

Atherosclerotic Cardiovascular Disease (ASCVD) CME

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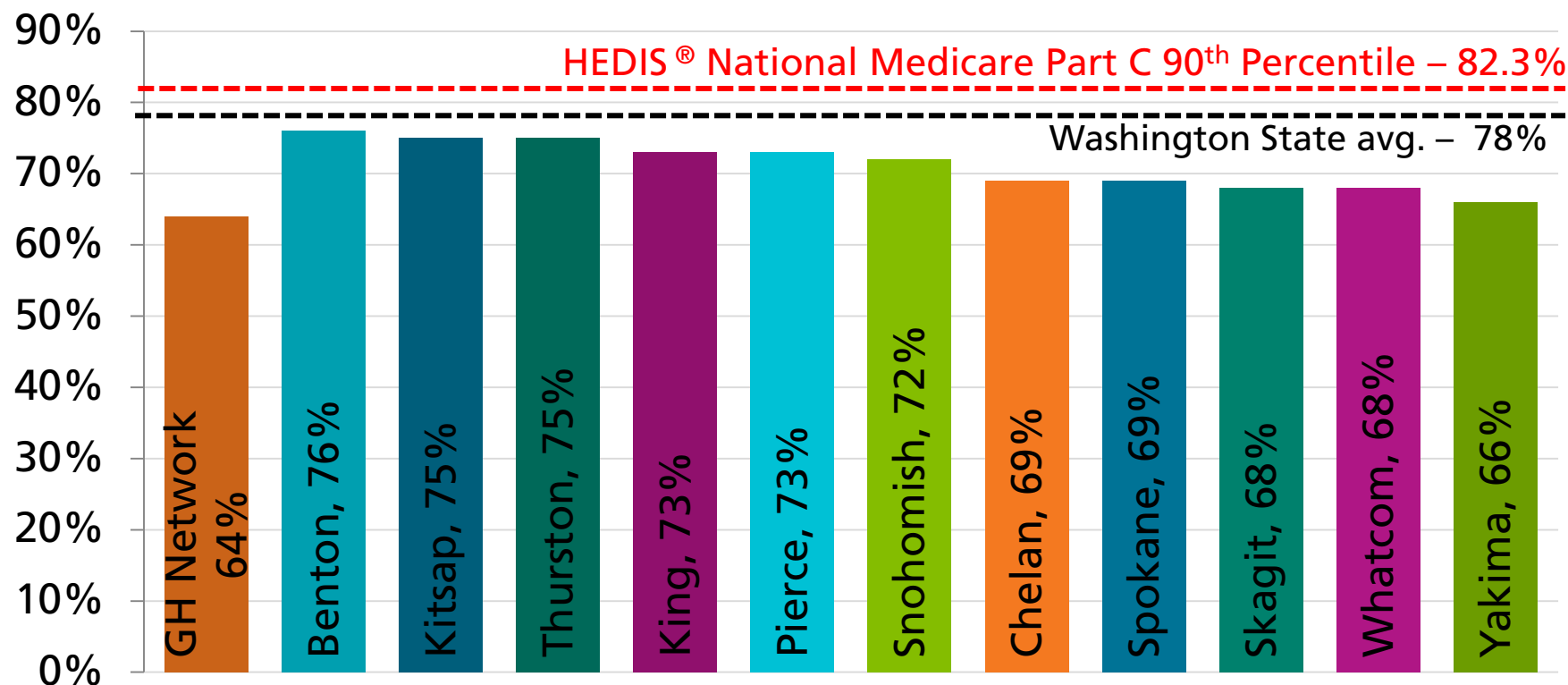
Agenda



- Why this topic was selected
- Background
- Pharmacologic therapy
- Statin tolerance
- Targets
- Risk calculators
- HEDIS metrics



Statin Therapy*



*Counties shown had over 200 eligible patients

Sources: Washington State Health Alliance Community Check-up 2015-All Payers, NCQA Medicare Performance 2016, Group Health Cooperative September 2016



Influences

Group Health's guidelines informed by:

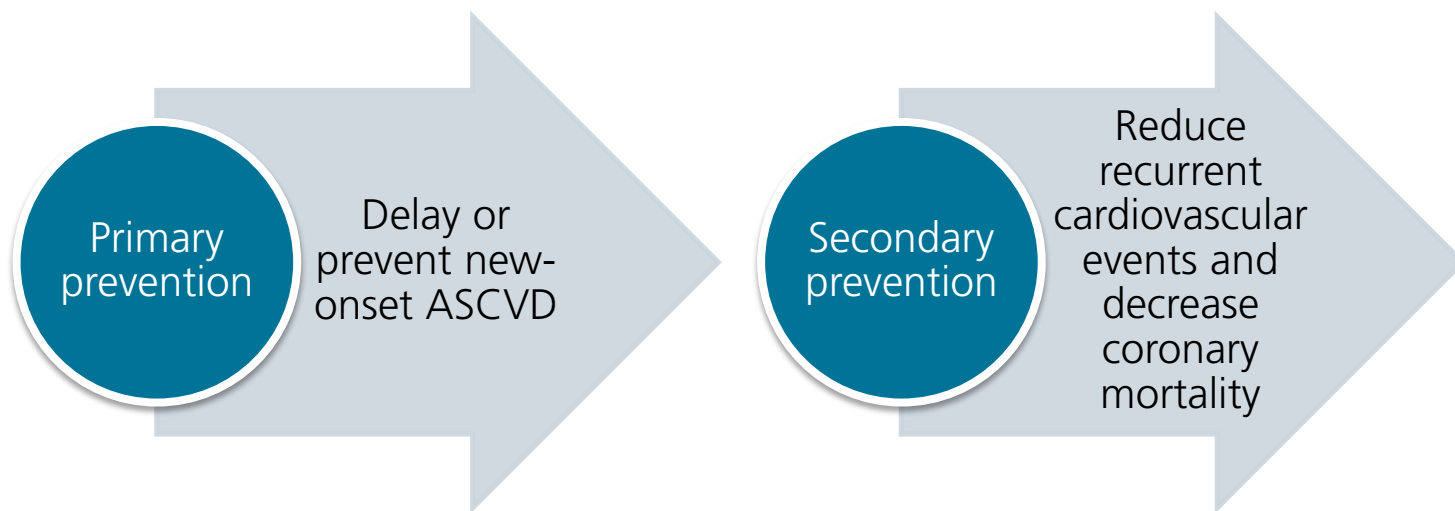




Background

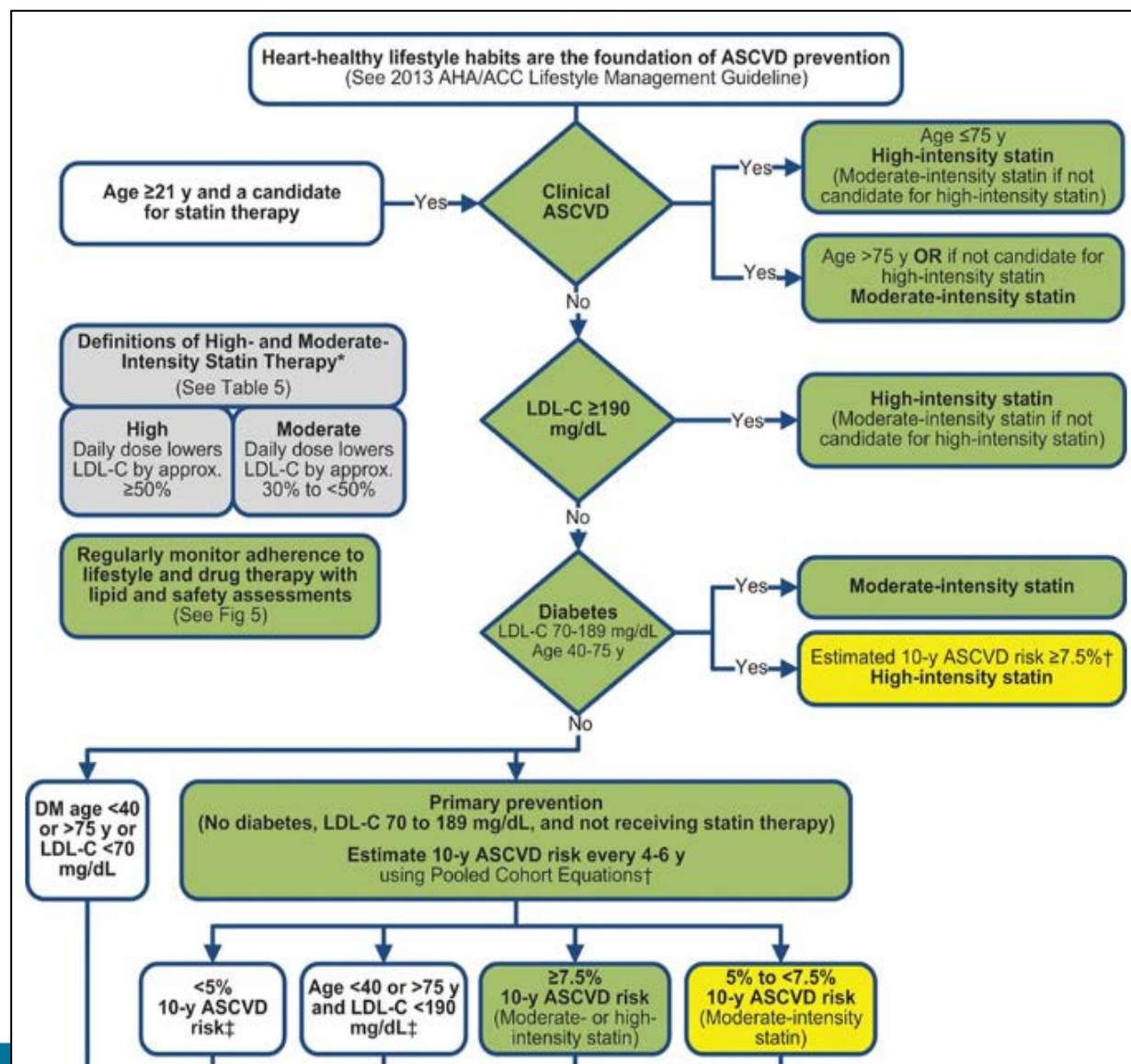
Conditions:

- Coronary heart disease (myocardial infarction, angina)
- Cerebrovascular disease (transient ischemic attack, ischemic stroke)
- Peripheral artery disease (claudication)
- Aortic atherosclerotic disease (abdominal aortic aneurysm)





2013 ACC/AHA Guideline





Guideline Comparison

Provider.ghc.org > Caring for our members > Clinical Guidelines

	GH	ACC/AHA
Primary Prevention	Moderate-intensity statin	Moderate to high intensity statin ^{¥€}
LDL Goal	<100 if primary prevention <70 if secondary prevention	None (statin intensity based on estimated risk)
Risk Calculator	Customized 5-year risk calculator for total ASCVD	2013 ACC/AHA 10-year risk calculator

¥ High-intensity statin recommended in patients with LDL ≥ 190 mg/dL, diabetic patients aged 40-75 years with estimated 10-yr ASCVD risk $\geq 7.5\%$

€ Moderate to high intensity statin recommended for patients without diabetes and 10-yr risk of $\geq 7.5\%$

→ Lifestyle Modifications



Tobacco
cessation



Mediterranean
or DASH diet

- Fish consumption 2 days/week may reduce CHD mortality



Moderation of
alcohol
consumption



Physical activity

- ≥ 30 minutes of moderate-intensity aerobic activity ≥ 5 days/week
- Moderate-to-high intensity muscle-strengthening activity ≥ 2 days/week



Weight
management



Blood pressure
management

- Age ≤ 79 years, goal $< 140/90$ mm Hg
- Age ≥ 80 years, goal $< 150/90$ mm Hg



GHC ASCVD Primary Prevention Guideline: Pharmacologic Therapy

Population	Statin (Moderate)	Antiplatelet	ACEI
Diabetic patients	Recommended for age ≥ 40	Use SDM	Recommended: <ul style="list-style-type: none">• 40-54 yr with $>10\%$ risk• ≥ 55 yr at any risk
Low CVD risk ($<5\%$ over 5 yr)	Not recommended	Not recommended	Not routinely recommended in patients without diabetes
Moderate CVD risk (5-10% over 5 yr)	Can be considered; use SDM, hs-CRP if needed	Use SDM	
High CVD risk ($>10\%$ over 5 yr)	Recommended	Recommended	
LDL ≥ 190 mg/dL	Should be considered, use SDM	Use SDM	

SDM: shared decision-making

hs-CRP: high-sensitivity C-reactive protein

Adapted from GHC ASCVD Primary Prevention Guideline Table 3



GHC Primary Prevention: Statin Therapy

For Primary Prevention, use ***moderate-intensity statin*** (30 to <50% LDL-lowering)

- Moderate is Simvastatin 40 mg or Atorvastatin 20 mg

Table 4. STANDARD (moderate-intensity) statin dosing for primary prevention of ASCVD

Standard dosing applies to patients for whom there are no concerns about their ability to tolerate moderate-intensity statin therapy.

Line	Medication	Initial dose	Maximum dose
1st	Simvastatin	40 mg daily at bedtime	40 mg ¹ daily at bedtime
	Atorvastatin	20 mg daily	80 mg daily
1. For patients already on simvastatin 80 mg daily, it is acceptable to maintain the dose if they have been taking the drug for 12 months or longer, are not taking interacting medications, are at LDL goal, and are without myopathy.			

Source: GHC ASCVD Primary Prevention Guideline



GHC Primary Prevention: Statin Therapy

Use reduced dosing (simva/atorva 1st, prava 2nd) if ability to tolerate moderate-intensity dose is in question

Use SDM to decide whether to change existing therapy

Table 5. REDUCED (low-intensity) statin dosing for primary prevention of ASCVD

Reduced dosing applies only to patients with questionable ability to tolerate moderate-intensity statin therapy, including those who are elderly/frail, have hepatic/renal impairment or untreated hypothyroidism, or are taking interacting drugs.

Line	Medication	Initial dose	Maximum dose
1st	Simvastatin	10–20 mg daily at bedtime	40 mg daily at bedtime
	Atorvastatin	10 mg daily	80 mg daily
2nd	Pravastatin ¹ (Alternative in cases of drug interactions or side effects)	20–40 mg daily at bedtime	80 mg daily at bedtime
1. Pravastatin has about half the potency of simvastatin; however, it is less likely to interact with other medications, particularly medications that are strong CYP3A4 inhibitors.			

Source: GHC ASCVD Primary Prevention Guideline



Standard Pharmacologic Therapy for Secondary Prevention

Statin (High Intensity*)	ACEI/ARB	Antiplatelet	Beta-blocker Post-MI
<ul style="list-style-type: none">• Atorvastatin 80 mg daily• Rosuvastatin 20-40 mg daily (2nd) <p><i>*Age >75 yr OR not candidate for high-intensity statin: use moderate-intensity statin</i></p>	<ul style="list-style-type: none">• Lisinopril 5-40 mg daily• Ramipril 5-20 mg daily• Losartan 25-100 mg/d in 1-2 doses (2nd)	<ul style="list-style-type: none">• Aspirin 81 mg daily• Clopidogrel 75 mg daily (2nd)	<ul style="list-style-type: none">• Metoprolol 25-100 mg BID (EF ≥50%)• Carvedilol 3.125-25 mg BID (EF <50%)• Metoprolol LA 12.5-200 mg daily (EF <50%, 2nd)

Dose ranges are initial to max.

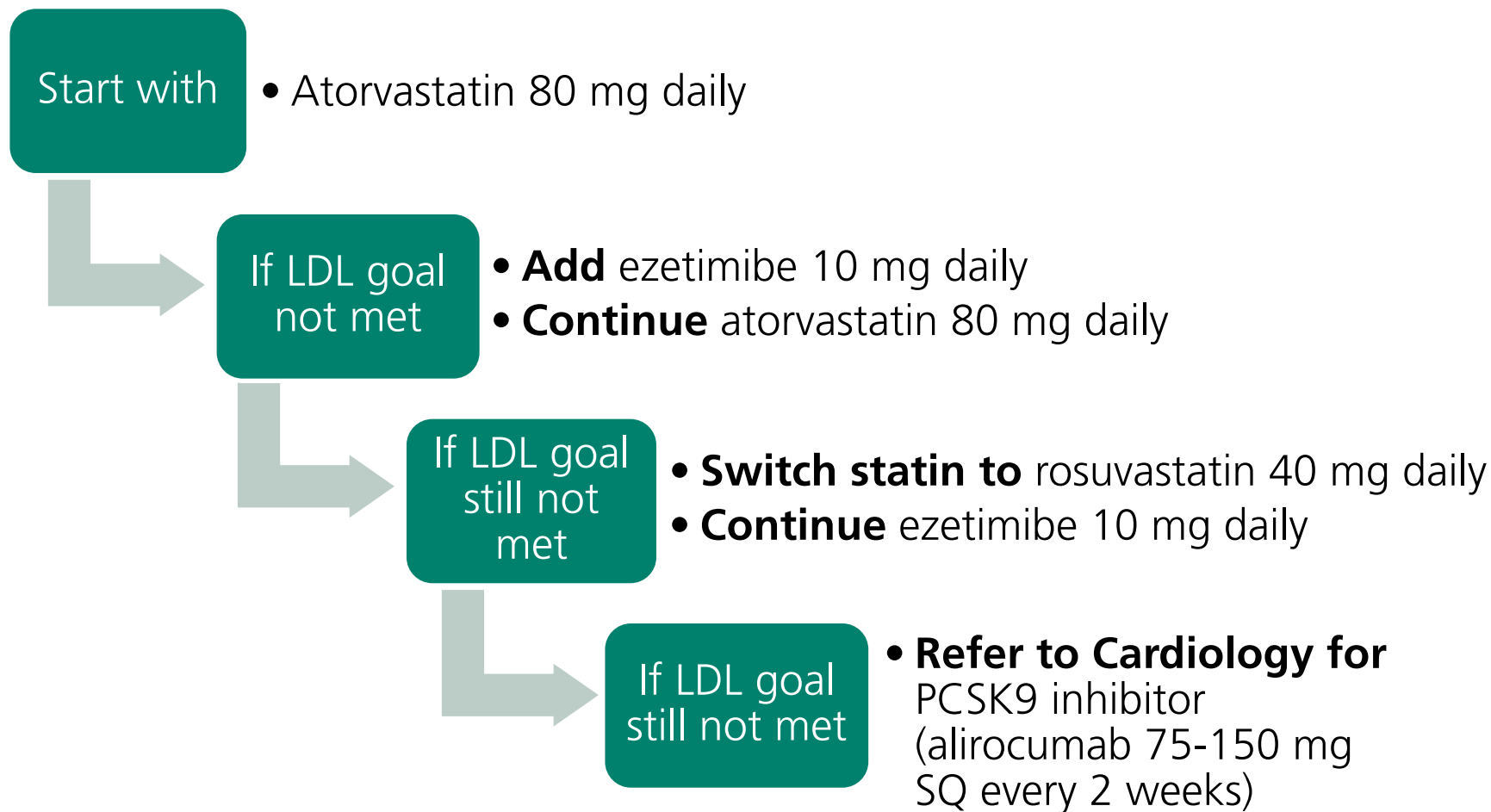
Adapted from GHC ASCVD Secondary Prevention Guideline Tables 1a, 3, 4, and 5



Secondary Prevention: Statin Therapy

Standard Dosing*

*Age >75 yr OR not candidate for high-intensity statin: use moderate-intensity statin

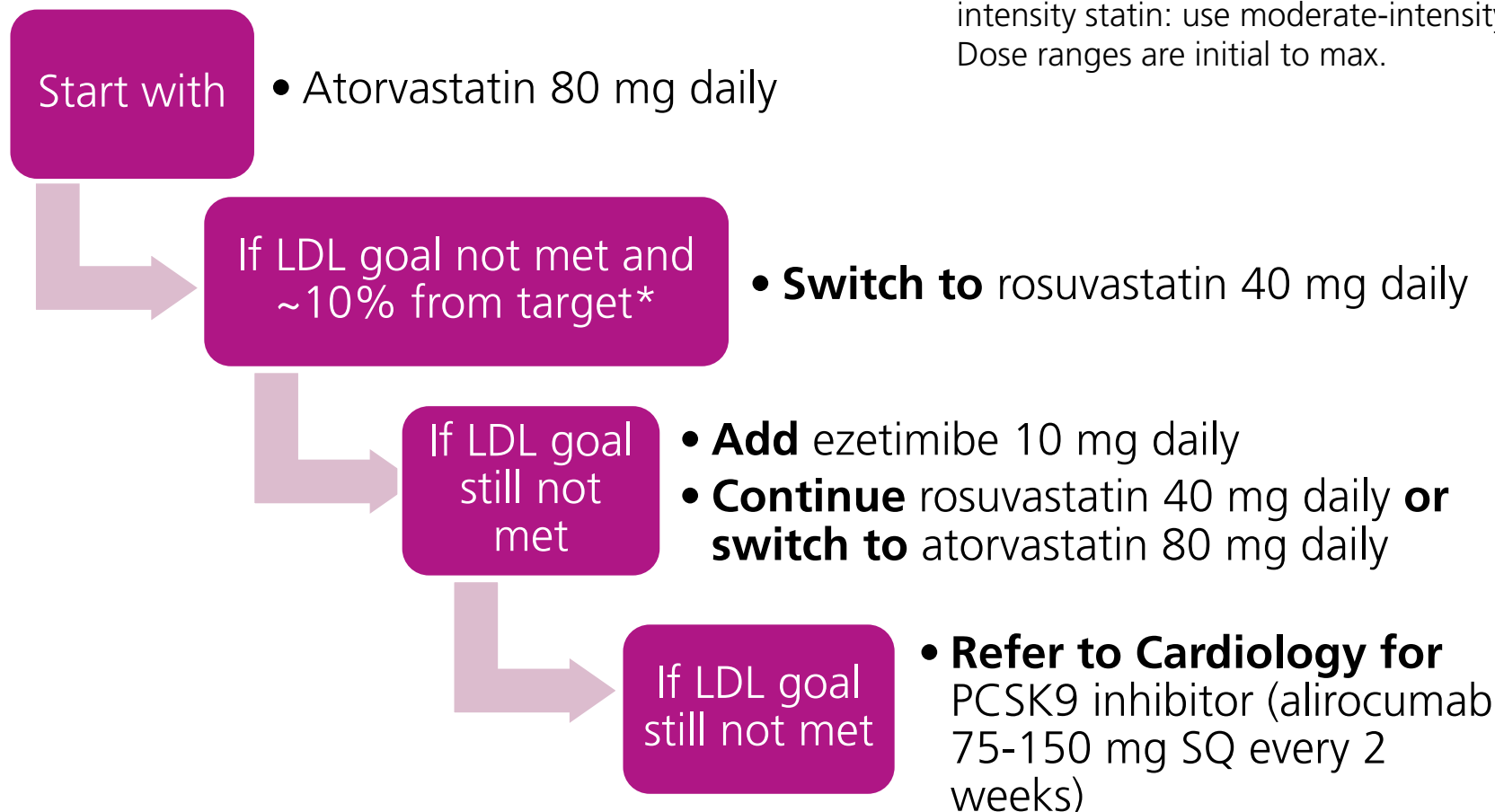




Secondary Prevention: Statin Therapy

Standard Dosing* Alternative

*Age >75 yr OR not candidate for high-intensity statin: use moderate-intensity statin. Dose ranges are initial to max.



Modified from GHC ASCVD Secondary Prevention Guideline Table 1a. IMPROVE-IT. N Engl J Med. 2015 Jun 18;372(25):2387-97. SATURN. N Engl J Med. 2011 Dec 1;365(22):2078-87.



Secondary Prevention: Statin Therapy Reduced Dosing

Use shared decision-making to decide whether to change existing therapy.

Table 1b. REDUCED dosing: Statins for lowering cholesterol for secondary prevention of ASCVD

Reduced dosing applies to patients with questionable ability to tolerate high-intensity statin therapy, including those who are frail/elderly, have hepatic/renal impairment or untreated hypothyroidism, or are taking interacting drugs.

Line	Medication	Initial dose ¹	Maximum dose
1st	Simvastatin	10–40 mg daily at bedtime	40 mg ² daily at bedtime
	Atorvastatin	10–40 mg daily	80 mg daily
2nd	Pravastatin ³ (Alternative in cases of drug interactions or side effects)	20–40 mg daily at bedtime	80 mg daily at bedtime
<ol style="list-style-type: none">1. Start statin at the highest dose you believe the patient will be able to tolerate. It is then very important to move the patient up from there to as close to standard high-intensity therapy as possible.2. For patients already on simvastatin 80 mg daily, it is acceptable to maintain the dose if they have been taking the drug for 12 months or longer, are not taking interacting medications, are at LDL goal, and are without myopathy.3. Pravastatin has about half the potency of simvastatin; however, it is less likely to interact with other medications, particularly medications that are strong CYP3A4 inhibitors.			

Source: GHC ASCVD Primary Prevention Guideline



Triglycerides

Labs needed for both 1° and 2° Prevention

- HbA1c
- TSH
- Protein/creatinine ratio
- Pregnancy

Other causes of ↑ TG

- Obesity
- Alcohol
- Medications (estrogen/oral contraceptives, HIV antiretrovirals, corticosteroids, cyclosporine, etc.)



Investigation/treatment required when TG > 500 mg/dL (or > 1000 mg/dL - use SDM)

1st line: Atorvastatin 80 mg daily

If TG still not < 500 mg/dL: Add fenofibrate (preferred) or niacin IR/SR

If TG still not < 500 mg/dL, add fish oil

Statin-intolerant: Gemfibrozil **monotherapy**



LDL Targets

LDL measurement verifies that patients are:

- Taking their statin (or other LDL-lowering drug)
- Achieving the appropriate reduction in LDL

ACC/AHA (2013) and Kaiser (2014)

- No recommendation for or against specific LDL-C or non-LDL-C targets

National Lipid Association (2015)

- Low, Moderate, or High Risk: LDL-C <100 mg/dL
- Very High Risk*: LDL-C <70 mg/dL

*Very high risk: ASCVD or DM with
≥2 other major ASCVD risk factors
or evidence of end-organ damage

Group Health Guideline (2016)

- Primary prevention at moderate or high CVD risk: <100
- ASCVD: <70

Source: ACC/AHA. *Circulation*. 2014 Jun 24;129(25 Suppl 2):S1-45.
National Lipid Association. *J Clin Lipidol*. 2015 Mar-Apr;9(2):129-69.



Why Lower Targets?

Larger reductions in LDL show a linear relationship with larger reductions in major vascular events

A 2010 meta-analysis found that for **every 1 mmol/L** (39 mg/dL) LDL reduction:

All-cause mortality ↓ **10%**

Major vascular events ↓ **22%**



Source: Cholesterol Treatment Trialists' (CTT) Collaboration



How Low Is Too Low?

If a patient has achieved a very low LDL, **do not lower** the intensity of statin therapy (provided patient is tolerating therapy).

Expert opinion is that no LDL level is too low.





Statin-Associated Muscle Symptoms (SAMS)

SAMS may occur with or without creatine kinase (CK) elevation

Pain and weakness usually symmetrical and proximal

Generally affect large muscle groups (thighs, buttocks, calves, back muscles)

Discomfort and weakness usually occur early (within 4-6 weeks after starting statin), but can occur after many years on treatment

Onset may occur with ↑ statin dose or initiating interacting drug

Appear more frequently in physically active patients

SAMS appear more promptly when re-exposed to the same statin

Source: EASC Consensus Panel. Eur Heart J. 2015 May 1;36(17):1012-22.



American College of Cardiology Statin Intolerance App

Determine if myalgia symptoms are related to statin

<http://www.acc.org/statintoleranceapp>

Select symptom type.

☒ **Any from this group – Possible intolerance**
Muscle ache, Weakness, Soreness, Stiffness, Cramping, Tenderness, General Fatigue

☐ **Any from this group – Unlikely intolerance**
Tingling, Twitching, Shooting Pain, Nocturnal Cramps, Joint Pain

Select symptom area.

☒ **Bilateral - Possible intolerance**
Muscle symptoms are generalized (e.g., neck and shoulder pain, lower extremity pain)

☐ **Unilateral - Unlikely intolerance**
Muscle symptoms are isolated (e.g., knee or shoulder ache)

Answer questions to evaluate possible intolerance to a patient's current statin prescription.

Value	Result	Statin-Related Muscle Symptoms	
		Possible	Unlikely
Symptom timing allows for statin intolerance	Yes		
Symptom Type	Muscle ache, Weakness, Soreness, Stiffness, Cramping, Tenderness, General Fatigue	✓	
Symptom Location	Bilateral	✓	
Sex	Male		
Age	≤ 18 Statin intolerance is rare in the pediatric population		✓
Race/Ethnicity	Native Hawaiian or Other Pacific Islander		
CK Elevated > 5x ULN?	Don't Know		

Answer questions to evaluate possible intolerance to a patient's current statin prescription.

⌂

Eval

Follow-Up

Compare

⬅

Back to Follow-Up Reasons

Patient has been rechallenged with original statin

Current Follow-Up

Did muscle symptoms return after rechallenge?

☒ Yes ☐ No

Recommendation

Next Steps

- Stop original statin.
- Wait for muscle symptoms to resolve

Follow steps to manage and treat a patient who reports muscle symptoms on a statin.

Statin's Interactions with Drugs You Selected

The tables below are compiled only from the following sources and may not represent all possible interactions:†
Prescribing Information - § Expert Opinion - ‡ FDA Recommendation - * ACC/AHA Guideline Recommendation

HIV Protease Inhibitors		
Atazanavir plus ritonavir (selected)	Use lowest possible dose of atorvastatin; titrate slowly; monitor for muscle symptoms§	⚠
Darunavir plus ritonavir (selected)	Do not exceed atorvastatin 20 mg daily†	⚠
Hepatitis C Protease Inhibitors		
Boceprevir (selected)	Do not exceed atorvastatin 40 mg daily†	⚠
Other		
Amiodarone (selected)	May require lower starting and maintenance dose of atorvastatin†	⚠
Colchicine	Use caution§	⚠

Compare statin characteristics and drug interactions to inform management of LDL-related risk.



If Patient *Appears* Intolerant to Statins

Consider decreasing dose

(can also use alternate day or 1-2x/week dosing regimen with atorvastatin or rosuvastatin)

If patient is still intolerant, **use SDM** to determine whether to switch statin. Consider consult with Cardiology.

Supplementation

- GHC ASCVD Guideline: Consider Coenzyme Q10. Evidence is conflicting, although some studies suggest benefit.
- Effectiveness of vitamin D for SAMS also controversial
- EASC does not recommend either CoQ10 or vitamin D

Adapted from GHC ASCVD Guidelines and EASC Consensus Panel. Eur Heart J. 2015 May 1;36(17):1012-22.

➔ Definition of Statin Intolerance

Inability to tolerate at least 2 statins due to objectionable symptoms (real or perceived) or abnormal labs

1 statin at lowest starting daily dose

Another statin at any daily dose

Symptoms are temporally related to statin treatment and reversible upon discontinuation but reproducible by re-challenge

Other known causes excluded

Hypothyroidism, interacting drugs, concurrent illnesses, significant changes in physical activity/exercise, underlying muscle disease

Lowest starting statin daily dose defined as:

rosuvastatin
5 mg

atorvastatin
10 mg

simvastatin
10 mg

lovastatin
20 mg

pravastatin
40 mg

fluvastatin
40 mg

pitavastatin
2 mg

Source: National Lipid Association Statin Intolerance Panel. *J Clin Lipidol*. 2014 May-Jun;8(3Suppl): S72-81.



If Patient *Still* Intolerant or Contraindications: Primary Prevention

Patients
not at
high risk

Stop the statin and
do not prescribe
further medications.

High
risk
patients

If not able to achieve
an LDL <100 mg,
**stop the statin and
consider prescribing
ezetimibe.**

High risk based on:

5-year risk >10% based on GHC CVD risk calculator, *or*

10-year risk $\geq 7.5\%$ based on ACC/AHA risk calculator, *or*

Patient aged 40 or older with diabetes, *or*

Any patient with LDL ≥ 190 mg/dL



If Patient *Still* Intolerant or Contraindications: Secondary Prevention

Start with

- Ezetimibe 10 mg daily

If LDL goal not met

- **Continue** ezetimibe 10 mg daily **and add one of the following:**
 - Niacin IR 100 mg BID-1000 mg TID
 - Niacin SR (Slo-Niacin) 250 mg-1000mg BID
 - Gemfibrozil 600 mg BID
 - Cholestyramine resin 4 g 1-2x/day to 24 g divided 1-6x/day

If LDL goal still not met

- **Refer to Cardiology for** PCSK9 inhibitor (alirocumab 75-150 mg SQ every 2 weeks)

Adapted from GHC ASCVD Secondary Prevention Guideline Table 2. Dose ranges are initial to max.

Cardiovascular Risk Calculators



Consider calculators as risk *estimators*



Interpret results using clinical judgment



Use tool as a starting point for discussion with patients



Use shared decision-making



Group Health Risk Calculator

Customized version of the Framingham CVD risk calculator

Approximates absolute 5-year risk of ASCVD and CHF

<https://www.ghc.org/html/public/tools/heart/>



HEART DISEASE AND STROKE

What's your risk?

Cardiac Risk Calculator

Cardiovascular disease — damage to your heart or blood vessels that can cause heart attacks or strokes — is the leading cause of death in this country. This calculator can help you understand your own risk. You'll also learn ways to lower your risk.

Note: This tool calculates risk for persons aged 30-79. You'll need to enter values for your cholesterol levels (routine screening starts at 35 for men and 45 for women) and blood pressure.

All fields are required.

What is your age?

What is your gender?

- ☐ Female
☐ Male

Do you have heart disease or cardiovascular disease? This includes being diagnosed with angina, a heart attack, a stroke, a mini-stroke (TIA), or peripheral artery disease (PAD).

- ☐ No
☐ Yes

Did your father or a brother have heart disease before the age of 55?

- ☐ No
☐ Yes
☐ Don't know



2013 ACC/AHA Risk Calculator

Assesses absolute 10-year risk of CVD and stroke

<http://tools.acc.org/ASCVD-Risk-Estimator/>

ASCVD Risk Estimator*

All fields are required to compute ASCVD risk.

Gender	<input type="radio"/> M <input type="radio"/> F	Age	<input type="text" value="20-79"/>
Total Cholesterol (mg/dL)	<input type="text" value="130-320"/>	Race	<div><input checked="" type="radio"/> White</div> <div><input type="radio"/> African American</div> <div><input type="radio"/> Other</div>
HDL - Cholesterol (mg/dL)	<input type="text" value="20-100"/>	Treatment for Hypertension	<input type="radio"/> Y <input type="radio"/> N
Systolic Blood Pressure	<input type="text" value="90-200"/>	Smoker	<input type="radio"/> Y <input type="radio"/> N
Diabetes	<input type="radio"/> Y <input type="radio"/> N		



MAYO
CLINIC

Statin/Aspirin Choice
Decision Aid

Back

Current Risk

Select Risk Calculator

ACC/AHA ASCVD Framingham Reynolds

Do you have a history of events such as prior heart attack or stroke, acute coronary syndromes, history of angioplasty or stents, etc?

No

These figures are used to calculate my risk of having a heart attack in the next 10 years:

Age 63

Gender M F

Population Group White or other

Smoker No

Diabetes Yes

Treated SBP No

Conv. Unit SI Unit

Systolic Blood Pressure 145 mmHg

HDL Cholesterol 45 mg/dL

Total Cholesterol 230 mg/dL

Select Current Intervention

Statins No Std Dose High Dose

Aspirin No Low Dose

Current Risk

Notes Document

Benefits vs Downsides according to my personal health information
Using ACC/AHA ASCVD Risk Calculator

Current Risk

heart attack

you who do take



Group Health Formulary Drug Price Comparison

Medication	AWP (30-day supply)	GH formulary status
Atorvastatin 80 mg tablets	\$173	Formulary
Rosuvastatin 40 mg tablets	\$268	Formulary, Step therapy
Ezetimibe 10 mg tablets	\$343	Formulary, prior auth
Alirocumab 75 mg syringes	\$1344	<u>Non</u> -formulary, prior auth



Source: Group Health Formulary, November 2016



Retail Generic 30-day Discounts

Conversation indicates
cost is barrier

Encourage mail-
order Rx

90-day fill

Retailers offer discounted cash-only purchases for generics

- May not be moderate/high intensity as defined by HEDIS
- Doesn't allow for monitoring or treat-to-target
- Claims not submitted to health plan (not reflected in performance rates)

Similar problems exist when offering drug samples to patients

Walgreens \$5

- Lovastatin 10/20/40 mg
- Pravastatin 10/20/40/80 mg
- Simvastatin 5/10/20/40/80 mg

Rite-Aid \$9.99

- Lovastatin 10/20/40 mg
- Pravastatin 10/20/40/80 mg
- Simvastatin 5/10/20/40/80 mg

Walmart \$4

- Lovastatin 10/20 mg

Target \$4

- Lovastatin 10/20 mg
 - Pravastatin 10/20/40 mg
-



New HEDIS ASCVD Measures

Introduced 2016

Initiation: At least **one statin medication dispensed** during time period

Adherence: **Remain** on statin for at least 80% of treatment period

Population

Males age 21–75 and females age 40–75 identified as having ischemic vascular disease (IVD) in the last two years via:

- IVD event (AMI, CABG, PCI) or
- Two or more events where IVD is diagnosed in an office visit or inpatient/emergency room setting

Exclusions

- Pregnancy
- In vitro fertilization
- Dispensed at least 1 prescription for clomiphene
- ESRD
- Cirrhosis
- Myalgia, myositis, myopathy, or rhabdomyolysis

Source: HEDIS 2017 Technical Specifications



Exclusion Codes for Statin Myopathy

Value Set: Muscular Pain and Disease

Definition	Coding
Drug-induced myopathy	ICD10: G72.0
Myopathy due to other toxic agents	ICD10: G72.2
Myopathy, unspecified	ICD10: G72.9
Rhabdomyolysis	ICD10: M62.82
Myalgia	ICD10: M79.1
Toxic myopathy	ICD9: 359.4
Myopathy NOS	ICD9: 359.9
Rhabdomyolysis	ICD9: 728.88
Myalgia and myositis NOS	ICD9: 729.1

Source: HEDIS 2017 Technical Specifications



HEDIS Definition: Statin Initiation

Received Statin Therapy

Patients with IVD who were dispensed at least one **high** or **moderate-intensity statin** medication during the measurement year.

Description	Statin Medications	
High-intensity statin therapy	Atorvastatin 40-80 mg	Rosuvastatin 20-40 mg
	Amlodipine-atorvastatin 40-80 mg	Simvastatin 80 mg
	Ezetimibe-atorvastatin 40-80 mg	Ezetimibe-simvastatin 80 mg
Moderate-intensity statin therapy	Atorvastatin 10-20 mg	Sitagliptin-simvastatin 20-40 mg*
	Amlodipine-atorvastatin 10-20 mg	Pravastatin 40-80 mg
	Ezetimibe-atorvastatin 10-20 mg	Lovastatin 40 mg
	Rosuvastatin 5-10 mg	Niacin-lovastatin 40 mg
	Simvastatin 20-40 mg	Fluvastatin XL 80 mg
	Ezetimibe-simvastatin 20-40 mg	Fluvastatin 40 mg bid
	Niacin-simvastatin 20-40 mg	Pitavastatin* 2-4 mg

**Non-formulary at Group Health*

Source: HEDIS 2017 Technical Specifications



HEDIS Definition: Statin Adherence

Statin Adherence 80%

Members with IVD who remained on a high or moderate-intensity statin medication for at least **80% of the treatment period**.

*Proportion of days covered =
Days covered by statins ÷ Days in treatment period*

Example:

*90 days of medication dispensed Apr 1 (first date) +
90 days of medication dispensed Sep 15 = 180 days*

April 1 through Dec 31 = 274 days

*180 days covered ÷ 274 day treatment period =
65.7%*

Source: HEDIS 2017 Technical Specifications



Statin Adherence Strategies



Patient Engagement Conversations

- Determine root cause
- Utilize Cardiac Risk tools
- Employ shared decision-making



Cost

- Use generics: atorvastatin and rosuvastatin
- May have a reduced cost benefit via GH mail-order



Intolerance

- Try different statin, lowering dose, or alternating days of therapy
- ACC intolerance app
- Consider CoQ10



Convenience

- 90 day supply at mail order



Tools

Provider.ghc.org

- HEDIS® Insight: Provider Communications > HEDIS® Insight
- Clinical guidelines: Caring For Our Members > Guidelines
- Patient education: Caring For Our Members > Patient Health Education
- Newsletters: Provider Communications
- Drug Formulary, Clinician Prescribing Tools: Caring For Our Members > Pharmacy
- Cardiac Risk Calculator: <https://www.ghc.org/html/public/tools/heart/>

Care Gap Report: Ask your Provider Services Consultant for regular patient lists for your practice.

Thank you!



GroupHealth®