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Plenary - 2021 Updated Approach to Lipid Management

McGill ANNUAL REFRESHER COURSE FOR FAMILY PHYSICIANS | 2021

November 29, 2021

C-CHANGE Health Education Program

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Plenary Development & Disclosures

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Faculty/Presenter Disclosure

- **Presenter:** Rahul Jain, MD CCFP MScCH (HPTE)

- **Relationships with financial interests:**
  - **Grants/Research Support:** none
  - **Speakers Bureau/Honoraria:** none
  - **Consulting Fees:** none
  - **Other:** none

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- **Presenter:** Sheldon Tobe, MD, FRCPC, MScCH, FACP, FAHA

- **Relationships with financial interests:**
  - **Grants/Research Support:** CIHR, KMH
  - **Speakers Bureau/Honoraria:** Astra-Zeneca, Bayer, Janssen, Otsuka, Pfizer
  - **Consulting Fees:** none
  - **Other:** none

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C-CHANGE: The ultimate CV "matchmaker" bringing together the "dream team"

Guideline Groups participating in C-CHANGE

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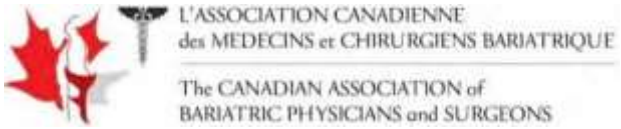

Mitigating Potential Bias

- Altering control over content: information and recommendations given in the program are evidence based and sourced from multiple clinical practice guidelines/scientific professional associations.
- Program material is peer reviewed by a committee with members representative of the target audience.

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Disclosure of Financial Support

- **This program has received financial support from** the Ontario Ministry of Health and Long-Term Care, Public Health Agency of Canada **in the form of** educational grants.

- **This program has received no in-kind financial support**.

- **Potential for conflict(s) of interest: none**

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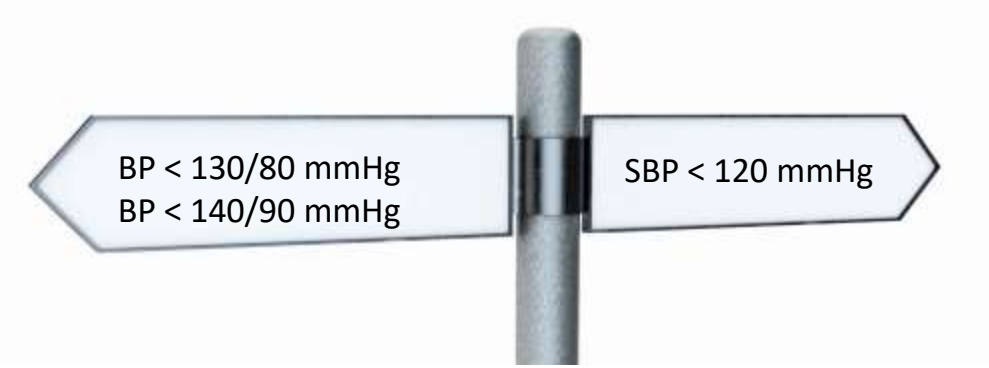
Clinical Practice Guidelines are Signposts, not Policies

The application of an individual guideline recommendation in clinical practice must remain at the discretion of the individual clinician who best knows their patient

- Guidelines help us manage populations
- HCPs should be able to explain a guideline to patient and why it does or does not apply to them
- Person-centred, individualized care informed by evidence/best practice



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Learning Objectives

As a result of attending this session, participants will be able to:

1. Review the updated 2021 Canadian Cardiovascular Society (CCS) Dyslipidemia Guidelines.

2. Develop a step-wise approach to screening and treating patients with dyslipidemia.

3. Identify clinical pearls which can be implemented in your practice to reduce cardiovascular risk.

Pragmatic Approach to Lipid Management – 4 messages

1. Who to screen for risk of ASCVD
2. How to screen for ASCVD risk

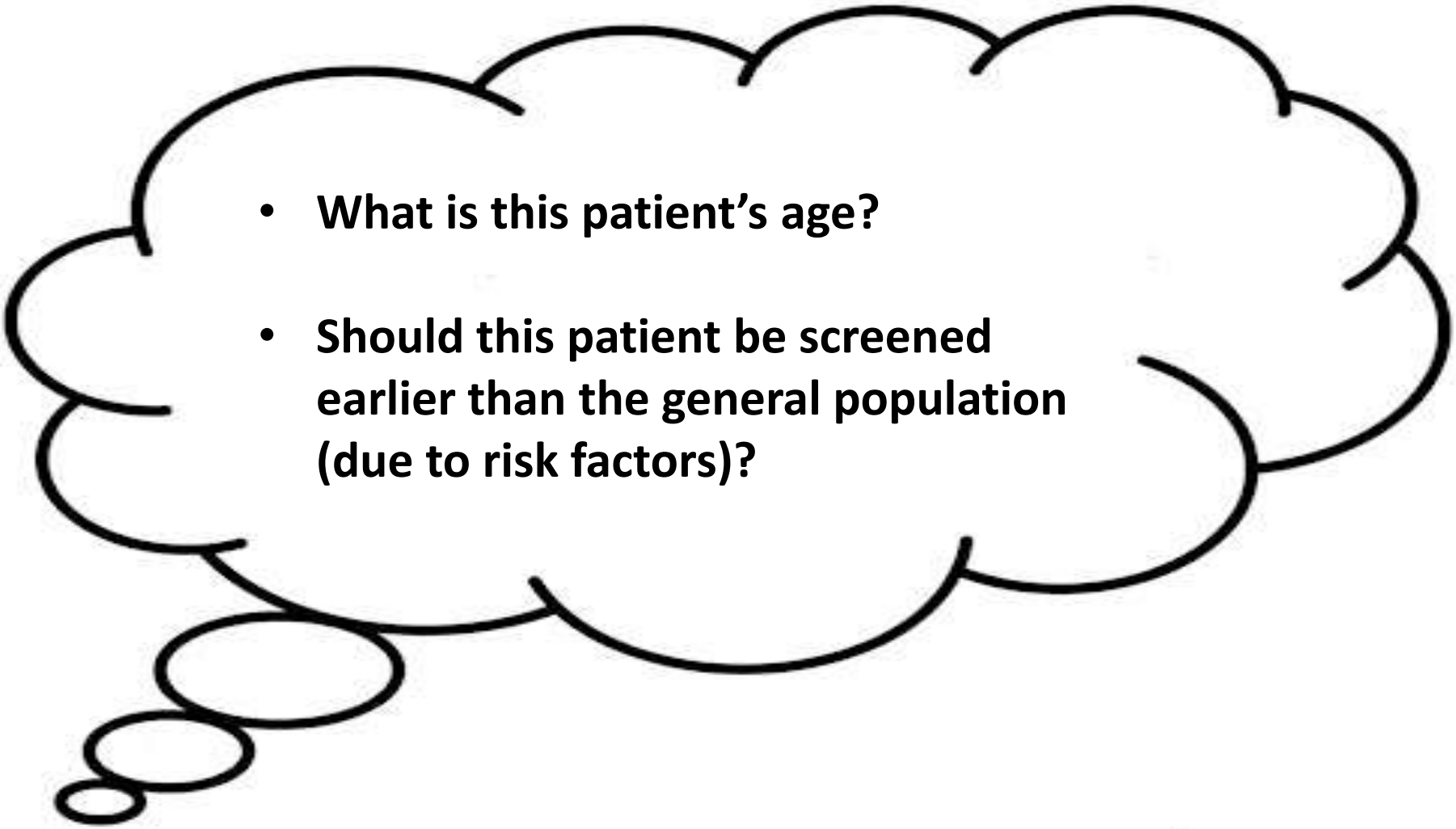
Screening

3. Who to treat to reduce ASCVD risk
4. How to treat patients (lipid guidelines)

Treatment

**** updates/changes to 2021 CCS Guidelines noted (in blue)**

Step 1 - Who to Screen for risk of ASCVD?



- What is this patient's age?
- Should this patient be screened earlier than the general population (due to risk factors)?

Step 1 - Who to Screen for risk of ASCVD?

A. Men and Women ≥40 yrs old (or postmenopausal)
   - consider screening at younger age in Indigenous and South Asian ethnic groups

B. Patient at any age with:

a. Clinical ASCVD
b. Abdominal aortic aneurysm (AAA)
c. Diabetes mellitus
d. Arterial hypertension
e. Current smoking
f. Chronic Kidney Disease
g. Family history of premature CVD in first degree relative (male <55 yrs old; female <65 yrs old)
h. Family history of dyslipidemia (**including elevated Lp(a), especially ≥50 mg/dL or ≥100 nmol/L**)
i. Stigmata of dyslipidemia: tendinous xanthomas (also corneal arcus, xanthelasmas if <45 yrs old)
j. Evidence of preclinical ASCVD (e.g. CACS or carotid ultrasound abnormalities)
k. Chronic obstructive pulmonary disease (COPD)
l. Obesity (BMI ≥30 kg/m^2)
m. Inflammatory diseases (e.g., RA, SLE, PsA, AS, IBD)
n. HIV/AIDS
o. Erectile dysfunction
p. Pregnancy-related complications (hypertensive disease of pregnancy, gestational diabetes, pre-term birth, stillbirth, low birthweight infant, placental abruption)

Step 2 – How to Screen for ASCVD risk (DYSLIPIDEMIA)?

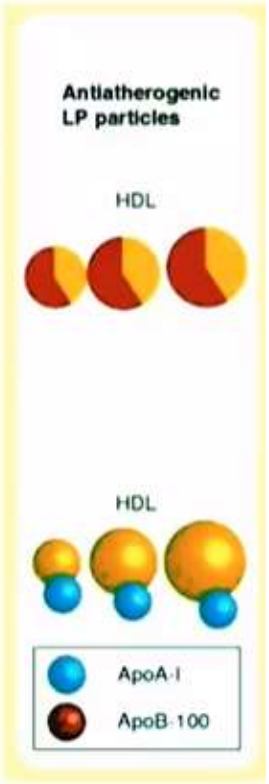
- **What are the standard lipid profile results?**
  - Fasting or non-fasting?
  - When should **non-HDL-C** and **Apo-B** be used in interpretation of results (instead of LDL) and why?
  - What is **Lp(a)**?

Step 2 – How to Screen for ASCVD risk (DYSLIPIDEMIA)

- For all patients:
  - history and physical examination
  - standard lipid profile*:* TC, LDL-C, HDL-C, non-HDL-C*, TG
    - Non-fasting lipid testing is recommended in most adults for screening; however, for individuals with a history of TGs >4.5 mmol/L, fasting lipid levels are recommended.
    - ***it is now generally preferable to follow non-HDL-C or ApoB levels over LDL-C when interpreting lipid results, particularly when TG is ≥1.5 mmol/L**
  - eGFR
  - **lipoprotein(a) -- once in patient's lifetime, with initial screening**

- Optional:
  - Apolipoprotein B (ApoB)
  - Urine ACR (if eGFR <60 mL/min/1.73 m^2, hypertension, or diabetes)

LDL-C measures only a portion of atherogenic particles – although non-HDL or ApoB captures all -



Source: Clin Lipidol © 2011 Future Medicine Ltd

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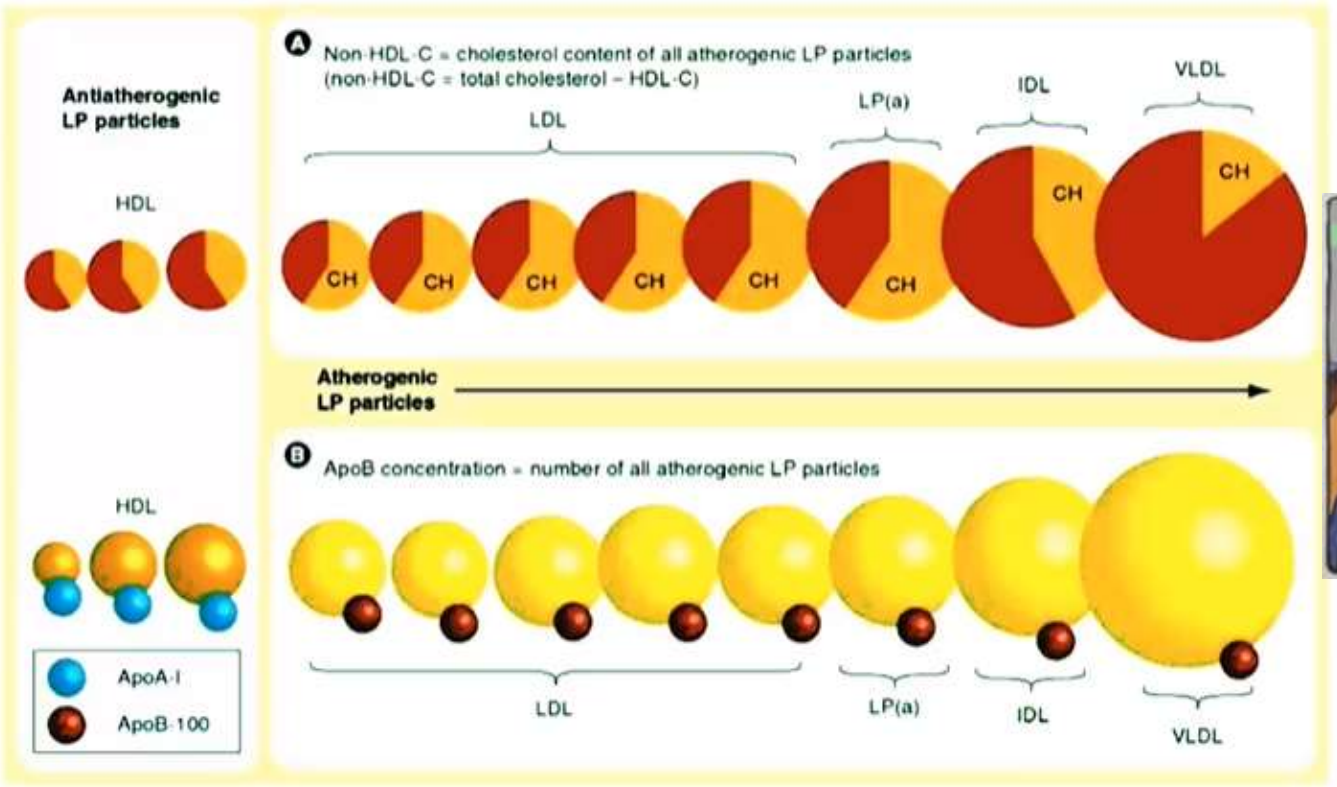

Non-HDL-C = (TC) – (HDL-C)

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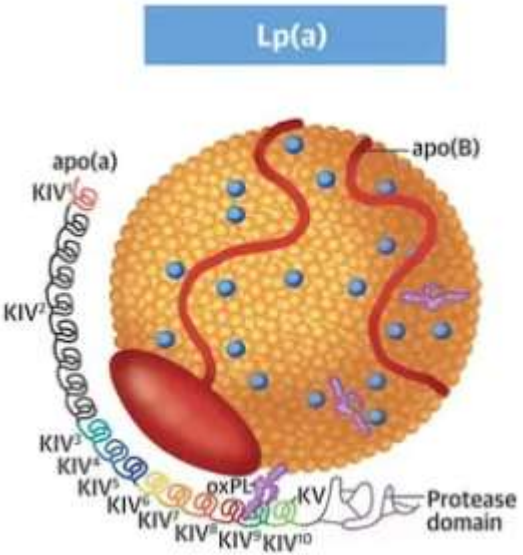
Source: Clin Lipidol © 2011 Future Medicine Ltd

What is Lipoprotein(a)?



Lp(a) = LDL-C + apo(a)

- A "bad" LDL with a "sticky" tail → **highly atherogenic**
  - Poorly correlated with LDL-C
- Lp(a) levels are almost entirely **genetically determined** (levels are determined at birth and remain stable over lifetime).
  - Higher in South Asians, Latin Americans and African Americans
- Independent marker of CV risk (independent of other lipids and risk factors)
  - The higher the Lp(a), the higher the risk for ASCVD and recurrent events
- Most common genetic dyslipidemia
  - Estimated 6 million Canadians have high Lp(a) defined as >50 mg/dL

Lp(a):

Clinical Pearls

- CCS recommends measuring Lp(a) level **once** in a person's lifetime as part of the initial lipid screening

- For all patients with Lp(a) ≥50 mg/dL (or ≥100 nmol/L), this is associated with a >2-fold increased CV risk and thus recommend earlier screening, health behaviour counselling and management of other CV risk factors in the setting of primary prevention.

- **Not a covered benefit** in Ontario and Manitoba, cost is $25-50.
  - Ontario Pilot (Nov 1-Mar 31/21) – ApoB and Lp(a) covered by community labs given evidence from 2021 CCS Lipid Guidelines Update
  (https://www.health.gov.on.ca/en/pro/programs/ohip/bulletins/redux/bul211102.aspx)

- Currently a **marker of risk and not a treatment target** – only test once in each adult's lifetime
  - Patients with high Lp(a) should have **earlier consideration of LDL-lowering therapies** (and be more aggressive in when to start therapy).
  - Possible future therapies reducing Lp(a) (?early thoughts re: PCSK9i)

Step 3 – Who to Treat to reduce ASCVD risk?

Does this patient have a statin-indicated condition?

- **If YES, may be for secondary prevention (i.e. history of ASCVD) or other high risk condition.**
- **If NO, primary prevention patient (risk stratify using Framingham Risk Score).**

Step 3 – Who to Treat to reduce ASCVD risk?

A. Based on Clinical Factors (Framingham Risk Calculation not req'd):

1. Patients with Statin-Indicated Conditions:
   a. Clinical ASCVD *("**secondary prevention**")* or AAA
   b. Diabetes mellitus if >40 yo, or >30 yo with microvascular disease or >15 yrs duration
   c. Chronic kidney disease (non-dialysis, eGFR <60 mL/min or urine ACR ≥ 3.0 mg/mmol)
   d. FH or LDL-C ≥5.0 or non-HDL-C ≥5.8 mmol/L or ApoB ≥ 1.45 g/L

Secondary Prevention

2. Patients with very high TG ≥10 mmol/L and/or history of TG-related pancreatitis → fibrates.

Step 3 – Who to Treat to reduce ASCVD risk?

Primary Prevention

B. Based on Calculation of Framingham Risk Score (FRS):

1. High FRS (≥20%/10yrs) – all patients should be treated with statins

2. Intermediate FRS (10-19.9%/10-yrs) and LDL-C ≥3.5 mmol/L or non-HDL-C ≥4.2 mmol/L or ApoB ≥ 1.05 g/L

3. Intermediate FRS (10-19.9%/10-yrs) and LDL-C <3.5 mmol/L or nonHDL-C <4.2 mmol/L or ApoB <1.05 g/L or other risk enhancers:
   - Men ≥50 yrs and women ≥60 yrs with one additional risk factor: low HDL-C, IFG, high waist circumference, smoker or HTN **or the presence of other risk modifiers: hsCRP ≥2.0 mg/L, CAC >0 AU, family history of premature CAD, Lp(a) ≥ 50 mg/dL (100 nmol/L)**

4. Low FRS (<10%/10-yrs) – statin therapy (beyond health behaviour modification) not recommended for most low-risk individuals, exceptions include:
   - LDL-C ≥ 5.0 mmol/L (or non-HDL-C ≥ 5.8 mmol/L or ApoB ≥ 1.45 g/L) or
   - FRS (5-9%/10 years) LDL-C ≥ 3.5 mmol/L (or non-HDL-C ≥ 4.2 mmol/L or ApoB ≥ 1.05 g/L), particularly with **other CV risk modifiers (e.g., FHx, Lp(a) ≥50 mg/dL [or ≥100 nmol/L] or CAC >0 AU)**

Step 4 – How to treat patients (dyslipidemia)?

**Reminder: multimodal approach to CV risk reduction and addressing all vascular risk factors (BP, glucose, lipids), diet, exercise, weight goals, alcohol and smoking.

- Start with health behaviour modifications
- Pharmacotherapy: Statins
  - Shift from 'targets' to 'thresholds' – *lower is better!*
  - What are 'thresholds to intensify therapy' beyond maximally tolerated statins with Ezetimibe and/or PCSK9i (FH and secondary prevention).
- Reducing Residual Risk: Secondary Prevention (ASCVD) or DM w/ RFs (and elevated TG): Icosapent ethyl (IPE)

Step 4 – How to treat patients (dyslipidemia)?

1. *Health Behaviour Modifications*:
   - behavioural advice and referral where appropriate to:
     - develop a healthy diet including limiting alcohol use;
     - optimizing weight;
     - improving physical activity levels; and
     - promoting smoking cessation

2. *Statins are recommended as the initial lipid-lowering agent of choice for treatment.*
   - maximum dose or maximally tolerated statin should be used for all patients in whom treatment is indicated.

Step 4 – How to treat patients (dyslipidemia)?

Primary Prevention

3. In CV primary prevention of patients with FH, using the thresholds of LDL-C ≥2.5 mmol/L, non-HDL-C ≥3.2 mmol/L, ApoB ≥0.85 g/L, or <50% lowering of LDL-C, consider adding PCSK9 inhibitor, with or without ezetimibe.

4. In other settings of CV **primary prevention**, using threshold of LDL-C ≥2.0 mmol/L, non-HDL-C ≥2.6, ApoB ≥0.80 g/L or <50% lowering of LDL-C, consider adding ezetimibe (or bile acid sequestrant)

Step 4 – How to treat patients (dyslipidemia)?

Secondary Prevention

5. Add therapy in CV secondary prevention, using thresholds of LDL-C ≥1.8 mmol/L, non-HDL-C ≥2.4, ApoB ≥0.70 g/L:

a) Ezetimibe ± PCSK9 inhibitor

- if LDL-C 1.8-2.2 mmol/L, non-HDL-C 2.4-2.9 mmol/L, or ApoB 0.7-0.8 g/L, ezetimibe may suffice

b) PCSK9 inhibitor ± ezetimibe

- PCSK9 inhibitor particularly if LDL-C >2.2 mmol/L, non-HDL-C >2.9 mmol/L or ApoB >0.8 g/L or in very high risk patients who derive the most benefit from PCSK9 inhibitors:

Recent acute coronary event (ACS) • hospitalized index ACS to 52 weeks post index ACS
Clinically evident ASCVD and any of the following: i. diabetes mellitus or metabolic syndrome ii. polyvascular disease (vascular disease in ≥2 arterial beds) iii. symptomatic PAD iv. recurrent MI v. MI in the past 2 years vi. previous CABG surgery vii. LDL-C ≥ 2.6 mmol/L or heterozygous FH viii. lipoprotein (a) ≥ 60 mg/dL (120 nmol/L)

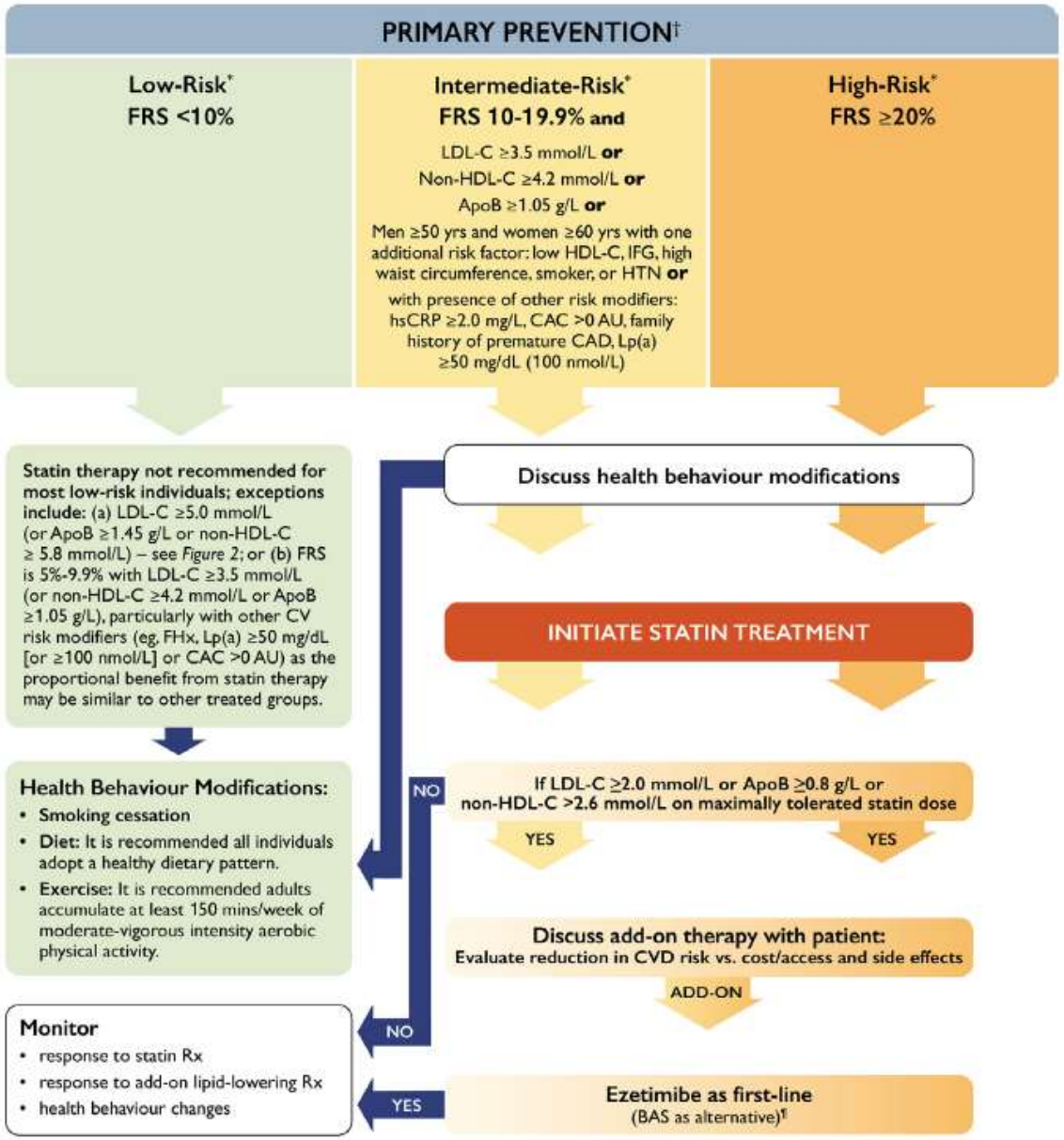
Step 4 – How to treat patients (dyslipidemia)?

6. **Icosapent ethyl in primary prevention patients with diabetes and an additional risk factor or secondary prevention patients when, in both instances, TG is ≥1.5 mmol/L and ≤5.6 mmol/L, on maximally tolerated statin**

7. When icosapent ethyl is not indicated but TG requires management (e.g., very high TG ≥10 mmol/L or concern about TG-related pancreatitis), use micronized fenofibrate

Treatment Approach for Primary Prevention Patients
(without a statin-indicated condition)

Primary Prevention



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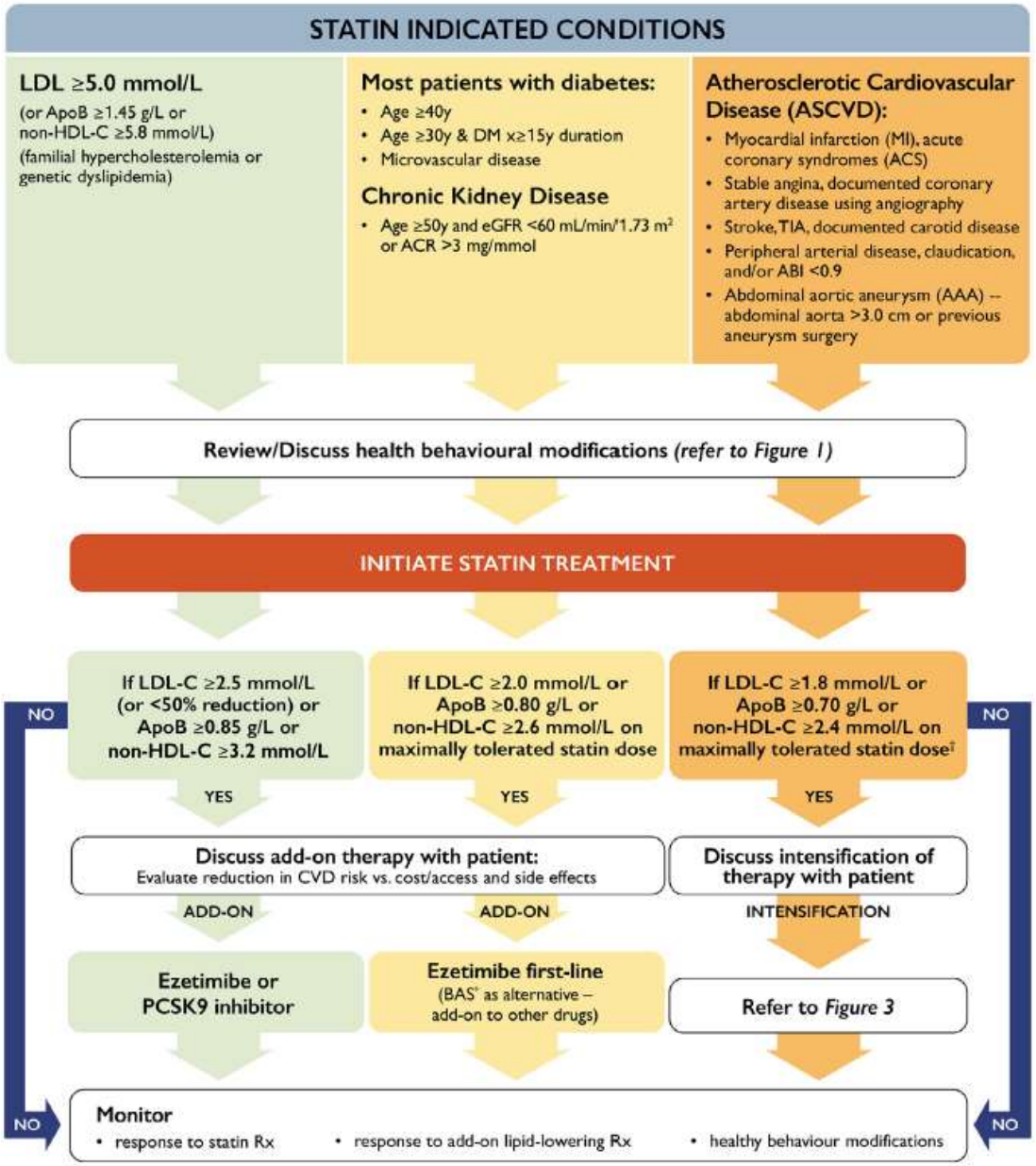
Treatment Approach for Patients with a Statin-Indicated Condition



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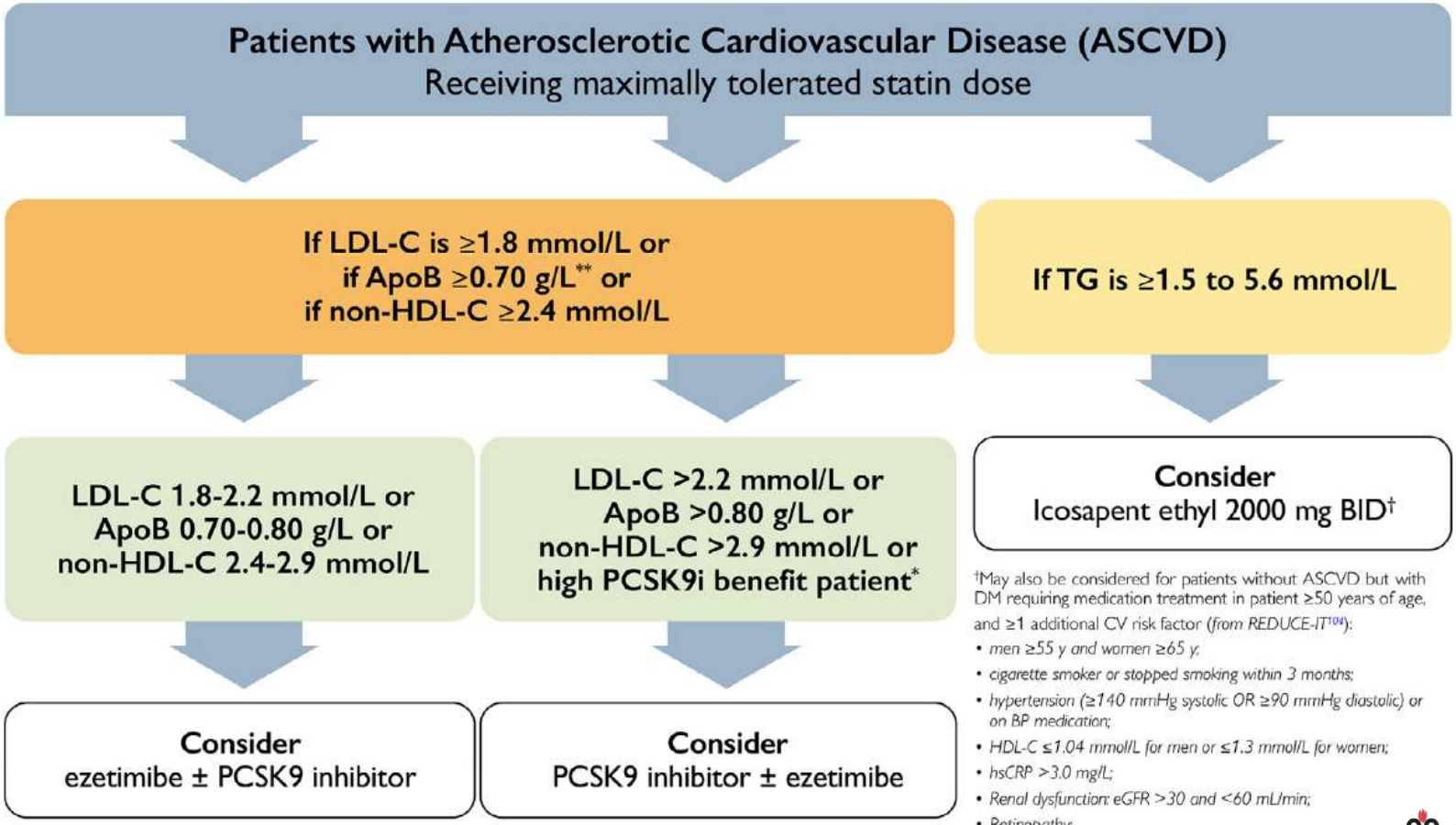
Treatment Intensification Approach for Patients with ASCVD

Secondary Prevention



†May also be considered for patients without ASCVD but with DM requiring medication treatment in patient ≥50 years of age, and ≥1 additional CV risk factor (*from REDUCE-IT*[104]):

- *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)*

*Patients shown to derive largest benefit form intensification of statin therapy with PCSK9 inhibitor therapy are identified in Table 3.

**At low levels of LDL-C or non-HDL-C, measurement of apoB is more accurate than other markers.

Case 1 – Putting it all together

Isabelle

- 50 years old
- HTN
- Non-smoker
- No personal or Fm Hx of ASCVD
- Moderate activity

Primary Prevention Patient

Who to screen?
>40 years old
Hx of HTN

How to screen?
Hx and P/E
Lipid Profile

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Who to screen?
>40 years old
Hx of HTN

How to screen?
Hx and P/E
Lipid Profile

Physical Examination:
BP: 134/82 mmHg
HR: 80 regular
BMI: 27 kg/m^2

Lab Values:
A1c: 5.8%
eGFR: 76 mL/min
Urine ACR: 1.1 mg/mmol
TC: 5.3 mmol/L
TG: 2.3 mmol/L
LDL: 3.3 mmol/L
HDL-C: 0.9 mmol/L
Non-HDL-C: 4.4 mmol/L

Medications:
Perindopril 8 mg po daily
Amlodipine 2.5 mg po daily

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Who to treat?

Does Isabelle have a statin-indicated condition?

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NO

Patients with Statin-Indicated Conditions:

- Clinical ASCVD (*"**secondary prevention**"*) or AAA
- Diabetes mellitus if >40 yo, or >30 yo with microvascular disease or >15 yrs duration
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POLL 1

What is Isabelle's Framingham Risk Score (FRS)?

1) Low
2) Intermediate
3) High
4) Unsure

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Case 1 – Putting it all together

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POLL 1

What is Isabelle's Framingham Risk Score (FRS)?

1) Low
2) Intermediate
3) High
4) Unsure

FRS = 13.7%

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Case 1 – Putting it all together

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HDL-C: 0.8 mmol/L
Non-HDL-C: 4.5 mmol/L

Medications:
Perindopril 8 mg po daily
Amlodipine 2.5 mg po daily

POLL 2

Which lipid parameter best evaluates Isabelle's CV risk?

1) LDL-C
2) Non-HDL-C
3) Apo-B
4) TG
5) Unsure

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Case 1 – Putting it all together

Isabelle

- 50 years old
- HTN
- Non-smoker
- No personal or Fm Hx of ASCVD
- Moderate activity

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POLL 2

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1) LDL-C
2) Non-HDL-C
3) Apo-B
4) TG
5) Unsure

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Medications:
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Amlodipine 2.5 mg po daily

POLL 3

Based on Isabelle's case, which is TRUE regarding who and how to treat (beyond health behaviours)?

1) She is not a candidate for statin therapy based on her profile.
2) She should be Rx a statin due to FRS and LDL-C.
3) She should be Rx a statin due to FRS and non-HDL.
4) Additional info is required to determine need for statin therapy.

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Case 1 – Putting it all together

Isabelle

- 50 years old
- HTN
- Non-smoker
- No personal or Fm

Physical Examination:
BP: 134/82 mmHg
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HDL-C: 0.8 mmol/L
Non-HDL-C: 4.5 mmol/L

PRIMARY PREVENTION†		
Low-Risk* FRS <10%	Intermediate-Risk* FRS 10-19.9% and LDL-C ≥3.5 mmol/L **or** Non-HDL-C ≥4.2 mmol/L **or** ApoB ≥1.05 g/L **or** Men ≥50 yrs and women ≥60 yrs with one additional risk factor: low HDL-C, IFG, high waist circumference, smoker or HTN **or** with presence of other risk modifiers: hsCRP ≥2.0 mg/L, CAC >0 AU, family history of premature CAD, Lp(a) ≥50 mg/dL (100 nmol/L)	High-Risk* FRS ≥20%

POLL 3

Based on Isabelle's case, which is TRUE regarding who and how to treat (beyond health behaviours)?

1) She is not a candidate for statin therapy based on her profile.
2) She should be Rx a statin due to FRS and LDL-C.
3) She should be Rx a statin due to FRS and non-HDL.
4) Additional info is required to determine need for statin therapy.

Case 2 – When treatment intensification is necessary

Brian

- 64 years old
- HTN
- Non-smoker
- CAD – STEMI (3 months ago)

Secondary Prevention Patient

Physical Examination:
BP: 128/74 mmHg
HR: 70 regular
BMI: 32 kg/m^2

Lab Values:
A1c: 5.6%
eGFR: 66 mL/min
Urine ACR: 2.6 mg/mmol
TC: 3.8 mmol/L
TG: 0.9 mmol/L
LDL: 2.6 mmol/L
HDL-C: 0.8 mmol/L
Non-HDL-C: 3.0 mmol/L

Medications:
ASA 81 mg po daily
Ticagrelor 90 mg po BID
Candesartan 8 mg po daily
Bisoprolol 2.5 mg daily
Atorvastatin 80 mg po daily

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POLL 4

Based on Brian's profile, what would be your next course of action (to reduce residual risk)?

1) Nothing at this point – he is on high intensity statin and further LDL-C reduction will lead to little additional benefit.
2) Add ezetimibe.
3) Add a PCSK9 inhibitor
4) Add icosapent ethyl (IPE)
5) Start a combination of the above meds

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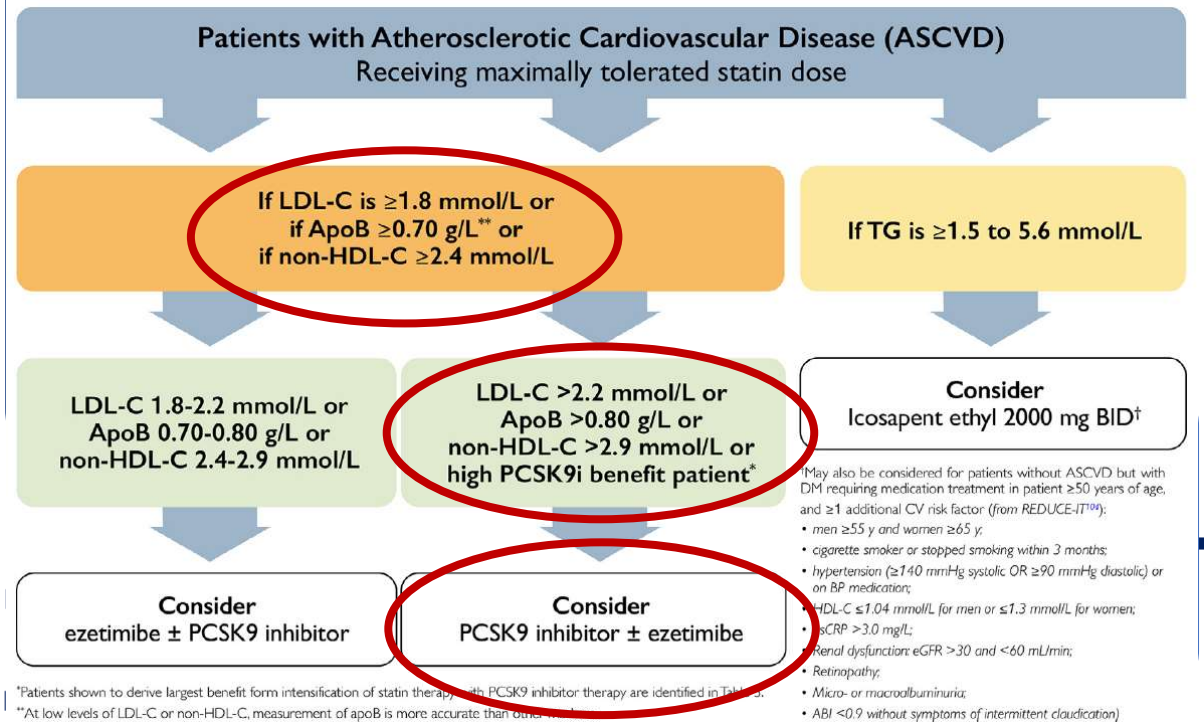

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Pragmatic Approach to Lipid Management – 4 messages

1. Who to screen for risk of ASCVD
2. How to screen for ASCVD risk

Screening

3. Who to treat to reduce ASCVD risk
4. How to treat patients (lipid guidelines)

Treatment

**** updates/changes to 2021 CCS Guidelines noted in blue**

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– Plenary – 2021 Updated Approach to Lipid Management

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November 29, 2021

C-CHANGE Health Education Program

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