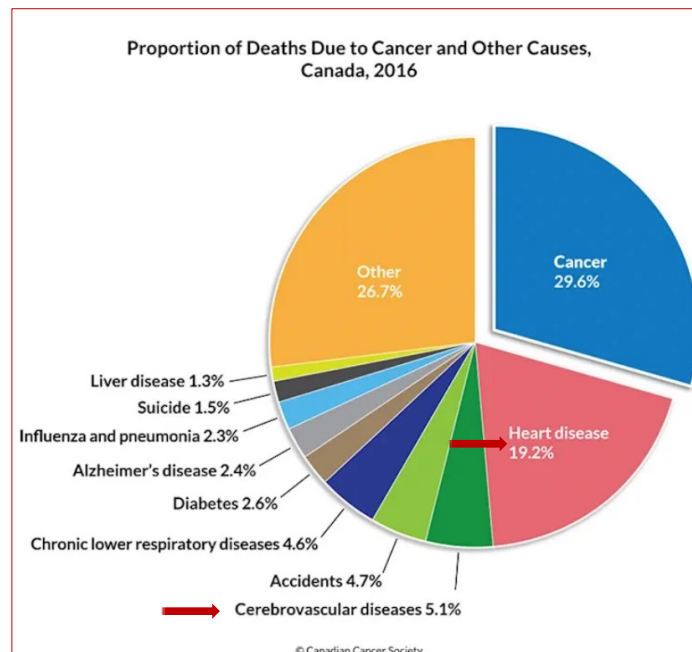


Cholesterol Session Handout

Not to be shared without permission
Information up to date as of November 2023

1

- Heart Disease and Stroke kill approximately a **quarter** of Canadians.
- These are **atherosclerotic** Disease of the Blood Vessels
- High Cholesterol contribute to atherosclerosis



2

ATHEROSCLEROSIS TIMELINE

- Atherosclerosis is a smoldering, **inflammatory disease** of medium to large arteries, **fueled by lipids** (lipids = Fats, including Cholesterol)
- Develops early on in life, and many cardiovascular events take place in young people < 65
- So it's important to alter the disease course as early as possible

3

- Atherosclerosis impacts the **whole body** – e.g. vessels in your legs, abdomen, kidneys etc
- Optimizing Cholesterol Profile with healthy eating patterns and/or medications reduces these complications

Carotid arteries and cerebral arteries

- Stroke
- Transient ischaemic attack (TIA)

• Recurrent TIAs

• Vascular dementia

Coronary arteries

- Acute coronary syndromes (unstable angina and myocardial infarction)

• Stable angina

• Silent ischaemia

Thoracic aorta

- Aortic rupture
- Aortic dissection

Abdominal aorta

- Aortic occlusion (rare)

• Aortic aneurysm

Renal arteries

- Renal artery occlusion (rare)

• Worsening renal function

• Renovascular hypertension

Peripheral arteries (aortoiliac, common or superficial femoral arteries; popliteal, tibial or peroneal arteries)

- Acute peripheral arterial occlusion

• Chronic limb ischaemia

• Intermittent claudication

Superior and inferior mesenteric arteries

- Acute mesenteric ischaemia

• Chronic mesenteric ischaemia

• Abdominal angina

■ Acute presentation

■ Chronic presentation

4

Cholesterol 101: Nomenclature



- Cholesterol = Waxy Substance made by the LIVER and released into the bloodstream
- Cells in your body uses for important function
- Because fats and water (i.e. your blood) don't mix, Cholesterol is stored and carried inside a waterproof carrier made of fat + proteins (lipoproteins)
- Think of lipoproteins as a dump truck carrying load (cholesterol and triglycerides)

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Cholesterol 101: LDL and HDL

Lipids

~~Cholesterol~~
 LDL Cholesterol

HDL Cholesterol
 Chol/HDL (Risk Ratio)
 Non HDL Cholesterol

- **LDL** = **LOW** Density Lipoprotein
- **HDL** = **HIGH** Density Lipoprotein
- **LDL Cholesterol** = Amount of Cholesterol carried inside a Low Density Lipoprotein Truck
- **HDL Cholesterol** = Amount of Cholesterol carried inside a High Density Lipoprotein Truck
- **90%** of Cholesterol that ends up in the artery walls are delivered by LDL particles.
- **HDL particles** can extract it and bring it back to the liver

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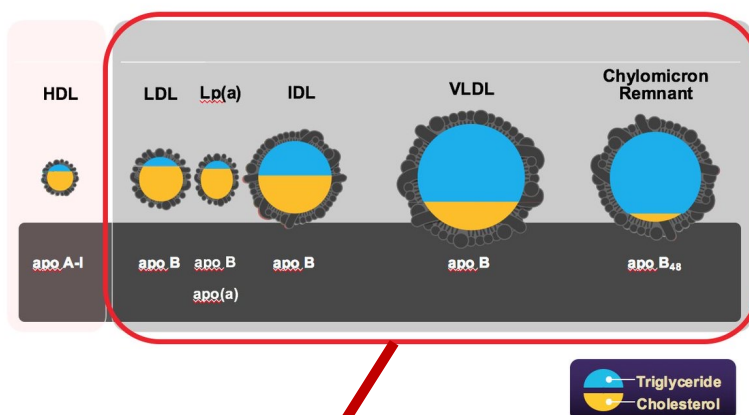
Cholesterol 101: Non-HDL

Lipids

Cholesterol
LDL Cholesterol

HDL Cholesterol
Chol/HDL (Risk Ratio)
Non HDL Cholesterol

Triglycerides



Non-HDL Cholesterol Captures All Lipoproteins known to cause atherosclerosis including LDL-C = My test of choice

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Cholesterol 101: Triglycerides (TGs)

- A type of fat (lipid) in your blood which is used to store unused calories
 - “When you eat, your body converts any calories it doesn’t need to use right away into triglycerides. The triglycerides are stored in your fat cells.
- Hormones release triglycerides for energy between meals.
- If you regularly eat more calories than you burn, *particularly from high-carbohydrate foods*, you may have high triglycerides”
- Why do High Triglycerides matter?
 1. Contribute to Atherosclerosis
 2. Very high TG levels can also cause Pancreatitis
 3. High TGs are often a sign of other conditions like metabolic syndrome, diabetes/prediabetes

*Source: Mayo Clinic

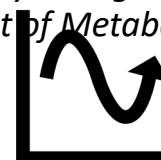
8



Takeaway: Follow these tests over time

- **LDL-C**
 - **Non – HDL-C** or
 - **ApoB** levels **over time**
- “It is now generally preferable to follow non-HDL-C or Apob levels over LDL-C” – 2021 CCS Guidelines

• **Triglycerides** as they are very responsive to dietary changes, and is a component of Metabolic Syndrome



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Framingham Risk Score for Hard Coronary Heart Disease ☆

Estimates 10-year risk of heart attack.

INSTRUCTIONS
There are several distinct Framingham risk models. MDCalc uses the 'Hard' coronary Framingham outcomes model, which is intended for use in **non-diabetic** patients age 30-79 years with no prior history of coronary heart disease or intermittent claudication, as it is the most widely applicable to patients without previous cardiac events. See the [official Framingham website](#) for additional Framingham risk models.

When to Use ▼ Pearls/Pitfalls ▼

Age	55	years
Sex	<input checked="" type="radio"/> Female	<input type="radio"/> Male
Smoker	<input checked="" type="radio"/> No	<input type="radio"/> Yes
Total cholesterol	5	mmol/L ↔
HDL cholesterol	0.91	mmol/L ↔
Systolic BP	128	mm Hg
Blood pressure being treated with medicines	<input type="radio"/> No	<input checked="" type="radio"/> Yes

2.6 % 10-year risk of MI or death for this patient	7 % Average 10-year risk of MI or death
Copy Results	Next Steps

Risk Calculator Most Commonly Used -

Framingham Risk Score (2008 ATPIII)



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Scenario 1: Benefits outweigh Risks of Medications Treatment in High Risk

(Greater Than 20% risk of CV disease in 10 years)

You are likely to benefit from Medications **regardless** of your Cholesterol Level **if**:

- You already have known Atherosclerotic disease
- Your cholesterol level is so high that you likely have a genetic condition
- You had Diabetes for some duration
- You have Kidney disease and are older than 50



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The Official Guideline

STATIN INDICATED CONDITIONS

LDL ≥ 5.0 mmol/L

(or ApoB ≥ 1.45 g/L or non-HDL-C ≥ 5.8 mmol/L)
(familial hypercholesterolemia or genetic dyslipidemia)

Most patients with diabetes:

- Age ≥ 40 y
- Age ≥ 30 y & DM ≥ 15 y duration
- Microvascular disease

Chronic Kidney Disease

- Age ≥ 50 y and eGFR < 60 mL/min/1.73 m² or ACR > 3 mg/mmol

Atherosclerotic Cardiovascular Disease (ASCVD):

- myocardial infarction (MI), acute coronary syndromes (ACS)
- stable angina, documented coronary artery disease by angiography
- stroke, TIA, document carotid disease
- peripheral arterial disease, claudication and/or ABI < 0.9
- Abdominal aortic aneurysm (AAA) -- abdominal aorta > 3.0 cm or previous aneurysm surgery



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Scenario 2: Risks of Taking Medications Outweigh Benefits If you are at Low CV Risk (Less than 5 – 10% Risk of CV disease in 10 years)

- Health Behaviour Modifications
- Smoking Cessation
- Adopt a Healthy Dietary Pattern
- Exercise Regularly

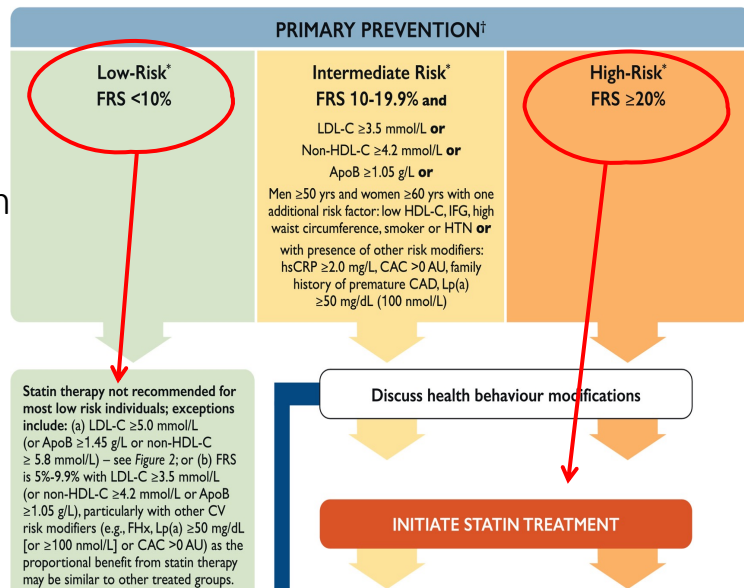
Note: These Recommendations Apply to Individuals at All Risk Levels



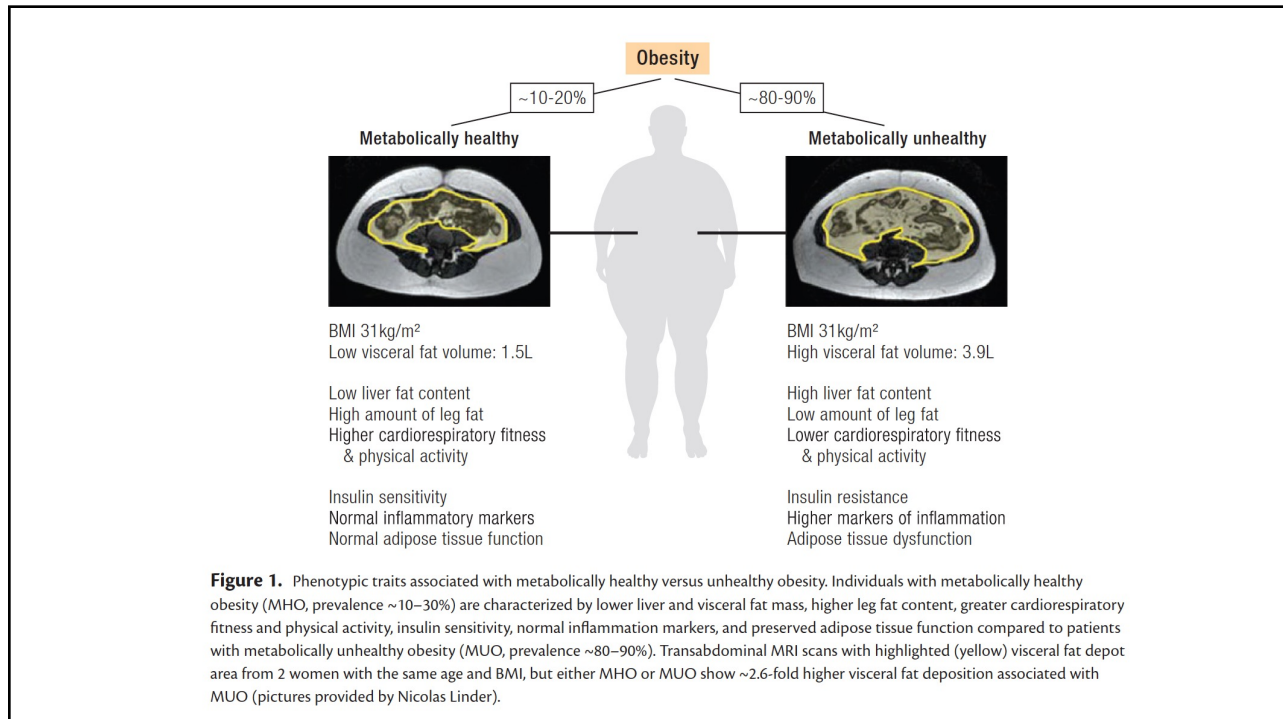
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Scenario 3: You're Somewhere In-between Between 10 – 20 % Risk of CV disease in 10 years

Treatment Approach for Primary Prevention Patients (without a statin indicated condition²)



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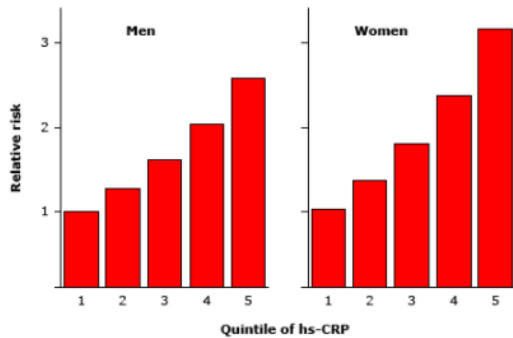
The Following Factors would Favor Cholesterol-lowering Medications:

1. Cholesterol levels are high enough
 - LDL-C 3.5mmol/L or
 - Non-HDL-C ≥ 4.2 mmol/L or
 - ApoB ≥ 1.05 g/L
2. Men ≥ 50 and Women ≥ 60 yrs with any one of:
 - Low HDL-C
 - Impaired Fasting Glucose
 - Elevated Waist Circumference
 - Smoker
 - Hypertension
3. Presence of "Risk Modifiers"
 - **CRP** ≥ 2.0 mg/L – an *Inflammatory Marker*
 - **Coronary Artery Calcium Score** > 0
 - **Family History** of Premature CAD → Multiply your base risk by 2x
 - **Lp(a)** ≥ 50 mg/dL (100 nmol/L)*

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The C-Reactive Protein (CRP)

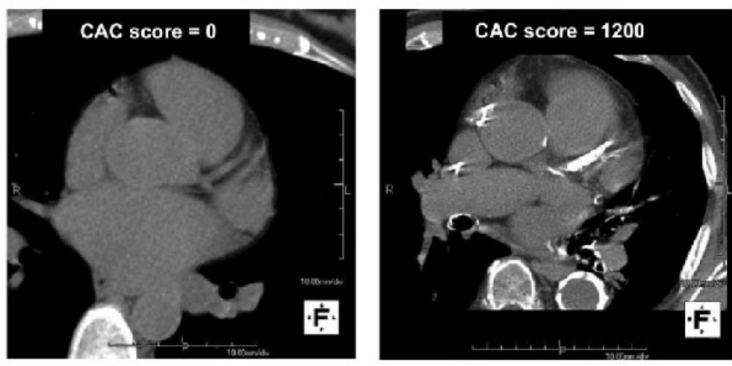
Increasing concentrations of C-reactive protein predict the risk of myocardial infarction



- An Inflammatory Marker
- Goes up with Inflammation (e.g. If you have Rheumatoid Arthritis, Inflammatory Bowel Disease), Infections (Viral or Bacterial), Malignancies
- Also tends to be a bit higher with excess adiposity
- Higher Levels *Linked to* Cardiovascular Disease

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Coronary Artery Calcium Score (CAC)

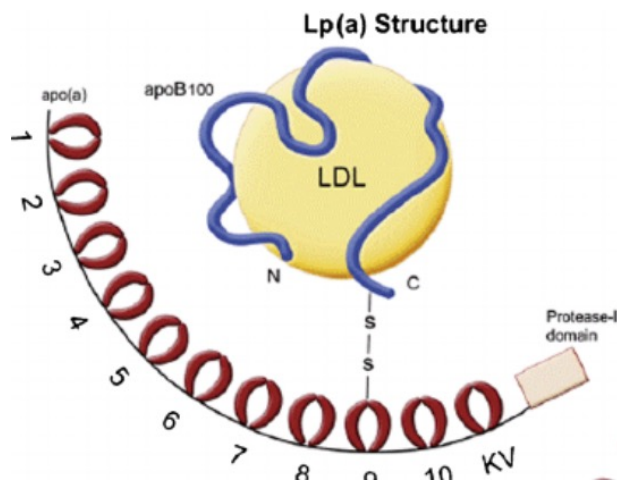


Score	Category
0	No atherosclerosis
1-99	Mild disease
100-399	Moderate disease
≥ 400	Severe disease

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Do you need to have your Lp(a) Tested?

- Essentially an LDL particle with a long tail called apo(a).
- Levels in blood robustly associated with coronary heart disease risk* and mostly determined by a single gene
- Recommend Measuring Lp(a) level once in a person's lifetime as part of the initial screening
- If Lp(a) \geq 50 mg/dL, earlier, more aggressive health behavior modification



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Takeaways

- Your Cholesterol is but one of many factors that determine your cardiovascular risk – it should not be interpreted in isolation.
- The decision is easy if someone is clearly low risk for high risk
- If you fall in the Intermediate Risk Category, have a dedicated discussion with your doctor and consider the additional tests - Lp(a), CRP, Coronary Artery Calcium



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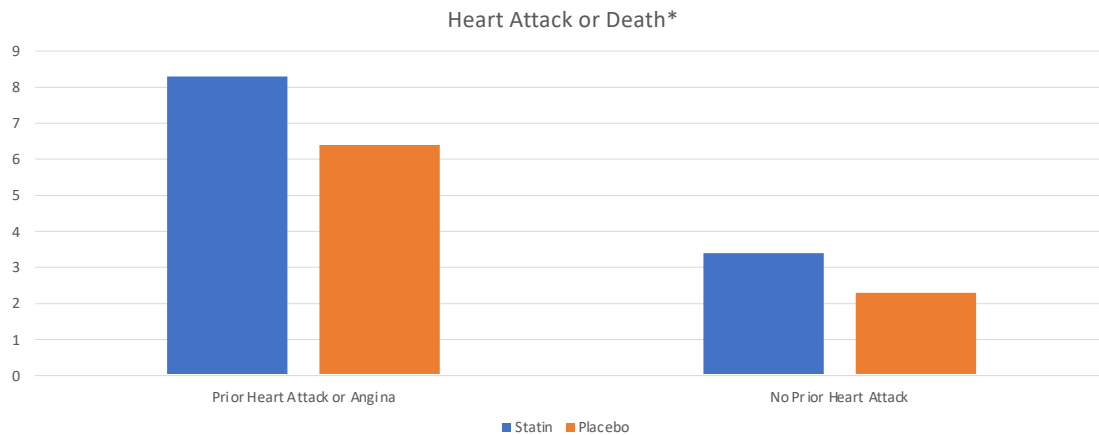
Statins

- Most effective, most commonly used drug for preventing CVD
- One of the best-studied classes of drugs
- Action
 1. Decreases the body's production of cholesterol, and
 2. Increases removal of cholesterol by the liver
- **LDL – cholesterol** reduction: **25 – 55%** (Depending on potency of drug, dosing)
- May also reduce inflammation, stabilize vulnerable Plaque
- Can **lower Triglycerides** and **raise HDL** (variable)
- some foods, such as grapefruit or grapefruit juice, can increase the risk of side effects of statins. - Simva, Lova



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Statins – What's the benefit?



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Statins – Adverse Events: Muscle Aches and/or Weakness

Discontinue, see if symptoms resolve and CK (muscle enzyme) normalizes

Check for Drug Interactions (E.g. CCBs + Simva, Certain Antibiotics, Grapefruit Juice)

Check Thyroid Function, Vitamin D deficiency

Switch to Low potency, water-soluble statin

Alternate Day or MWF dosing

Careful Monitoring for Recurrence

TIP:

- Whenever you start a new drug, remember to check with your doctor for drug Interactions
- If you are on Atorvastatin or Simvastatin, limit your consumption of grapefruit juice to 8 oz (240 mL) or less or ½ a grapefruit or less

Grapefruit juice inhibits intestinal CYP3A4

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Statins – Rarer Adverse Events

- Liver Enzyme Abnormality – Significance unclear as liver failure is extremely rare. Often in the first 3 months.
 - Generally only addressed if Liver enzymes > 3 times normal.
 - We measure liver enzymes prior to starting, routine monitoring not necessary
- New onset Diabetes – *Intensive therapy* associated with 1 additional case of diabetes for every 500 patients
 - Likely due to genetic differences; benefits outweigh risks in most instances
- ?Cognitive Change
 - Mechanism, causal association and incidence not well understood

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Non-Statin Drugs to Lower your Risk

- **Ezetimibe**
 - Works in small intestine selectively blocks cholesterol uptake.
 - 10mg taken any time of day
 - Low Side Effect Rate, Myalgia Rare
 - Most commonly used after statins, either as:
 - **Add-on** to Statins – additional **20 – 25% lowering** of LDL-C (Synergistic)
 - **An alternative** to statins – 15 - 20% lowering of LDL-c
- **PCSK9 Inhibitors (Evolocumab, Alirocumab)**
 - Blocks an enzyme that breaks down LDL Receptors, i.e. increased clearance
 - Lowers LDL-C by an additional **50-60% on top of statin**
 - **53% lowering CVD events**
 - Injections, every 2 or 4 weeks
 - Currently only covered for familial hypercholesterolemia from BC Pharamcare LCD
 - Costs \$7844/mo



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Who benefits from Ezetimibe or PCSK9 inhibitor?

Current Guidelines recommend Intensification with either Ezetimibe or PCSK9 inhibitors for patients:

- With prior MI/Stroke
- On maximally tolerated statin
- Not Meeting Lipid Targets
 - LDL-C ≥ 1.8 mmol/L or
 - Non-HDL- C ≥ 2.4 mmol/L or
 - ApoB ≥ 0.7 g/L

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Recommended Target Levels if on Treatment

1. You have No Known Atherosclerotic Disease

Includes patients recommended to be on statins due to Diabetes and CKD)

- NonHDL-C < 2.6 mmol/L
- LDL-C < 2.0 mmol/L
- ApoB < 0.8 g/L

2. You have known Atherosclerotic Diseases like:

Prior Heart Attack, Stroke or TIA, Leg or Neck Vessel narrowing or Aortic Aneurysm
– Even if found incidentally on imaging

- NonHDL-C < 2.4 mmol/L
- LDL-C < 1.8 mmol/L
- ApoB < 0.7 g/L

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CCS Guidelines

Recommended Dietary Patterns

*Note, not a single-nutrient in isolation with the exception of Trans Fats

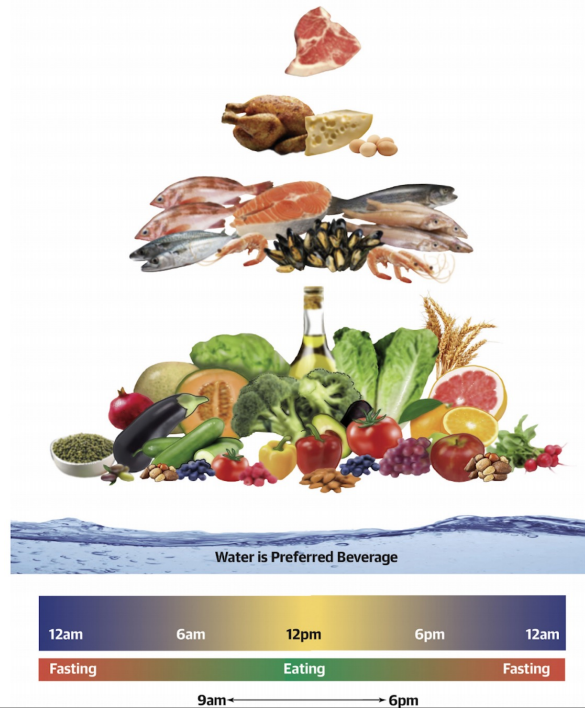
May Lower LDL by up to 17 – 29 %, especially in poor baseline diets

- Mediterranean Dietary Pattern
- Portfolio Diet or other Plant based
- Dietary Approaches to Stop Hypertension (DASH)
- Low-Glycemic (GI)/Glycemic Load (GL)
- Dietary patterns high in nuts, legumes (particularly Soy), olive oil, fruits and vegetables, total fiber and whole grains

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A Pesco-Mediterranean Diet Pyramid

- A primarily plant-based eating plan that includes daily intake of fruits, vegetables, beans and other legumes, nuts, herbs, olive oil and whole grains.
- Animal proteins are eaten in smaller quantities (fish and seafood preferred)
- Olive oil is recommended as the primary added fat, replacing other oils and fats (butter, margarine).



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Portfolio Diet (Vegan Diet)

WHAT DOES THE PORTFOLIO DIET LOOK LIKE?

Expected LDL-Cholesterol lowering:

<p>1 NUTS 45g DAILY</p> <p>All nuts are good for your heart and cholesterol and contrary to concerns do not contribute to weight gain. Add nuts as a snack between meals, adding to salads, cereals, or yogurt. Trying nut butter on your toast is an option. 45g is about a handful of nuts. If allergic to peanuts or tree nuts, try seeds.</p>		<p>• 5 - 10%</p>
<p>2 PLANT PROTEIN 50g DAILY</p> <p>This is the most challenging component of the Portfolio diet. Start by trying to get 25g daily. Consider replacing milk with soy milk, try tofu, soy nuts and beans.</p>		<p>• 5 - 10%</p>
<p>3 VISCOUS (STICKY) FIBRE</p> <p>Aim to eat 2 servings of oatmeal, beans, lentils, and chickpeas a day. Replace bread with rye or pumpernickel or oatcakes. Eat at least 5 servings of fruit and vegetables every day. Aim to eat 2 servings per day of oatmeal, barley, or cereals enriched with psyllium or oat bran. Replace white bread with whole grain oat breads. Put oat bran or psyllium into smoothies. Eat at least 5 servings per day of vegetables (eggplant, okra) and fruit (apples, oranges, berries) high in viscous fibre.</p>		<p>• 5 - 10%</p>
<p>4 PLANT STEROLS 2g DAILY</p> <p>These occur naturally (soyabean, corn, squash, etc.) but to get this amount of sterol you will require fortified foods such as spreads, juices, yogurt, milk and even supplements as part of a meal.</p>		<p>• 5 - 10%</p>

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DASH (Dietary Approaches to Stop Hypertension) Eating Plan

- Eating vegetables, fruits, and whole grains
- Including fat-free or low-fat dairy products, fish, poultry, beans, nuts, and vegetable oils
- Limiting foods that are high in saturated fat, such as fatty meats, full-fat dairy products, and tropical oils such as coconut, palm kernel, and palm oils
- Limiting sugar-sweetened beverages and sweets

<https://www.nhlbi.nih.gov/education/dash-eating-plan>

DASH Eating Plan

The Benefits: Lowers blood pressure & LDL "bad" cholesterol.

Eat This	Limit This
Vegetables	Fatty meats
Fruits	Full-fat dairy
Whole grains	Sugar sweetened beverages
Fat-free or low-fat dairy	Sweets
Fish	Sodium intake
Poultry	
Beans	
Nuts & seeds	
Vegetable oils	

www.nhlbi.nih.gov/DASH



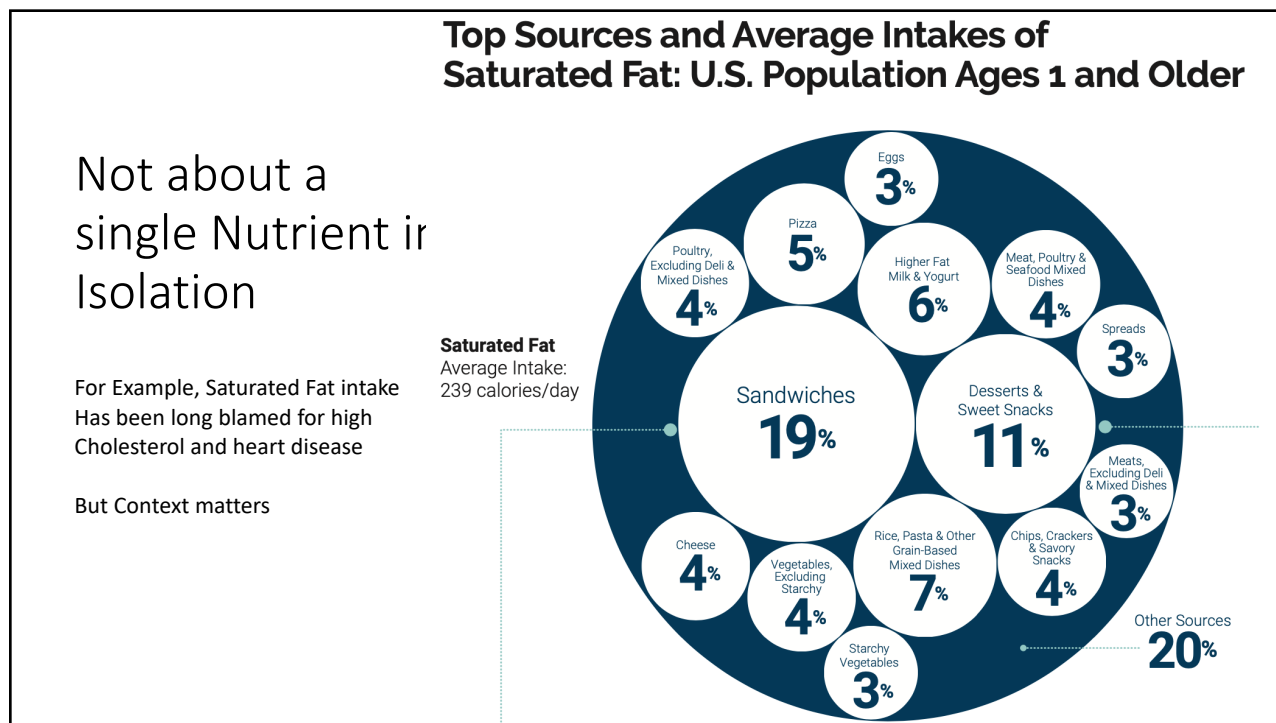
31

Low Carbohydrate Diet

- Roughly around 100g of



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Specific Foods and Dietary Components

- **Dietary fiber** – Certain Soluble fibers reduce LDL cholesterol due to its gel-forming attributes, slower gastric emptying, enhanced excretion of cholesterol and inhibition liver synthesis of new cholesterol.
 - Examples: Psyllium, pectin, wheat dextrin, certain beans, lentils, nuts, and oat products
 - One Analysis showed adding 10g/day of psyllium lowered LDL-c by average 0.33mmol/L
- **Nuts** – High in mono- or polyunsaturated fatty acids (particularly walnuts, almonds, pistachios, macadamia nuts, pecans, and hazelnuts)
- **Soy** – Excellent source of protein and isoflavones, which are phytoestrogens. Only modest benefit when incorporating soy products alone (Tofu, Soy butter, Edamame, Soy burgers)
- **Plant Sterols and Stanols** (Phytosterols) – May lower cholesterol by inhibiting absorption from the gut; but decrease is modest because your liver makes more cholesterol to compensate.
 - Naturally Occurring in Nuts, Legumes, Whole Grains, Fruits, Vegetables and Plant Oil
 - Enriched Products – E.g. Margarins like Becel® Pro-Activ, Benecol – promising addition, but little evidence for safety beyond 2 years. There are patients with rare genetic condition (Sitosterolemia) which makes increased consumptions of plant sterols and stanols

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If You Can't Make Sweeping Changes

INSTEAD OF

- Any Meat In Recipes
- Red Meats
- Refined Grain Products
- Soft drinks and fruit juices
- Dairy Butter

TRY

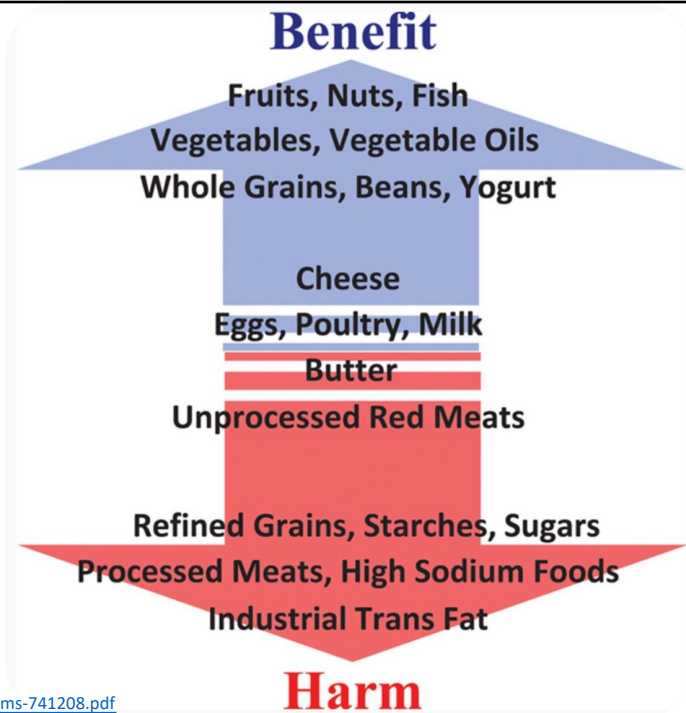
- Soy or other legumes
- Lean Cuts of meats, fish
- Higher Fiber Whole Grain Products
- Tea, Carbonated Water or Plain water
- Nut butter Spread

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A Summary of Evidence-Based Dietary Priorities for Heart and Metabolic Health

- You can adapt your current diet to fit this list or
- Pick any of the recommended eating patterns that suit your palate and lifestyle the best
- Don't get overwhelmed, there's more similarities than differences among well-formulated diets



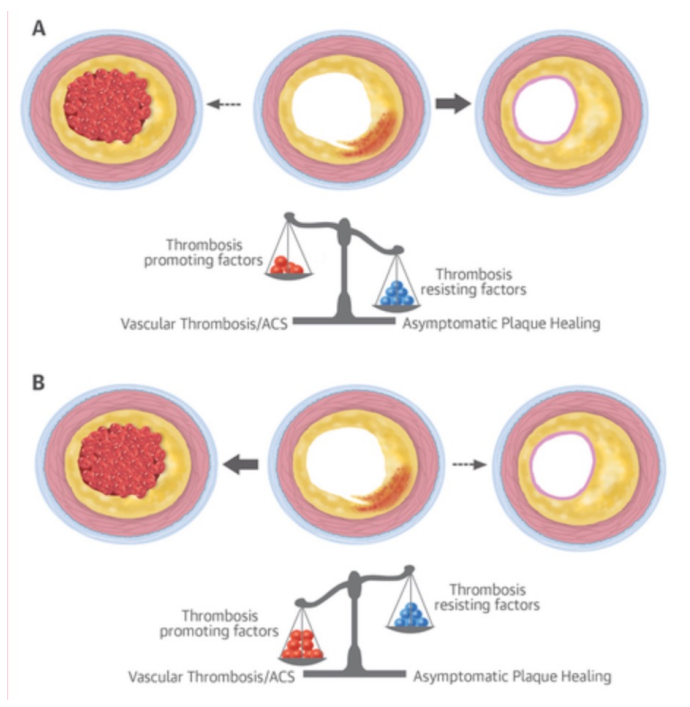
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4814348/pdf/nihms-741208.pdf>

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Let's Pan Out a Bit:
Back to
Atherosclerosis..

A plaque is like a **pimple**
in the artery, rather than
a clogged pipe

Depending on the
balance of factors, it may
heal or pop.



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How are you
managing the
the other
factors that
increases your
Cardiovascular
Risk?

Hypertension

Diabetes

Psychosocial Stressors

Sleep/Sleep Apnea

Smoking

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Key Takeaways

- Track your Non HDL (or Apo B or LDL) and TG Over Time
- Discuss your Cardiovascular Risk with your Doctor, not just cholesterol in isolation
- Everyone regardless of their risk levels benefits from lifestyle interventions
- Dietary pattern likely to improve your outcome includes:
 - High in Fruits, nuts, fish, vegetables, beans/whole grains and yogurt
 - Low in Refined grains, starches, sugars, processed meats, high sodium foods
- High Cholesterol level is a necessary but not sufficient condition for atherosclerotic disease

