analogy:**
 - *Imagine your heart health is like the weather forecast. The Framingham risk score is like predicting the chance of rain over the next 10 days. It doesn't mean it will definitely rain, but it gives you an idea of the likelihood so you can plan accordingly.*
- **Explain the Framingham risk score result:**
 - *The score gives us an estimate of your chance of having a heart-related event, like a heart attack or stroke, over the next 10 years. For example, your score is 16%, that means that out of 100 people with similar health profiles, about 16 might experience such an event in the next decade.*
- **Consider integrating heart age:**
 - *You have a heart of the average 64-year-old. Having a heart that is older than you are means that you are at much higher risk of heart disease*
- **Reassure, engage and motivate:**
 - *The good news is there are things we can do today to lower your risk and improve your heart health*



Interactive Question 5

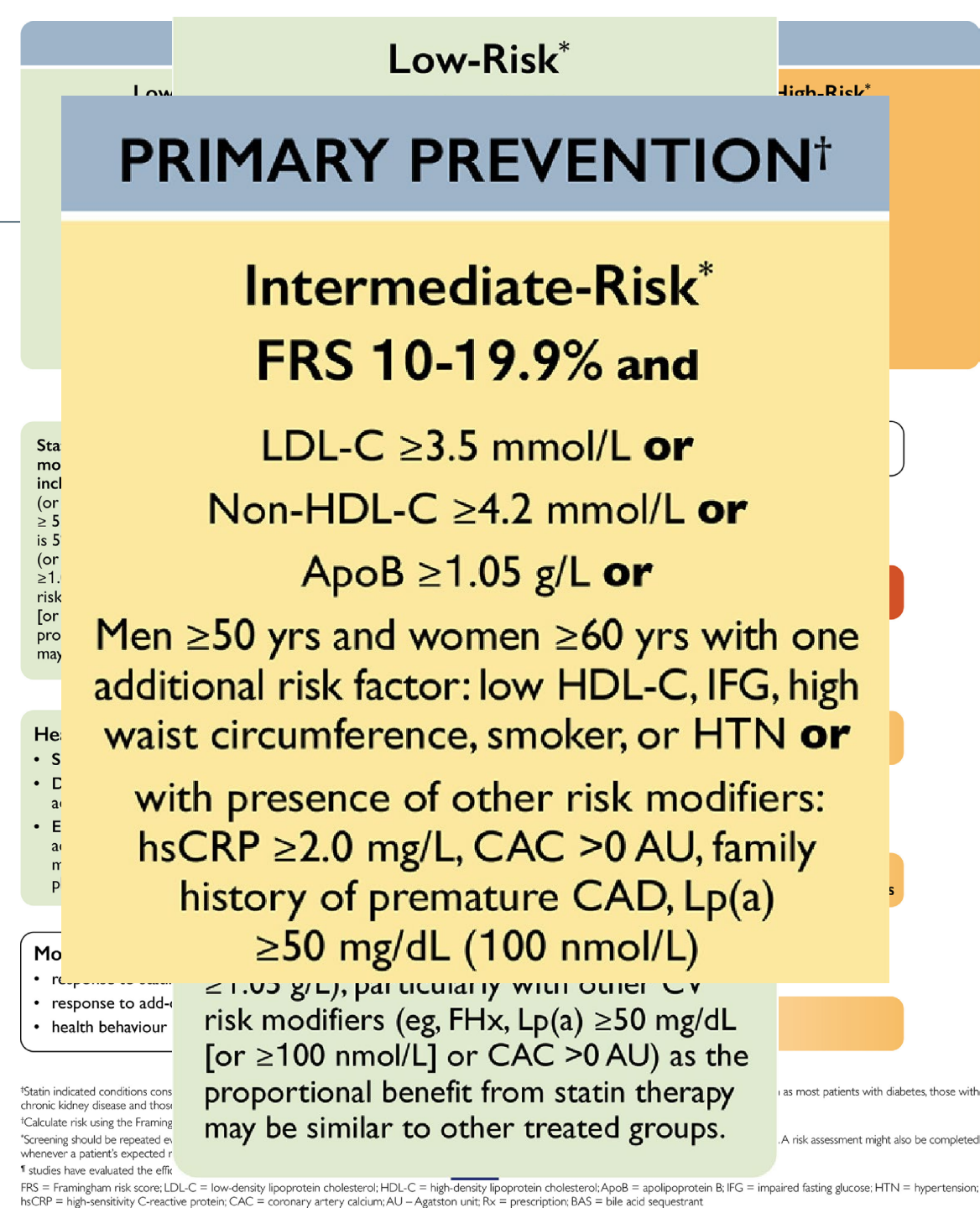
The pharmacist has calculated the FRS for this patient as 15.6%. The pharmacist is determining the most appropriate course of action. What should she do? (check all that apply)

- a) Behavioural modifications
- b) Low-potency statin
- c) High-potency statin
- d) Ezetimibe



FRS Provides Some But Not All the Information

- Many high- and intermediate-risk will require statin therapy in addition to behavioural changes
- Low-risk will depend on other factors that further increase the risk
- Behaviour Changes:
 - **Nutrition:** Portfolio dietary pattern, DASH dietary pattern, low-glycemic index/glycemic load dietary pattern, and plant-based dietary pattern, as well as dietary patterns high in nuts, legumes, olive oil, fruits and vegetables, total fibre, and whole grain
 - **Physical activity:** at least 150 minutes of moderate to vigorous aerobic activity per week. It might also be beneficial to add muscle- and bone-strengthening activities at least 2 days per week
 - **Smoking cessation**



Want to Teach on the Benefits of Behaviour Changes?



Intervention (minimal dose for effect)	Expected CV outcomes	Expected lipid outcomes
Mediterranean dietary pattern	↓ major CV events 28-30% (0.6-1% absolute risk reduction [NNT=100-167])	
Portfolio dietary pattern	↓ 10y-FRS by 11%	Efficacy: ↓ LDL-C 21-29% (comparable to Lovastatin 20mg) Effectiveness: ↓ LDL-C 8-14%
DASH (Dietary Approaches to Stop Hypertension) dietary pattern	↓ CVD 20%; ↓ 10y-FRS by 13%	↓ LDL-C 3%
Dietary patterns high in nuts (≥ 30 g/day)	↓ Major CV events 28% (1% absolute risk reduction [NNT=100])	↓ LDL-C 5-7%, ↓ TG 5-10%
Dietary patterns high in legumes (≥ 4 servings/week)	↓ CHD events 14%	
Dietary patterns high in Olive oil (≥ 60 mL/day)	↓ major CV events 30% (0.6% absolute risk reduction [NNT=167])	
Dietary patterns rich in fruits and vegetables (≥ 5 servings/day)	↓ CV mortality 4% per serving/day	
Dietary patterns high in total fibre (≥ 30 g/day)	↓ CVD events 9% reduction per 7g/day	
Dietary patterns high in whole grains (≥ 3 servings/day)	↓ CVD events 21%	
Low-glycemic index (GI)/glycemic load (GL) dietary patterns	↓ CHD and CVD events 10-12%/19-21%	↓ LDL-C 5% (for low-GI dietary patterns)
Vegetarian dietary patterns	↓ CHD events 19%	
Saturated fats intake ≤ 9% energy 107	↓ CVD events 21%	
Replacement of Saturated fats with polyunsaturated fats (PUFAs) especially from omega-3/omega-6 sources	↓ CVD events 28% (5.4% absolute risk reduction [NNT=18.5])	
Replacement (≥ 5% energy) of Saturated fats with polyunsaturated fats (MUFAs) from plant sources	↓ CHD events 15% for 5% energy replacement	
Replacement of saturated fats with whole grains	↓ CHD events 9% for 5% energy replacement	

Replacement (≥ 5% energy) of Saturated fats with low-GI carbohydrates	↓ CHD events 23% for 5% energy replacement	
Omega -3 PUFAs eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) from marine, algal, or yeast sources (2-4 g/day)	No CV benefit	↓ TG 25-30% in hypertriglyceridemia
Reduced saturated fats/dietary cholesterol NCEP Step I diet: ≤10% energy/≤300 mg/day NCEP Step II diet: ≤7% energy/≤ 200 mg/day		↓ LDL-C 10-12% 12-16%
Dietary patterns supplemented with plant sterols/stanols 1-2 gm/day		↓ LDL-C 6-12%;
Dietary patterns high in soy protein ≥30g/day		↓ LDL-C 3-5%; ↓ TG 4%
Dietary patterns high viscous soluble fibre from oats, barley, psyllium, pectin, or konjac mannan (≥10 g/day)		↓ LDL-C 5-10%;
Dietary patterns high in dietary pulses (beans, peas, chickpeas, and lentils) (≥ 1 serving/day or ≥130 g/day)		↓ LDL-C 5%
Moderate Alcohol intake 1-2 drinks/day	↓ CHD events 32%	↑ HDL-C 5-10%,
Weight loss and reduction of abdominal obesity 5-10% of body weight loss	↓ CVD risk 6% per 4.56 kg/m ² lower BMI and 9% per 12.6cm lower waist circumference (based on a minimum BMI of 20 kg/m ²)	↓ LDL-C 11%, ↑ HDL-C 3% (12% once weight stable), ↓ TG 32%
Exercise 30-60 min/day moderate to vigorous intensity	↓ CVD events 20-30%	↑ HDL-C 5-10%
Smoking cessation	↓ CV mortality 52% for never smoking and 10-39% for smoking cessation (< 5 years to ≥ 20 years)	↑ HDL-C 7-12%
Combined low-risk lifestyle behaviours (healthy body weight, healthy diet, regular exercise, smoking cessation, moderate alcohol intake, moderate sleep duration).	↓ CVD events and mortality 75%	



Holistic Approach to CVD Management

Canadian Journal of Cardiology 36 (2020) 596–624

Guidelines

Hypertension Canada's 2020 Comprehensive Guidelines for the Prevention, Diagnosis, Risk Assessment, and Treatment of Hypertension in Adults and Children

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SECONDARY PREVENTION POST ACS AND BEYOND			
Lifestyle Recommendations • Stop smoking • Weight reduction • Increased physical activity • Stress management • Depression counselling • Healthy diet		Refer to Cardiac Rehabilitation	
Recommended		Comments	Considerations
• Dual APT • Extended APT or Dual pathway (ASA + rivaroxaban)	→ ASA 81 mg daily + ticagrelor 90 mg BID x 1 yr → ASA 81 mg daily + ticagrelor 60 mg BID or clopidogrel 75 mg daily → ASA 81 mg daily + rivaroxaban 2.5 mg BID	• Extended DAPT or Dual pathway therapy should be considered ~1 year post-ACS	
• Lipid lowering	→ atorvastatin 80 mg daily or equivalent with LDL target <1.8 mmol/L (2016 Canadian guidelines or <1.4 mmol/L (2019 ESC/EAS guidelines) → icosapent ethyl 2 g BID if TG 1.5–5.6 and LDL <2.6 mmol/L	• LDL not at target • Statin intolerance • Very high risk*	ezetimibe 10 mg daily and/or alirocumab 75–150 mg Q2 weeks evolocumab 140 mg Q2 weeks (or 420 mg Q4 weeks)
• ACE inhibition /ARB	→ ramipril 10 mg daily or perindopril 8 mg daily or telmisartan 80mg		
• Beta-blocker	→ atenolol 50 mg daily or bisoprolol 10mg daily, or carvedilol 25 mg BID, or metoprolol 50 mg BID		
• BP Control	→ CHEP based algorithm	As needed	DHP CCB + ACEi or ARB ± chlorthalidone or indapamide
• CV protection and glycemic control in diabetes	→ Diabetes Canada based algorithm	Add agent with CV benefit	empagliflozin and/or dapagliflozin and/or liraglutide, semaglutide, dulaglutide

* Recent ACS, ≥2 prior MIs, multivessel CAD (e.g., ≥40% stenoses in ≥2 vessels, prior CABG), polyvascular disease (e.g., CAD + PAD or cerebrovascular disease, diabetes mellitus, LDL-C far from target (e.g., ≥2.6 mmol/L)



UPDATED FOR 2024



Clinical Practice Guidelines

Quick Reference Guide

CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Secondary Prevention of Stroke

Seventh Edition, Update 2020



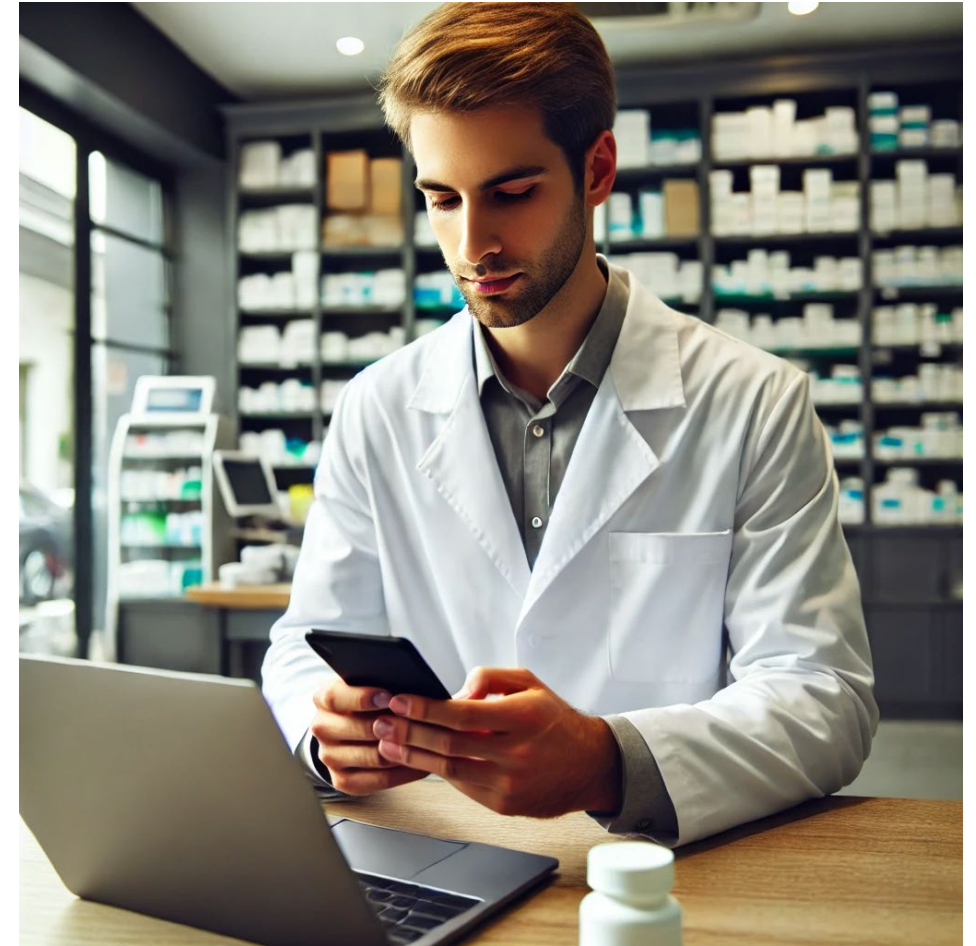
Section 3 – Statins



Interactive Question 6

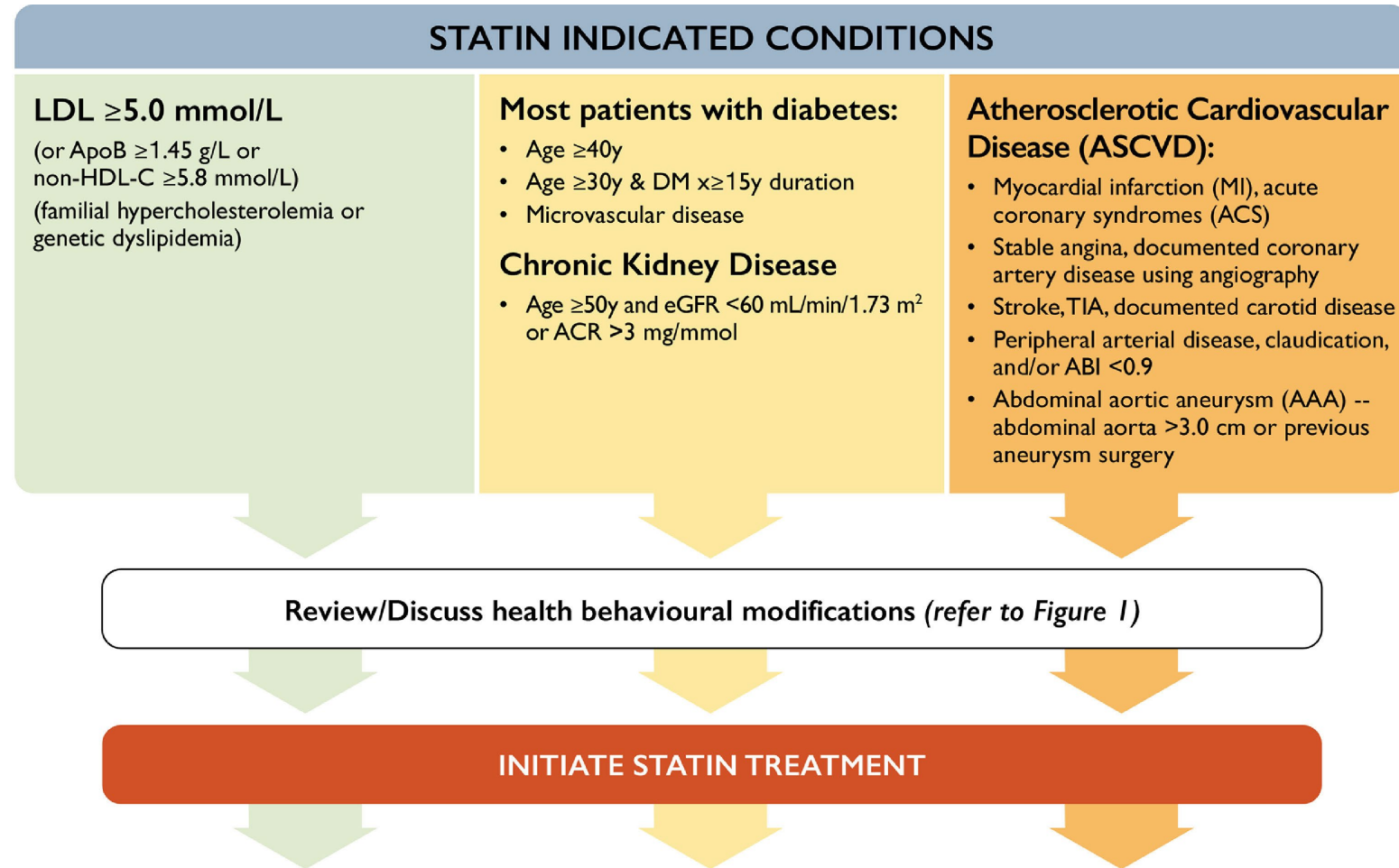
A 52-year-old has an LDL-C level of 1.8 mmol/L, non-HDL-C = 2.4 mmol/L with an FRS score of 8.2% (low risk). Which of the following situation would you consider starting a statin? (select all that apply)

- a) Statin therapy would not be indicated for this patient
- b) If they have chronic kidney disease
- c) If they have a BMI > 35 kg/m²
- d) If they have type 2 diabetes
- e) If they have had a history of transient ischemic attacks



Statin Indicated Conditions

- Statin-indicated condition refers to any condition for which pharmacotherapy with statins is indicated
- **Practice Tip:**
 - If you have any of these patients with ASCVD, CKD or type 2 diabetes that meet these criteria:
 - No screening is required
 - You would add statin **regardless of the patient's lipid levels**
- For each of these conditions, the patient is at high-risk and can benefit from statin therapy



Interactive Question 7

A pharmacist has prescribing authority and is going to initiate statin for a patient for primary prevention. Which of the following statements is TRUE?

- a) Ideally, they should start on a low to mid-potency statin first (e.g. simvastatin)
- b) Start on rosuvastatin 5-10 mg or atorvastatin 10-20 mg daily
- c) Book recheck lipids in 21 days
- d) Lipid targets are LDL-C < 1.8 mmol/L, non-HDL-C < 2.4 mmol/L or apoB < 0.70 g/L



Lipid Lowering Therapy – Primary Prevention

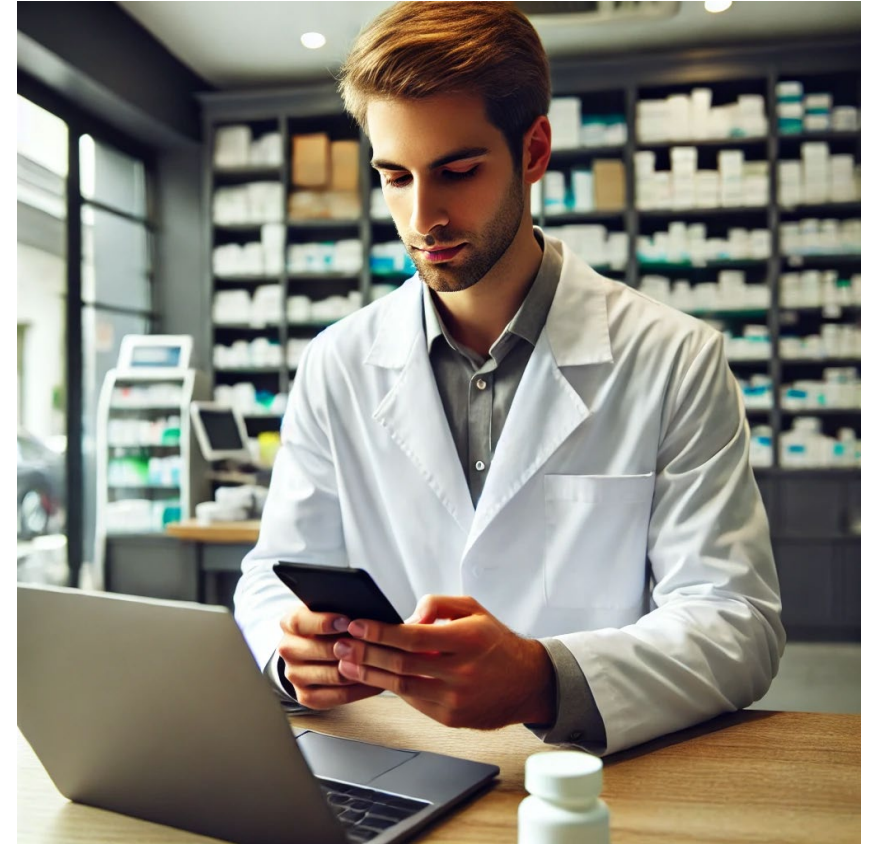
- **Starting statin (choose one of the following):**
 - Atorvastatin 10 mg daily
 - Rosuvastatin 5 mg daily
- **Key education for patient**
 - Statin is prescribed to lower their risk of a heart attack or stroke
 - Must be taken every day
 - Tolerated well. Some people have some mild muscle pain, this is normally temporary and improves by staying on the medication
- **Monitoring**
 - Conduct lipid profile in 4 to 6 weeks
 - If **LDL-C ≥ 2.0 mmol/L** or **non-HDL-C > 2.6 mmol/L** or **ApoB > 0.8 g/L**:
 - Increase dose of rosuvastatin by 5-10 mg (max dose 40 mg/day) or atorvastatin by 10 mg (max dose 80 mg/day)



Interactive Question 8

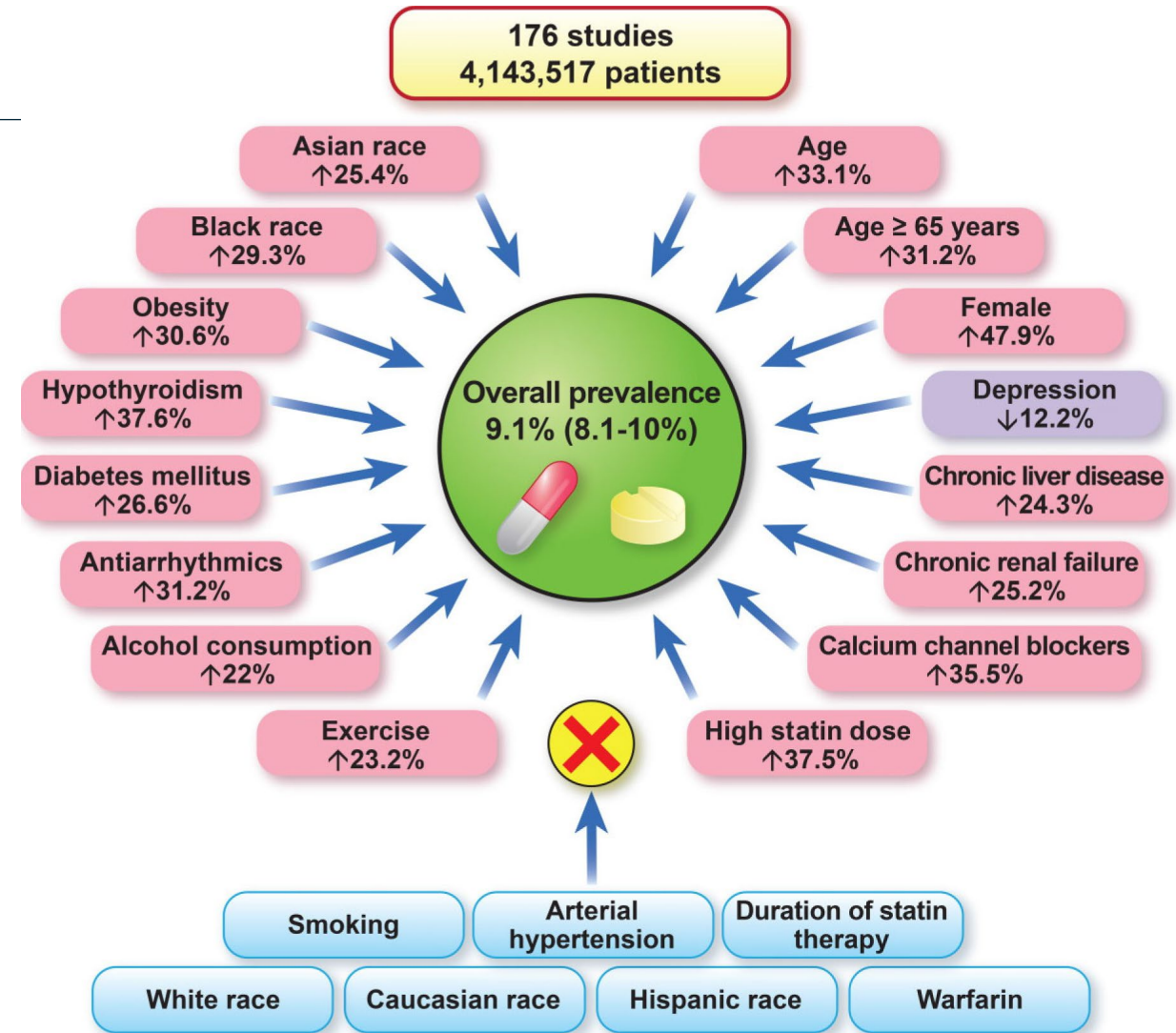
A patient has recently started on rosuvastatin 10 mg daily and is calling 3 weeks later and explaining about muscle pain. She read online that this is very common with her medication, and she needs to stop it. Which of the following is the most appropriate course of action?

- a) She should discontinue the atorvastatin today
- b) She should be given Co-enzyme Q10
- c) Recommend that she dose her statin 3 times per week and reassess in a couple of weeks
- d) She should be considered for ezetimibe or a PCSK9 inhibitor

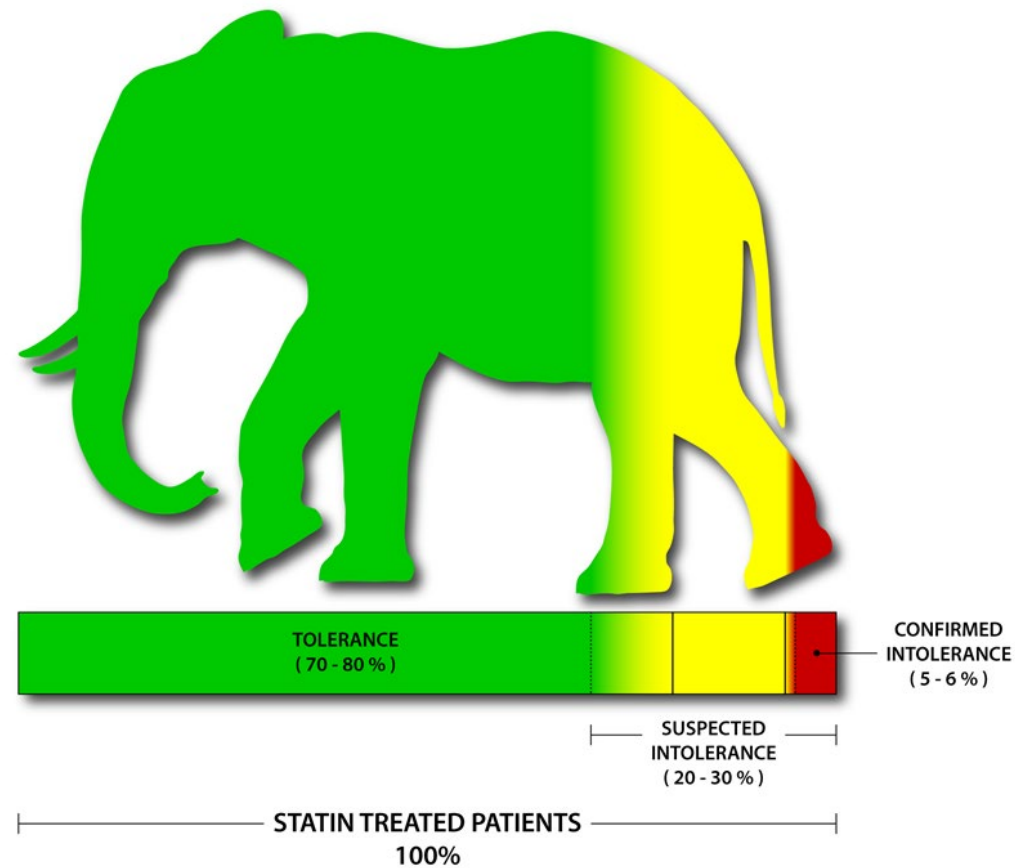


Statin Intolerance Risk is Small

- The overall prevalence is 9.1% (< 1 in 10)
- Risk factors: (significant)
 - Age
 - Female gender
 - Asian and Black race
 - Obesity
 - Diabetes mellitus
 - Hypothyroidism C
 - Chronic liver
 - Renal failure



Statin Intolerance is an Elephant in the Room

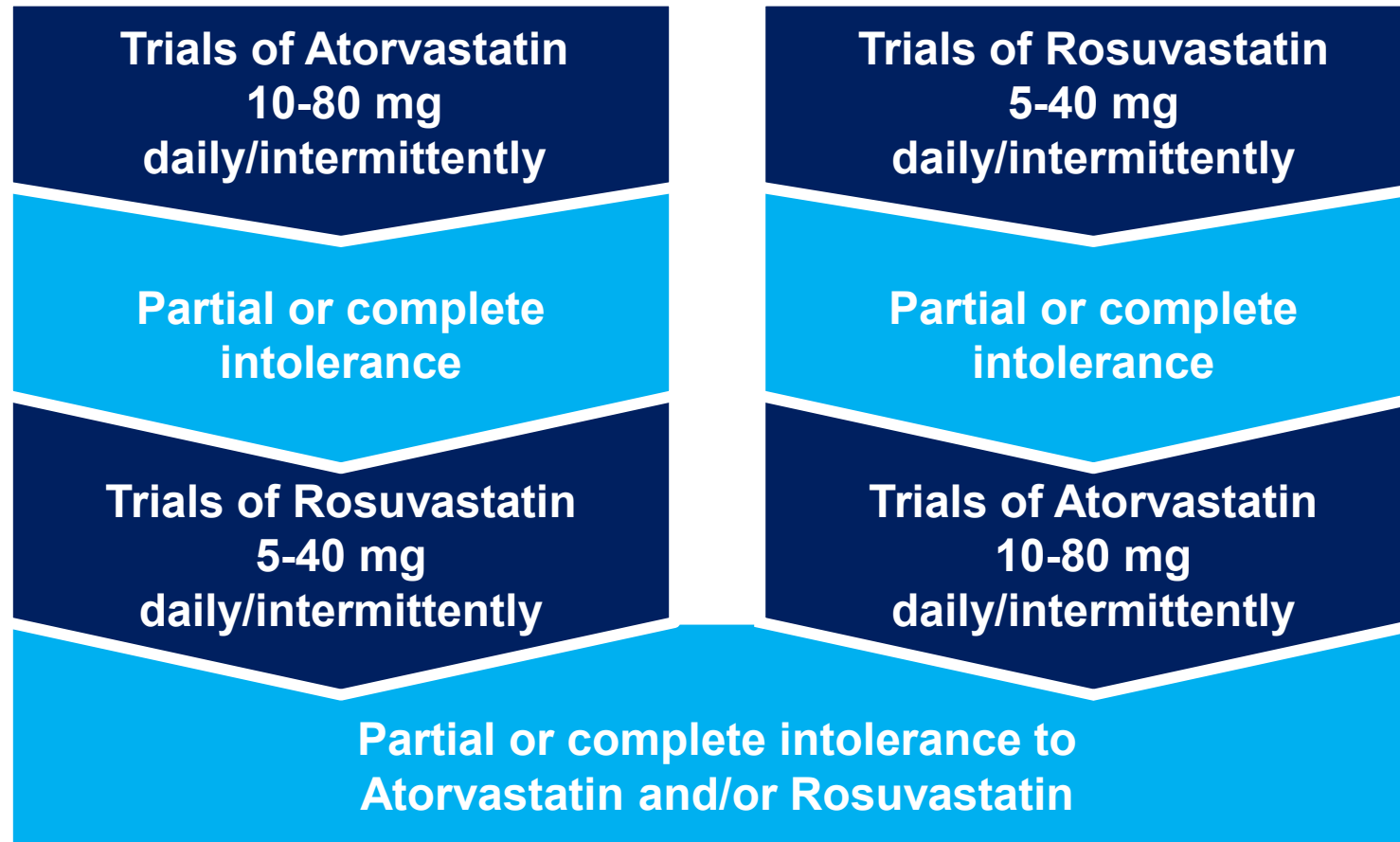


Managing Statin Intolerance

- Important to remind patients that statins lower CV risk
- **Strategies to prevent**
 - Start low dose of atorvastatin or rosuvastatin
 - Counsel patients that these side effects are common, but temporary and to let you know if they experience them
 - Watch for drug interactions that can lead to higher statin levels
- **Management strategies in a nutshell:**
 - Start/Stop
 - Lower
 - Add
- **Measurement of creatine kinase and ALT**
 - Guidelines provides recommendations for:
 - Myalgia (Stopping if CK > 5 X ULN)
 - Suspected liver disease (ALT > 3 x ULN)



Identification and Management: Try a switch



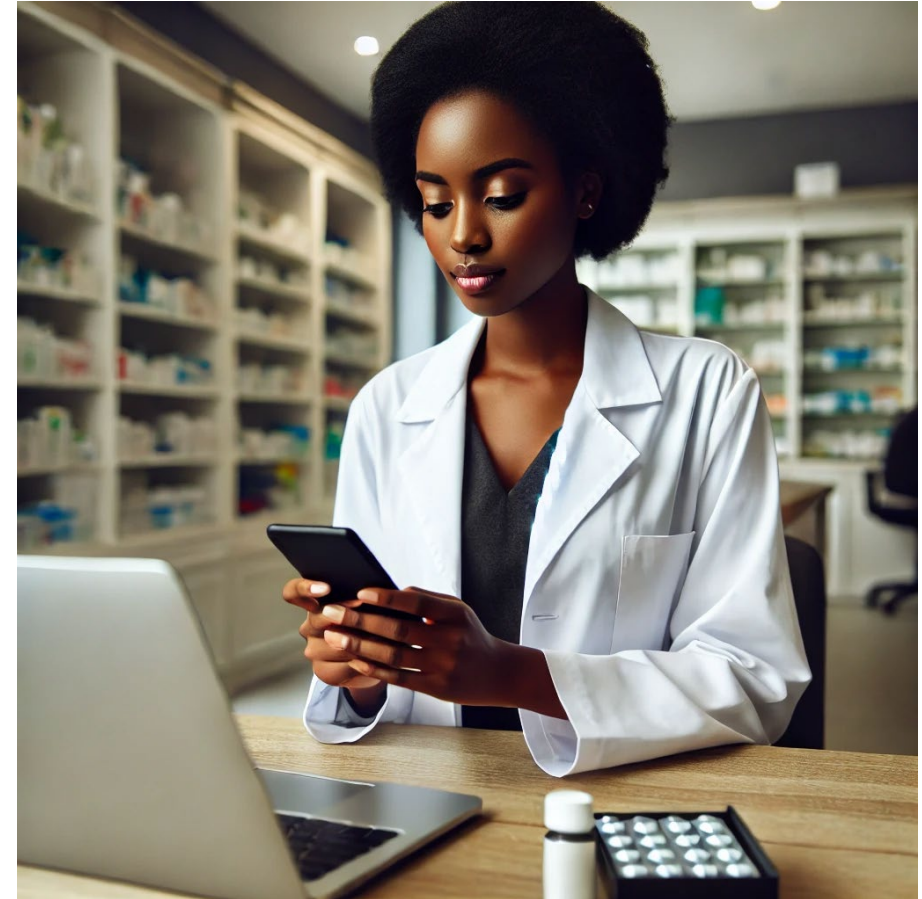
Section 4 – Other Therapies and Secondary Prevention



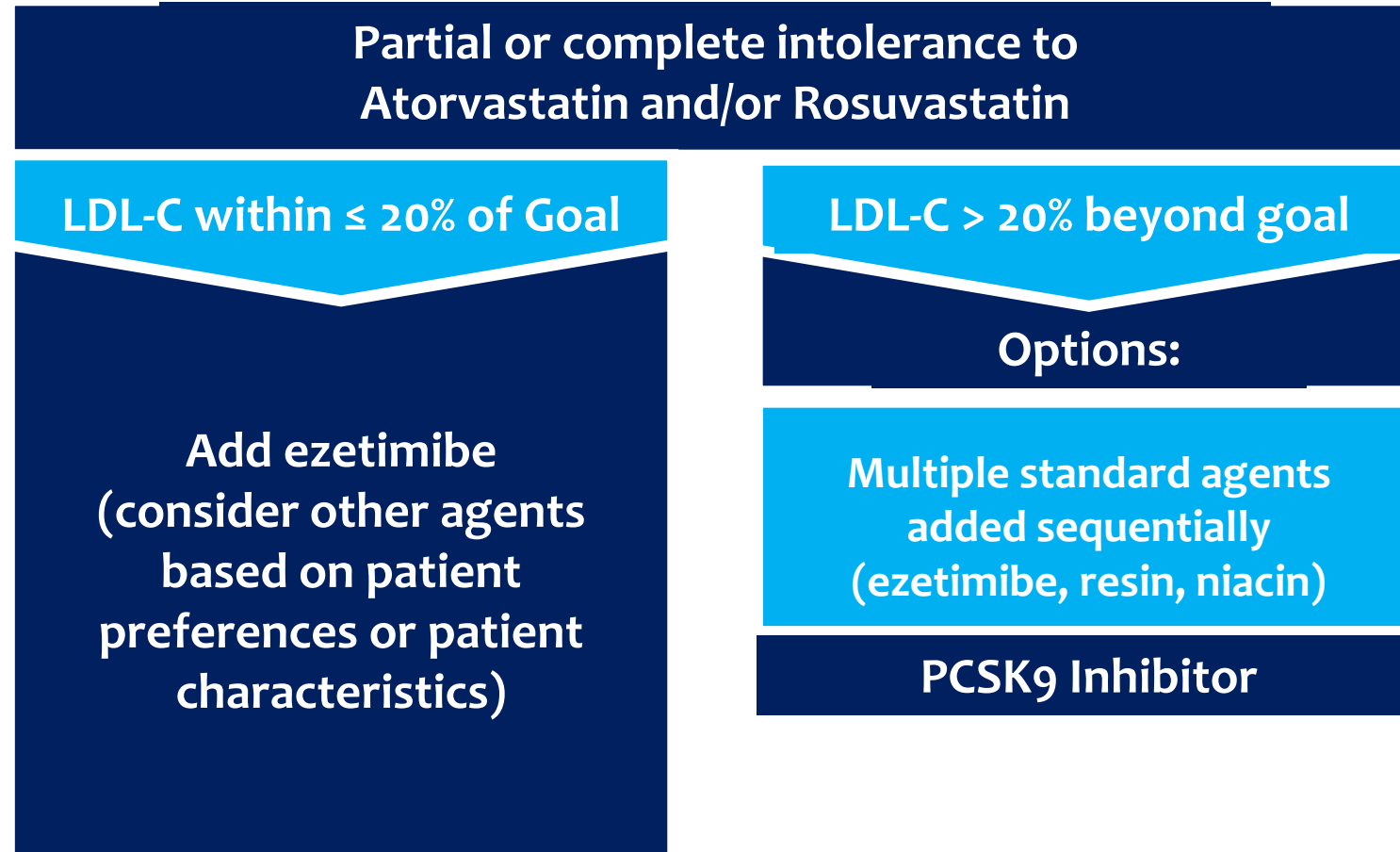
Interactive Question 9

A 60-year-old is currently taking atorvastatin 40 mg for primary prevention. Her LDL-C is 2.2 mmol/L, her non-HDL-C = 2.8 mmol/L. When her dose was increased to 80 mg, she had muscle pain and returned to 40 mg. Which of the following is the guideline recommended option?

- a) Switch to rosuvastatin
- b) Add ezetimibe
- c) Add bile-acid sequestrant
- d) Add PCSK9i

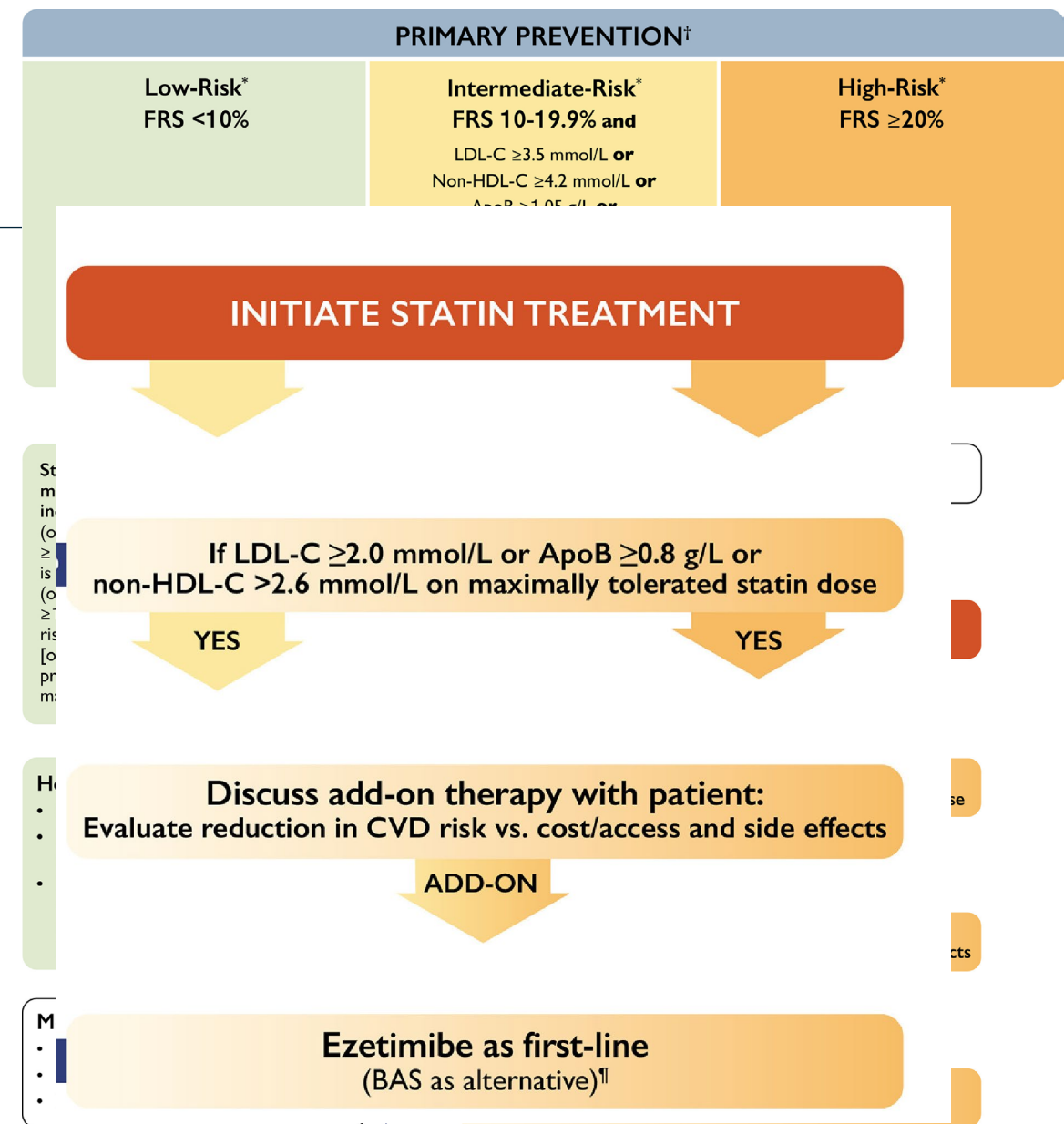


Management is dependent on proximity to LDL-C goal



Beyond Statins for Primary Prevention

- Check:
 - **Reaching targets:**
 - Could an increase in statin help get us there
 - What other therapies can be considered?
 - **Adherence to therapy** – many patients stop statin therapy
 - **Statin tolerability** – adverse effects that the patient may attribute to their statin



†Statin indicated conditions consists of all documented ASCVD conditions, as well as other high-risk primary prevention conditions in the absence of ASCVD, such as most patients with diabetes, those with chronic kidney disease and those with a LDL-C ≥5.0 mmol/L.

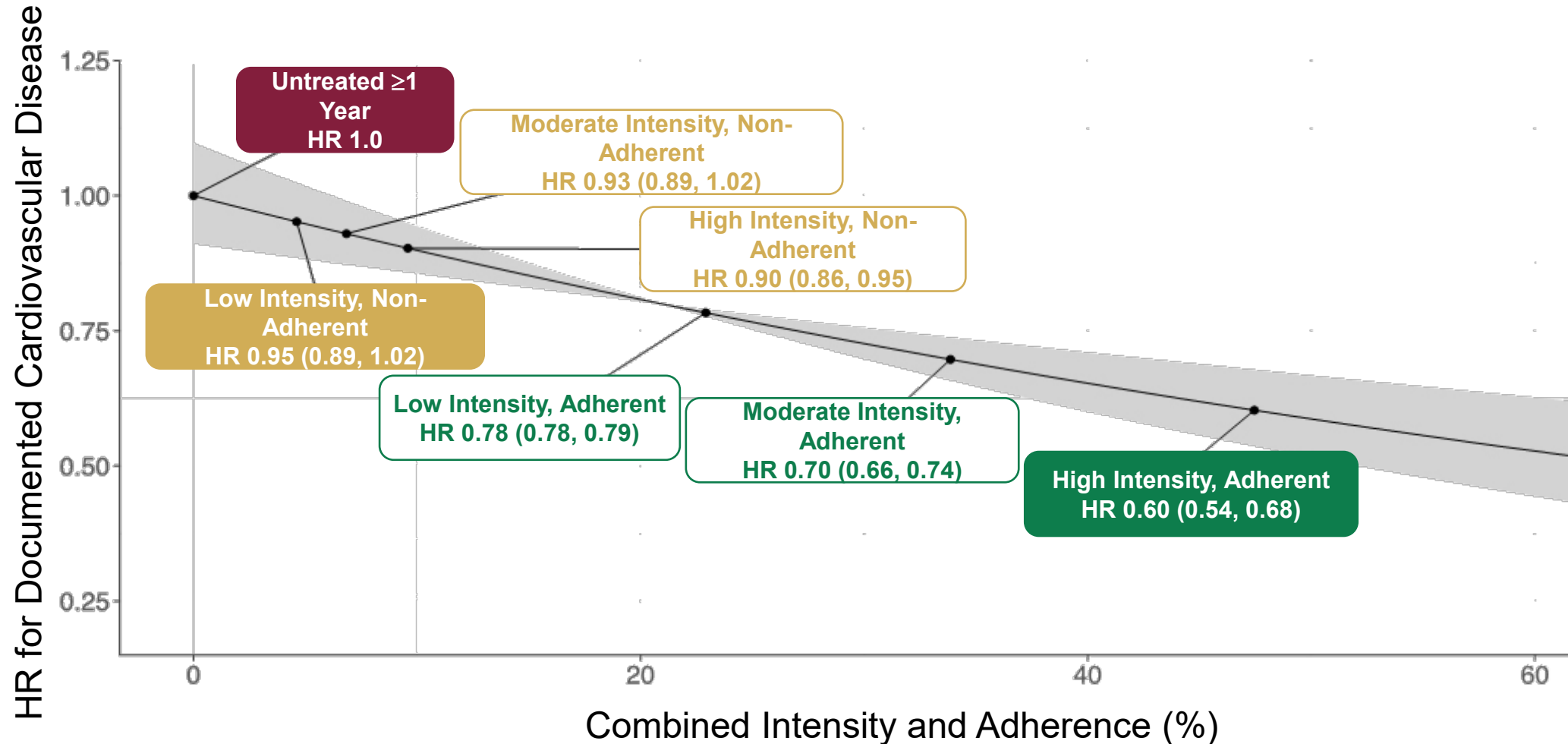
‡Calculate risk using the Framingham Risk Score (FRS) – refer to the iCCS available on the App Store or on Google Play.

*Screening should be repeated every 5 years for men and women aged 40 to 75 years using the modified FRS or CLEM to guide therapy to reduce major CV events. A risk assessment might also be completed whenever a patient's expected risk status changes.

‡ studies have evaluated the efficacy of BAS for the prevention of ASCVD, but results have been inconclusive.

FRS = Framingham risk score; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; ApoB = apolipoprotein B; IFG = impaired fasting glucose; HTN = hypertension; hsCRP = high-sensitivity C-reactive protein; CAC = coronary artery calcium; AU – Agatston unit; Rx = prescription; BAS = bile acid sequestrant.

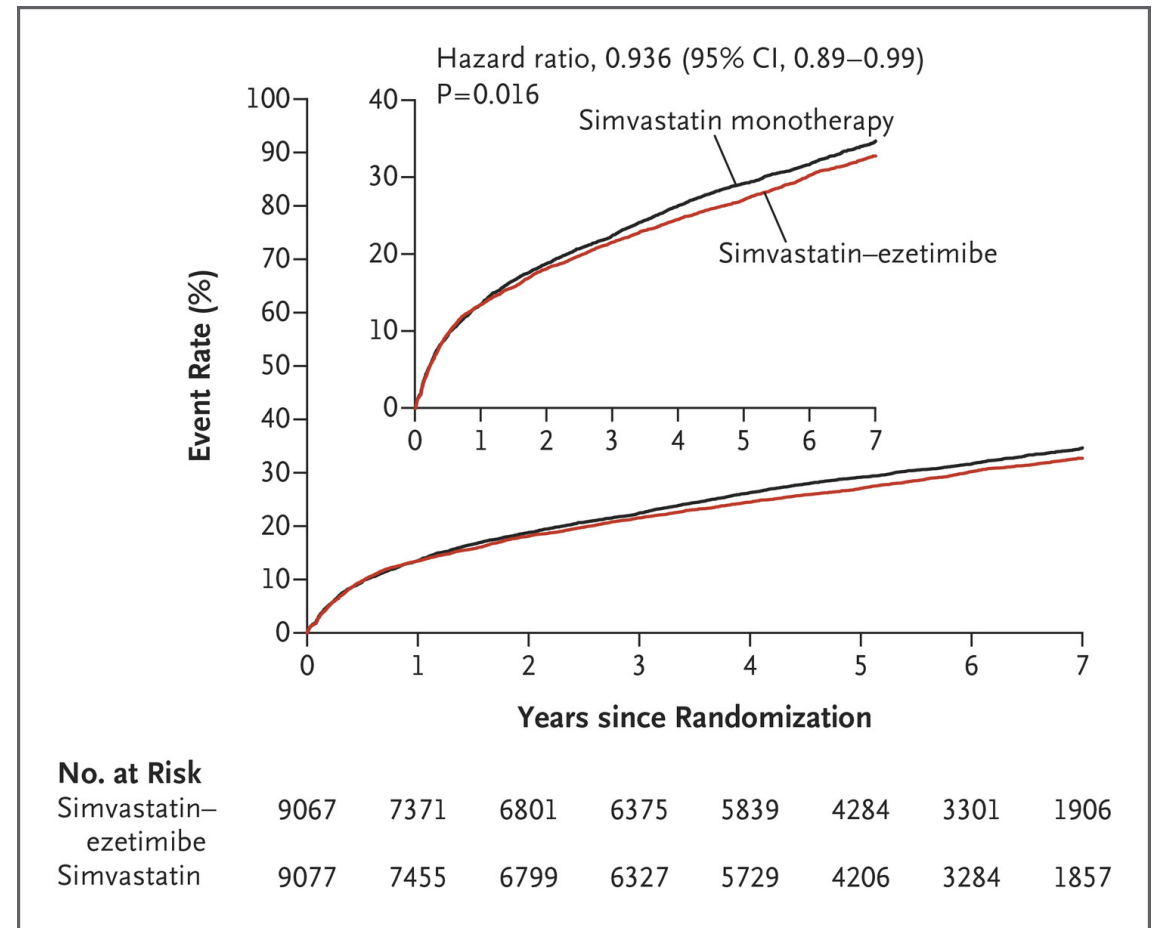
Poor Adherence is Associated with Adverse Outcomes



Ezetimibe is an Option to Help Reach Target and Reduce Risk

- Ezetimibe prevents the absorption of cholesterol at the small intestine brush border
- ↓ LDL-C by ~20% in addition to statin
- **A paucity of side effects and well documented safety profile**
 - Diarrhea, arthralgia, and upper respiratory tract symptoms
- Linked with rare reports of muscle-related side effects but there are no known mechanisms that confirm a causal relationship
- **IMPROVE-IT (Secondary Prevention)**
 - Patients with a recent ACS on statin therapy
 - Ezetimibe 10 mg PO daily vs placebo
 - ↓ MACE (NNT=50 over 7 yr)
 - CV death – not significant

Reduction in the risk of MACE (CV death, MI, unstable angina, revascularization, or stroke)



Bile Acid Sequestrants

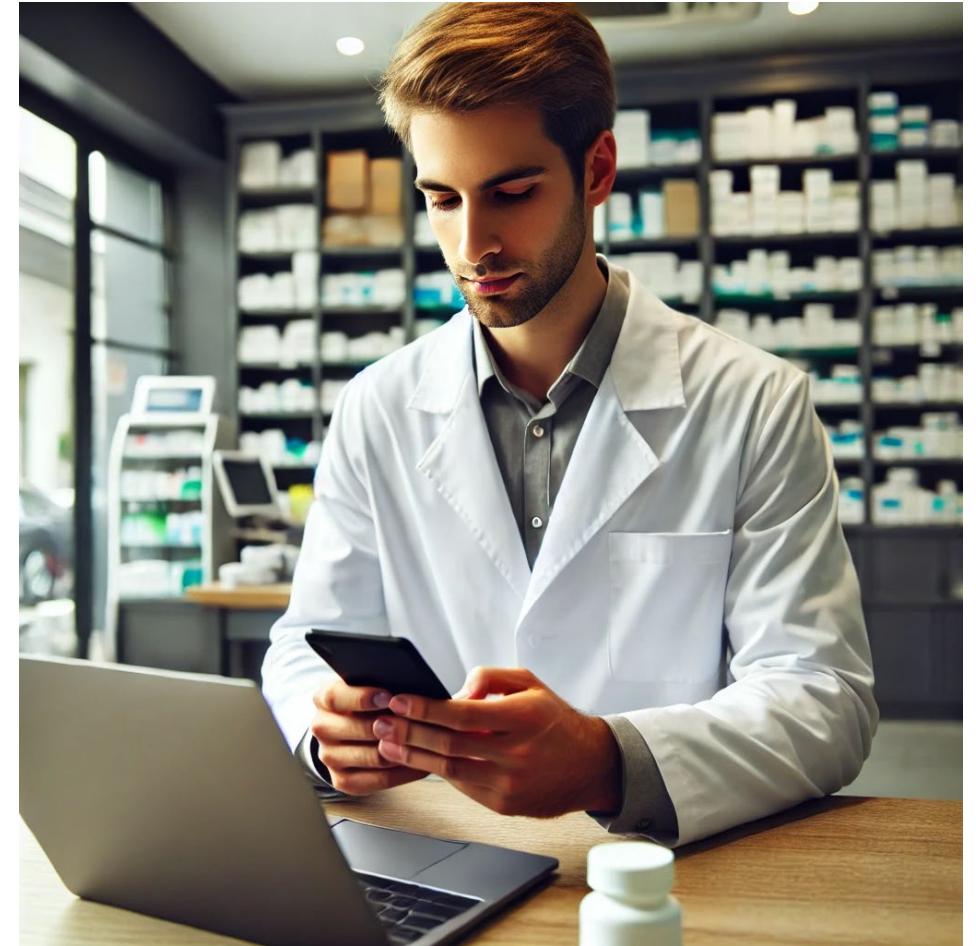
- Prevents the reabsorption of bile acid in the ileum, which results in lowering the LDL-C levels
- Their use is limited due to:
 - The large number of pills
 - Multiple drug-drug interactions
 - Gastrointestinal side effects
 - The need for suspensions
- Includes: colestipol, cholestyramine, and colesevelam
- **Guideline:** We suggest that bile acid sequestrants be considered for LDL-C lowering in high-risk patients whose levels remain above target despite statin treatment +/- ezetimibe therapy
- Adverse effects are common:
 - Bloating, constipation, nausea, and abdominal pain
- Colesevelam, compared to colestipol and cholestyramine, has fewer drug interactions



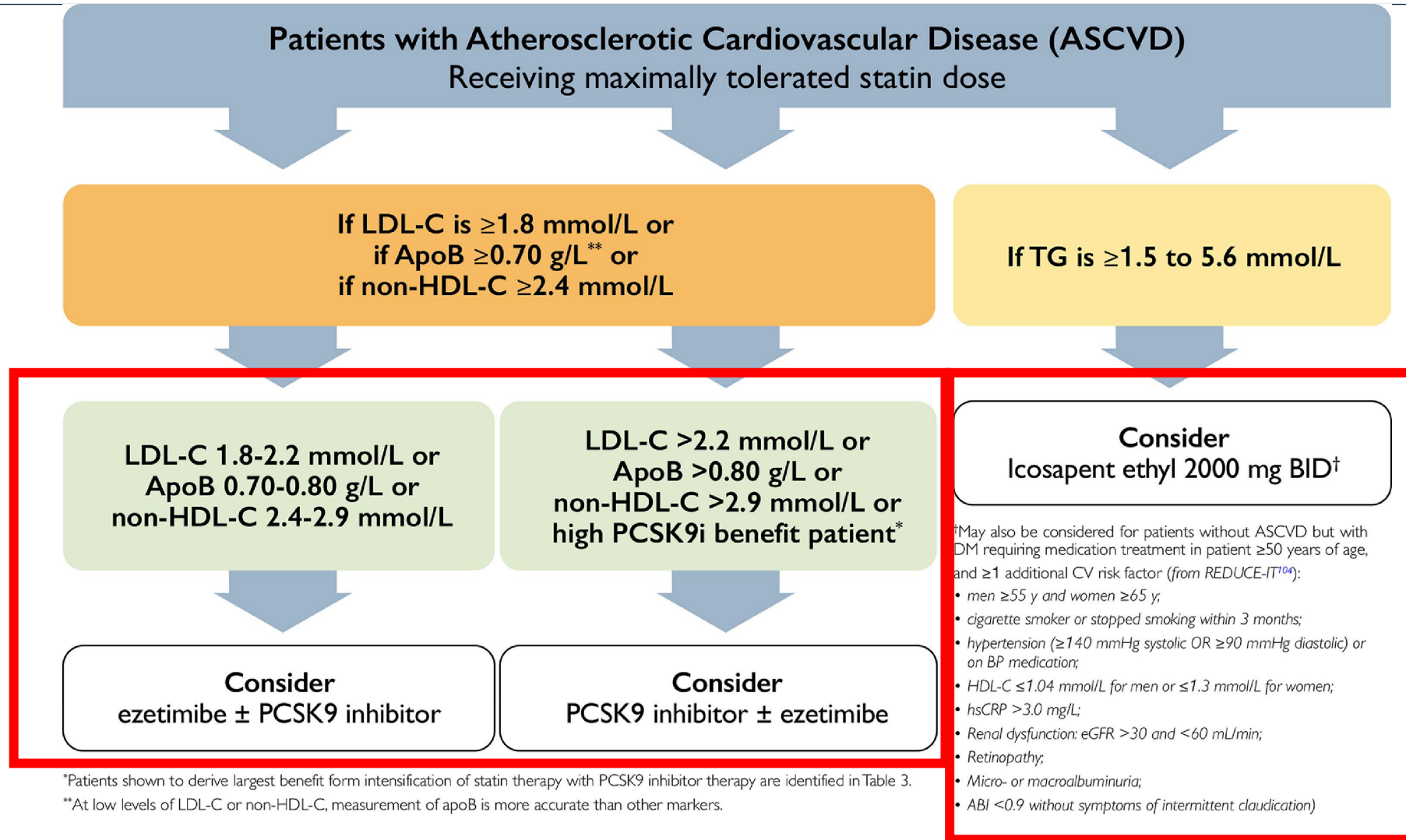
Interactive Question 10

A 64-year-old has an LDL-C level of 2.3 mmol/L, non-HDL-C = 2.9 mmol/L and a triglyceride = 3.8 mmol/L. They are currently taking rosuvastatin 40 mg daily for secondary CV protection. What would be the appropriate course of action? (Select all that apply)

- a) Change to atorvastatin 80 mg
- b) Add ezetimibe
- c) Add PCSK9 inhibitor
- d) Add icosapent ethyl
- e) Add omega-3 supplements

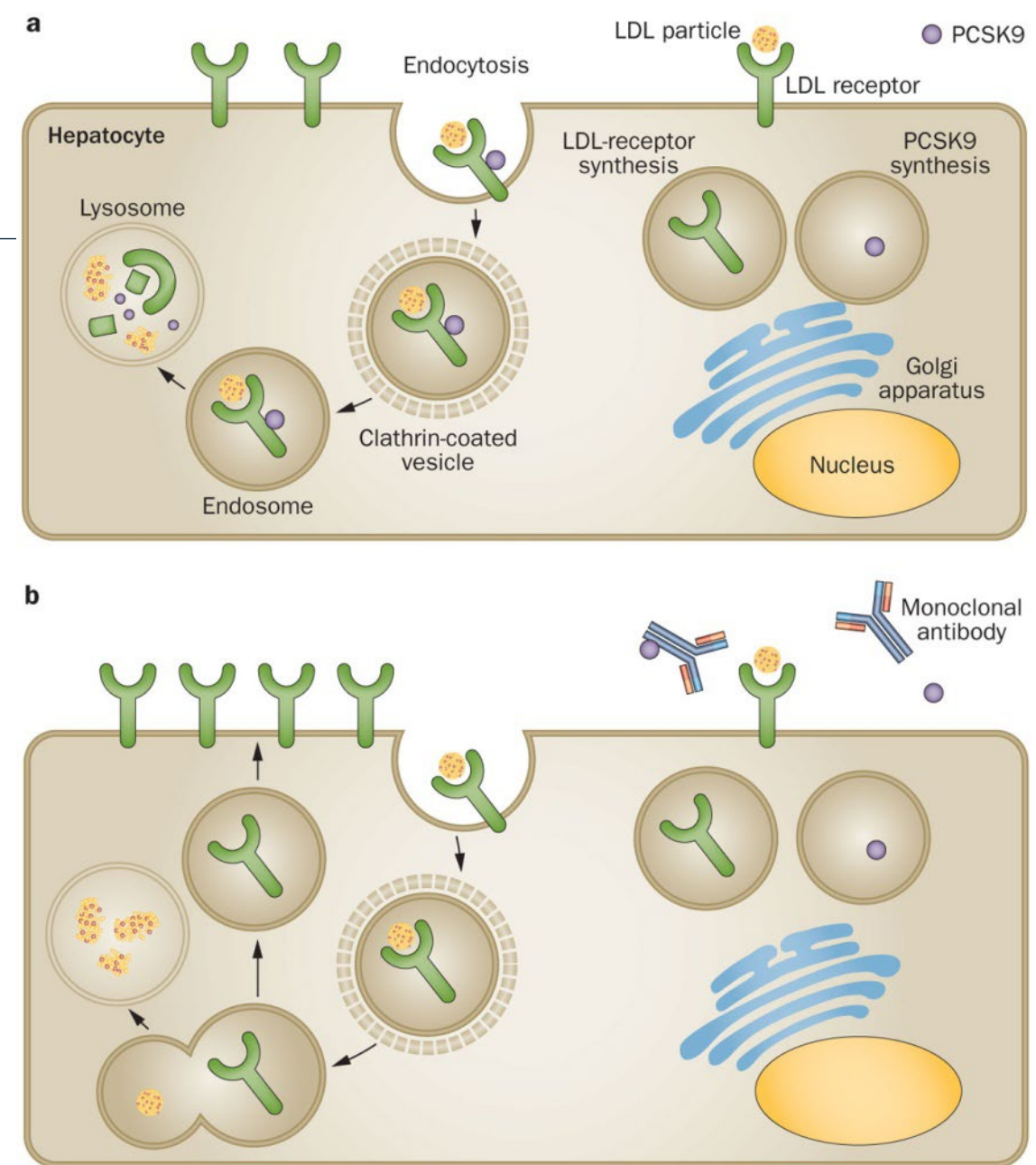


Managing Dyslipidemia in Patients with ASCVD



PCSK9 Inhibitors

- Monoclonal antibodies that bind PCSK9
 - Protein that regulates the breakdown of LDL-C receptor
 - Higher levels = more breakdown of the receptor
- PCSK9i
 - Block PCSK9
 - This allows for more recycling of LDL-C
 - Higher uptake of LDL-C by hepatic tissues and a reduction in circulating LDL-C
- **Addresses the concept that:**
 - High LDL-C is bad
 - Average is not good
 - Low is better
 - Lowest is best

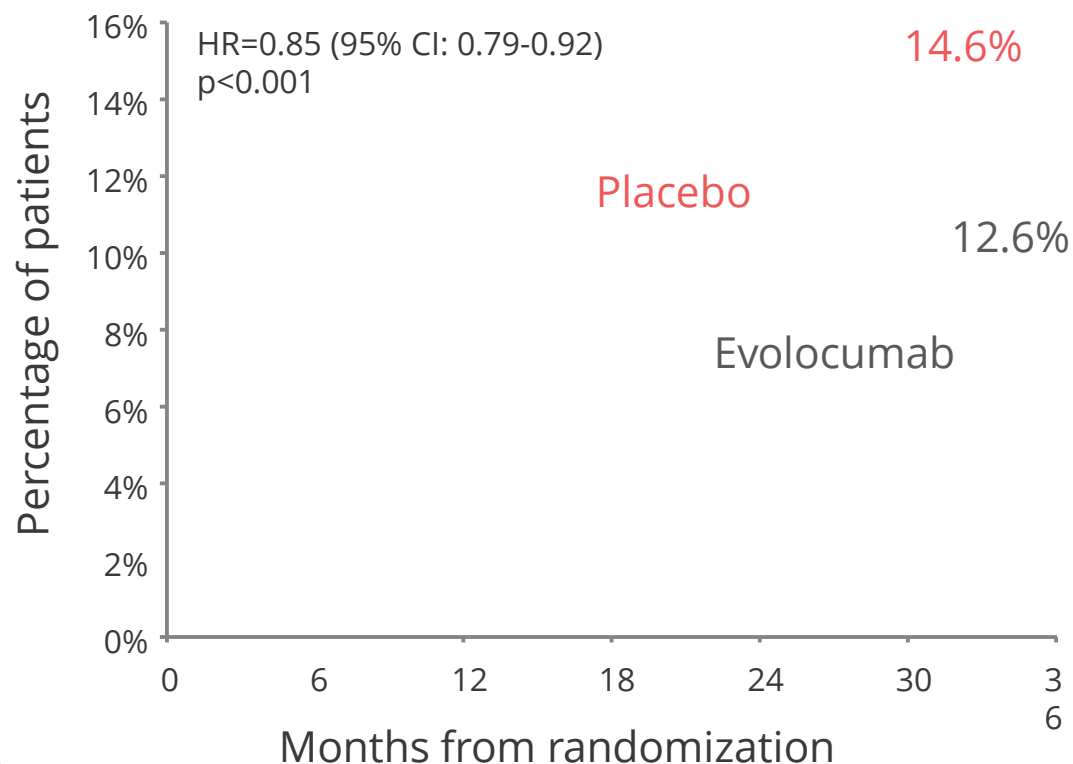


Evolocumab in ASCVD (FOURIER)



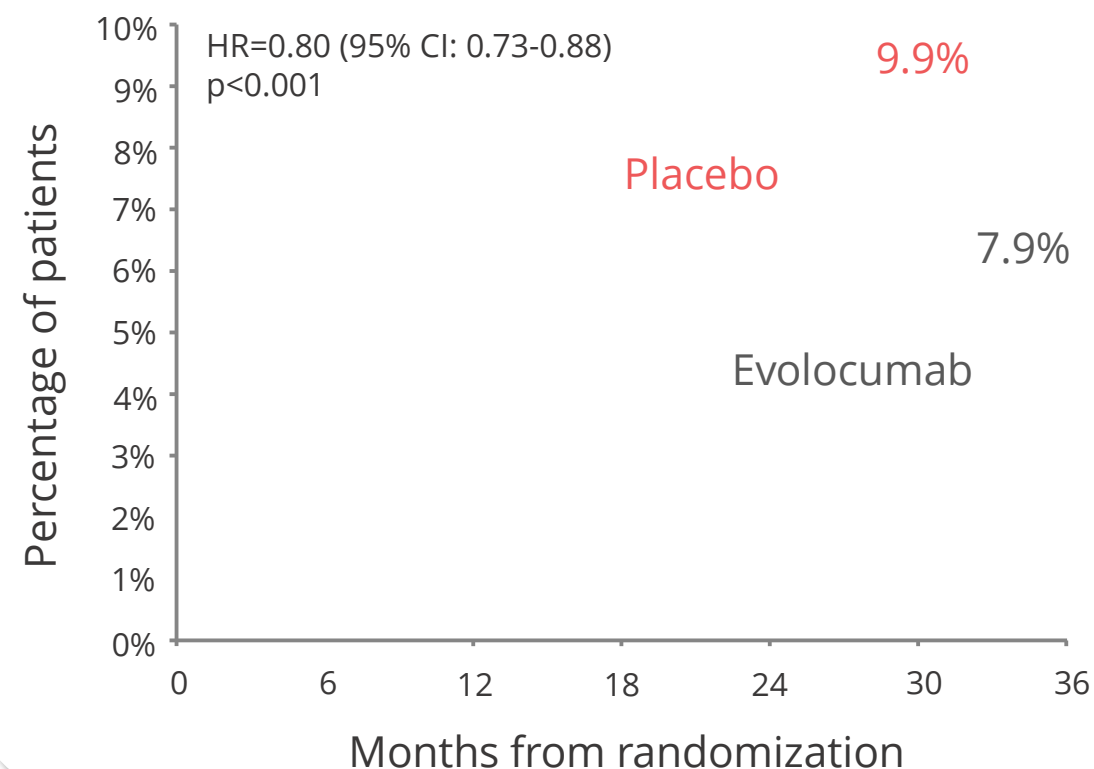
Primary endpoint

CV death, MI, stroke, hospitalization for UA, coronary revascularization

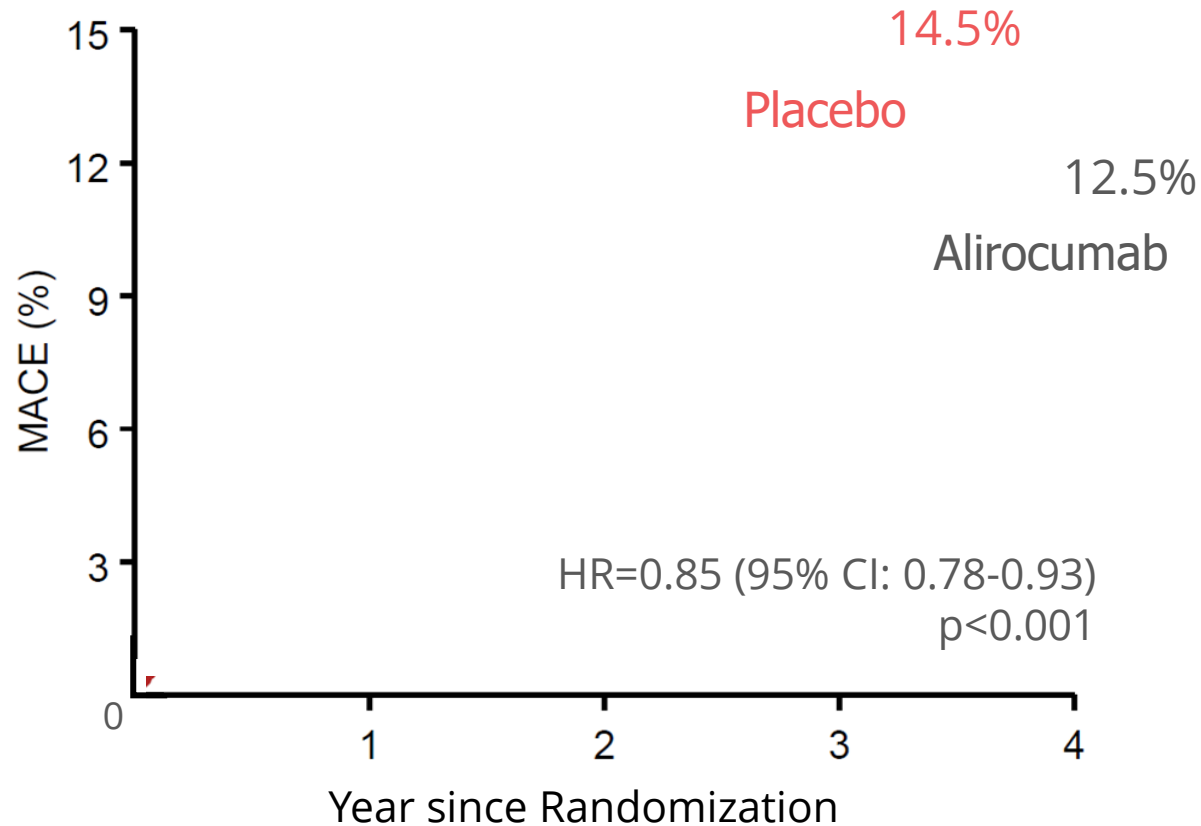


Key secondary endpoint

CV death, MI, or stroke



Alirocumab Post-ACS – ODYSSEY



Primary endpoint

Composite of:

- Death from coronary heart disease
- Non-fatal MI
- Fatal or non-fatal ischemic stroke
- Hospitalization for unstable angina

PCSK9i Summary

- **Dosing**

- Alirocumab: 75 mg SC Q2W or 300 mg Q4W
- Evolocumab: 140 mg SC Q2W or 420 mg Q1M

- **Efficacy**

- Decreases LDL-C by 45% to 65%.
- Decreases apoprotein B by 40% to 50%.
- Decreases lipoprotein (a) by 30% to 40%.
- Decreases triglyceride by 8% to 10%.
- Increases HDL cholesterol by 8% to 10%.
- Increases apoprotein A1 by 4% to 5%
- ↓ MACE (NNT=63-67 over ~2 yr)

- **Adverse effects**

- Generally well tolerated: injection site reactions, nasopharyngitis, headache, upper respiratory tract infection, musculoskeletal pain, back pain, diarrhea, and myalgia.

- **Monitoring**

- After 4 to 8 weeks, repeat an LDL-C level

Patients who can benefit the most from PCSK9i

Recent acute coronary event (ACS)

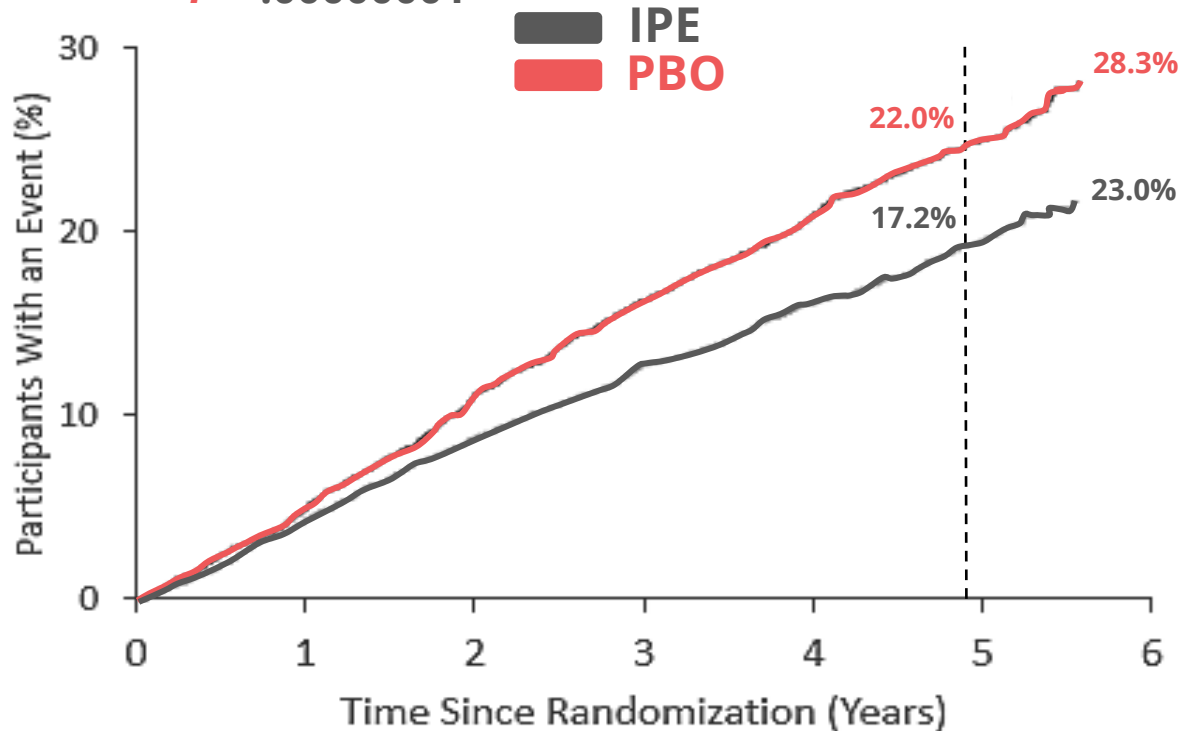
- Hospitalized index ACS to 52 weeks post index ACS

Clinically evident ASCVD and any of the following:

- Diabetes mellitus or metabolic syndrome
- Polyvascular disease (vascular disease in ≥ 2 arterial beds)
- Symptomatic PAD
- Recurrent MI
- MI in the past 2 years
- Previous CABG surgery
- LDL-C ≥ 2.6 mmol/L or heterozygous FH
- Lipoprotein (a) ≥ 60 mg/dL (120 nmol/L)

Icosapent Ethyl Reduces CV Risk in People with ASCVD and Elevated TGs

- **HR (95% CI): 0.75 (0.68-0.83)**
- **ARR: 4.8%**
- **NNT = 21**
- **$P = .00000001$**



Primary composite endpoint:

- CV death
- Non-fatal MI
- Non-fatal stroke
- Coronary revascularization
- Unstable angina

Guidelines Recommend Icosapent Ethyl in Two High-Risk Groups

Patients with diabetes

requiring medication treatment in patient ≥ 50 years of age and ≥ 1 additional risk factor (from REDUCE-IT):

- *Men ≥ 55 y and women ≥ 65 y;*
- *Cigarette smoker or stopped smoking within 3 months;*
- *Hypertension (≥ 140 mmHg systolic OR ≥ 90 mmHg diastolic) or on BP medication;*
- *HDL-C ≤ 1.04 mmol/L for men or ≤ 1.3 mmol/L for women;*
- *hsCRP > 3.0 mg/L;*
- *Renal dysfunction: eGFR > 30 and < 60 mL/min;*
- *Retinopathy;*
- *Micro- or macroalbuminuria;*
- *ABI < 0.9 without symptoms of intermittent claudication*

OR

Patients with Atherosclerotic Cardiovascular Disease (ASCVD)

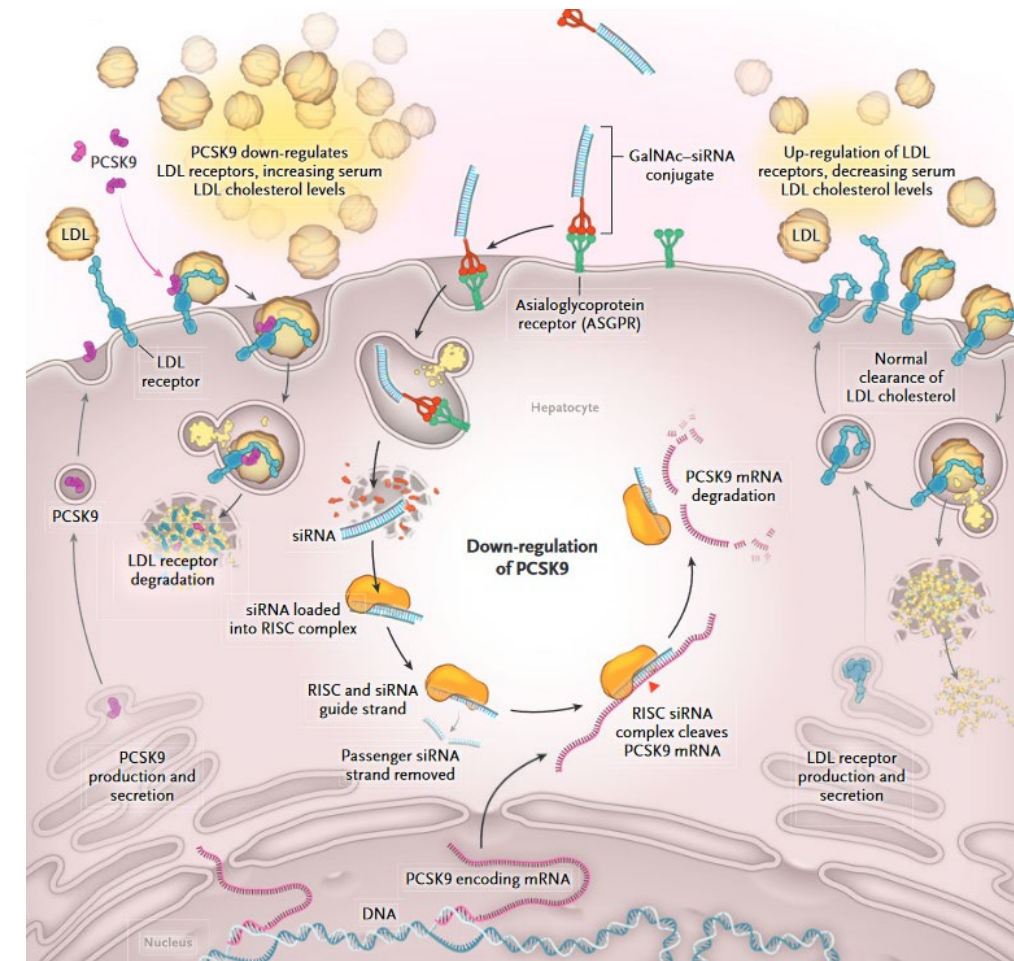
Receiving maximally tolerated statin dose.

If TG is ≥ 1.5 to 5.6 mmol/L

Consider icosapent ethyl 2000 mg BID

Inclisiran

- Targets PCSK9 mRNA in the liver
 - Leads long-term reduction in PCSK9 levels
- Dosing
 - 284 mg SC: Day 0, day 90, then Q 180 days
- Key points
 - Used as adjunct to diet and maximally tolerated statin dose
 - Mean % reduction in LDL-C: 48-52%
 - CV outcome trials have not been completed (2026-2027)
 - No major contraindications or warning in monograph
- Adverse effects
 - Injection site reaction, arthralgia, urinary tract infection, diarrhea, bronchitis, pain in extremities, dyspnea



Putting it all Together

1. What should you do tomorrow?
 - Look for opportunities to lower CV risk in your patientsa
2. Look for people to screen, based on age and conditions
 - If in scope, order labs
 - Remember 1 in 4-5 Canadians don't have a primary care provider
3. Ensure candidates are taking guideline treated therapy
 - Ensure patients are meeting targets – ordering and reviewing labs
 - Holistic approach to CV risk reduction (BP, dyslipidemia, obesity, type 2 diabetes, smoking cessation)
 - Assess and address adherence
4. Crucial for secondary prevention, many will require multiple therapies to reach their targets
 - Dyslipidemia is still a major issue that needs to be regularly addressed and managed
5. Small changes you can make with your patients may have a dramatic effect on their overall CV risk

Thank you



Canadian
Pharmacists
Association

Association des
pharmaciens
du Canada

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