

It's Time to "Treat to Target" for Lipid Management: Optimizing Clinical Care and Primary Prevention for High-Risk Patients

Dr. Natalie Levy

December 3, 2025

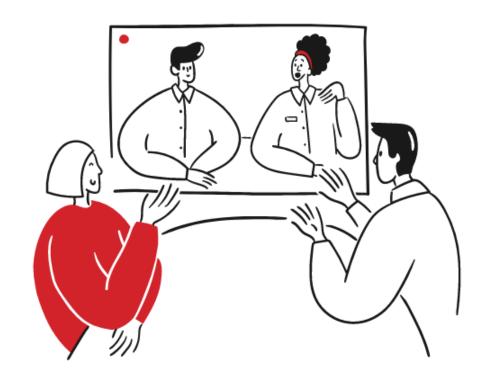
HRSA Funding Acknowledgment

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Housekeeping

- Phones have been muted to prevent background noise
- Use the chat box to type questions during the webinar
- This webinar is being recorded and will soon be available to all participants
- A webinar evaluation will be shared with participants









CHCANYS

Getting LDL-C to Goal: A Team-based Approach

Natalie Levy, MD

Director, Primary Care Diabetes Program, Bellevue Hospital Associate Professor, NYU Grossman School of Medicine December 3, 2025





CHCANYS

Getting LDL-C to Goal: A Team-based Approach Primary Prevention

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Disclosures



- I have no financial disclosures
- I am not a lipid specialist



Logistics



- 90-minute Webinar
- Part I: 60 min Presentation, Type Questions in the Chat
- Part II: 30 min Panel Discussion with 3 CHCANYS sites:
- Neighborhood Health Center of Western NY
- Ryan Health, NYC
- ConnextCare, Oswego County



Objectives



- ACC/AHA LDL Goals for the Primary Prevention of ASCVD.
- The landscape of Statin Intolerance among CHC patient populations.
- Alternatives and related barriers or facilitators to statins (i.e., Ezetimibe, PCSK9 inhibitors, Bempedoic acid).
- The role of multi-disciplinary Clinical Care Teams in supporting a "Treat to Target" framework for optimal cholesterol management and shared decision-making among high-risk patients.



Outline



- LDL-C Goals in Primary Prevention
- Statins: Potency / MOA/ Intolerance/ Alternatives
- My Workflow for getting patients to LDL-C goal
- Panel with CHCANYS sites: Neighborhood Health Center of Western NY, Ryan Health (NYC), ConnextCare (Oswego County)



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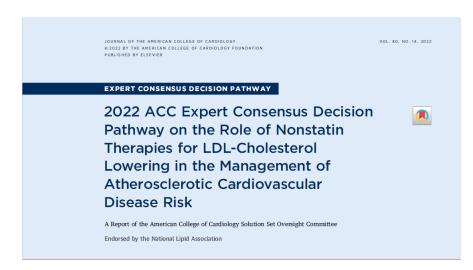
LDL-C Goals in Primary Prevention



• Importance of defining an LDL-C Goal



Review the Goals

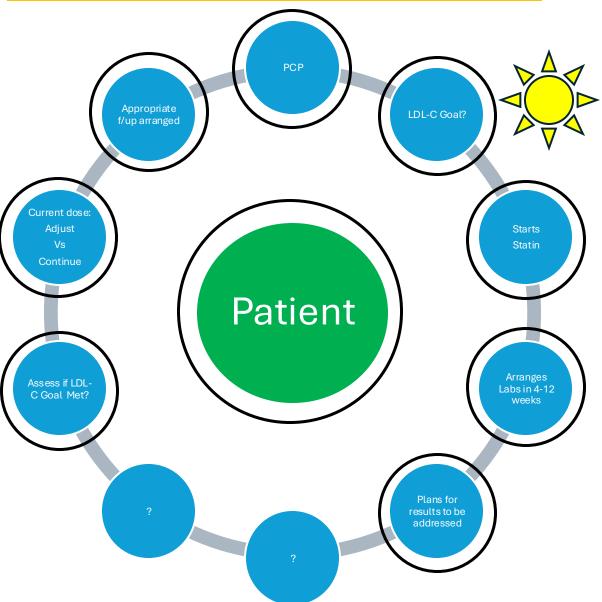






Getting to LDL-C Goal

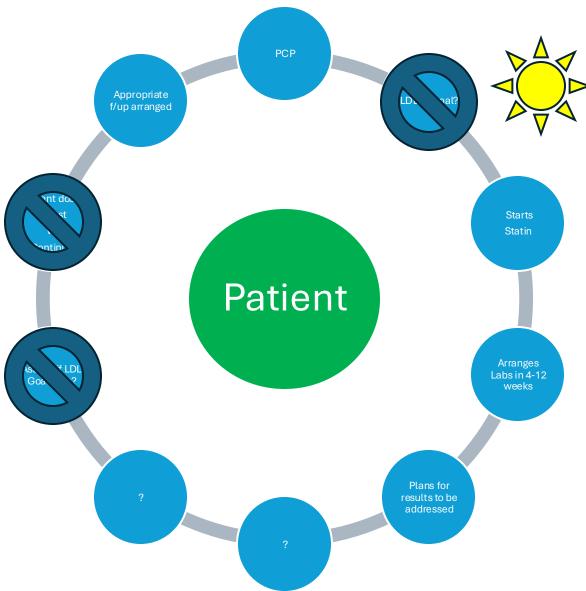






Getting to LDL-C Goal



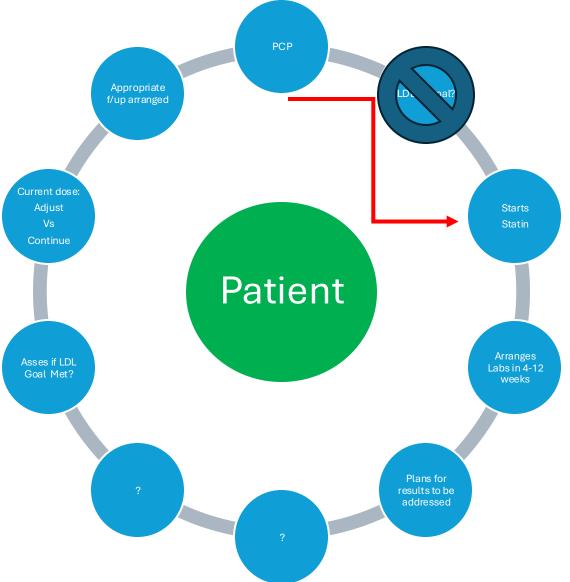


What usually happens instead?



Getting to LDL-C Goal





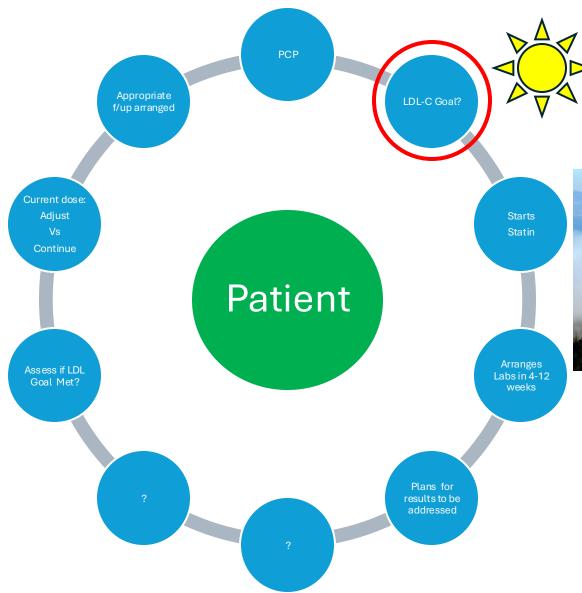


- High Risk Patient
- LDL High
- Advise on LS
- Start a Statin



Getting to LDL-C Goal

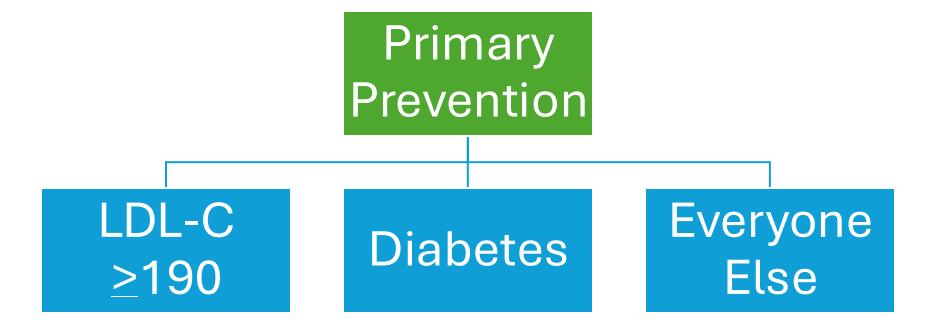






LDL-C Goals in Primary Prevention













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EXPERT CONSENSUS DECISION PATHWAY

Pathway on the Role of Nonstatin
Therapies for LDL-Cholesterol
Lowering in the Management of
Atherosclerotic Cardiovascular
Disease Risk

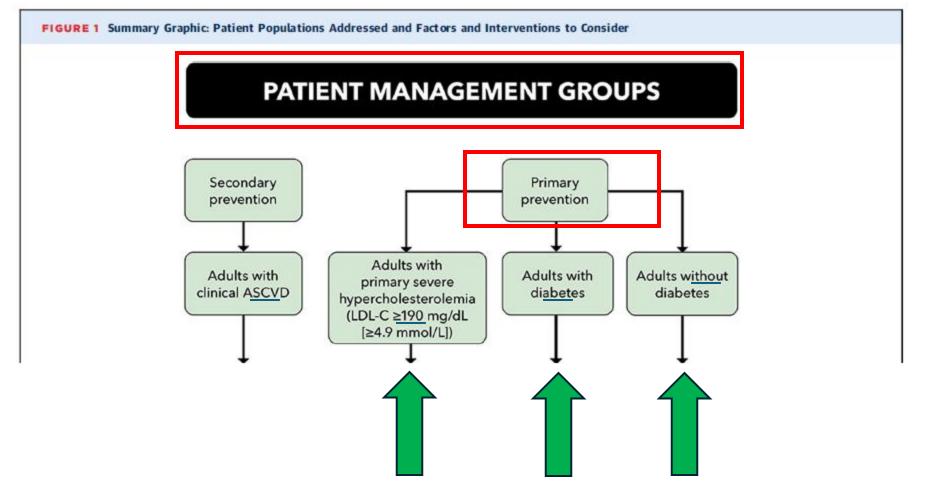


A Report of the American College of Cardiology Solution Set Oversight Committee

Endorsed by the National Lipid Association

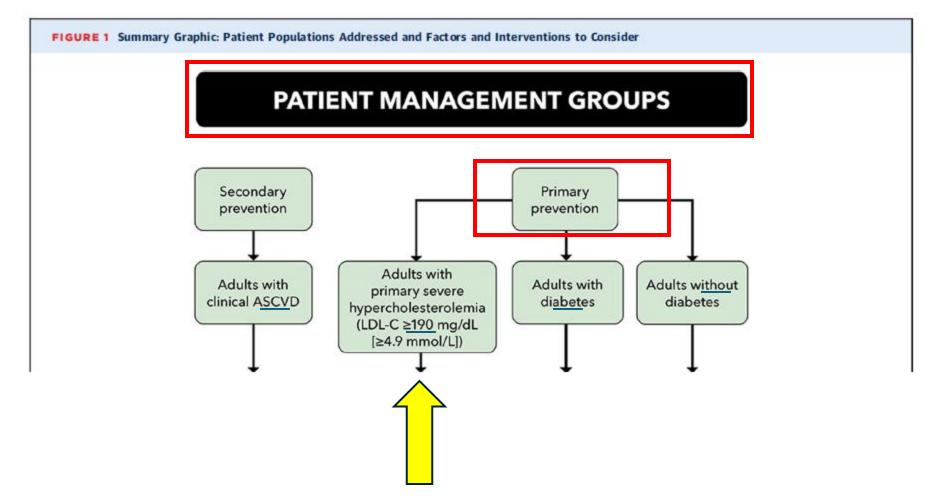




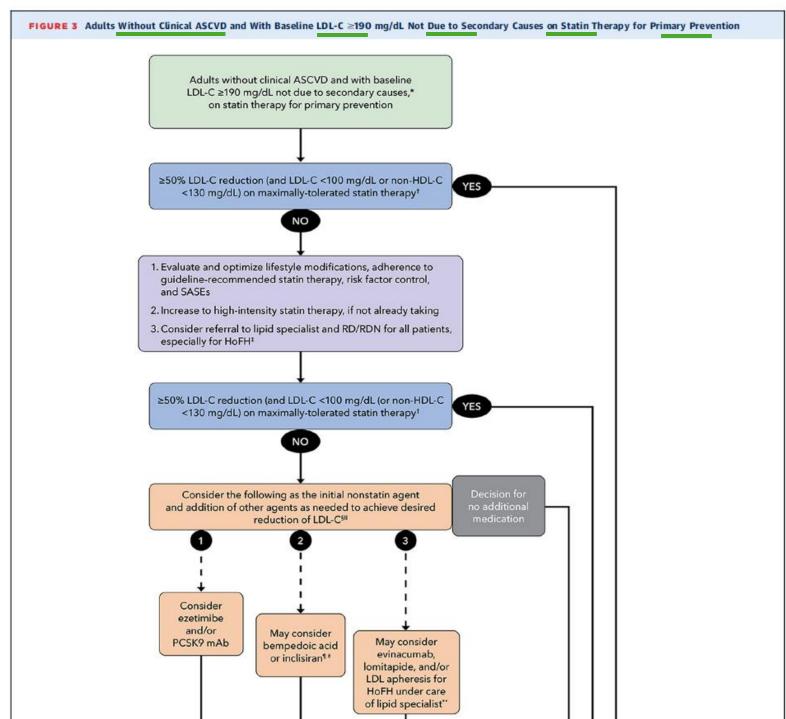






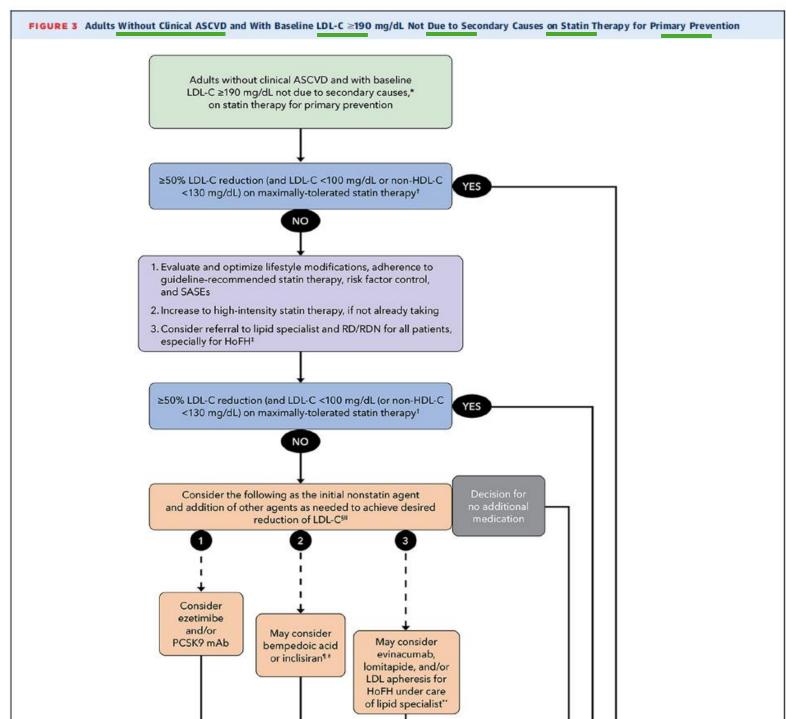






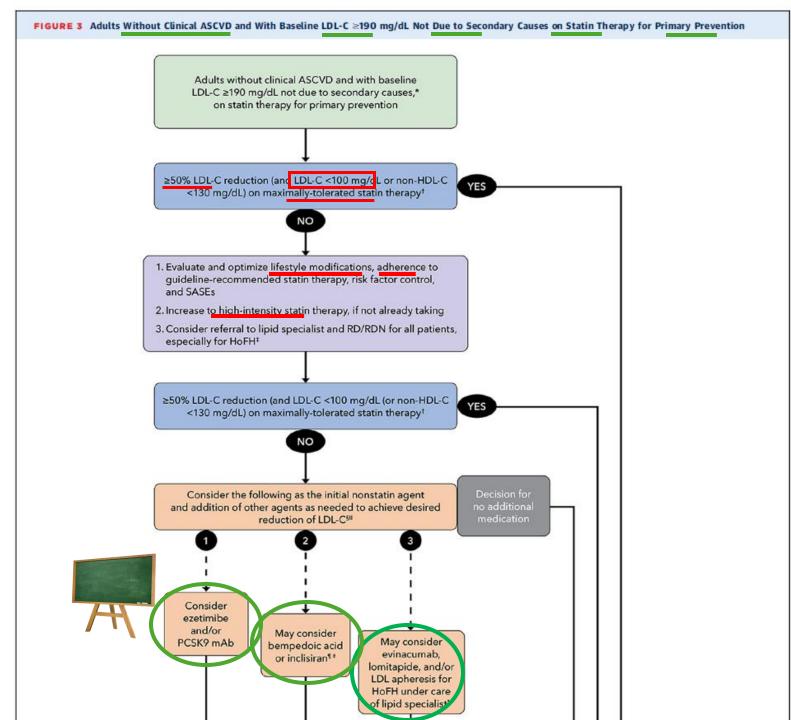










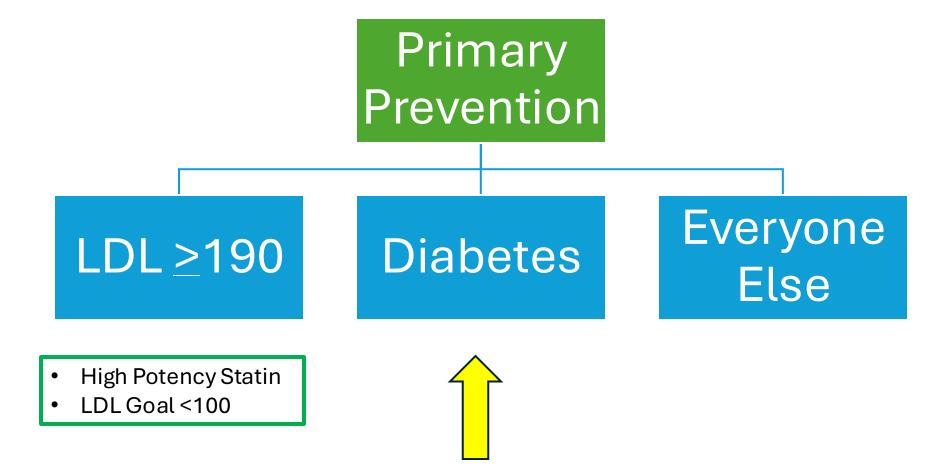




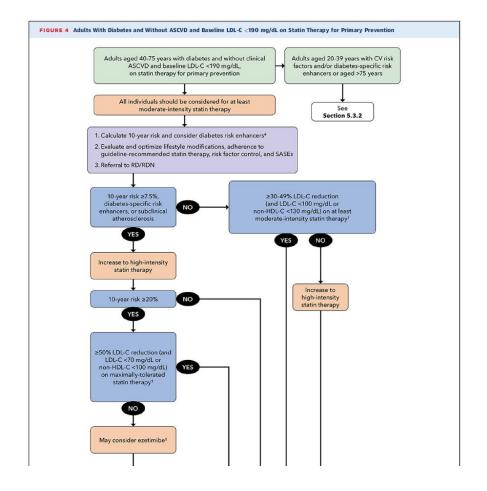


LDL-C Targets





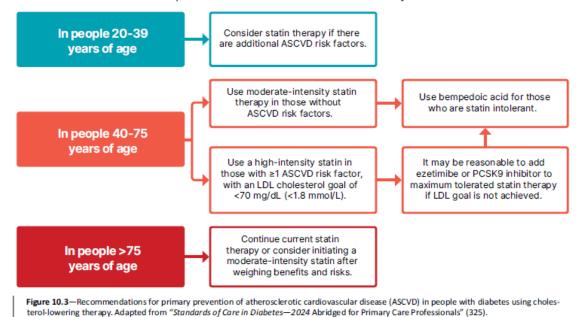




ACC 2022 ECDP



Lipid Management for Primary Prevention of Atherosclerotic Cardiovascular Disease Events in People With Diabetes in Addition to Healthy Behavior Modification



ADA 2025 Standards of Care

"This section has received endorsement from the American College of Cardiology"









Lipid Management for <u>Primary Prevention</u> of Atherosclerotic Cardiovascular Disease Events in People With Diabetes in Addition to Healthy Behavior Modification

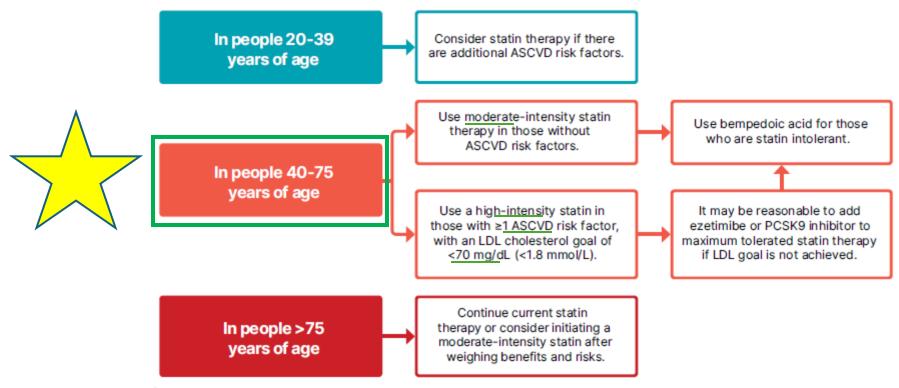
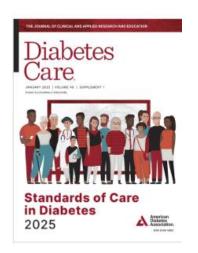


Figure 10.3—Recommendations for primary prevention of atherosclerotic cardiovascular disease (ASCVD) in people with diabetes using cholesterol-lowering therapy. Adapted from "Standards of Care in Diabetes—2024 Abridged for Primary Care Professionals" (325).







Lipid Management for <u>Primary Prevention</u> of Atherosclerotic Cardiovascular Disease Events in People With Diabetes in Addition to Healthy Behavior Modification

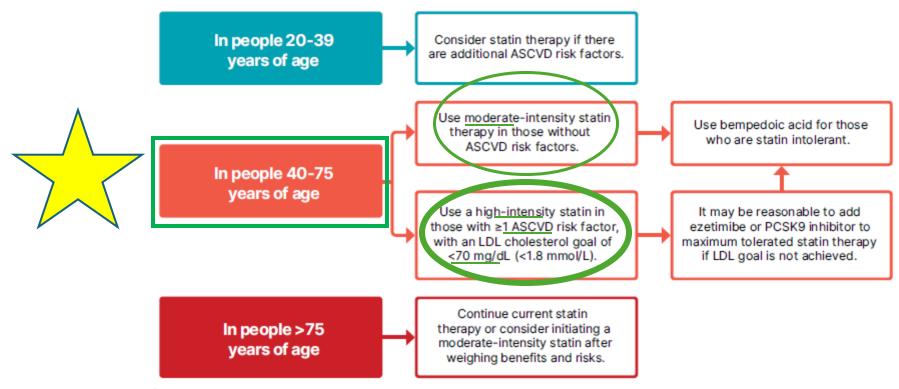
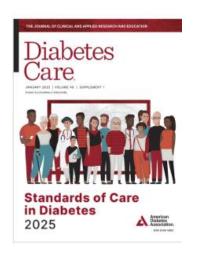


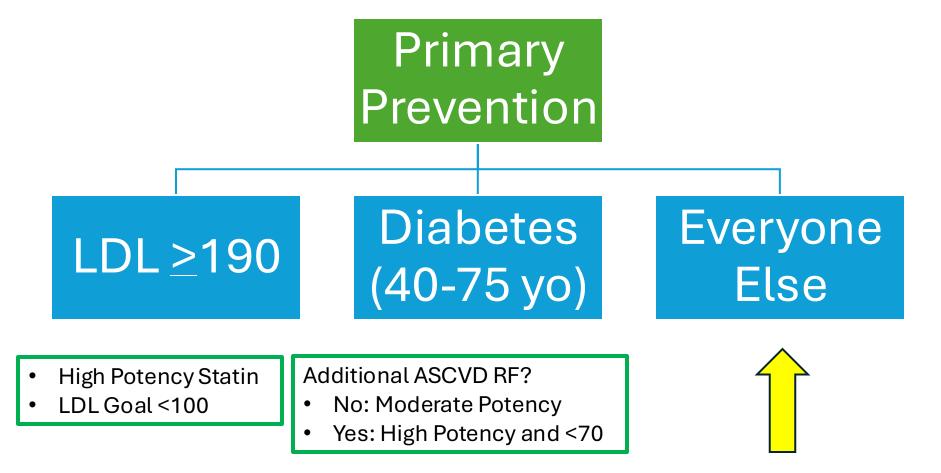
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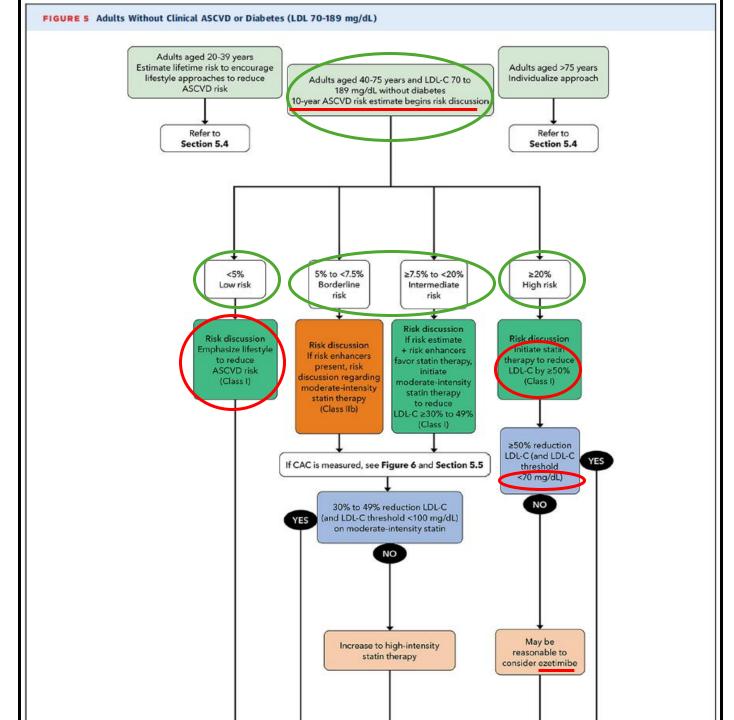


LDL-C Targets



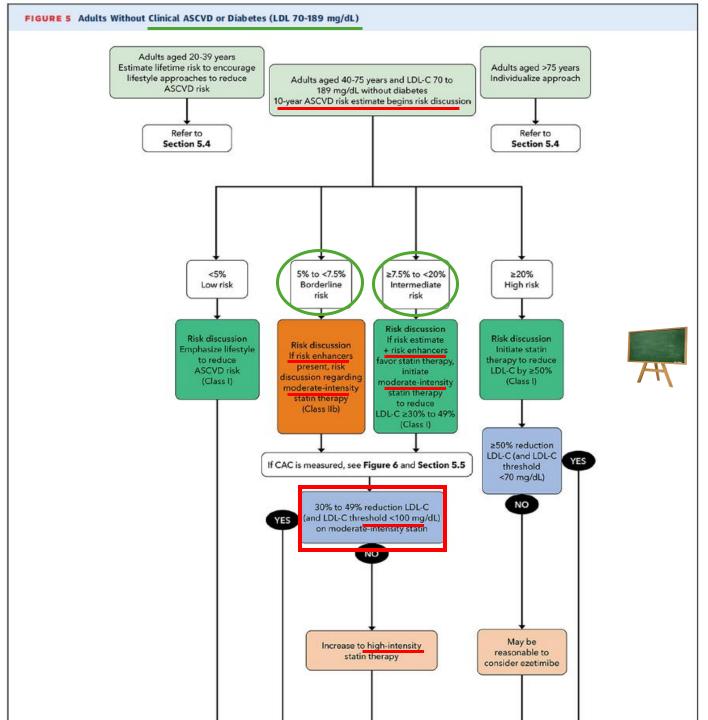






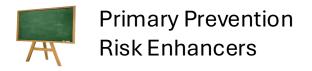








Primary Prevention: Risk Enhancers





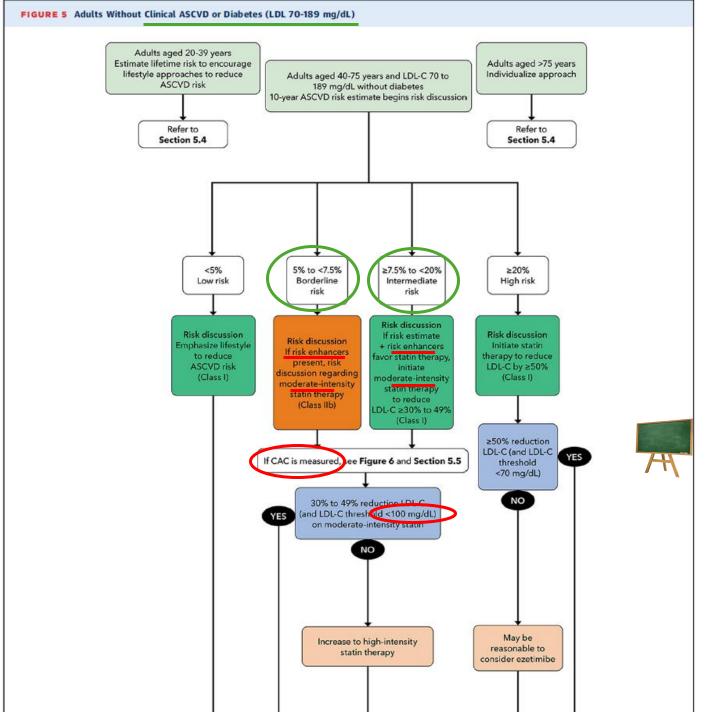
Risk-Enhancing Factors

- Family history of premature ASCVD (men aged <55 years; women aged <65 years)
- 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 [≥150 mg/dL], elevated blood pressure, elevated glucose, and low HDL-C [<40 mg/dL in men; <50 mg/dL in women] are factors; tally of 3 makes the diagnosis
- Chronic kidney disease (eGFR 15-59 mL/min/1.73 m² 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 years) and history of pregnancy-associated conditions that increase later ASCVD risk, such as preeclampsia
- High-risk races/ethnicities (eg, South-Asian ancestry)
- Lipids/biomarkers: Associated with increased ASCVD risk
 - Persistently* elevated, primary hypertriglyceridemia (≥175 mg/dL)
 - If measured:
 - Elevated high-sensitivity C-reactive protein (≥2.0 mg/L)
 - Elevated Lp(a): A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥50 mg/dL or ≥125 nmol/L constitutes a risk-enhancing factor, especially at higher levels of Lp(a).
 - Elevated apoB≥130 mg/dL: A relative indication for its measurement would be triglycerides ≥200 mg/dL. A level ≥130 mg/dL corresponds to LDL-C≥160 mg/dL and constitutes a risk-enhancing factor
 - 4. ABI < 0.9

ABI = ankle-brachial index; AIDS = acquired immunodeficiency syndrome; apoB = apolipoprotein B; ASCVD = atherosclerotic cardiovascular disease; eGFR = estimated glomerular filtration rate; HDL-C = high-density lipoprotein cholesterol; HIV = human immunodeficiency virus; LDL-C = low-density lipoprotein cholesterol; Lp(a) = lipoprotein (a); RA = rheumatoid arthritis.

^{*}Optimally, 3 determinations. Reprinted with permission from Grundy et al.7

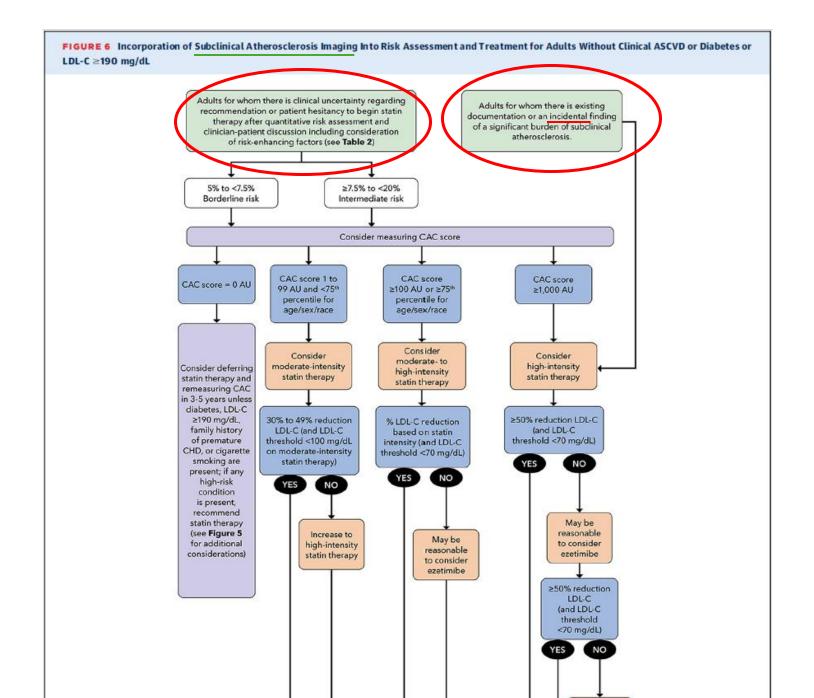






Primary Prevention: Coronary Artery Calcium Score

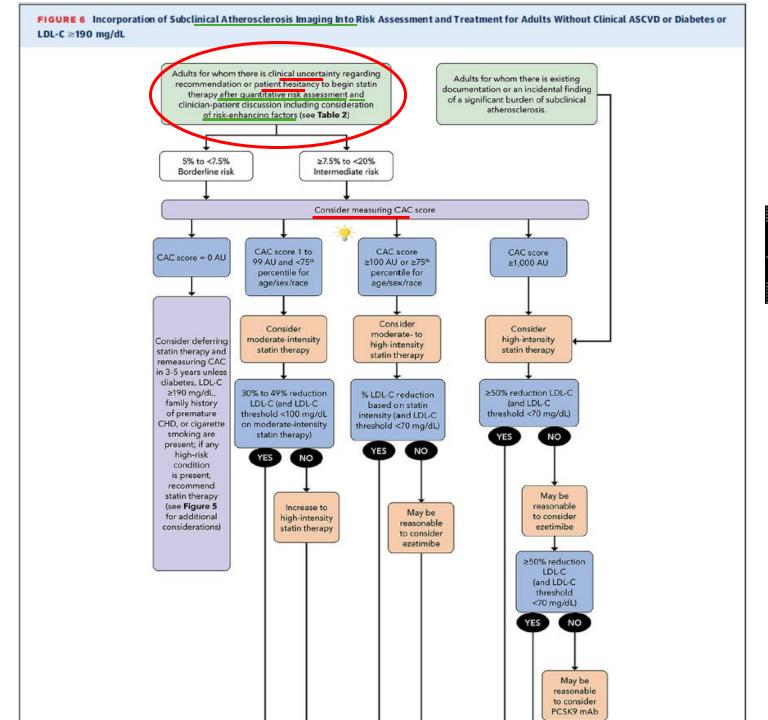




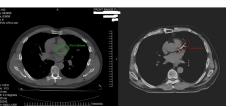




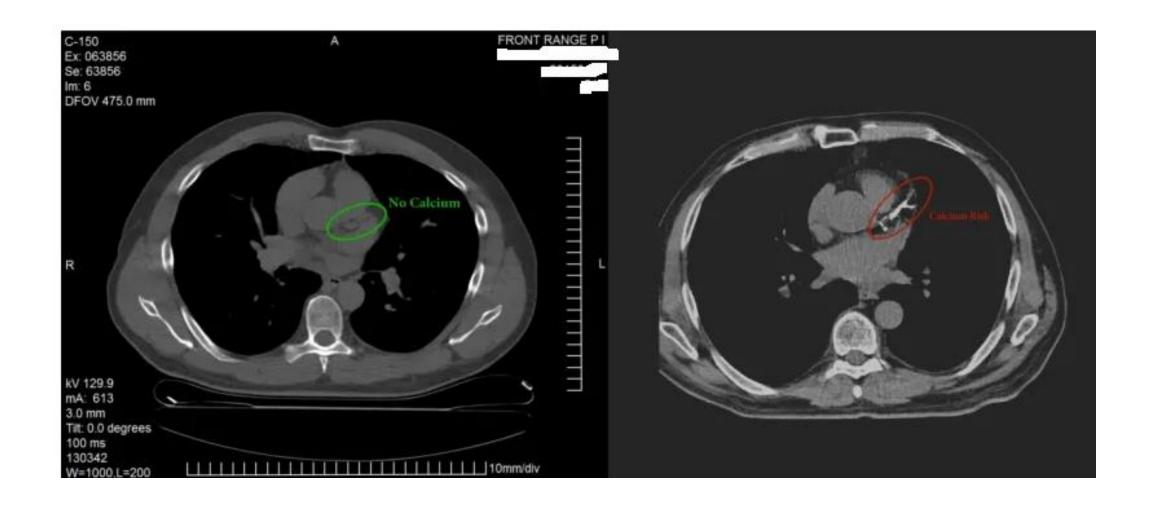




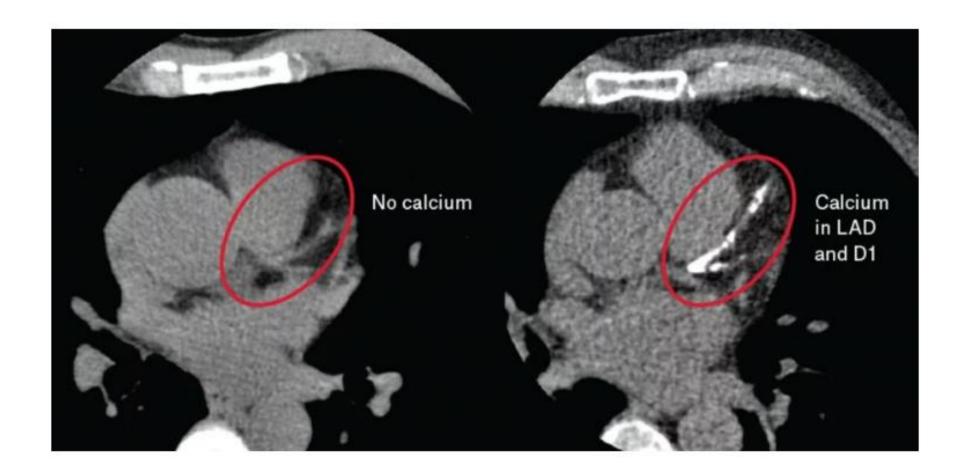




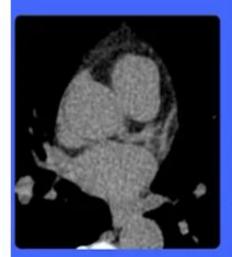
CAC

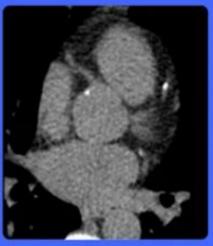


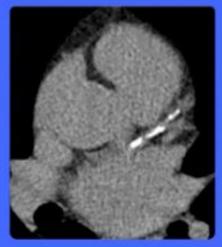
CAC



Coronary Calcium Test Scores









0 No calcium is detected 1-100
Mildly increased risk of heart disease

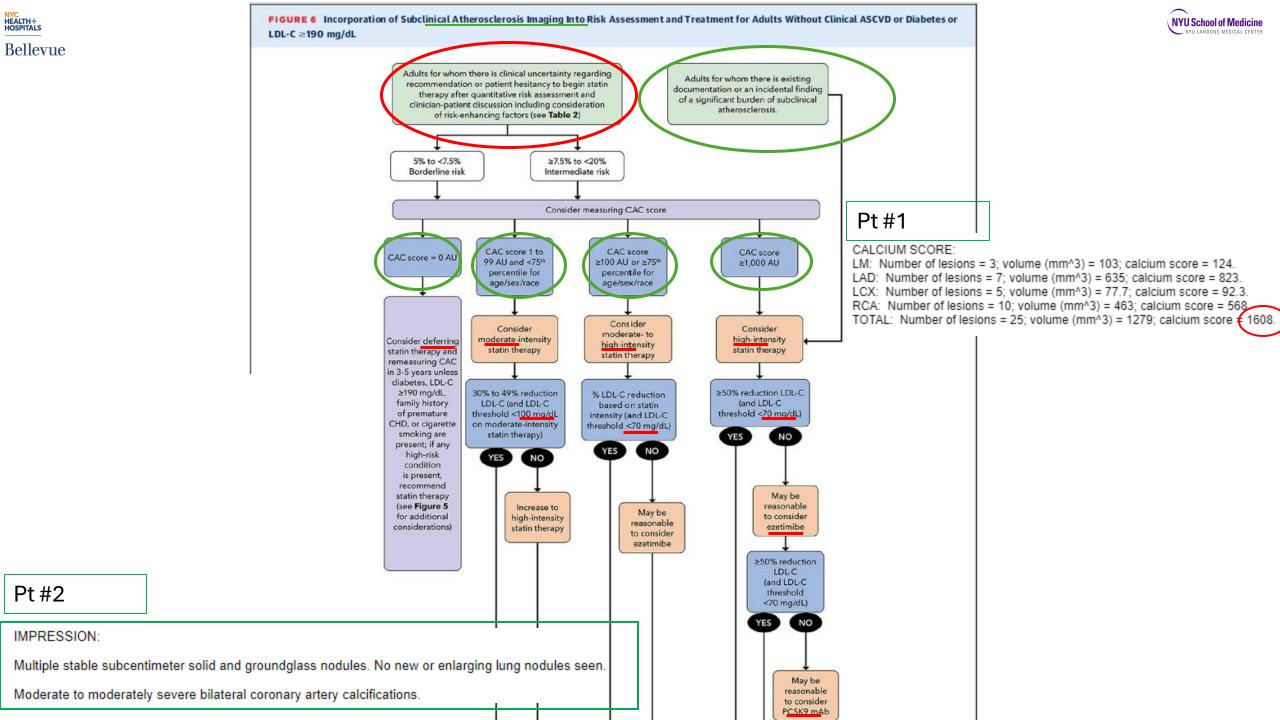
101-299 Moderately increased risk of heart disease 300+
Moderately to severely increased risk of heart disease

CAC Score: Predictor of Coronary Events

Coronary-Artery Calcium Score	Major Coronary Event†			Any Coronary Event		
	No./No. at Risk	Hazard Ratio (95% CI)	P Value	No./No. at Risk	Hazard Ratio (95% CI)	PValue
0	8/3409	1.00		15/3409	1.00	
1–100	25/1728	3.89 (1.72–8.79)	<0.001	39/1728	3.61 (1.96–6.65)	<0.001
101–300	24/752	7.08 3.05–16.47)	< 0.001	41/752	7.73 (4.13–14.47)	< 0.001
>300	32/833	6.84 2.93-15.99)	< 0.001	67/833	9.67 (5.20-17.98)	< 0.001

^{*} CAC denotes coronary-artery calcium score, and CI confidence interval.

[†] Major coronary events were myocardial infarction and death from coronary heart disease. ‡ Each unit increase in log₂(CAC+1) represents a doubling of the coronary-artery calcium score.





LDL Targets



Primary Prevention

LDL ≥190

Diabetes (40-75yo)

Everyone Else

- High Potency Statin
- LDL Goal < 100

Additional ASCVD Risk Factors?

- No: Moderate Potency
- Yes: High Potency and <70

10yr ASCVD risk score

<5% Lifestyle

>20% LDL <70

5-19.9% + Risk enhancers LDL < 100





- LDL-C Goals in Primary Prevention
- Statins: Potency / MOA/ Intolerance/ Alternatives
- My Workflow for getting patients to LDL-C goal
- Panel with CHCANYS sites: Neighborhood Health Center of Western NY, Ryan Health (NYC), ConnextCare (Oswego County)





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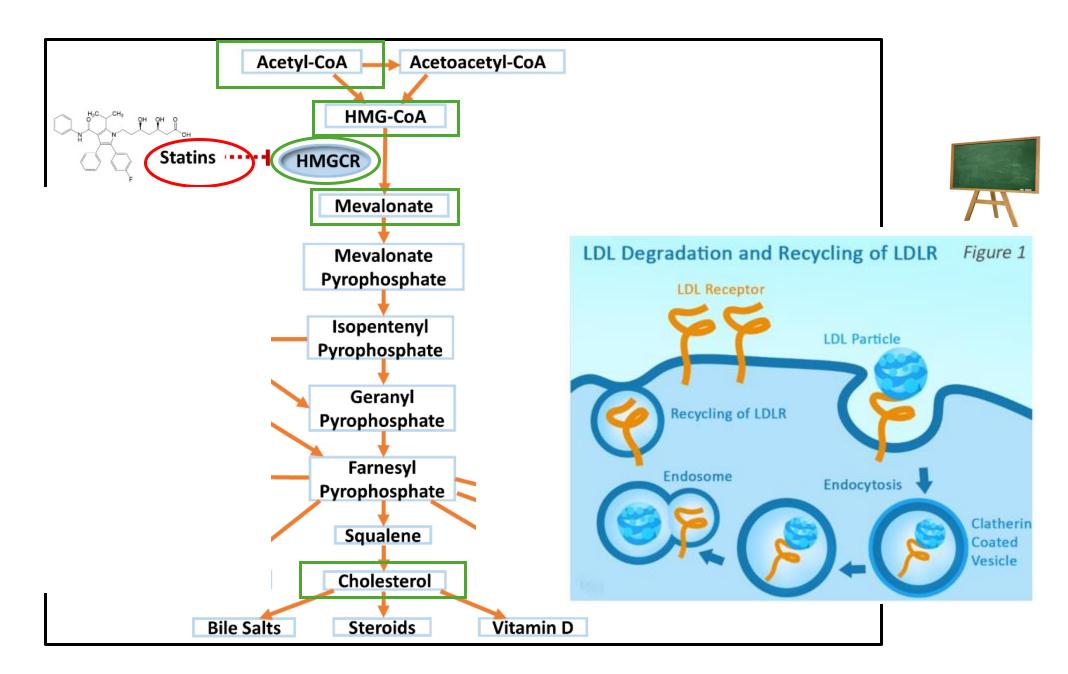


High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL on average by ≥50%	Daily dose lowers LDL on average by approximately 30-49%	Daily dose lowers LDL on average by <30%
Atorvastatin 40-80 mg Rosuvastatin 20-40 mg	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Fluvastatin 40 mg BID Pitavastatin 2-4 mg	Simvastatin 10 mg Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg





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Statin Intolerance- Topics



- Most common clinical presentation
- Definition
- Frequency
- Strategies



Statin Intolerance-Topics



- Most common clinical presentation: SAMS
- Definition
- Frequency
- Strategies



SAMS



- Statin Associated Muscle Symptoms
- Large, Symmetric / Bilateral Muscle Groups
- Usually starts w/in the first few weeks
- Usually resolves 2-4 weeks after stopping the statin
- Three levels
- Myalgia: discomfort- achy, soreness, fatigue, generally w/o CK elevation
- Myopathy: pain, weakness. CK > 10x ULN. 1/10,000 patients per year
- Rhabdomyolysis: myoglobinuria and acute renal failure, CK >40x ULN.
 1/100,000 patients per year



Statin Intolerance



- Most common clinical presentation: SAMS
- Definition
- Frequency
- Strategies



Statin Intolerance: Definition



- Symptoms
 - Start with statin use
 - Resolve/improve with statin dose reduction/discontinuation
- Tried 2 or more statins
- One of the statins was at the lowest approved daily dose
- Q: Meets Definition of Statin Intolerance?
 - Symptoms: while taking 20mg of daily atorvastatin





- Partial vs Complete Intolerance
 - Complete: cannot tolerate any statin at any dose or at any regimen
 - Partial: can tolerate a lower does of statin than required to meet goal



Statin Intolerance



- Most common statin intolerance: SAMS
- Definition of being statin intolerant
- Frequency
- Strategies



Statin Intolerance- Frequency?



- ILEP: International Lipid Expert Panel. 2022. Meta-analysis. 4 mill pts.
 - 112 RCT -- 4.9%
 - 64 Observational-17%



Statin Intolerance- Frequency?



- ILEP: International Lipid Expert Panel 2022. Meta-analysis. 4 mill pts.
 - 112 RCT -- 4.9%
 - 64 Observational-17%

The prevalence (or cumulative incidence) of statin intolerance was 4.9% (95% confidence interval [CI] 4.0%-6.0%) in the 112 RCTs included. However, the prevalence (or cumulative incidence) was 17% (95% CI 14%-19%) in the 64 observational cohort studies included.

The primary objectives of the RCTs included in this metaanalysis were generally to assess clinical outcomes other than adverse effects and tolerability. Self-selection of those who volunteer for clinical trials of statin therapy, coupled with design elements such as exclusion of patients with prior statin intolerance or co-morbid conditions that may predispose to statin intolerance and run-in phases on statin therapy for some trials, suggest that results from clinical trials may produce an underestimation of the true incidence of statin intolerance in the population. Therefore, estimates of prevalence from observational cohort data may more accurately reflect the real-world clinical experience. Meta-regression





Placebo Effect



Nocebo Effect





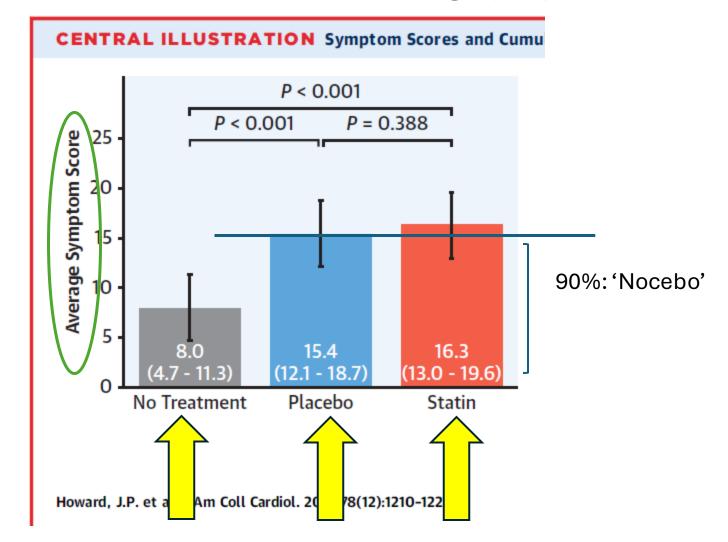


• SAMSON: 2021. 60 pts. Hx Statin Intol w/in 2 weeks of use. RCT. 3 Conditions: Atorva 20 vs Placebo vs NO PILL. Avg Symptom Score.

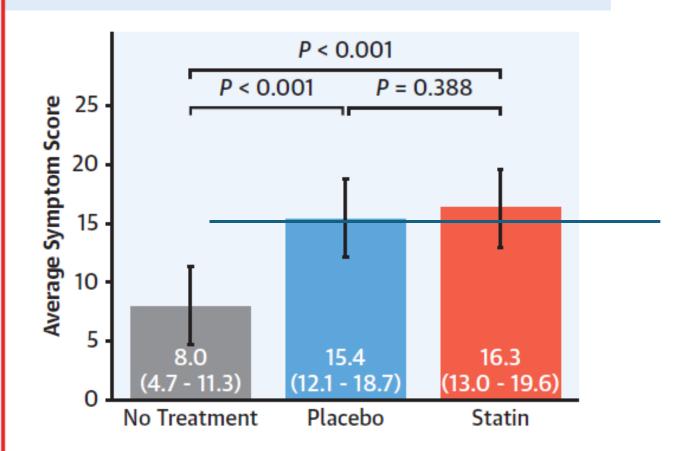




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CENTRAL ILLUSTRATION Symptom Scores and Cumu



Relevant?

Whether it is 'nocebo' or not, It's real to the person

Therefore, we need strategies to manage it

Howard, J.P. et al. J Am Coll Cardiol. 2021;78(12):1210-1222.





Statin Intolerance





- Most common statin intolerance: SAMS
- Definition of being statin intolerant
- Frequency
- Strategies



Statin Intolerance- Strategies



- Pre-Strategies
- Engage your patient in the #s!
- What LDL-C 1) Currently? 2)Goal? 3)What can be achieved with daily statin use?
- Set a date for a repeat lab draw
- High Intensity Statins- I avoid the very highest doses

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL on average by ≥50%	Daily dose lowers LDL on average by approximately 30-49%	Daily dose lowers LDL on average by <30%
Atorvastatin 40-80 mg Rosuvastatin 20-40 mg	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg	Simvastatin 10 mg Pravastatin 10-20 mg Lovastatin 20 mg



Statin Intolerance- Strategies



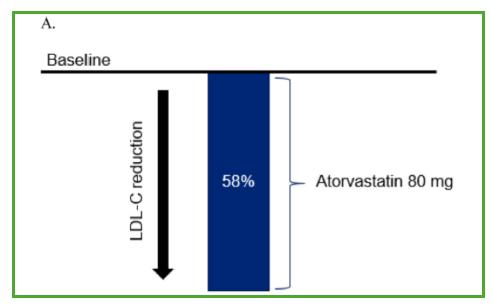
- Don't be judgy
- Wash out
- Then What?
 - Statin-based strategy?
 - Non-statin-based strategy / Statin Alternatives?



Statin Intolerance- Strategies



- Statin-based Strategies
- Same statin- lower dose, or non-daily dosing
- Try a different statin- low dose-and/or- non-daily dosing
- Ultimately 50+% of people with statin intolerance can tolerate some dose of a statin
- Low dose combination: Atorvastatin 10mg + Ezetimibe10mg: ?



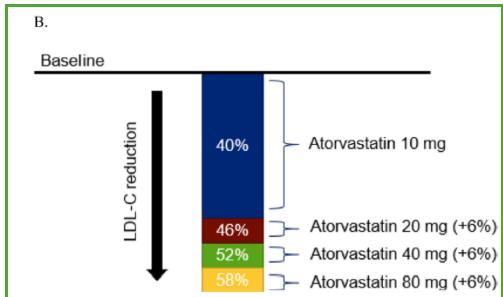
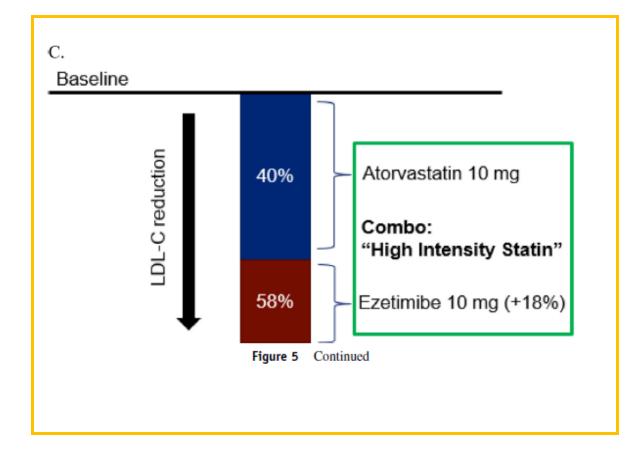


Figure 5 Approaches to achieving high-intensity statin LDL-C lowering in a patient with SAMS.

A. LDL-C lowering with the high-intensity statin – atorvastatin, B. LDL-C lowering across all atorvastatin dosing ranges, C. LDL-C lowering with low dose atorvastatin plus ezetimibe which equates to a high-intensity statin







Statin Intolerance-Strategies



Non-statin-based therapies / Statin Alternatives...





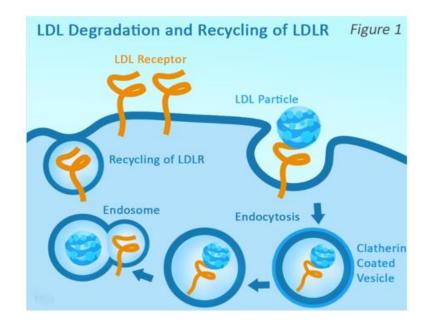
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Statin Alternatives



- Three Classes
 - Ezetimibe
 - PCSK9i: mAb and siRNA
 - o Bempedoic Acid
- Unique MOA but ultimately
 - o All lead to more LDLR
 - All lower LDL-C
- Improved CV Outcomes?
 - Ezetimibe
 - be 💙
 - o PCSK9 mAB
 - Bempedoic Acid
- Still being studied in CVOT
 - o PCSK9i: siRNA Inclisiran, ORION-4, 2026 🔞



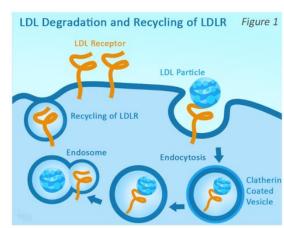
https://bpsbioscience.com/cholesterol-pcsk9-pathway



Statin Alternative-Ezetimibe



- Oral medication
- Inhibit NPC1L1 receptors in the small intestine
- Decreases absorption of cholesterol
- Less cholesterol gets delivered to the liver
- More LDLR
- Lowers LDL-C by about 20%



https://bpsbioscience.com/cholesterol-pcsk9-pathway

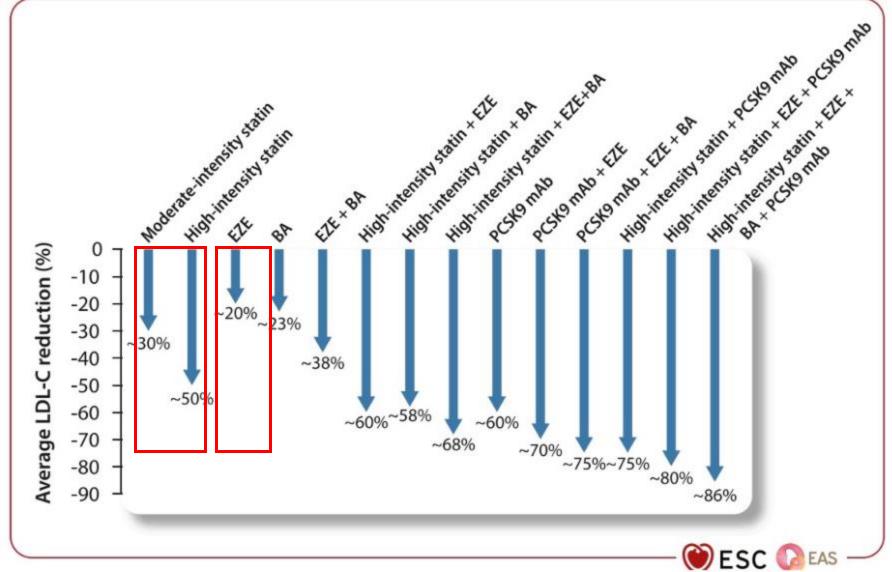
Improved outcomes in CVOT when combined with statins





Bellevi





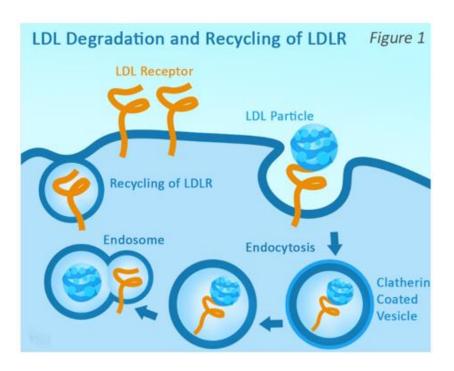


Statin Alternative-PCSK9i





PCSK9 targets our LDLR for degradation

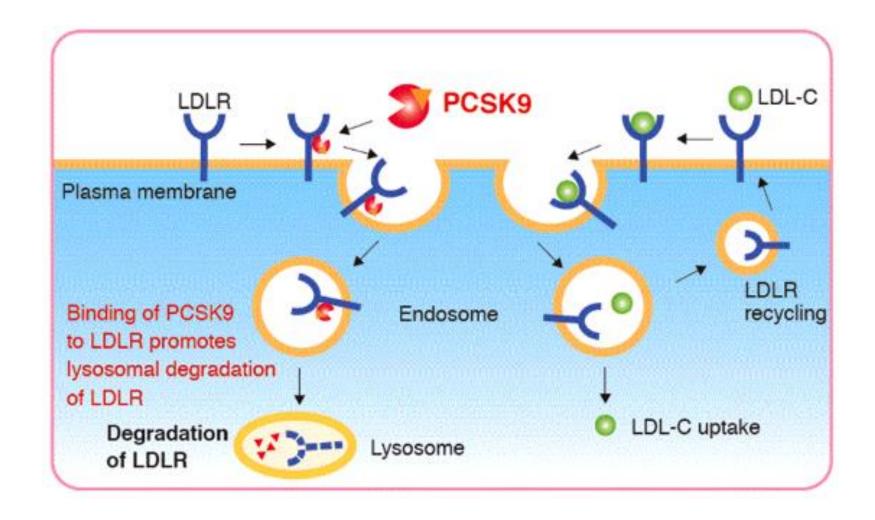


https://bpsbioscience.com/cholesterol-pcsk9-pathway





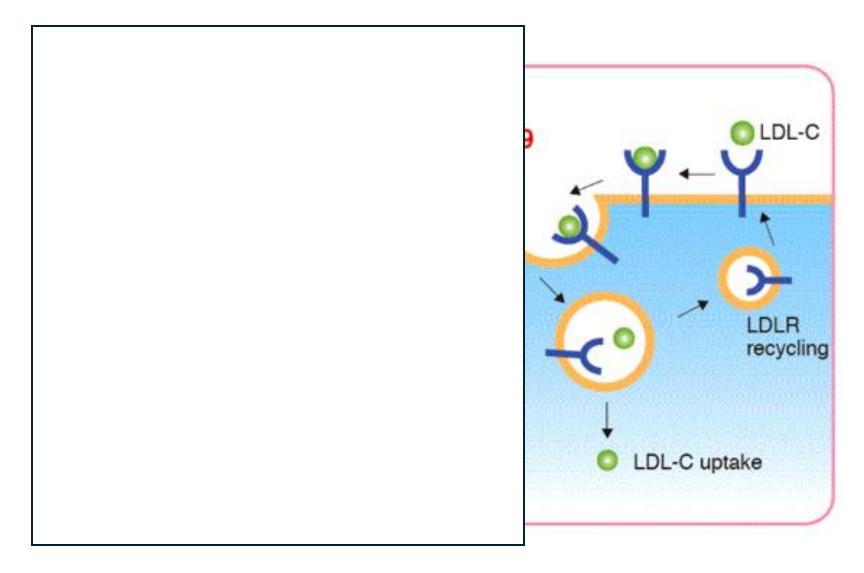








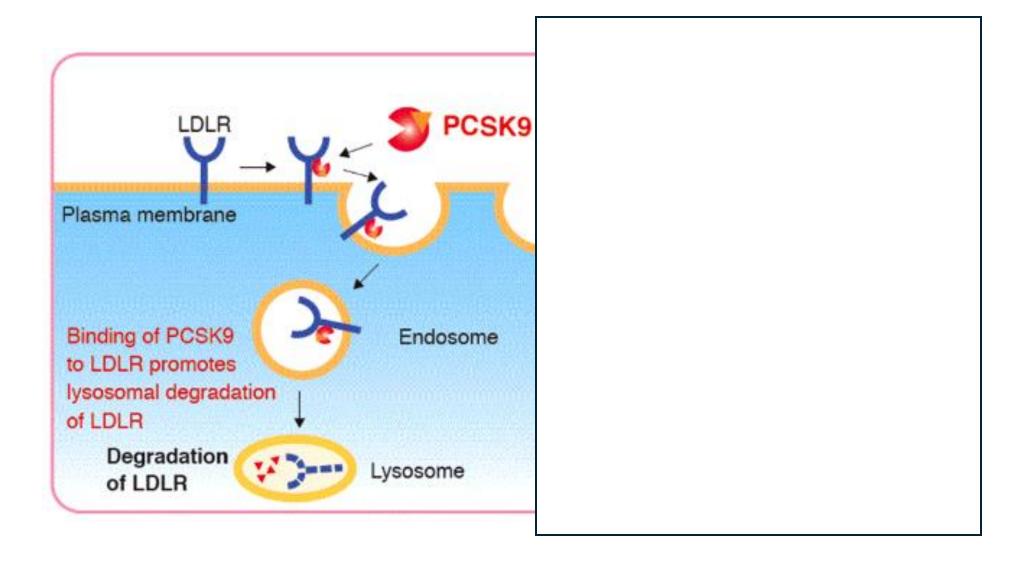
















- Two types of PCSK9i
- Both are injectable
- Monoclonal Ab
- siRNA





- Monoclonal Ab against PCSK9
- PCSK9 mAb
- Evolocumab
- Alirocumab
- SQ, by the patient
- Every 2 weeks or monthly
- Targets existing PCSK9 molecules for destruction
- Shown in trials to
 - Lower LDL
 - Improve Cardiovascular Outcomes







PCSK9i



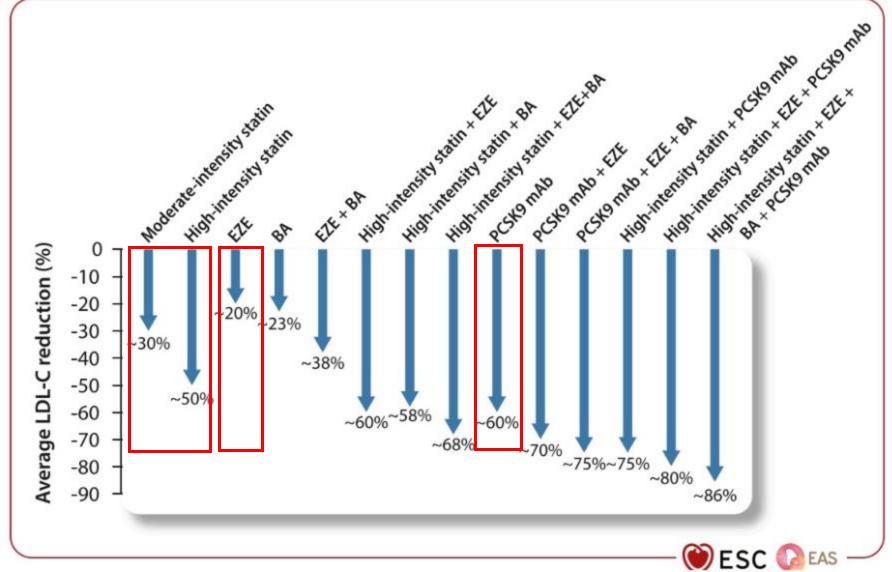
- Small interfering RNA Therapy
- siRNA
- Inclisiran
- SQ, in the clinic
- Maintenance is every 6 months
- Prevents the production of PCSK9
- Easier Adherence?
- Shown in trials to
 - Lower LDL
 - CVOT is in process





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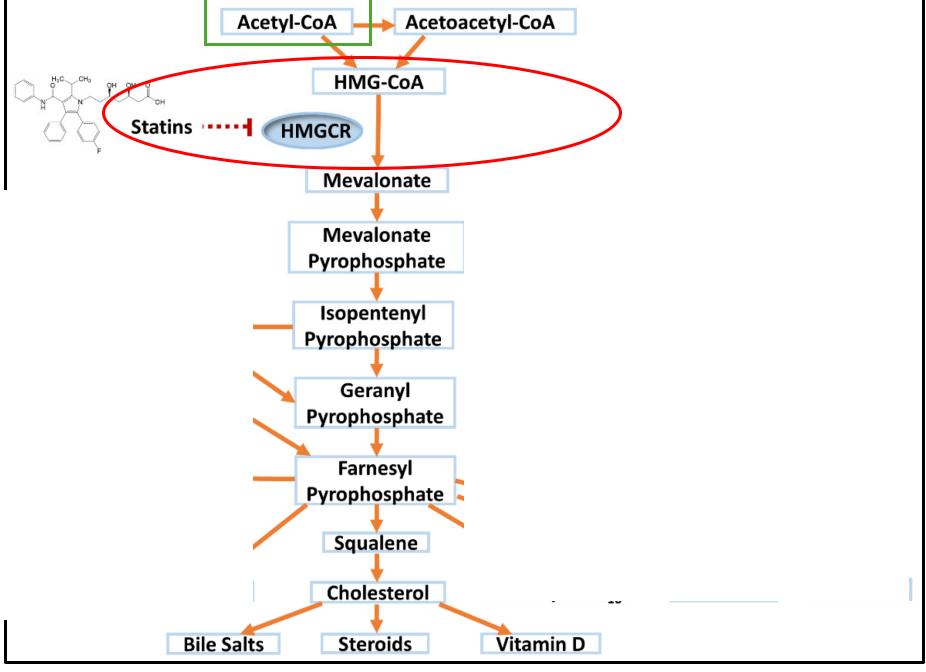
Statin Alternative-Bempedoic Acid



- Oral medication
- ATP Citrate Lyase Inhibitor
- Works in the same pathway as statins but upstream







NYU School of Medicine



Statin Alternative- Bempedoic Acid



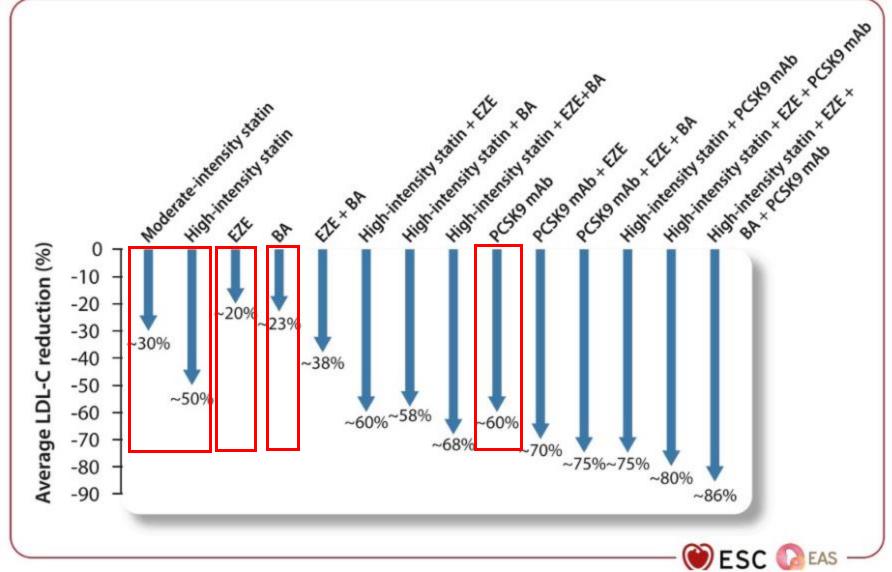
- ATP Citrate Lyase Inhibitor
- Works in the same pathway as statins but upstream
- Prodrug
- Activator is found in the liver but not skeletal muscles
- Avoids Statin Associated Muscle Symptoms
- Increases in Uric Acid, Caution in people with Gout
- Shown in CVOT to improve outcomes





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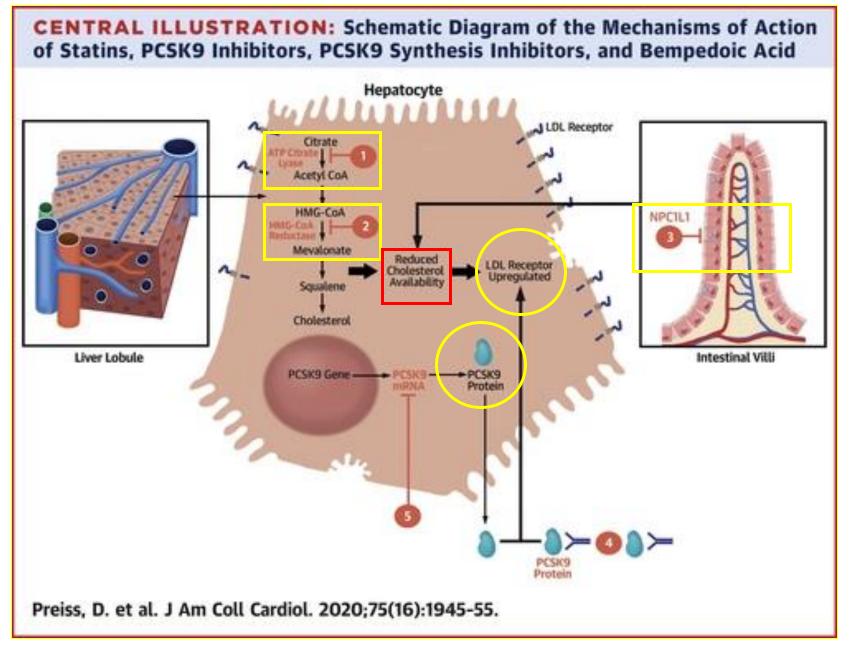






LDL Lowering



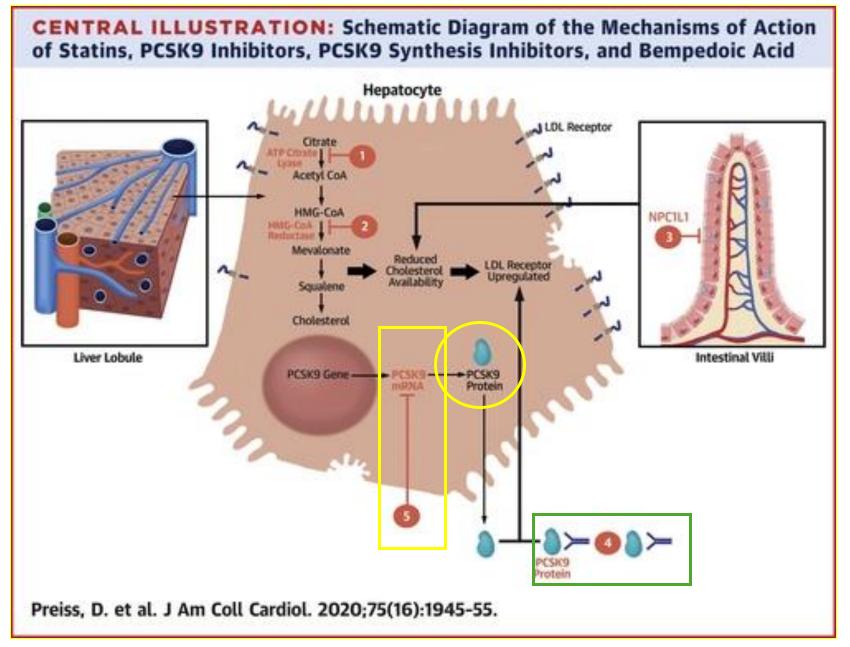






LDL Lowering





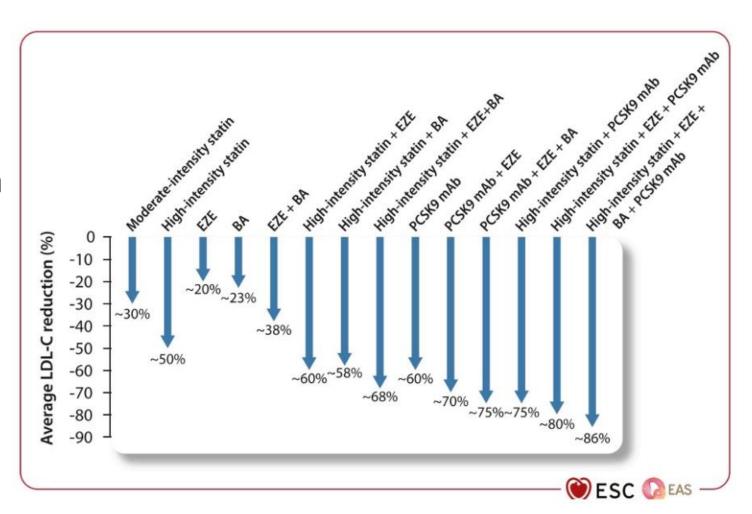




Statin Alternatives



- Used in 2 Situations:
- Statin Intolerance
- Statins alone are not enough





Outline



- LDL-C Goals in Primary Prevention
- Statins: Potency / MOA/ Intolerance/ Alternatives
- My Workflow for getting patients to LDL-C goal
- Panel with CHCANYS sites: Neighborhood Health Center of Western NY, Ryan Health (NYC), ConnextCare (Oswego County)





My Workflow: Getting LDL-C to Goal

- Same process development that I used when we designed our Primary Care Diabetes and HTN Programs
 - Embrace learning of guidelines
 - Carefully observe the needs of my own patients
 - Envision workflow
 - Involve the Core Chronic Disease Team
 - Work out a process
 - Disseminate to the whole clinic
- Now turning my attention to Getting LDL-C to Goal



- Work in Progress
- PCP setting the LDL-C goal is the first key step
- Then the conversation re how to help put that plan into action begins
- Here is how my workflow has gone so far: Index Visit





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My Workflow- @ Index Visit



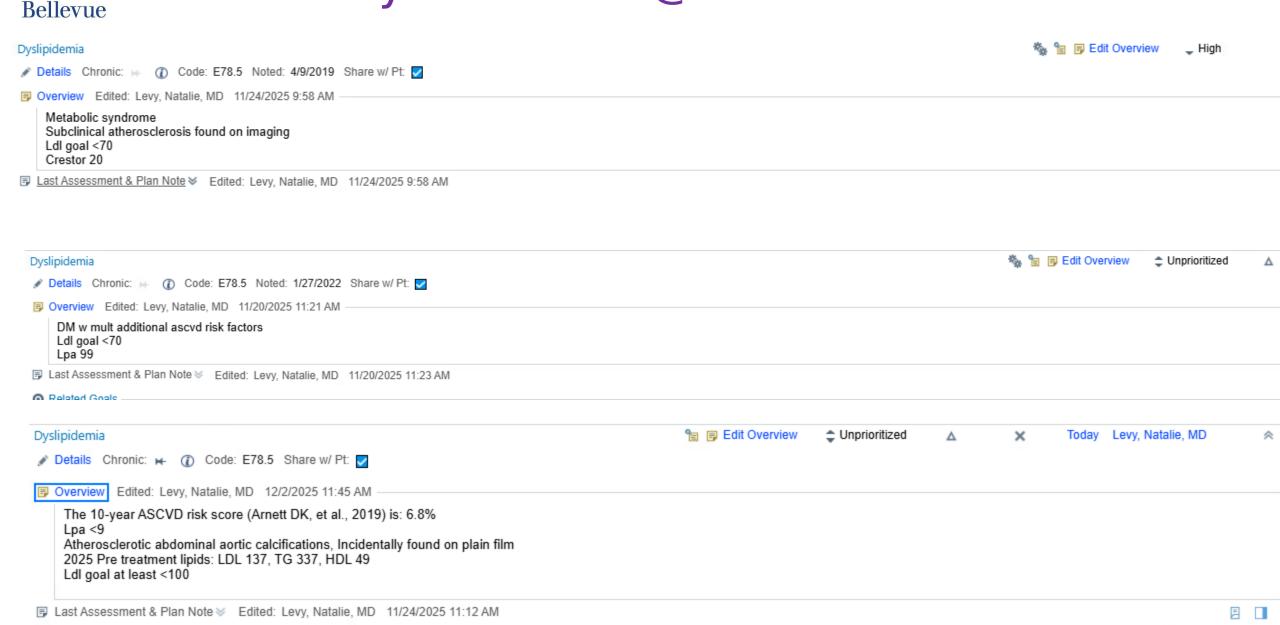
Assessing the LDL-C Goal

- Reflect on the patient's risk category and LDL-C Goal
- Engage the patient in the LDL-C #s
- Discuss Lifestyle
- Start a statin
- Write down the goal
 - In Epic in the Overview Section



My Workflow- @ Index Visit







My Workflow-@ Index Visit



Request a Lab Appointment in my "check out instructions"

- 4-12 weeks is the recommendation
- Actual Timing depends on
 - O How soon can they start statin, ease of return?
- 4 weeks?
 - o Rare option for me
 - Patient would have to pick up their medication right away
 - o Go for this if the person also needs a BP check- will get labs at time of BP check
- 6-8 weeks?
 - Ideal
 - I like to keep the momentum going if possible
- 12 weeks?
 - Their logistics make it tough for them to come back
 - I don't request a special lab appt
 - We follow up at our next visit



My Workflow-@Index Visit



Arrange for Someone to follow up and assess the results

- Three main options
- If patient agrees to come back in a few (~6-8) weeks for labs
 - Lab appt + APP appointment a few days later, Telehealth Visits
 - (Try to arrange the lab appointment on a day the patient will be here anyway)
- If the patient happens to have a T2DM Pharm D appt ~4-8 weeks later
 - Lab appt a few days prior to the Pharm D appt
 - I ask the Pharm D to follow up on the LDL-C result
- If the patient cannot come back for labs, we will check labs at our next visit
 - And at that next visit I will make a plan for who will f/up the results



My Workflow- @Index Visit



My Index Visit Checkout Note Most Frequent Options

- Option 1
 - Arrange Lab Appt 6-8 weeks
 - Arrange Advanced Practice Provider Telehealth Appointment 1-2 days later
- Option 2
 - I notice that the patient is seeing the Pharm D in 4-8 weeks
 - I request a Lab Appt 1-2 days prior to that Pharm D visit
 - I route my note to the Pharm D, I tell them the LDL-C goal, and ask them to f/up on the results
- Option 3
 - The patient cannot come back for labs before my next visit
 - Check out note says- schedule a f/up with me 12-16 weeks (next available)
- Option 4....Nursing Led T2T LDL-C Program?
 - Nurses run our T2T HTN Program, do a fantastic job.
 - I would love us to have a Nurse Led T2T LDL-C Program, I've thought about what this would look like, but the RNs are current at capacity.
 - If a Nurse led T2T LDL-C program interests anyone I would be happy to talk about this in the Q and A.

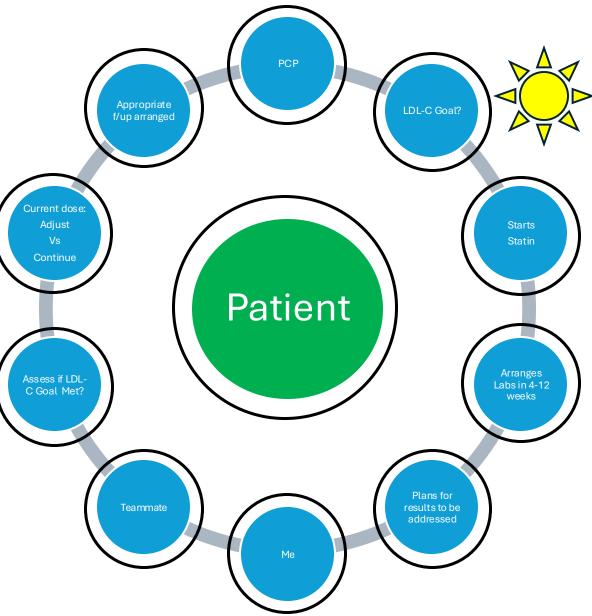


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Getting to LDL-C Goal







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