UT Southwestern Medical Center

Advanced Lipids

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11/07/2024

Outline

- Questions
- LDL/ApoB/Lp(a)
- Secondary Causes
- Therapeutic Modalities
  - Statin
  - Nonstatin therapies
- Tx for Clinical ASCVD – AKA Secondary Prevention
- Tx for High-Risk Groups
- Tx for Primary Prevention
- Take Home Points

Question 1

A 60-year-old man presents for the routine follow-up of intermittent claudication. He feels well. His medical history includes iliofemoral arterial disease status/post percutaneous revascularization, hypertension, hypercholesterolemia, and type 2 diabetes mellitus. He quit smoking a few months earlier. His medications include aspirin 81 mg, rosuvastatin 40 mg, lisinopril 20 mg, metformin 1000 mg twice daily, chlorthalidone 25 mg, and varenicline 0.5 mg.

His vital signs are pulse rate 70 bpm, blood pressure 139/81 mm Hg, and respiratory rate 14 breaths/min. His examination findings are remarkable only for decreased pedal and posterior tibial pulses. Laboratory evaluation findings include total cholesterol level 170 mg/dL, high-density lipoprotein cholesterol (HDL-C) level 34 mg/dL, low-density lipoprotein cholesterol (LDL-C) level 98 mg/dL, and triglyceride (TG) levels 190 mg/dL. His calculated 10-year atherosclerotic cardiovascular disease (ASCVD) risk is 24% using the Pooled Cohort Equation.

The addition of which one of the following is most appropriate for this patient?

A. Niacin
B. Clopidogrel
C. Fish Oil
D. Ezetemibe
E. Vitamin E

Question 2

A 54-year-old man with hypertension and myocardial infarction 11 months prior treated with stenting of the posterior descending artery is seen in clinic for routine follow-up. He denies any chest discomfort or dyspnea with activity. He would like to reduce his medications if possible. Since his previous visit 6 months prior, he has been diagnosed with diabetes mellitus, and he asks whether the statin is responsible. His daily medications include aspirin 81 mg, metoprolol succinate 25 mg, lisinopril 10 mg, and atorvastatin 40 mg. On examination, his heart rate is 62 bpm and blood pressure is 112/65 mm Hg. The remainder of his examination is normal. An echocardiogram reveals normal left ventricular ejection fraction (LVEF). Creatinine is 0.9 mg/dL and low-density lipoprotein is 68 mg/dL.

What would you advise regarding his medication regimen?

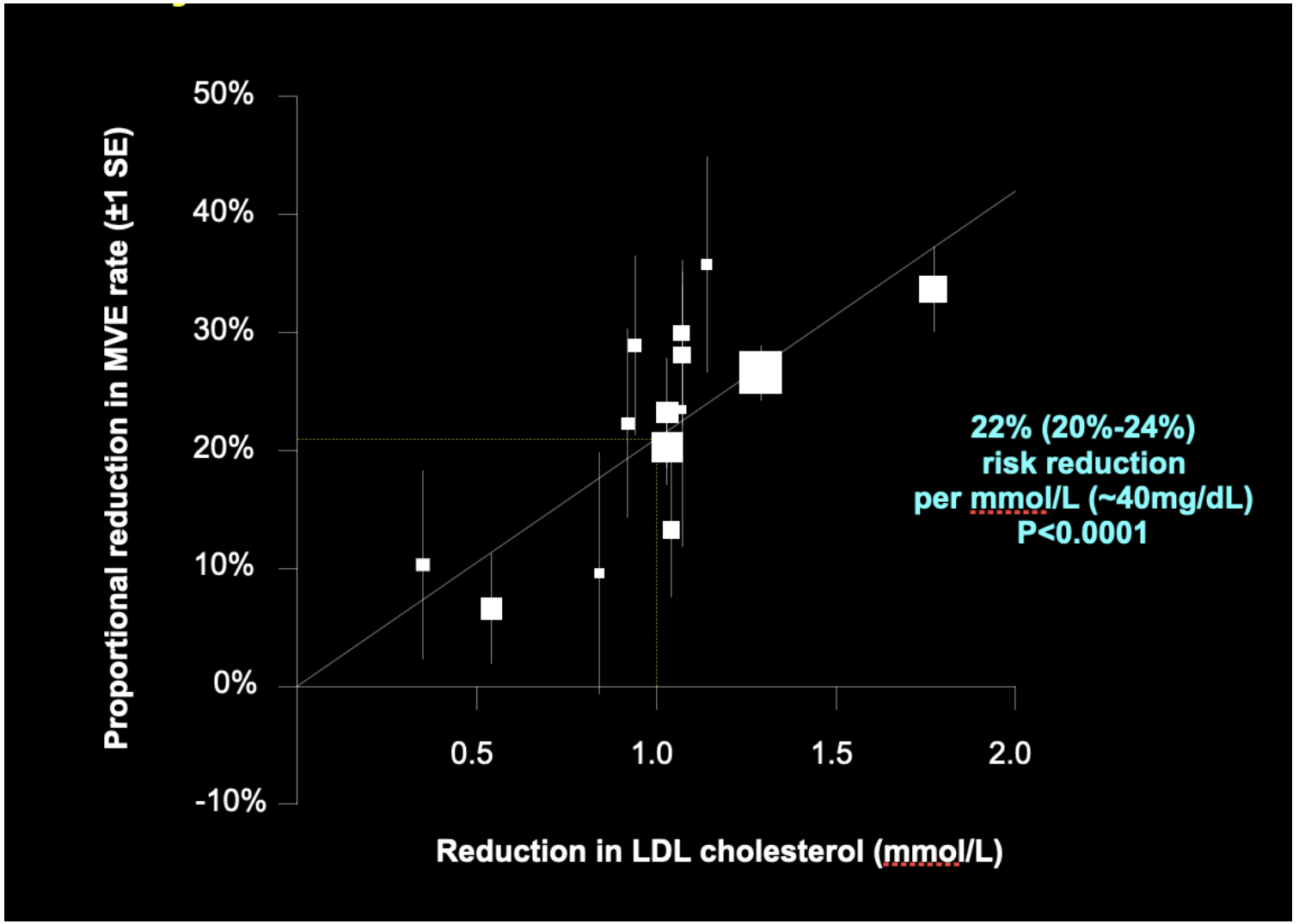
A. Discontinue Aspirin
B. Continue current therapy
C. Discontinue Metoprolol
D. Increase Lisinopril
E. Substitute Ezetimibe for Atorvastatin

Friedewald Equation for Estimating LDL-C

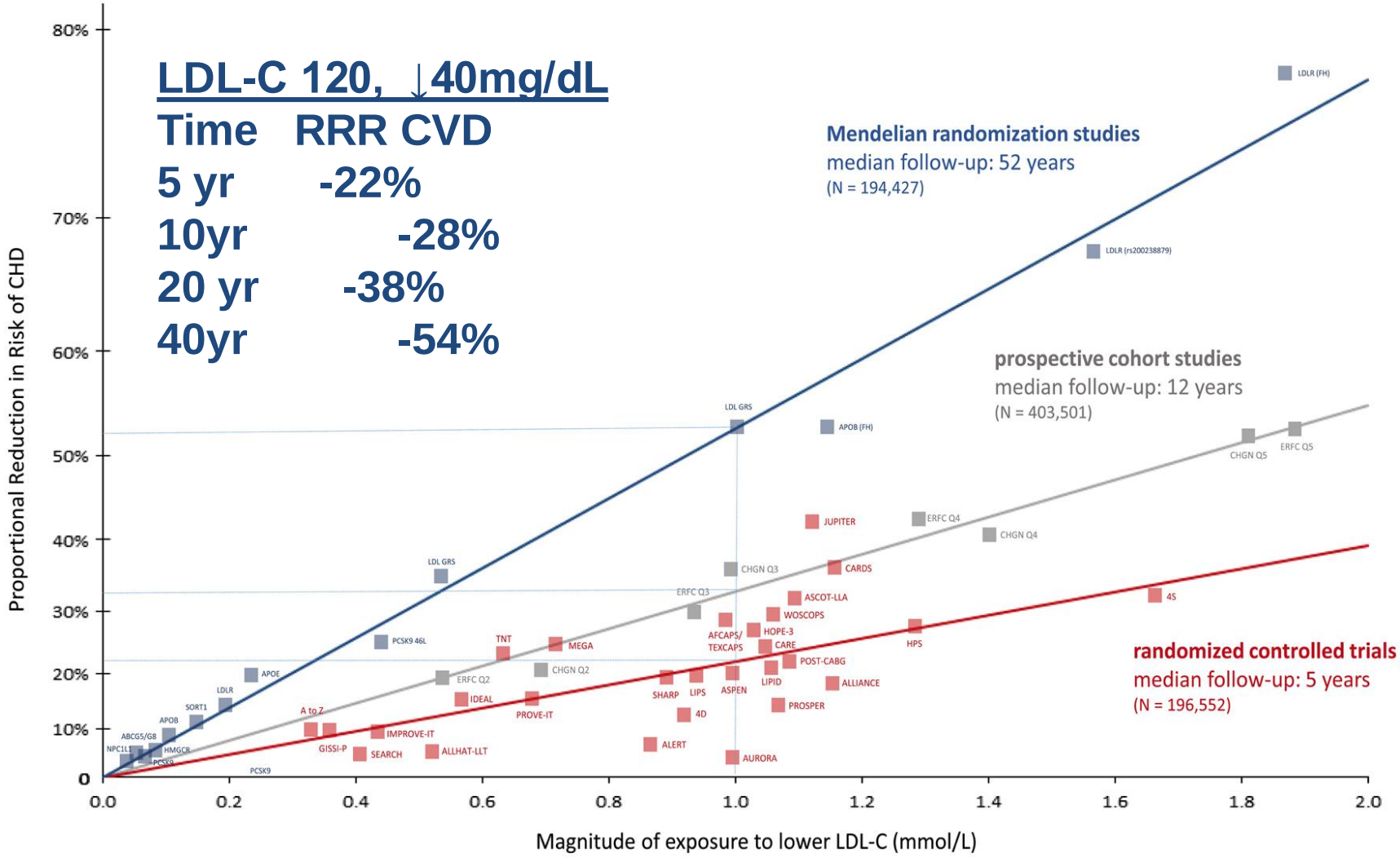
- Current lipid panel = calculated LDL-C
- *Total Cholesterol = LDL-C + VLDL-C + HDL-C*
  - LDL-C = Total Cholesterol – HDL-C - VLDL-C
    - VLDL-C ~ Triglycerides/5 (only for Trig <400)
  - **LDL-C = Total Cholesterol – HDL-C – Trig/5**

I	B-NR	1. In adults who are 20 years of age or older and not on lipid-lowering therapy, measurement of either a fasting or a nonfasting plasma lipid profile is effective in estimating ASCVD risk and documenting baseline LDL-C.[S2.2-1–S2.2-6]
I	B-NR	2. In adults who are 20 years of age or older and in whom an initial nonfasting lipid profile reveals a triglycerides level of 400 mg/dL or higher (≥4.5 mmol/L), a repeat lipid profile in the fasting state should be performed for assessment of fasting triglyceride levels and baseline LDL-C.[S2.2-1–S2.2-4]

CTT Metanalysis: Relation between LDL-C Reduction and Major Vascular Events in 14 statin trials



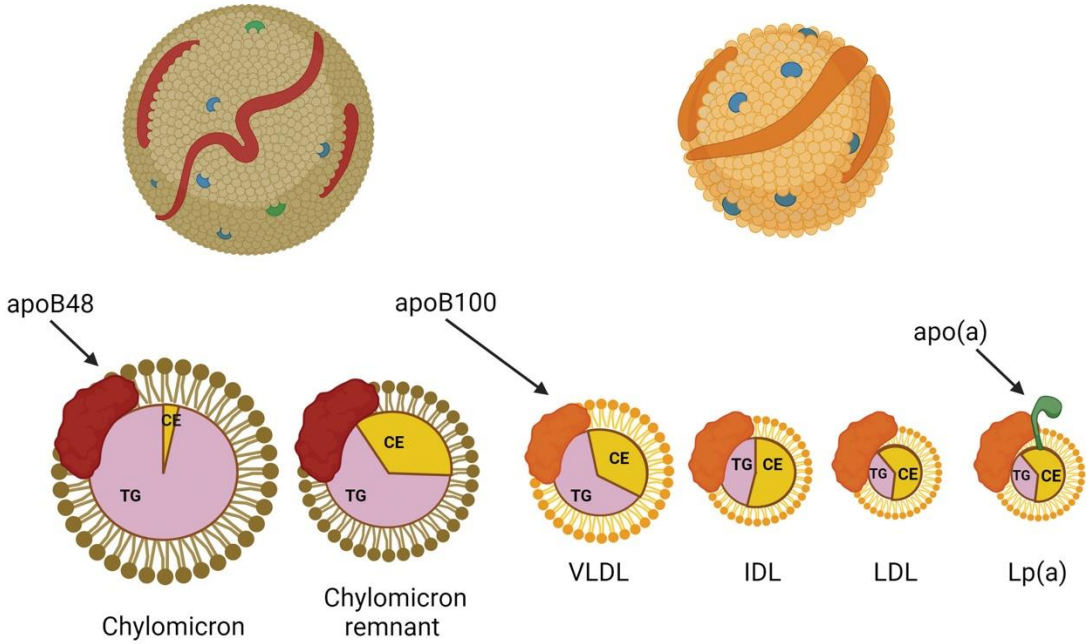
LDL-C Lowering-Not Just How Low, But How Long



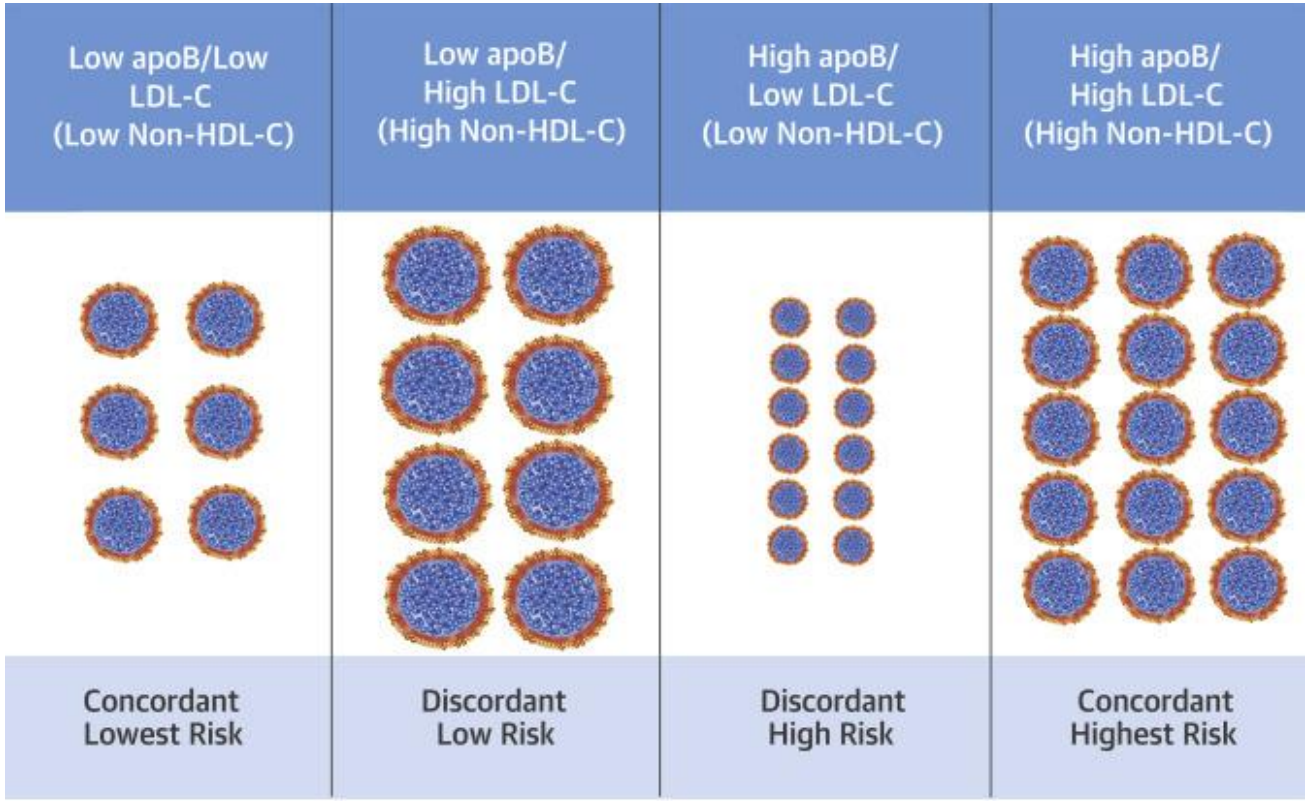
Ference B et al. *Eur Heart Journal 2017*;38:2459–2472.

ApoB

- ApoB is the major apolipoprotein embedded in LDL and VLDL



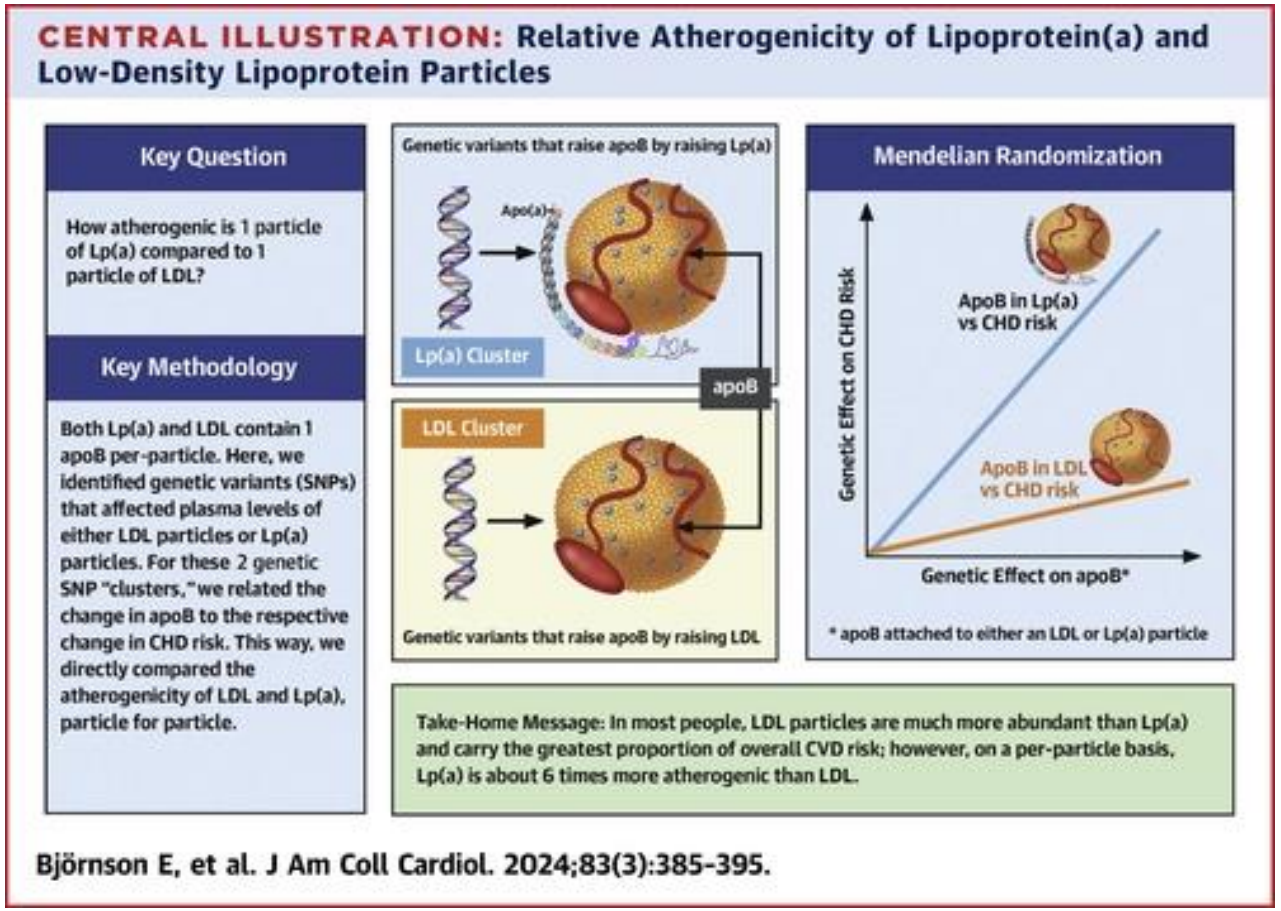
TG: Triglycerides
CE: Cholesterol ester



Wilkins, J.T. et al. J Am Coll Cardiol. 2016; 67(2):193-201.

Lipoprotein A

- Lp(a) is a modified form of LDL that appears to possess atherogenic potential
- Indications for measurement are family history of premature ASCVD or personal history of ASCVD not explained by major risk factors
- Lp(a) ≥50 mg/dL or ≥125 nmol/L, Lp(a) may be considered a risk-enhancing factor

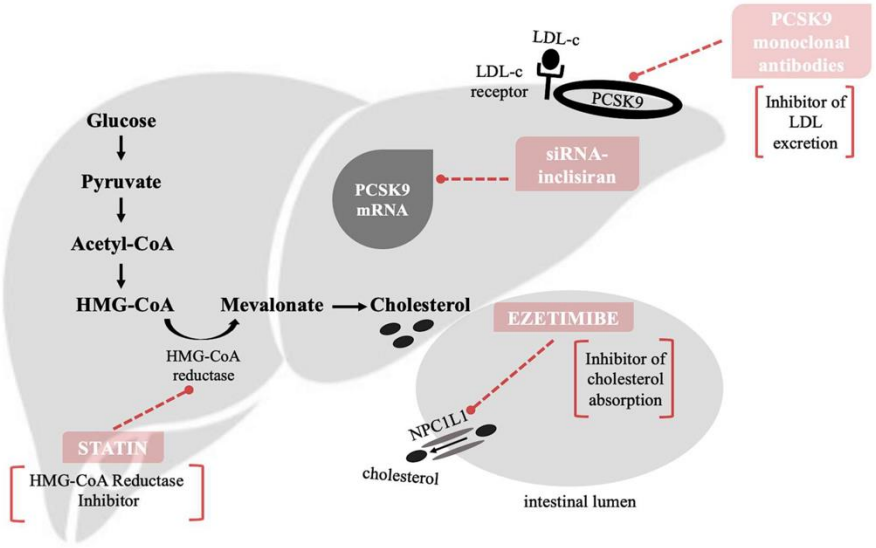


Lifestyle Therapies

- Emphasizes intake of vegetables, fruits, whole grains, legumes, healthy protein sources (low-fat dairy products, low-fat poultry (without the skin), fish/seafood, and nuts), and nontropical vegetable oils
- Limit intake of sweets, sugar-sweetened beverages, and red meats
- Engage in moderate aerobic physical activity 3-4 sessions per week, lasting on average 40 minutes per session
- Good adherence to various LDL-lowering diets will reduce LDL-C levels by 10% to >15%

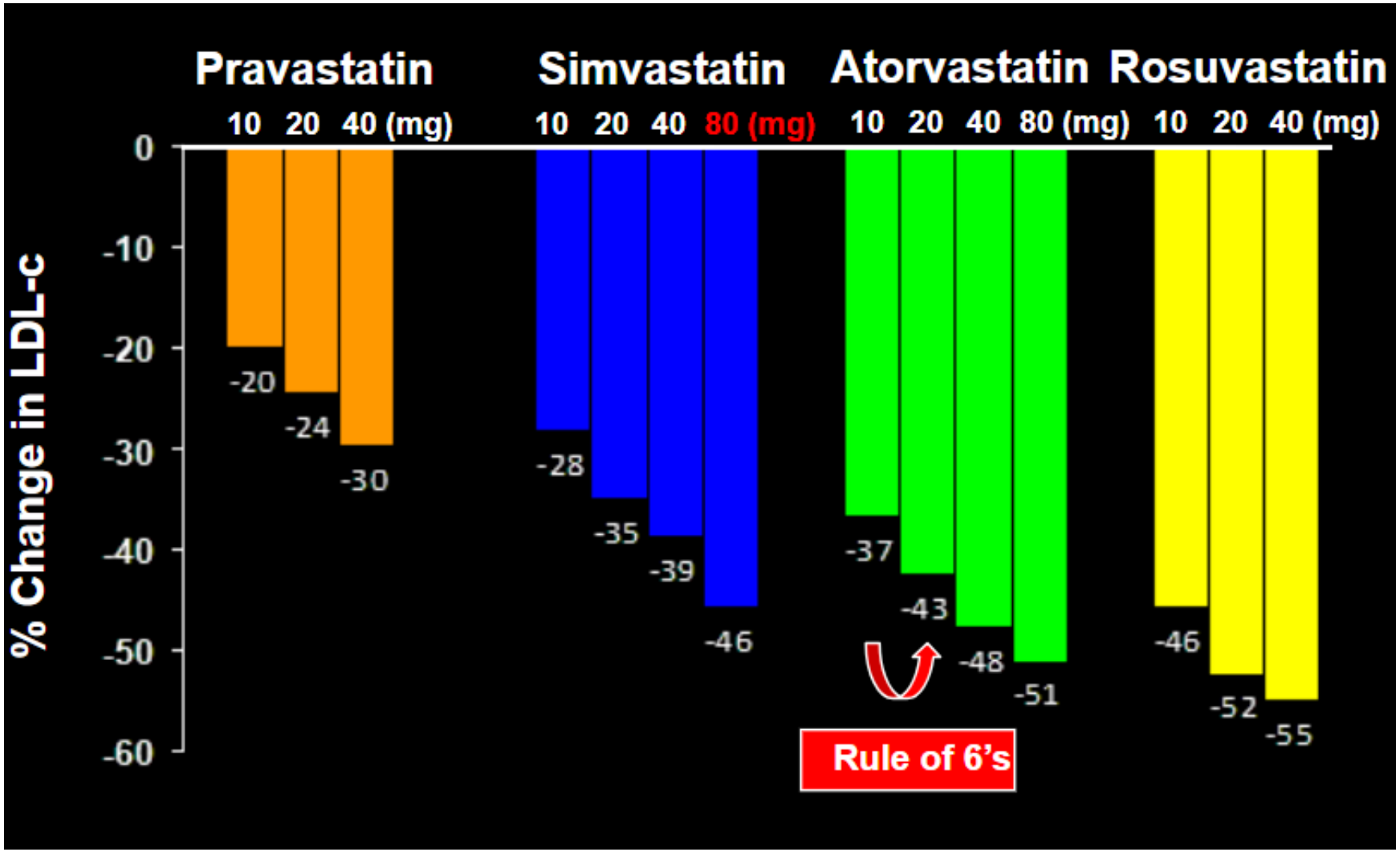
Statin Therapy

- Statins inhibit HMG-CoA reductase thereby lowering the amount of cholesterol the liver produces



	High Intensity	Moderate Intensity	Low Intensity
LDL-C lowering†	≥50%	30%–49%	<30%
Statins	**Atorvastatin (40 mg‡) 80 mg** **Rosuvastatin 20 mg (40 mg)**	**Atorvastatin 10 mg** (20 mg) **Rosuvastatin** (5 mg) **10 mg** **Simvastatin 20–40 mg§**	Simvastatin 10 mg
	…	**Pravastatin 40 mg** (80 mg) **Lovastatin 40 mg** (80 mg) Fluvastatin XL 80 mg **Fluvastatin 40 mg BID** Pitavastatin 1–4 mg	**Pravastatin 10–20 mg** **Lovastatin 20 mg** Fluvastatin 20–40 mg

Change in LDL Values with Different Statin Doses



Jones PH, *Am J Cardio*. 2003;92:152-160

Greater benefit of statin at higher baseline LDL-C levels

10-year risk of ASCVD 1%
<u>35% reduction with statin</u>
= 0.7% risk of CHD
0.3% absolute reduction minus harms

10-year risk of ASCVD 18%
<u>35% reduction with statin</u>
= 12% risk of CHD
6% absolute reduction minus harms

Statin Safety and Associated Side Effects

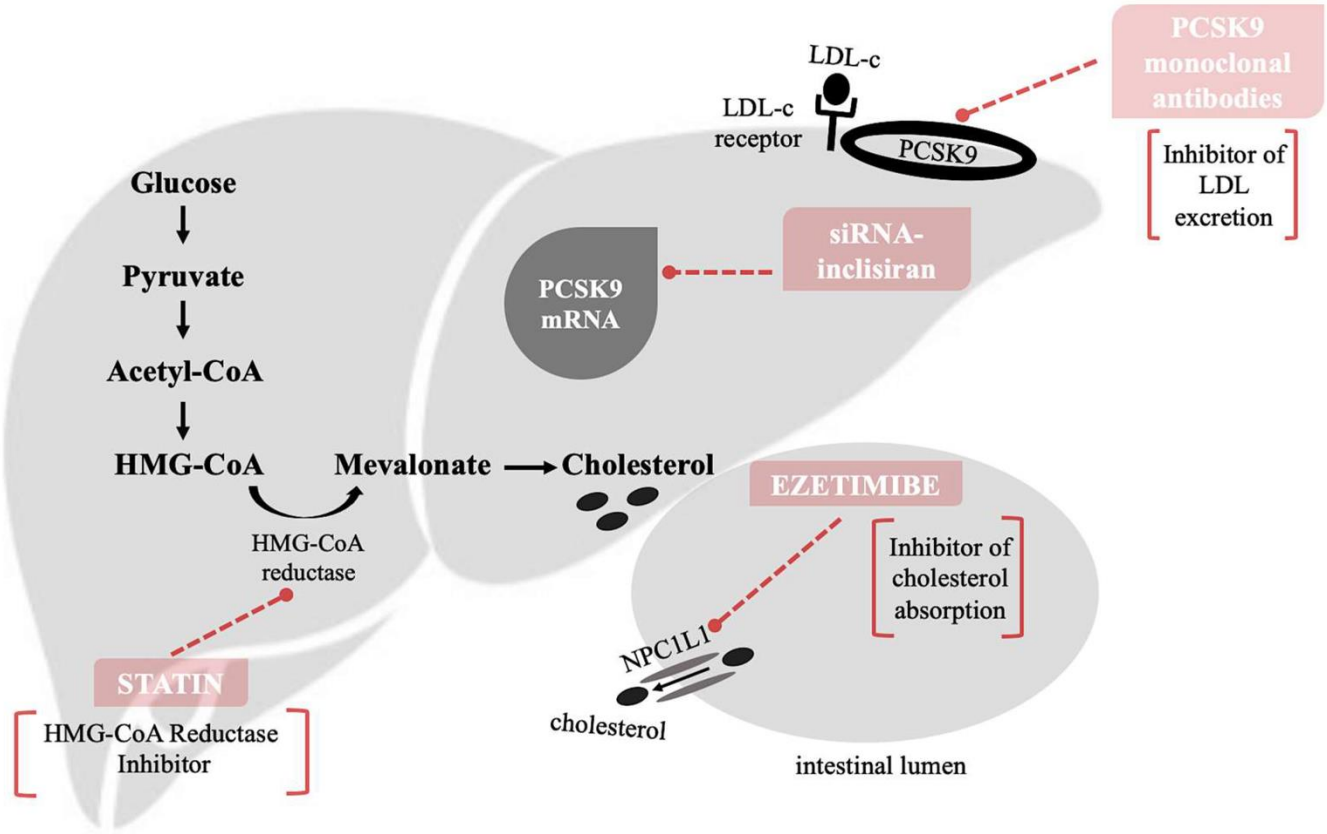
- Muscle aches – 1-10%
- Rhabdomyolysis- 1:10,000
- Elevated LFT's- inconsequential <3x ULN
  - No need for routine monitoring
- Diabetes- cross threshold 1:255 prescriptions
  - Mainly in those with IFG/obesity or treated with high-intensity statin
  - Still lowers CV risk in patients with DM
- Cognitive issues- case reports

Statin Safety Recommendations

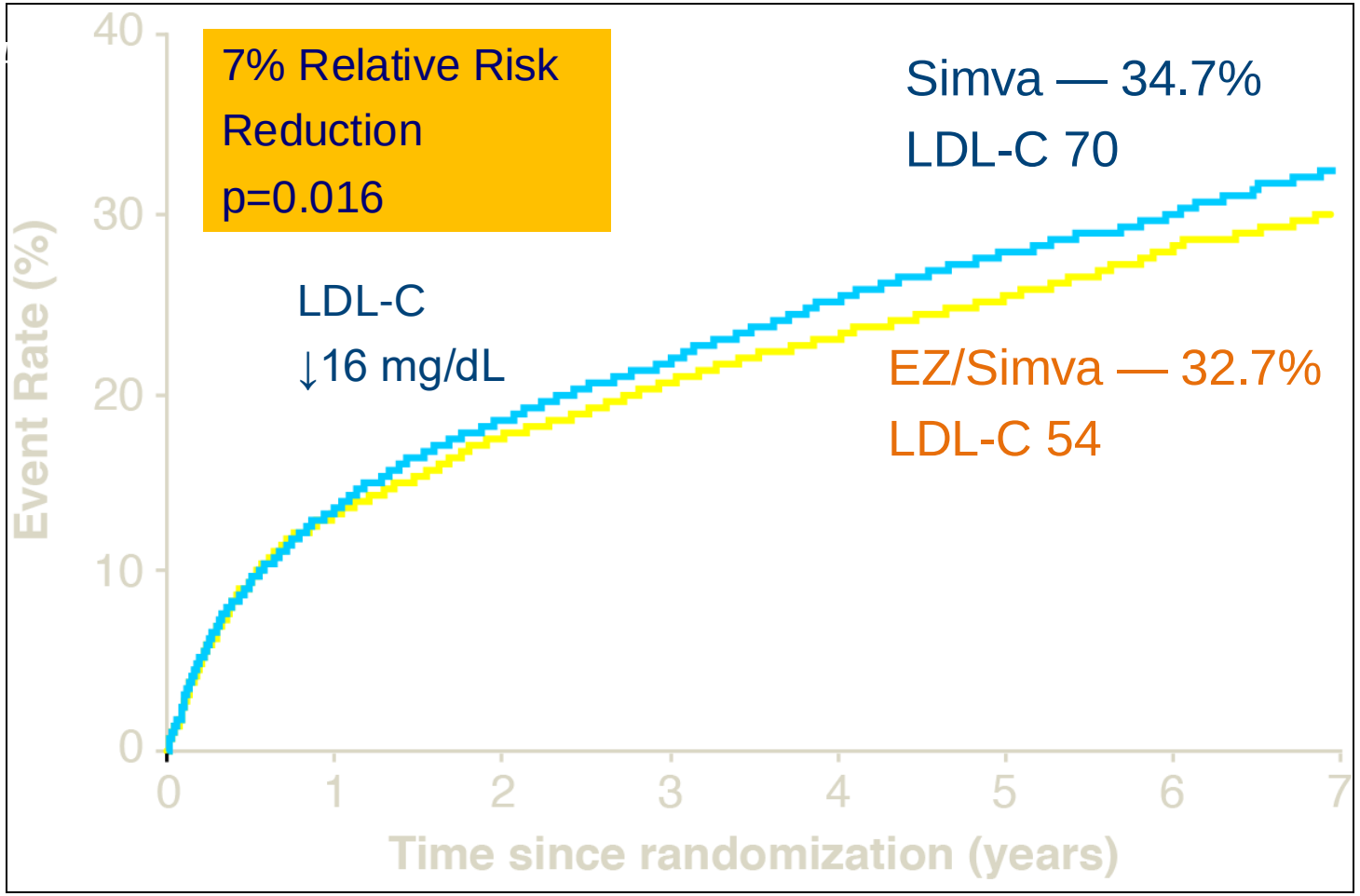
I	B-R	5. In patients with increased diabetes mellitus risk or new-onset diabetes mellitus, it is recommended to continue statin therapy, with added emphasis on adherence, net clinical benefit, and the core principles of regular moderate-intensity physical activity, maintaining a healthy dietary pattern, and sustaining modest weight loss.[S5-8–S5-12]
I	C-LD	6. In patients treated with statins, it is recommended to measure creatine kinase levels in individuals with severe statin-associated muscle symptoms, objective muscle weakness, and to measure liver transaminases (aspartate aminotransferase, alanine aminotransferase) as well as total bilirubin and alkaline phosphatase (hepatic panel) if there are symptoms suggesting hepatotoxicity.[S5-13–S5-15]
III: No Benefit	B-R	9. Coenzyme Q10 is not recommended for routine use in patients treated with statins or for the treatment of SAMS.[S5-20,S5-21]
III: No Benefit	C-LD	10. In patients treated with statins, routine measurements of creatine kinase and transaminase levels are not useful.[S5-13–S5-15]

Ezetimibe

- Ezetimibe inhibits absorption of cholesterol in the small intestine by blocking NPC1L1 protein.
- Lowers LDL-C levels by 13% to 20%.



IMPROVE IT: Effect of Ezetimibe in Patients with Recent Heart Attack



7-year event rates

Cardiovascular death, MI, documented unstable angina requiring rehospitalization, coronary revascularization (≥30 days), or stroke

Cannon CP, et al. *NEJM 2015*

Bile Acid Sequestrants

- Cholestyramine, colestipol, and colesevelam are a few examples
- Bile acid sequestrants can bind other drugs, so other medications must be avoided for 1 hour before and at least 3-4 hours after administration.
- Adding psyllium can minimize constipation and can reduce the bile acid sequestrant dose.

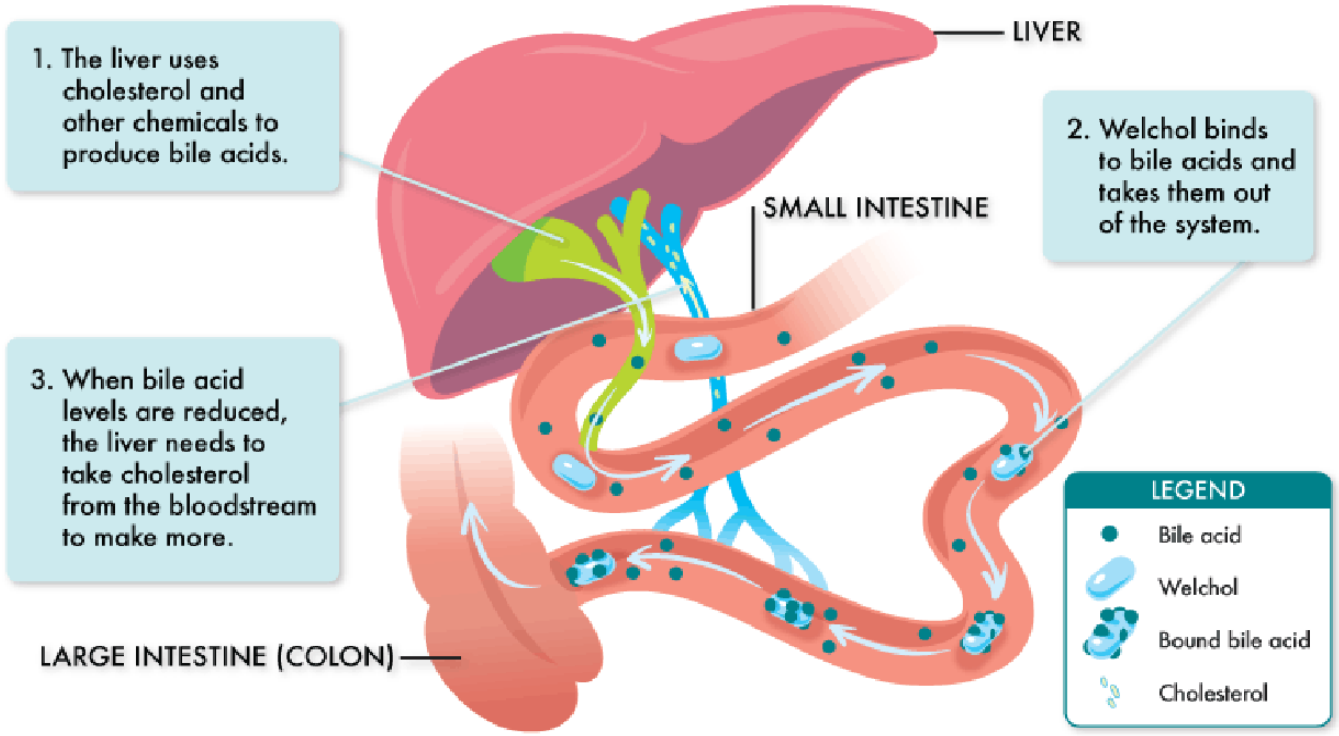
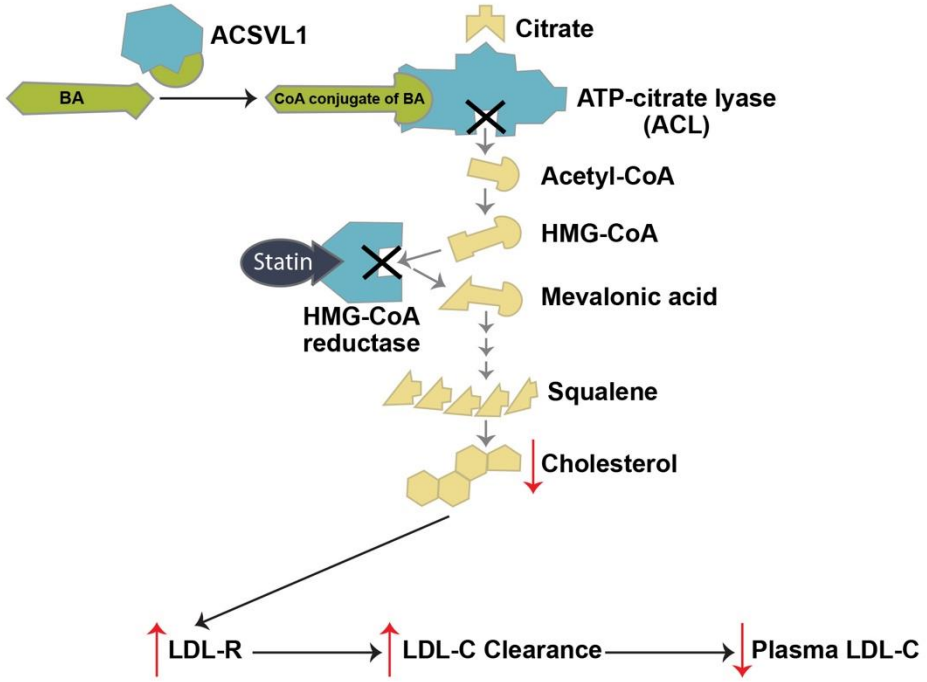


Figure 1.6 – Bile acid sequestrant (Welchol) effect on the enterohepatic

Bempedoic Acid Mechanism of Action

Converted to the CoA Conjugate of Bempedoic Acid, the Active Form, Only in Liver



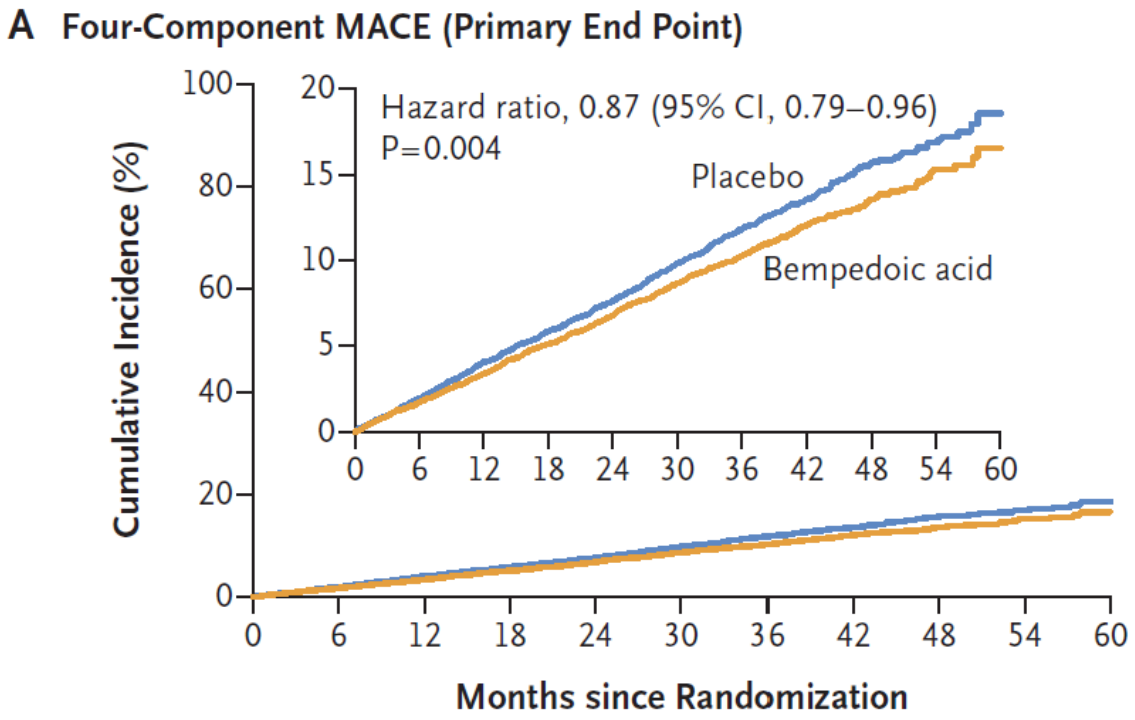
- Bempedoic acid (BA) acts in the same cholesterol biosynthesis pathway as statins
- BA targets ATP-citrate lyase (ACL), an enzyme upstream of HMG-CoA reductase
- Upregulates LDL receptors and lowers LDL-C
- Specific isozyme (ACSVL1) that converts BA into an active drug is not present in skeletal muscle

ACSVL1, very long-chain acyl-CoA synthetase-1;
CoA, coenzyme A; LDL-C, low-density lipoprotein cholesterol.

Ray KK et al. Presented at ESC, Munich, 2018.

Bempedoic Acid: and CV Outcomes

CLEAR OUTCOMES Trial



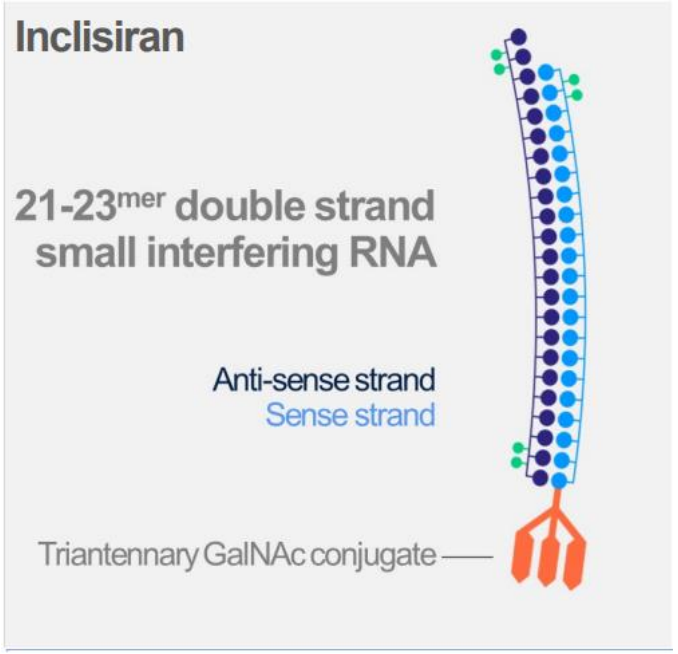
Clinical Considerations

- ***Oral***
- ***No ↑ glucose/DM***
- ***No ↑ myalgia***

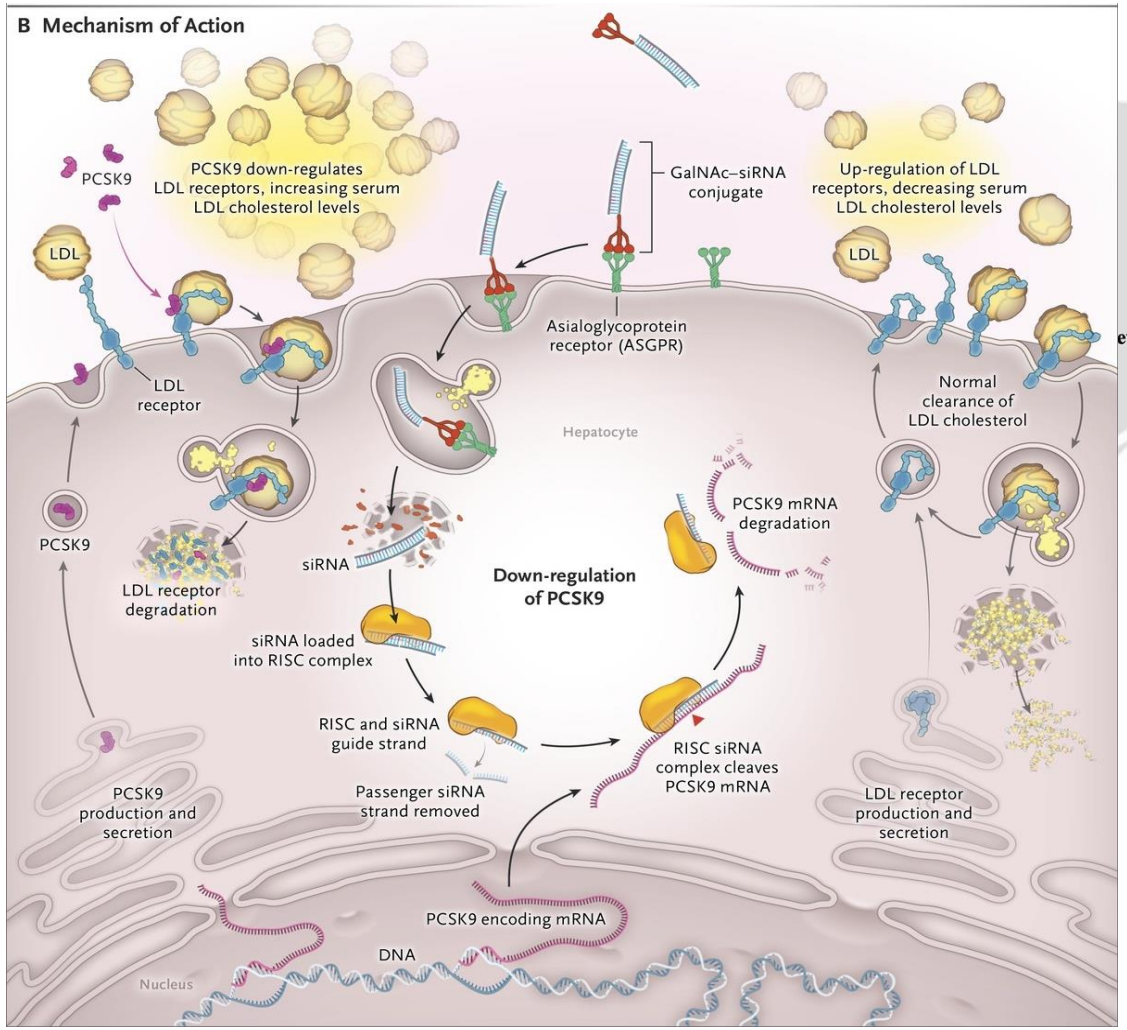
- ***↑ Hyperuricemia/Gout***
- ***0.5% Tendon rupture***
- ***Modest LDL-C lowering but combo with ezetimibe***

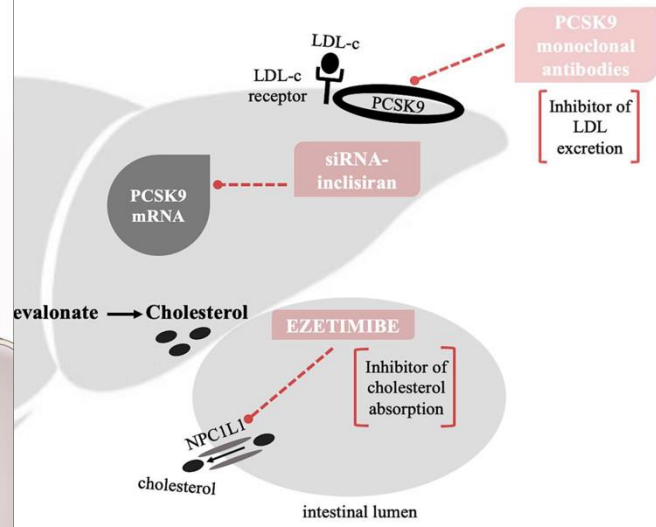
Nissen S et al NEJM 2023

Inclisiran: Chemical Configuration and Mechanism of Action



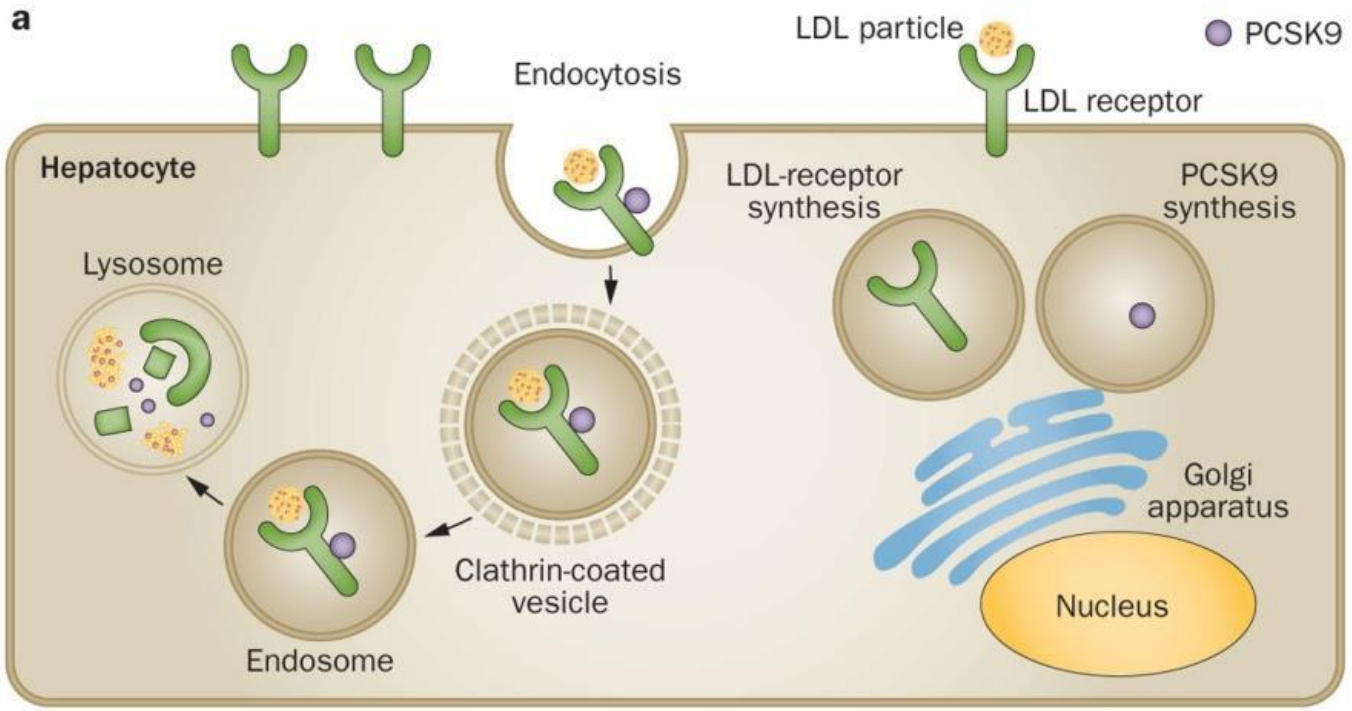
Dosed SQ baseline, 3 mo, Q6 months





Khvorova A. N Engl J Med 2017;376:4-7.

PCSK9 (proprotein convertase subtilisin/kexin type 9): Physiology

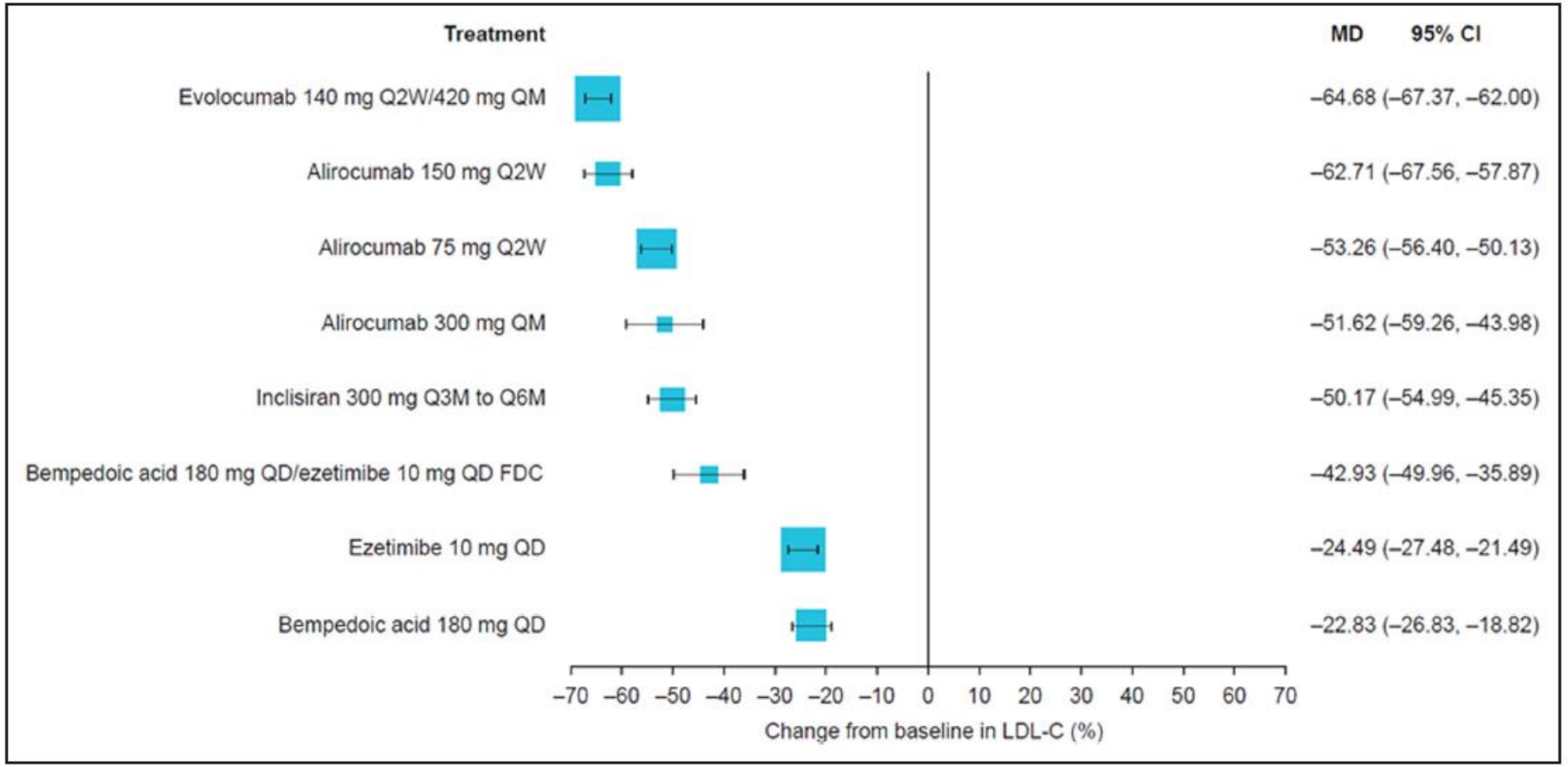


↑ PCSK9*
(↓LDL receptors)
↑ LDL-C

↓ PCSK9
(↑LDL receptors)
↓ LDL-C

*Abifadel M. *Nat Genet* 2003;34(2):154-6
Ballantyne. *Nat. Rev. Cardiol.* 2014.84
Jay D. Horton et al. *J. Lipid Res*. 2009;50:S172-S177

LDL-C Reduction of Non-Statin Therapies



Toth P et al. JAHA 2022;11:e025551. DOI: 10.1161/JAHA.122.025551

Approach to Patient Management

1. ***Rule out secondary causes***
2. ***Initiate Therapeutic Lifestyle Changes***
3. ***Determine the patient's risk level***
   - ***CAC testing, Risk Enhacing Factors***
4. ***Start statin therapy as necessary***
   - ***4 groups per ACC/AHA Guidelines***
5. ***Other targets?***
   - ***(OM3FA-high TG, 2◦ prevention)***

Secondary Causes of Dyslipidemia

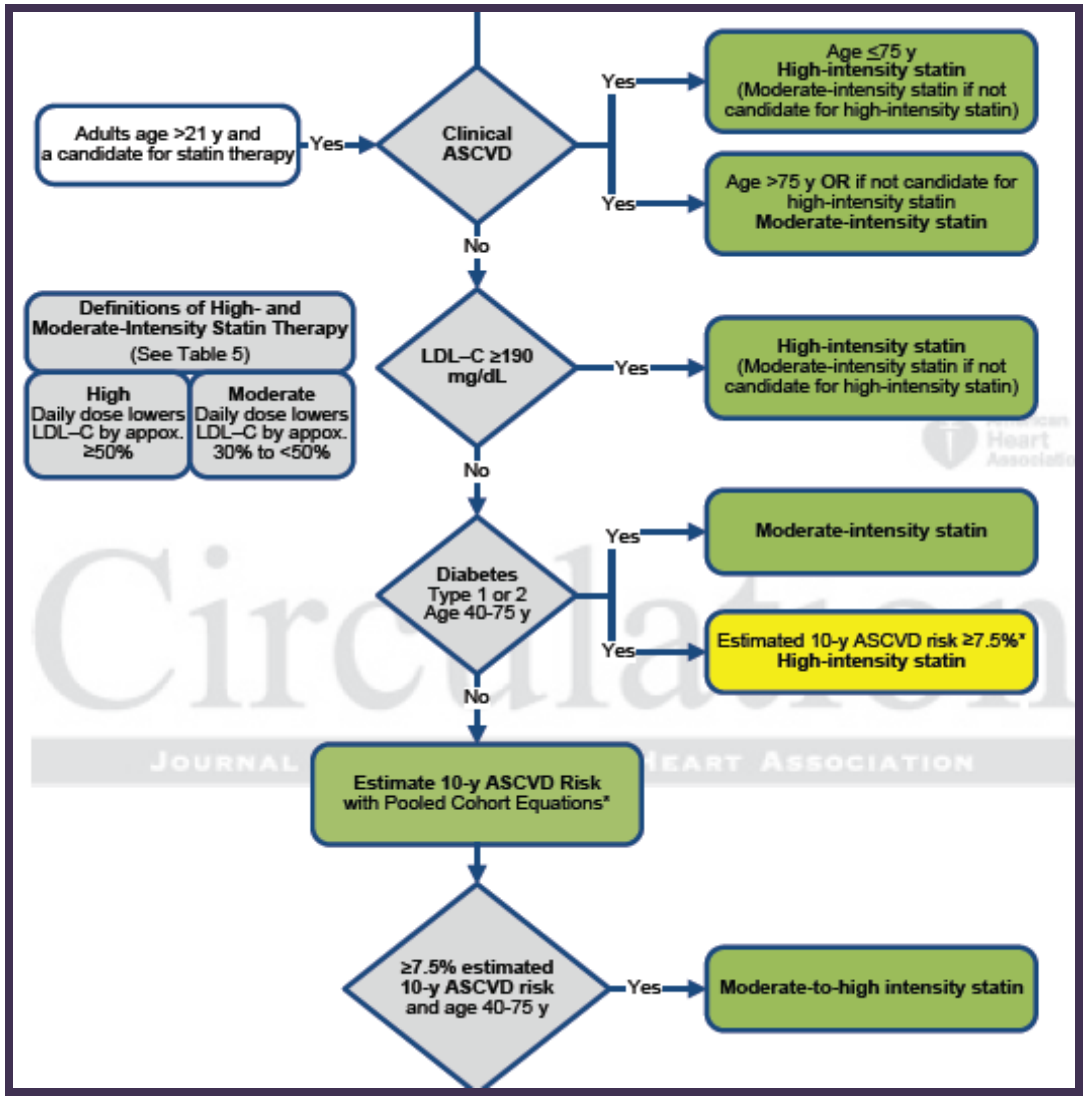
High LDL

- Nephrotic Syndrome
- Hypothyroidism
- Obstructive liver disease
- Keto Diet

High Triglycerides

- Diabetes
- Alcohol
- Glucocorticoids
- Thiazide diuretics
- Beta Blockers

Statin Therapy Recommendations- 4 Groups



Clinical ASCVD
-High

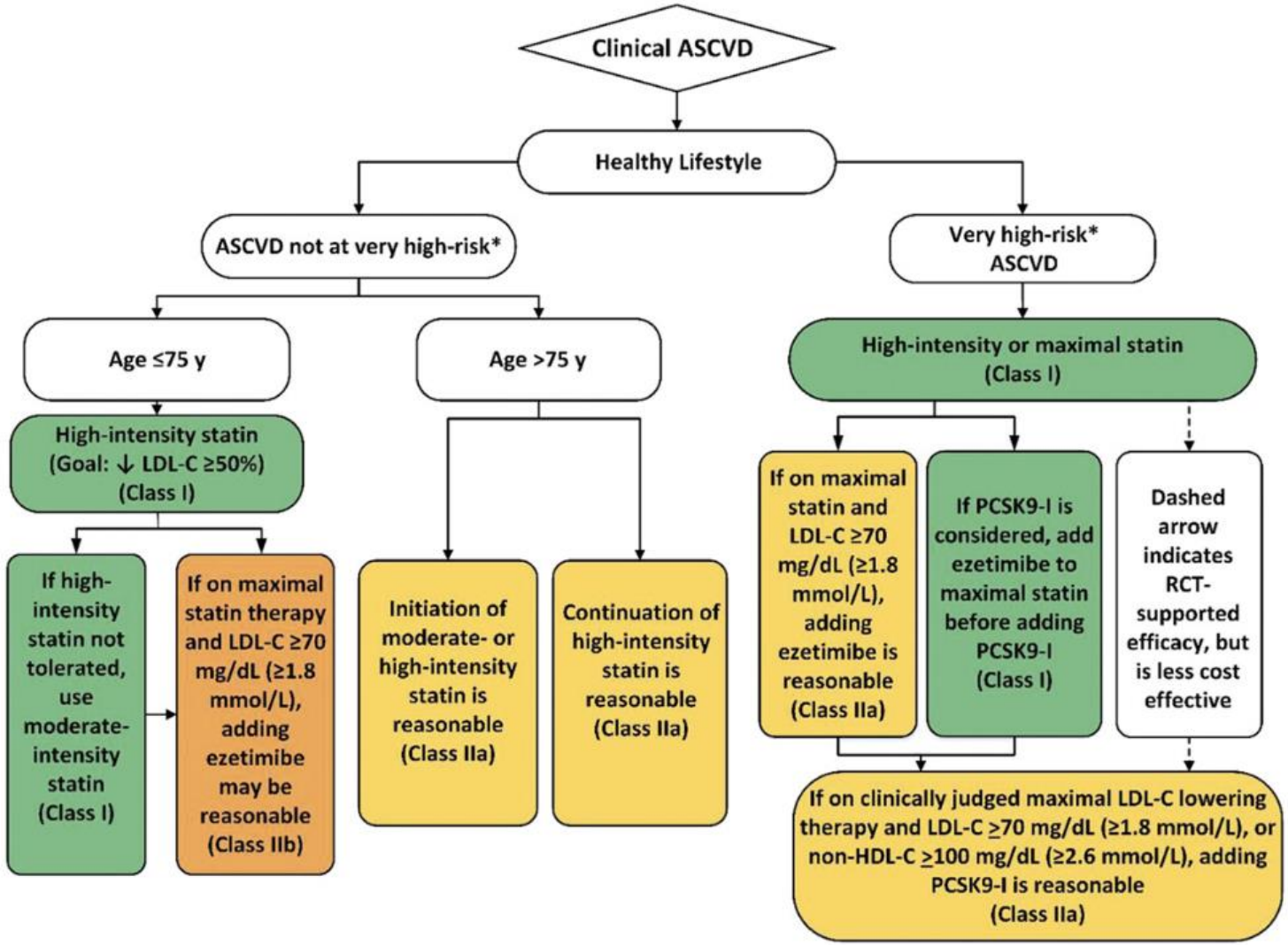
LDL-C ≥ 190
-High

Diabetes
(Age 40-75)
-Mod (High)

Risk ASCVD≥ 7.5%
(Age 40-75)
-Mod (High)

-statin intensity

Clinical ASCVD – AKA Secondary Prevention



Clinical ASCVD - Very High-Risk Features

Table 4. Very High-Risk* of Future ASCVD Events (Table view)

Major ASCVD Events
Recent ACS (within the past 12 mo)
History of MI (other than recent ACS event listed above)
History of ischemic stroke
Symptomatic peripheral arterial disease (history of claudication with ABI <0.85, or previous revascularization or amputation[S4.1-40])
High-Risk Conditions
Age ≥65 y
Heterozygous familial hypercholesterolemia
History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)
Diabetes mellitus
Hypertension
CKD (eGFR 15-59 mL/min/1.73 m^2)[S4.1-15,S4.1-17]
Current smoking
Persistently elevated LDL-C (LDL-C ≥100 mg/dL [≥2.6 mmol/L]) despite maximally tolerated statin therapy and ezetimibe
History of congestive HF

LDL-C Goal for Secondary Prevention in Current Cholesterol Guidelines

Guideline	LDL-C Goal
2018 US ACC/AHA Cholesterol	<70mg/dL*
2019 ESC Guidelines	<55mg/dL**
2022 ACC Consensus Statement	<55mg/dL*

* for “Very High Risk”
**Optional <40mg/dL

Patient Management – Severe Hypercholesterolemia

- ***Defined as LDL-C ≥190 mg/dL***
- ***Small proportion will have Familial Hypercholesterolemia (2-7%)***
- ***Up to 5-fold lifetime risk of CHD***

Khera A.V. et al. *JACC* 2016;67:2758-2789.
Bucholz E et al. Circulation 2018; 137:2218-2230.
Perak A et al Circulation 2016;134:9-19.

Familial Hypercholesterolemia(s)

- **Definition: Severe hypercholesterolemia with autosomal dominant inheritance pattern**
- ***Homozygous (~1:500,000); LDL-C >400mg/dl***
- ***Heterozygous (~1:250); LDL-C 200-400mg/dl***
- **Simon Broome Criteria or Dutch Lipid Criteria**

Total cholesterol >290 or LDL >190 mg/dl in adult,
or total cholesterol >260 or LDL>160mg/dl in child

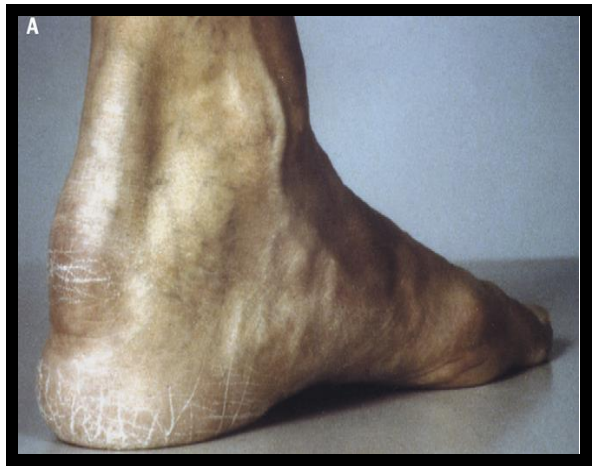
AND

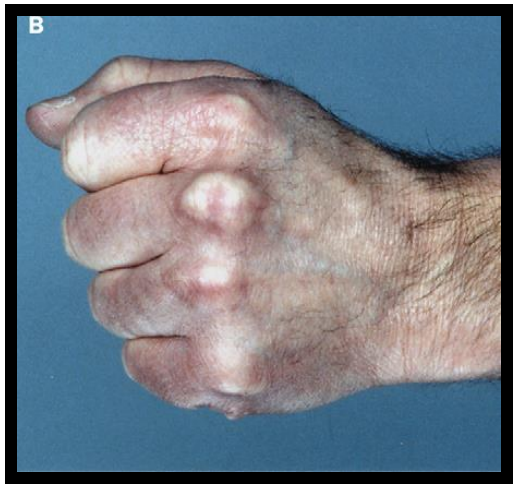
Definite: Tendon xanthoma or + gene in patient or relative

Probable: Family history of premature heart attack, OR Hypercholesterolemia in 1st or 2nd degree relative

Goldberg AC et al. J Clin Lipid 2011;5:S1-S8

Physical Exam Findings in FH





Tendinous Xanthomas (any age)

Corneal Acus (<45yo)

Xanthelasma (<25yo)

ACC/AHA Guidelines – Severe Hypercholesterolemia

I	B-R	1. In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL or higher (≥4.9 mmol/L), maximally tolerated statin therapy is recommended.[S4.2-1–S4.2-7]
IIa	B-R	2. In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL or higher (≥4.9 mmol/L) who achieve less than a 50% reduction in LDL-C while receiving maximally tolerated statin therapy and/or have an LDL-C level of 100 mg/dL or higher (≥2.6 mmol/L), ezetimibe therapy is reasonable.[S4.2-8–S4.2-10]
IIb	B-R	3. In patients 20 to 75 years of age with a baseline LDL-C level of 190 mg/dL or higher (≥4.9 mmol/L), who achieve less than a 50% reduction in LDL-C levels and have fasting triglycerides 300 mg/dL or lower (≤3.4 mmol/L), while taking maximally tolerated statin and ezetimibe therapy, the addition of a bile acid sequestrant may be considered.[S4.2-11,S4.2-12]

2018 AHA Cholesterol Guidelines: LDL-C Testing in Children

IIa	B-R	3. In children and adolescents 10 years of age or older with an LDL-C level persistently 190 mg/dL (≥4.9 mmol/L) or higher or 160 mg/dL (4.1 mmol/L) or higher with a clinical presentation consistent with FH (see Section 4.2.) and who do not respond adequately with 3 to 6 months of lifestyle therapy, it is reasonable to initiate statin therapy (S4.4.4.3-13–S4.4.4.3-16).
IIa	B-NR	4. In children and adolescents with a family history of either early CVD* or significant hypercholesterolemia,† it is reasonable to measure a fasting or nonfasting lipoprotein profile as early as age 2 years to detect FH or rare forms of hypercholesterolemia (S4.4.4.3-17–S4.4.4.3-21).

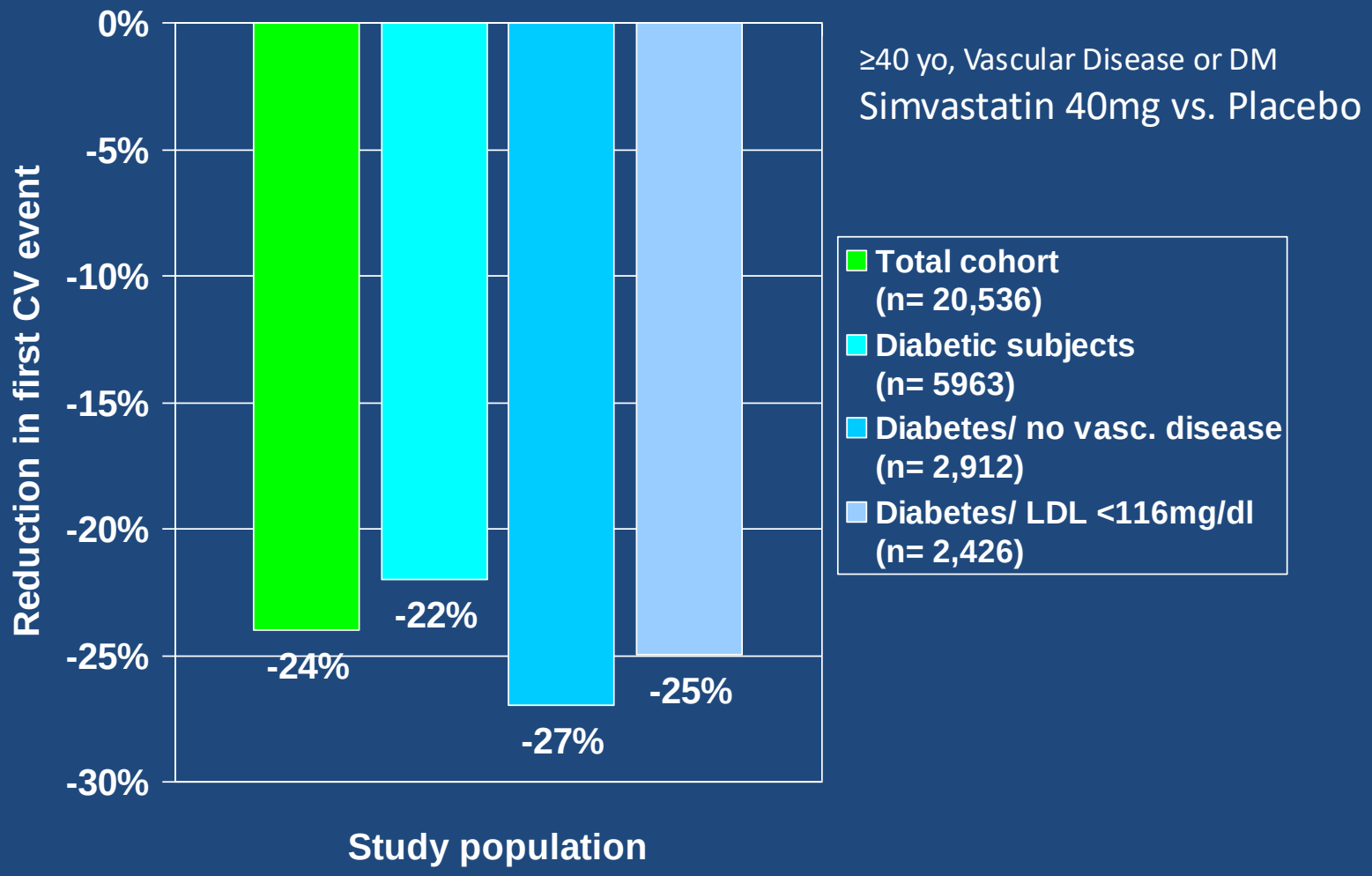
Statin option
≥ 10yrs

LDL-C testing
≥ 2yrs

	Acceptable, mg/dL	Borderline, mg/dL 75th	Abnormal, mg/dL 95th
TC	<170 (<4.3 mmol)	170-199 (4.3-5.1 mmol)	≥200 (≥5.1 mmol)
Triglycerides (0-9 y)	<75 (<0.8 mmol)	75-99 (0.8-1.1 mmol)	≥100 (≥1.1 mmol)
Triglycerides (10-19 y)	<90 (<1.0 mmol)	90-129 (1.0-1.5 mmol)	≥130 (≥1.4 mmol)
HDL-C	>45 (>1.2 mmol)	40-45 (1.0-1.2 mmol)	<40 (<1.0 mmol)
LDL-C	<110 (<2.8 mmol)	110-129 (2.8-3.3 mmol)	≥130 (≥3.4 mmol)
Non–HDL-C	<120 (<3.1 mmol)	120-144 (3.1-3.7 mmol)	≥145 (≥3.7 mmol)

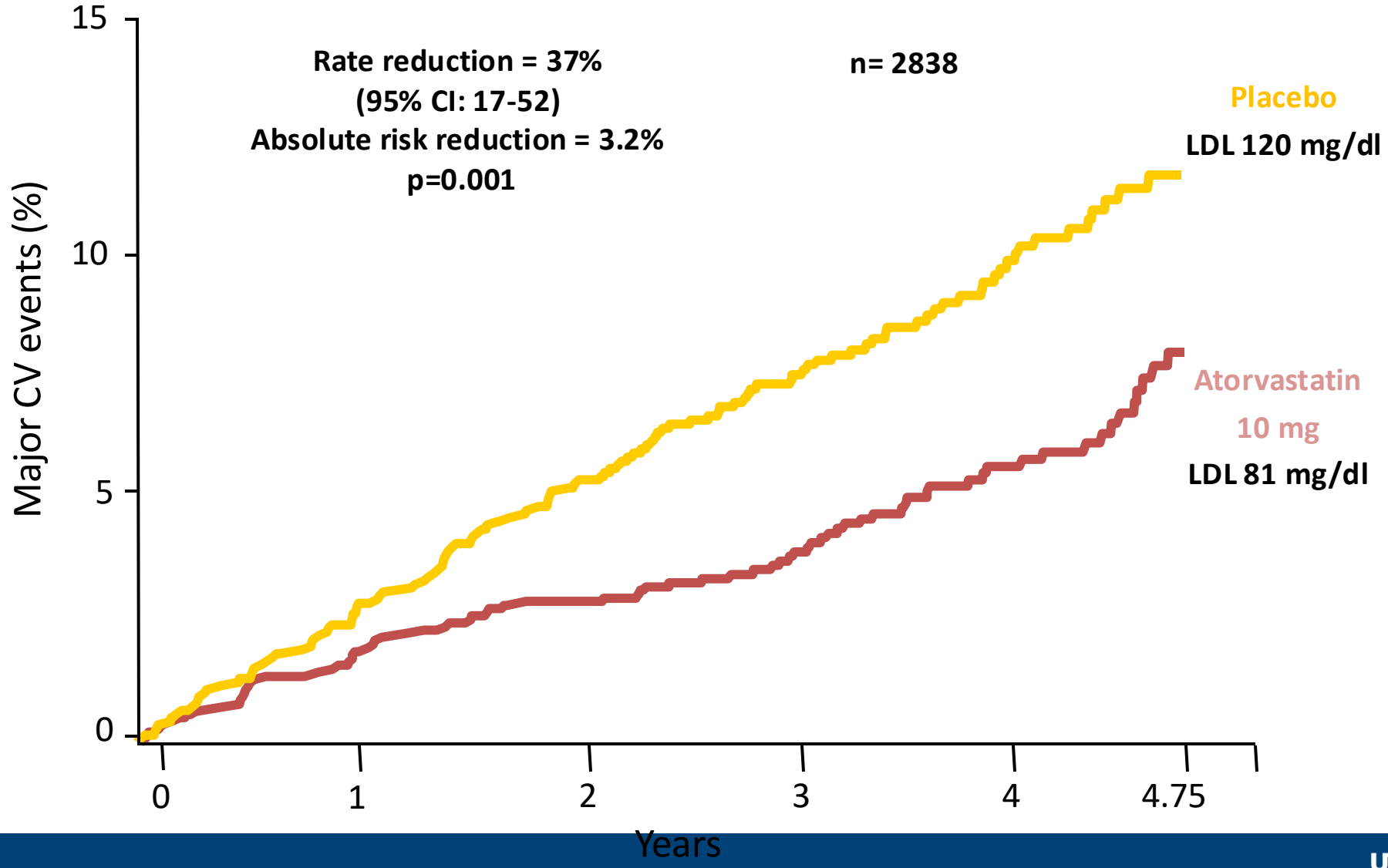
IIa	B-NR	5. In children and adolescents found to have moderate or severe hypercholesterolemia, it is reasonable to carry out reverse-cascade screening of family members, which includes cholesterol testing for first-, second-, and when possible, third-degree biological relatives, for detection of familial forms of hypercholesterolemia.[S4.4.4.3-22–S4.4.4.3-24]

Effect of Simvastatin in Diabetic Subgroup: Heart Protection Study



HPS. *Lancet.* 2002;360:7-22.

CARDS: Statins Lower CV Risk in Diabetic Patients



Colhoun HM, et al. *Lancet.* 2004;364:685-696.

Patient Management – Diabetes Mellitus

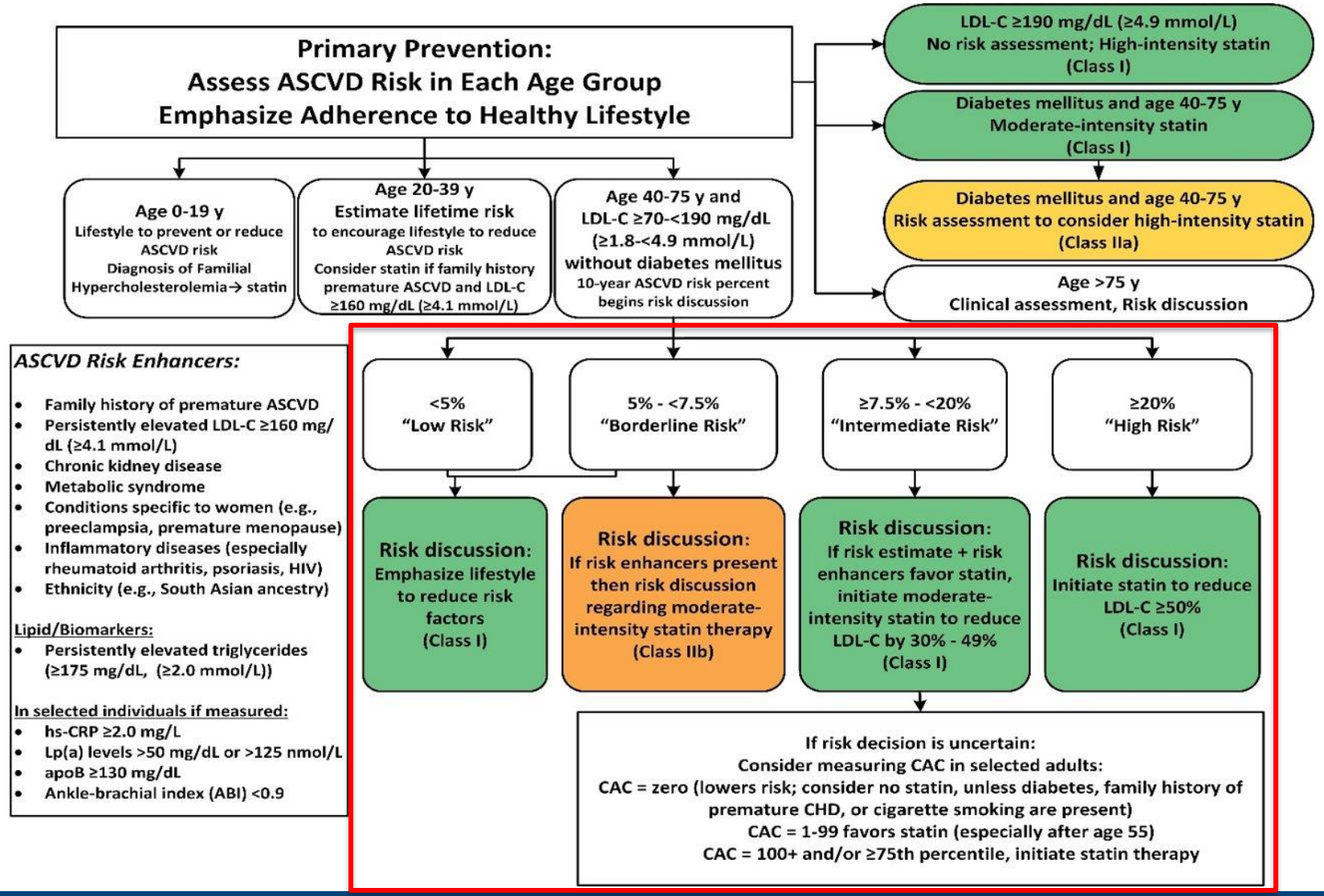
COR	LOE	Recommendations
I	A	1. In adults 40 to 75 years of age with diabetes mellitus, regardless of estimated 10-year ASCVD risk, moderate-intensity statin therapy is indicated.[S4.3-1–S4.3-9]
IIa	B-R	3. In adults with diabetes mellitus who have multiple ASCVD risk factors, it is reasonable to prescribe high-intensity statin therapy with the aim to reduce LDL-C levels by 50% or more.[S4.3-12,S4.3-13]

Table 5. Diabetes-Specific Risk Enhancers That Are Independent of Other Risk Factors in Diabetes Mellitus

Risk Enhancers
Long duration (≥10 years for type 2 diabetes mellitus[S4.3-20] or ≥20 years for type 1 diabetes mellitus[S4.3-6]
Albuminuria ≥30 mcg of albumin/mg creatinine[S4.3-25]
eGFR <60 mL/min/1.73 m^2[S4.3-25]
Retinopathy[S4.3-19]
Neuropathy[S4.3-16]
ABI <0.9[S4.3-22,S4.3-24]

ABI indicates ankle-brachial index; and eGFR, estimated glomerular filtration rate.

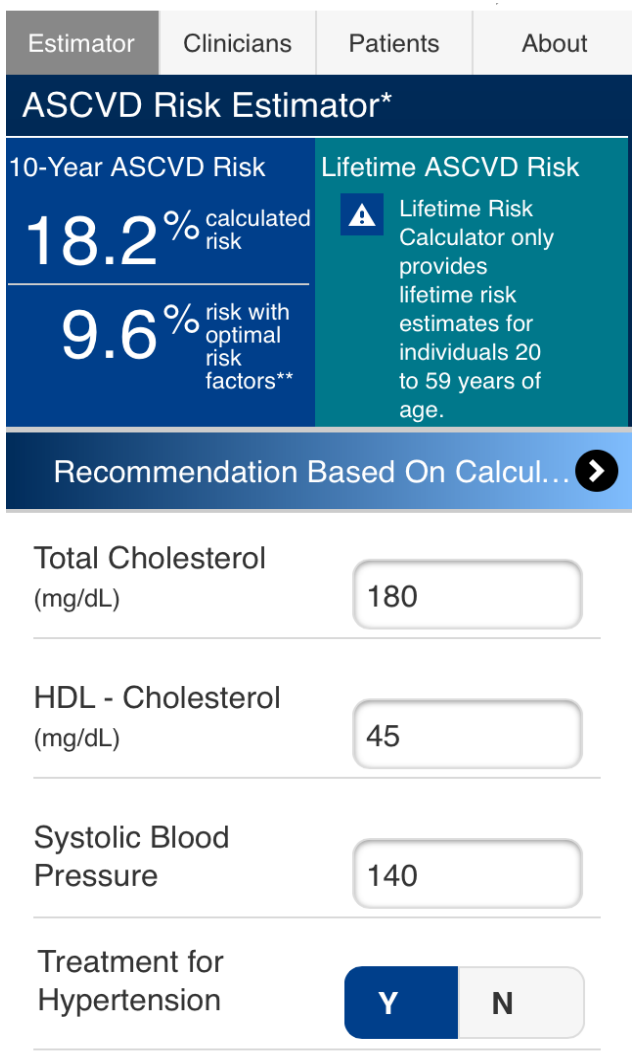
Patient Management – Primary Prevention



Patient Management – Primary Prevention

Pooled Cohort Equations

- Age
- Sex
- Race (Black/White/Other)
- Total Cholesterol
- HDL Cholesterol
- Systolic BP
- Hypertension
- Diabetes
- Tobacco Use



ASCVD Risk Enhancers

Risk-Enhancing Factors
• **Family history of premature ASCVD** (males, age <55 y; females, age <65 y) • **Primary hypercholesterolemia** (LDL-C, 160–189 mg/dL [4.1–4.8 mmol/L); non–HDL-C 190–219 mg/dL [4.9–5.6 mmol/L])* • **Metabolic syndrome** (increased waist circumference, elevated triglycerides [>175 mg/dL], elevated blood pressure, elevated glucose, and low HDL-C [<40 mg/dL in men; <50 in women mg/dL] are factors; tally of 3 makes the diagnosis) • **Chronic kidney disease** (eGFR 15–59 mL/min/1.73 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation) • **Chronic inflammatory conditions** such as psoriasis, RA, or HIV/AIDS • **History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk such as preeclampsia** • **High-risk race/ethnicities** (e.g., South Asian ancestry)

ASCVD Risk Enhancers

Risk-Enhancing Factors		
IIb	C-LD	2. In adults with advanced kidney disease that requires dialysis treatment who are currently on LDL-lowering therapy with a statin, it may be reasonable to continue the statin.[S4.5.4-2]
III: No Benefit	B-R	3. In adults with advanced kidney disease who require dialysis treatment, initiation of a statin is not recommended.[S4.5.4-3,S4.5.4-4]

Role of Coronary Calcium Testing

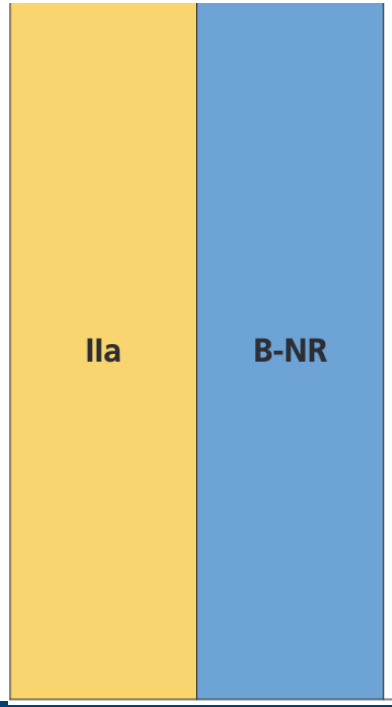
CAC Testing

0
Lifestyle
(unless smoking, DM, premature fam hx)

1-99,
Probably Statin

≥100 or ≥75th%
Statin

When the CAC score is zero, remeasure after 5 to 10 years.



7. In intermediate-risk adults or selected borderline-risk adults in whom a CAC score is measured for the purpose of making a treatment decision, AND
   - If the coronary calcium score is zero, it is reasonable to withhold statin therapy and reassess in 5 to 10 years, as long as higher risk conditions are absent (diabetes mellitus, family history of premature CHD, cigarette smoking);
   - If CAC score is 1 to 99, it is reasonable to initiate statin therapy for patients ≥55 years of age;
   - If CAC score is 100 or higher or in the 75th percentile or higher, it is reasonable to initiate statin therapy.[S4.4.2-17,S4.4.2-23]

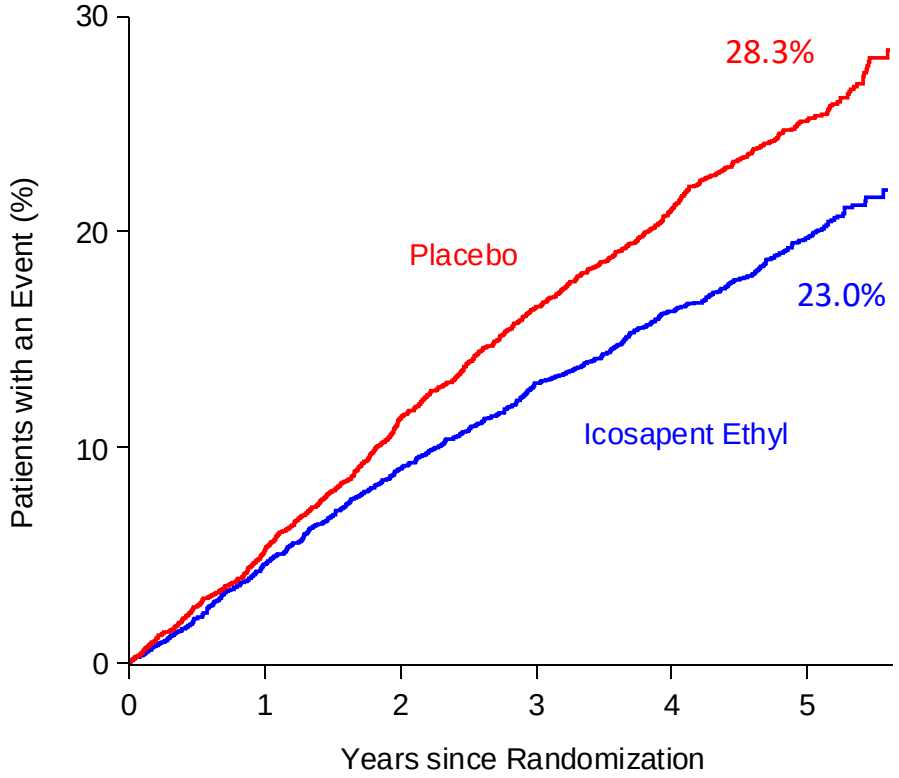
Recommendations for Older Adults

Recommendations for Older Adults Referenced studies that support recommendations are summarized in Online Data Supplements 18 and 19.		
COR	**LOE**	**Recommendations**
IIb	B-R	1. In adults older than 75 years of age with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), initiating a moderate-intensity statin may be reasonable[S4.4.4.1-1–S4.4.4.1-8]
IIb	B-R	2. In adults older than 75 years of age, it may be reasonable to stop statin therapy when functional decline (physical or cognitive), multimorbidity, frailty, or reduced life-expectancy limits the potential benefits of statin therapy.[S4.4.4.1-9]
IIb	B-R	3. In adults 76 to 80 years of age with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), it may be reasonable to measure CAC to reclassify those with a CAC score of zero to avoid statin therapy.[S4.4.4.1-10,S4.4.4.1-11]

Treatment of Hypertriglyceridemia Uncertain

Primary End Point:

CV Death, MI, Stroke, Coronary Revascularization, Unstable Angina



Hazard Ratio, 0.75

(95% CI, 0.68–0.83)

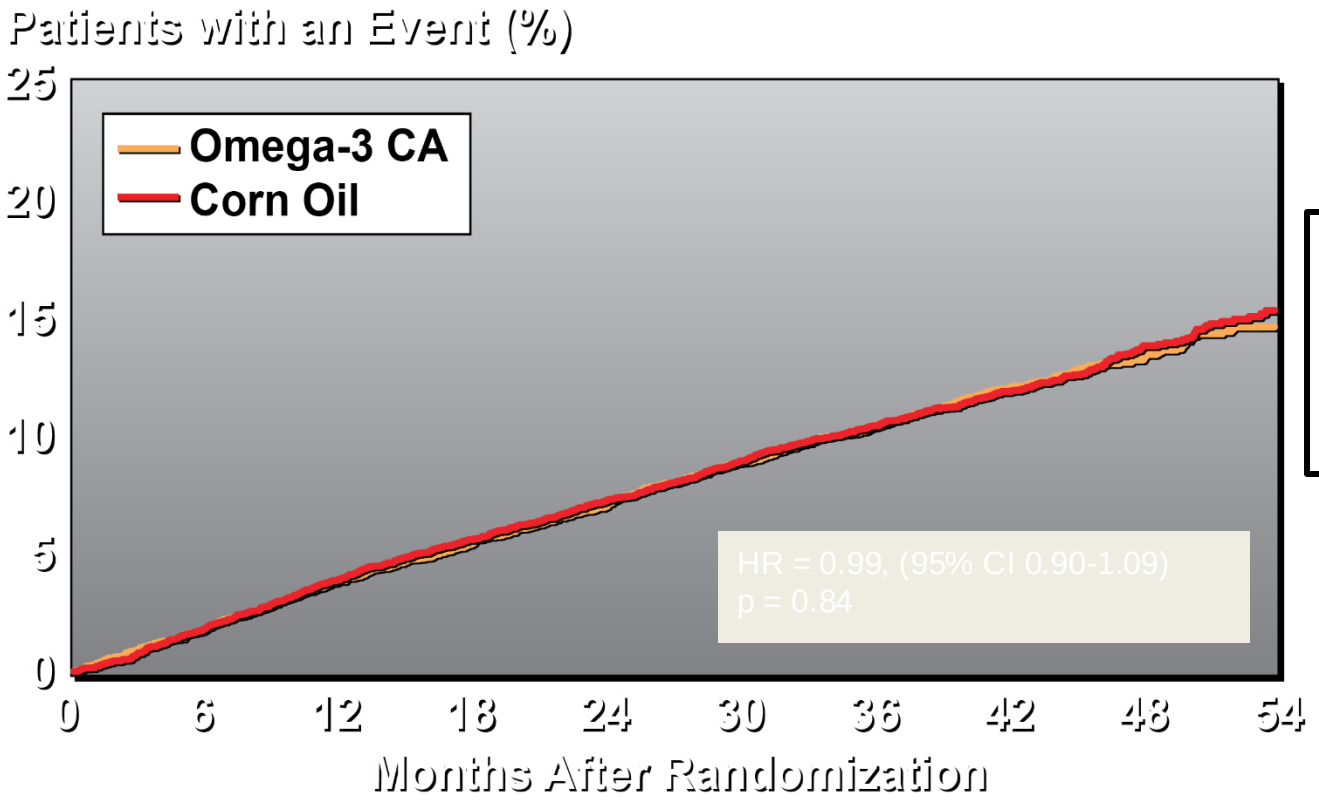
P=0.00000001

Bhatt DL, Steg PG, Miller M, et al. *N Engl J Med*. 2019.

Treatment of Hypertriglyceridemia Uncertain

STRENGTH TRIAL

1° Endpoint Components and All-Cause Death



↑ Afib
2.2 vs 1.3%
HR, 1.69 [95%CI, 1.29-2.21]

No ↑ bleeding

Why the Differences in REDUCE-IT vs. STRENGTH?

1.Harms of mineral oil placebo?

2.Beneficial effects of EPA vs. DHA (Icospent ethyl vs. other EPA?)

Hypertriglyceridemia

I	B-NR	1. In adults 20 years of age or older with moderate hypertriglyceridemia (fasting or nonfasting triglycerides 175 to 499 mg/dL [2.0 to 5.6 mmol/L]), clinicians should address and treat lifestyle factors (obesity and metabolic syndrome), secondary factors (diabetes mellitus, chronic liver or kidney disease and/or nephrotic syndrome, hypothyroidism), and medications that increase triglycerides.[S4.5.2-1]
IIa	B-R	2. In adults 40 to 75 years of age with moderate or severe hypertriglyceridemia and ASCVD risk of 7.5% or higher, it is reasonable to reevaluate ASCVD risk after lifestyle and secondary factors are addressed and to consider a persistently elevated triglyceride level as a factor favoring initiation or intensification of statin therapy (see Section 4.4.2.).[S4.5.2-2–S4.5.2-6]
IIa	B-NR	4. In adults with severe hypertriglyceridemia (fasting triglycerides ≥500 mg/dL [≥5.7 mmol/L]), and especially fasting triglycerides ≥1000 mg/dL (11.3 mmol/L)), it is reasonable to identify and address other causes of hypertriglyceridemia), and if triglycerides are persistently elevated or increasing, to further reduce triglycerides by implementation of a very low-fat diet, avoidance of refined carbohydrates and alcohol, consumption of omega-3 fatty acids, and, if necessary to prevent acute pancreatitis, fibrate therapy.[S4.5.2-7,S4.5.2-9]

Triglyceride Raising Drugs

- Oral estrogens
- Tamoxifen
- Raloxifene
- Retinoids
- Immunosuppressive drugs (cyclosporine, sirolimus, tacrolimus)
- Beta blockers
- Interferon
- Atypical antipsychotic drugs
- Protease inhibitors
- Thiazide diuretics
- Glucocorticoids
- Rosiglitazone
- Bile acid sequestrants
- L-asparaginase
- Cyclophosphamide.

Issues Specific To Women

I	B-NR	1. Clinicians should consider conditions specific to women, such as premature menopause (age <40 years) and history of pregnancy-associated disorders (hypertension, preeclampsia, gestational diabetes mellitus, small-for-gestational-age infants, preterm deliveries), when discussing lifestyle intervention and the potential for benefit of statin therapy.[S4.5.3-1–S4.5.3-6]

I	C-LD	2. Women of childbearing age who are treated with statin therapy and are sexually active should be counseled to use a reliable form of contraception.[S4.5.3-7–S4.5.3-12]
I	C-LD	3. Women of childbearing age with hypercholesterolemia who plan to become pregnant should stop the statin 1 to 2 months before pregnancy is attempted, or if they become pregnant while on a statin, should have the statin stopped as soon as the pregnancy is discovered.[S4.5.3-7–S4.5.3-12]

Top Take Home Points

- Emphasize healthy lifestyle
- Clinical ASCVD = High intensity statin
- Very-high risk patients = goal LDL 70mg/dL
  - Consider nonstatin medication if needed.
- LDL > 190 = high intensity statin
- DM + Age 40-75 = moderate intensity statin
- Calculate ASCVD risk for primary prevention patients
- Don't forget risk enhancing factors
- Consider coronary calcium scan to aid in treatment decisions
- Assess treatment response with repeat lipid measurements and adjust meds as needed

50

Question 1

A 60-year-old man presents for the routine follow-up of intermittent claudication. He feels well. His medical history includes iliofemoral arterial disease status/post percutaneous revascularization, hypertension, hypercholesterolemia, and type 2 diabetes mellitus. He quit smoking a few months earlier. His medications include aspirin 81 mg, rosuvastatin 40 mg, lisinopril 20 mg, metformin 1000 mg twice daily, chlorthalidone 25 mg, and varenicline 0.5 mg.

His vital signs are pulse rate 70 bpm, blood pressure 139/81 mm Hg, and respiratory rate 14 breaths/min. His examination findings are remarkable only for decreased pedal and posterior tibial pulses. Laboratory evaluation findings include total cholesterol level 170 mg/dL, high-density lipoprotein cholesterol (HDL-C) level 34 mg/dL, low-density lipoprotein cholesterol (LDL-C) level 98 mg/dL, and triglyceride (TG) levels 190 mg/dL. His calculated 10-year atherosclerotic cardiovascular disease (ASCVD) risk is 24% using the Pooled Cohort Equation.

The addition of which one of the following is most appropriate for this patient?

A. Niacin
B. Clopidogrel
C. Fish Oil
D. Ezetemibe
E. Vitamin E

Question 2

A 54-year-old man with hypertension and myocardial infarction 11 months prior treated with stenting of the posterior descending artery is seen in clinic for routine follow-up. He denies any chest discomfort or dyspnea with activity. He would like to reduce his medications if possible. Since his previous visit 6 months prior, he has been diagnosed with diabetes mellitus, and he asks whether the statin is responsible. His daily medications include aspirin 81 mg, metoprolol succinate 25 mg, lisinopril 10 mg, and atorvastatin 40 mg. On examination, his heart rate is 62 bpm and blood pressure is 112/65 mm Hg. The remainder of his examination is normal. An echocardiogram reveals normal left ventricular ejection fraction (LVEF). Creatinine is 0.9 mg/dL and low-density lipoprotein is 68 mg/dL.

What would you advise regarding his medication regimen?

A. Discontinue Aspirin
B. Continue current therapy
C. Discontinue Metoprolol
D. Increase Lisinopril
E. Substitute Ezetimibe for Atorvastatin

Thank You

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