

**Focused Update:
2013 ACC/AHA Guideline on
the Treatment of Blood
Cholesterol to Reduce
Atherosclerotic
Cardiovascular Risk in Adults**

Rachel Kile, Pharm.D.

PGY1 Pharmacy Resident

Memorial Health Care System

Objectives

- Upon completion of this presentation, you should be able to:
 - Evaluate evidence supporting the ACC/AHA recommendations
 - Explain differences between the current ACC/AHA and previous guidelines
 - Identify indications for HMG-CoA reductase inhibitor (“statin”) therapy based on the ACC/AHA guideline
 - Differentiate among pharmacokinetic & pharmacodynamic properties of statins
 - Apply the ACC/AHA guideline to patient case examples

Updated Guideline

- 2008- Initiated by National Heart, Lung, and Blood Institute (NHLBI)
- 2013- NHLBI partnered with the American College of Cardiology (ACC) and the American Heart Association (AHA)
 - To ensure highest quality, trustworthy guidelines

"ATP IV"

- "The Blood Cholesterol Expert Panel was originally convened as the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel [ATP] IV) appointed by the NHLBI."
- "ATP IV" is officially named:
 - "ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults "

Updated Guideline

- 2011- No evidence considered beyond this year by ACC/AHA
- 2013- Year of publication
- 2014- Guidelines will begin to be updated (again)

Scope of ACC/AHA Guideline

- Treatment of cholesterol for the primary and secondary prevention of atherosclerotic cardiovascular disease (ASCVD) in women and men age ≥ 21 years of age
- Recommendations based on randomized controlled trials (RCTs), systematic reviews, and meta-analyses of RCTs with ASCVD outcomes
- *Not* a comprehensive lipid management guideline
 - ASCVD risk reduction only

Guideline Focus

- 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitor (statin) therapy in secondary and primary prevention populations
 - NYHA Class II-IV heart failure and maintenance hemodialysis patients **excluded**
- Fixed-dose statins to reduce ASCVD risk
 - Multiple RCTs

RCT Evidence: ASCVD

- Fails to demonstrate support for targeting specific LDL-C and HDL-C goal levels
 - Titration of statin dose
 - Primary or secondary prevention
- Fails to demonstrate benefit for targeting non-HDL-C once LDL-C goal achieved
 - By adding additional medication therapy (e.g niacin)

RCT Evidence: ASCVD

- Lifestyle modification crucial
 - Prior to and during statin therapy
 - Heart healthy diet
 - Regular exercise
 - Avoid tobacco products
 - Maintain healthy weight



RCT Evidence: ASCVD

- **Fixed-dose** statin therapy at the *appropriate intensity* of cholesterol lowering is recommended
 - Most likely benefit
- Statin therapy far superior in lowering cholesterol levels
 - vs other cholesterol-lowering medications

Major Statin Benefit Groups

- 4 major groups
- RCT data shows consistent ASCVD risk reduction benefit > statin adverse effects in these populations
 - Higher risk primary prevention population
 - Secondary prevention population
- Excludes NYHA Class II-IV heart failure and maintenance hemodialysis patients
 - Guideline provides no recommendation

Major Statin Benefit Groups

- Statin therapy proven to reduce ASCVD events in this population:
 - Moderate intensity therapy
 - LDL-C lowering by 30-<50%
 - High intensity therapy
 - LDL-C lowering by $\geq 50\%$
 - Maximum tolerated statin intensity
- NO targeting of specific LDL goal levels
 - LDL goal targeting is not supported by RCTs

Major Statin Benefit Groups

Individuals with:

1. *Clinical* ASCVD
2. Primary elevations of LDL-C \geq 190 mg/dL
3. Diabetes aged 40-75 years with LDL-C 70-189 mg/dL
4. Without *clinical* ASCVD or diabetes who are 40-75 years of age with LDL-C 70-189 mg/dL and an estimated 10-year ASCVD risk \geq 7.5%

1. Clinical ASCVD

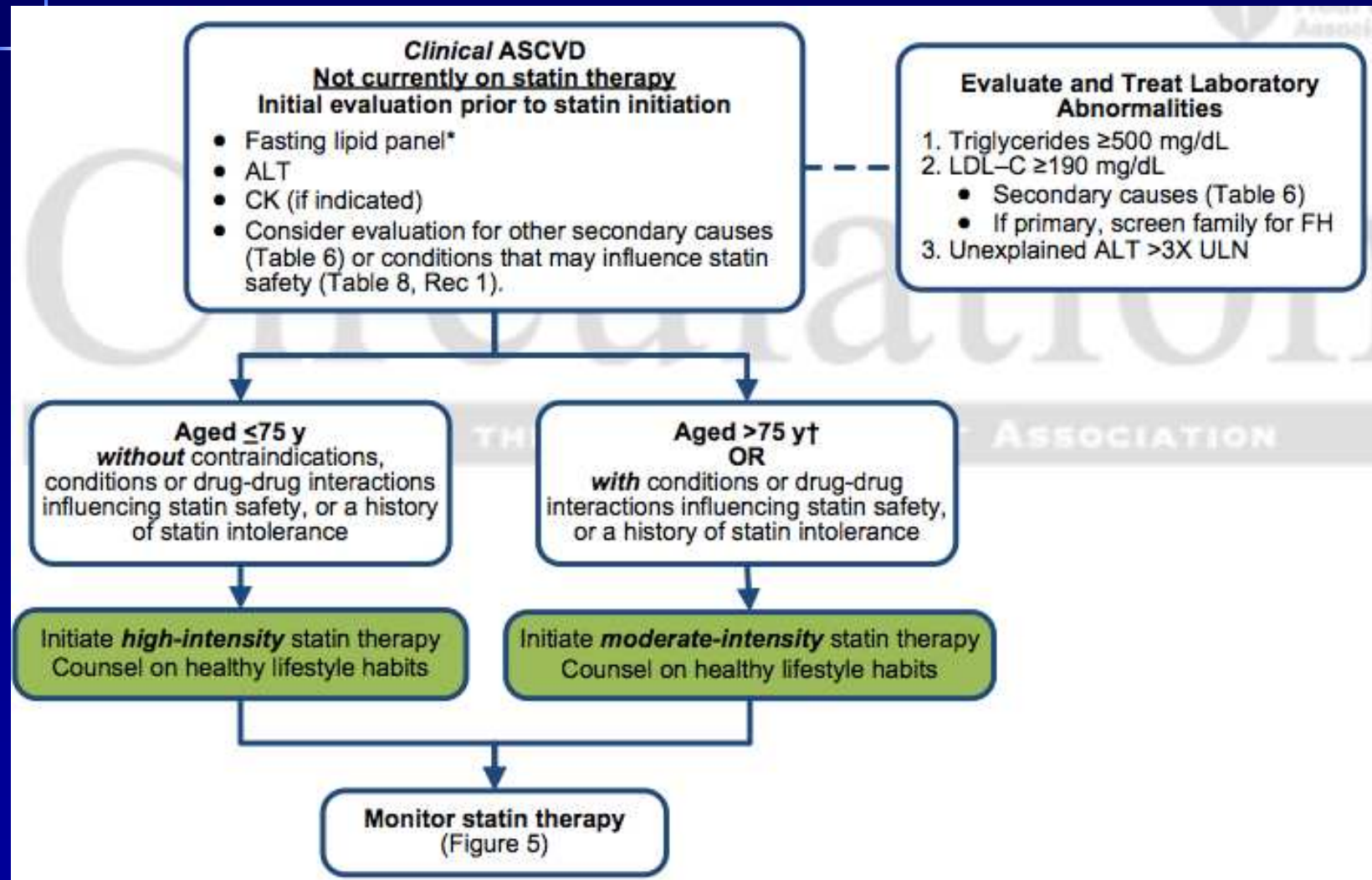
- Definition

- **Secondary** prevention

- Acute coronary syndromes
 - MI
 - Stable or unstable angina
 - Coronary or other arterial revascularization
 - Stroke or TIA
 - Peripheral arterial disease presumed to be of atherosclerotic origin



1. Clinical ASCVD



2. LDL-C \geq 190 mg/dL

- Large LDL-C reductions required
- High-intensity statin therapy
 - \geq 50% LDL-C reduction desired
- Non-statin cholesterol-lowering medications often needed to reduce ASCVD risk
- Evaluation of secondary causes
 - Diet, medications, disease, altered metabolism

3. Diabetes

- 40 to 75 years of age
- LDL-C 70-189 mg/dL
- Moderate-intensity statin therapy
 - If $\geq 7.5\%$ estimated 10-year ASCVD risk, use *high-intensity* statin therapy, unless contraindicated
- Maximum tolerated statin intensity is key

4. Without Clinical ASCVD/Diabetes

- 40-75 years of age
- LDL-C 70 to 189 mg/dL
- Estimated 10-year ASCVD risk of $\geq 7.5\%$
 - Pooled Cohort Equation
- High-intensity statin therapy

Pooled Cohort Equation

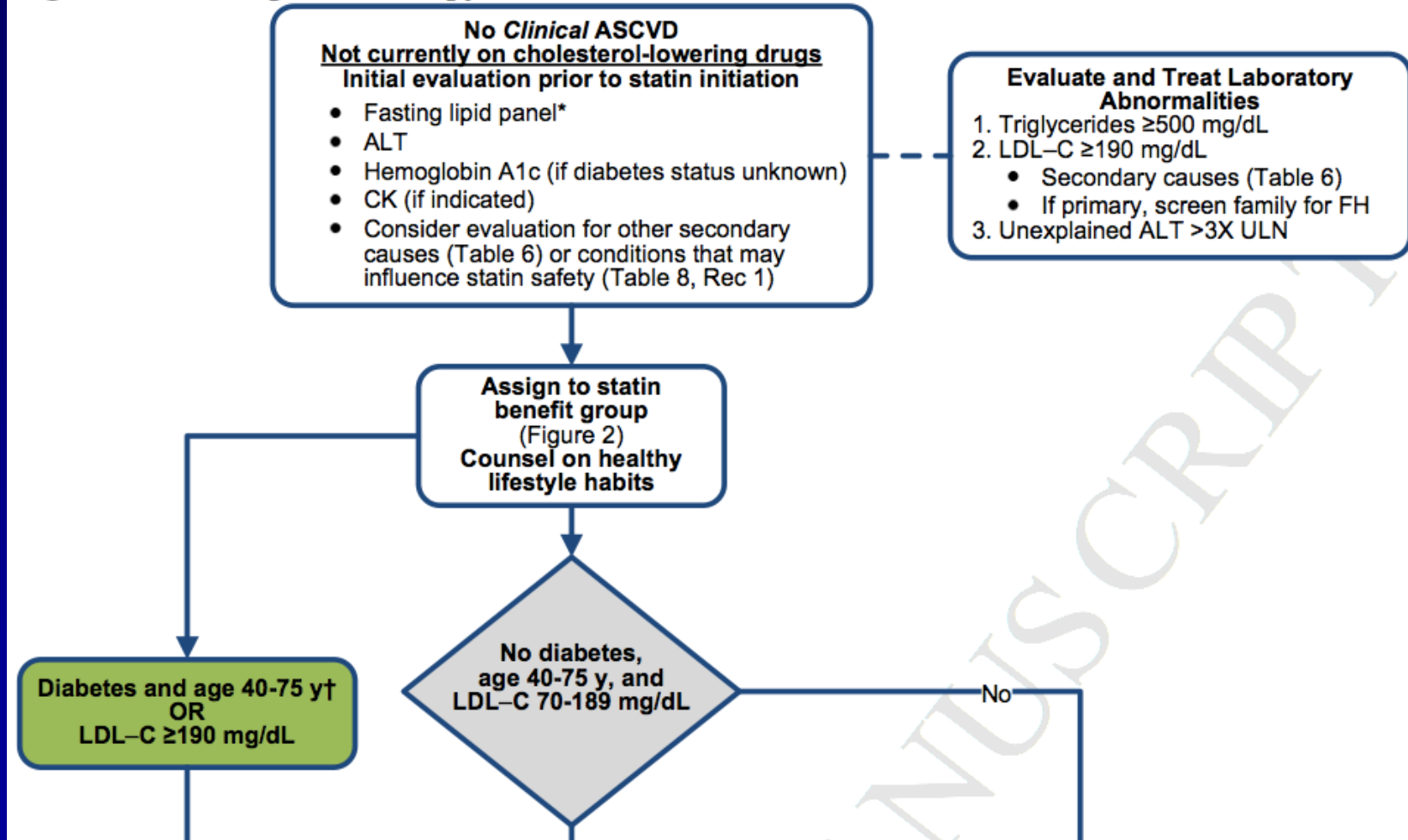
- Estimates absolute *10-year risk* of ASCVD
 - Pooled Cohort Equation calculator
 - Guides initiation of statin therapy
 - http://my.americanheart.org/professional/StatementsGuidelines/PreventionGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp
 - Nonfatal MI, CHD death, nonfatal and fatal stroke
- White and black men and women only
- Without clinical ASCVD

Pooled Cohort Equation

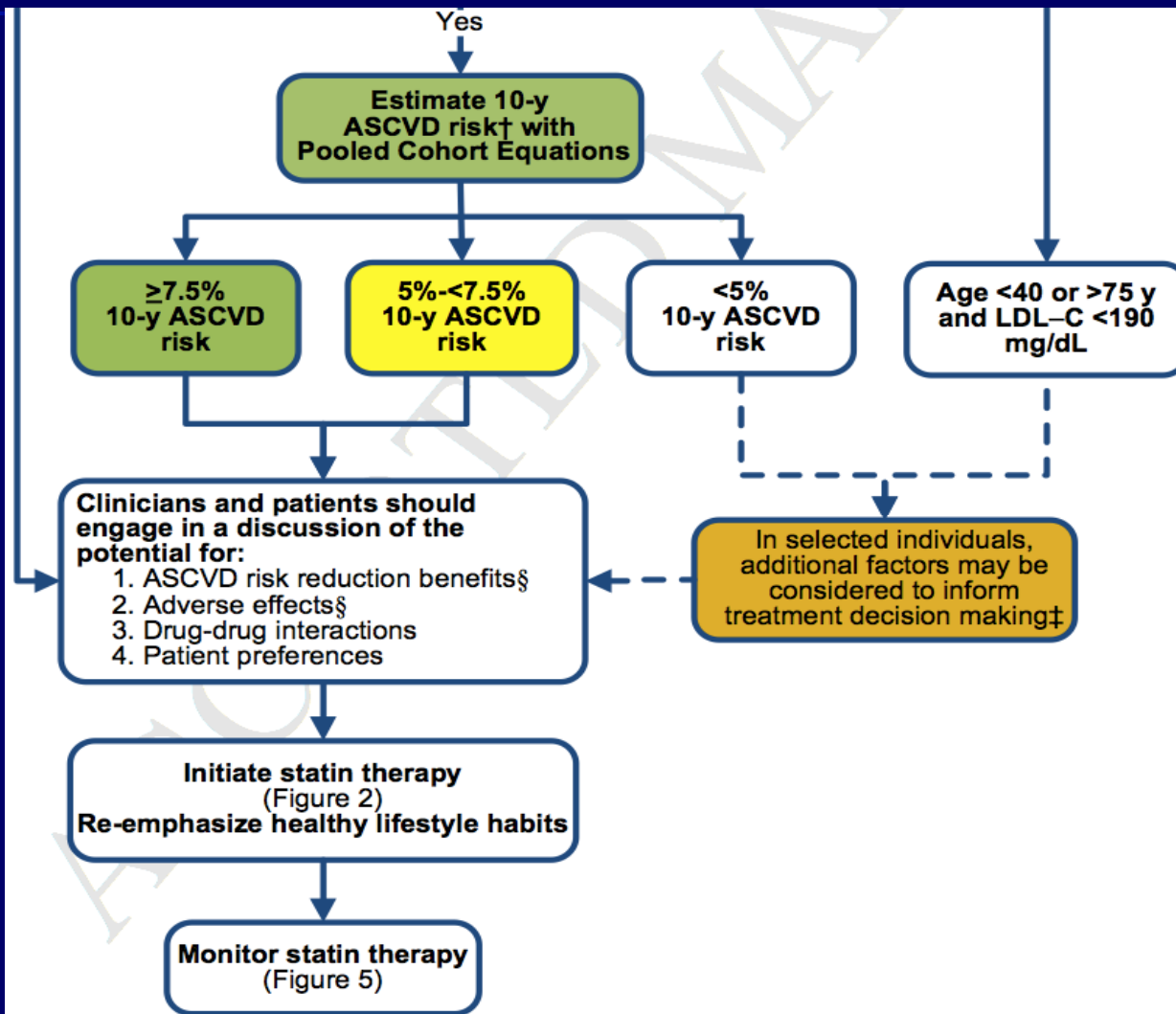
- Sex
- Age
- Race
- Total Cholesterol
- HDL
- Systolic Blood Pressure
- Treatment for Hypertension
- Diabetes
- Smoking status

Statin Therapy: Without ASCVD

Figure 4. Initiating statin therapy in individuals *without clinical* ASCVD



Statin Therapy: Without ASCVD



Intensity of Statin Therapy

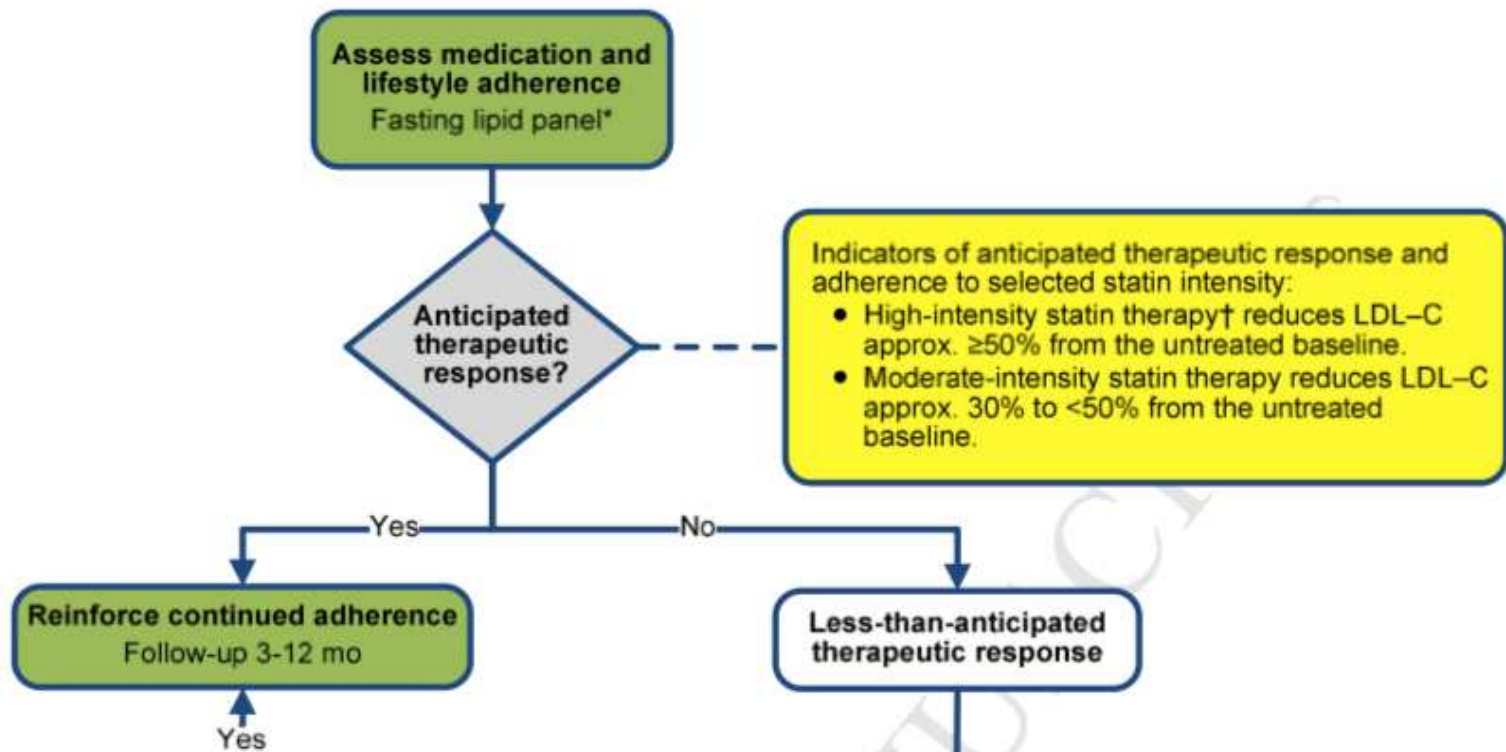
*Table 2. High-, Moderate-, and Low-Intensity Statin Therapy**

Statin Therapy	Daily Dose		
	High-Intensity†	Moderate-Intensity‡	Low-Intensity§
Atorvastatin	40 –80 mg	10 (20) mg	–
Rosuvastatin	20 (40) mg	(5) 10 mg	–
Simvastatin	–	20–40 mg¶	10 mg
Pravastatin	–	40 (80) mg	10–20 mg
Lovastatin	–	40 mg	20 mg
Fluvastatin	–	80 mg (Fluvastatin XL)	20–40 mg
Fluvastatin	–	40 mg**	–
Pitavastatin	–	2–4 mg	1 mg

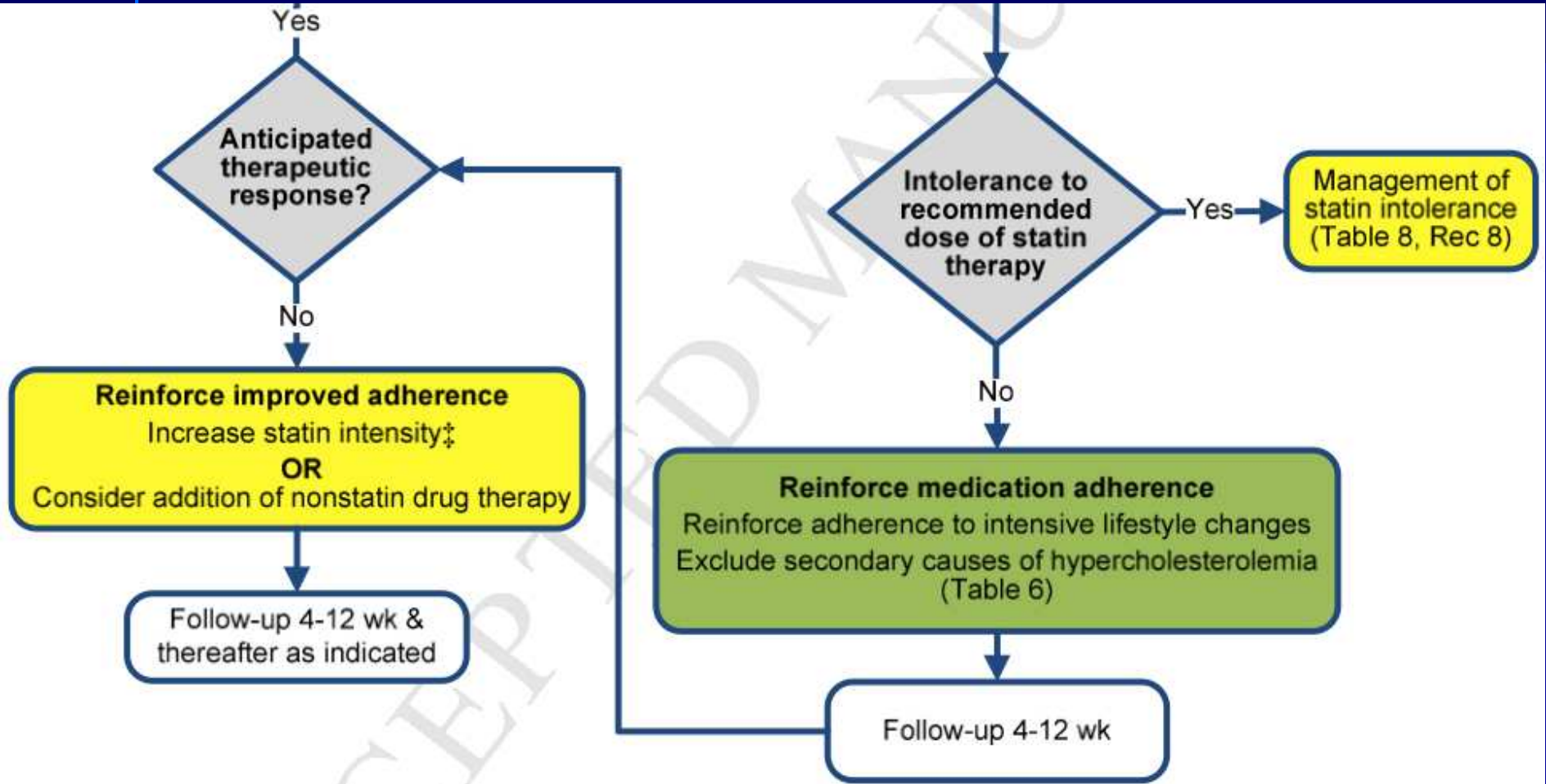
Statin	T_{1/2} (hrs)	L/H	Lipid Lowering	Metabolism /DDIs	Adverse Effects
Lovastatin	1-2	L	21-42%	Hepatic (major substrate CYP3A, P-gp) weakly inhibits CYP2C9, 3A4	Myalgias, increased CPK
Simvastatin	Unknown	L	26-47%	Hepatic (major substrate CYP3A4) inhibits CYP2C8, 2C9, 2D6	Increased transaminases and myalgias
Pravastatin	2-3	H	22-37%	Hepatic (minor substrate of 3A4, P-gp) Weakly inhibits CYP2C9, 3A4, 2D6	Myalgias, elevated transaminases
Rosuvastatin	19	H	45-63%	Hepatic (minor substrate of CYP2C9 and 3A4)	Myalgias, elevated transaminases
Atorvastatin	14	L	30-60%	Hepatic via CYP3A4, P-gp (inhibits CYP3A4 and P-gp)	Arthralgias, diarrhea, elevated transaminases (80mg/day)
Pitavastatin	12	L	30-45%	Hepatic via UGT 1A3 and UGT 2B7; minimal CYP2C9 and 8	Arthralgias, pain in extremities

Statin Monitoring

Figure 5. Statin Therapy: Monitoring therapeutic response and adherence



Statin Monitoring



Major Recommendations: Statins

ASCVD Statin Benefit Groups

Heart healthy lifestyle habits are the foundation of ASCVD prevention. In individuals not receiving cholesterol-lowering drug therapy, recalculate estimated 10-y ASCVD risk every 4-6 y in individuals aged 40-75 y without clinical ASCVD or diabetes and with LDL-C 70-189 mg/dL.

Adults age >21 y and a candidate for statin therapy

Yes

Clinical ASCVD

Yes

Age ≤75 y
High-intensity statin
(Moderate-intensity statin if not candidate for high-intensity statin)

Yes

Age >75 y **OR** if not candidate for high-intensity statin
Moderate-intensity statin

No

Definitions of High- and Moderate-Intensity Statin Therapy
(See Table 5)

High

Daily dose lowers LDL-C by approx. ≥50%

Moderate

Daily dose lowers LDL-C by approx. 30% to <50%

LDL-C ≥190 mg/dL

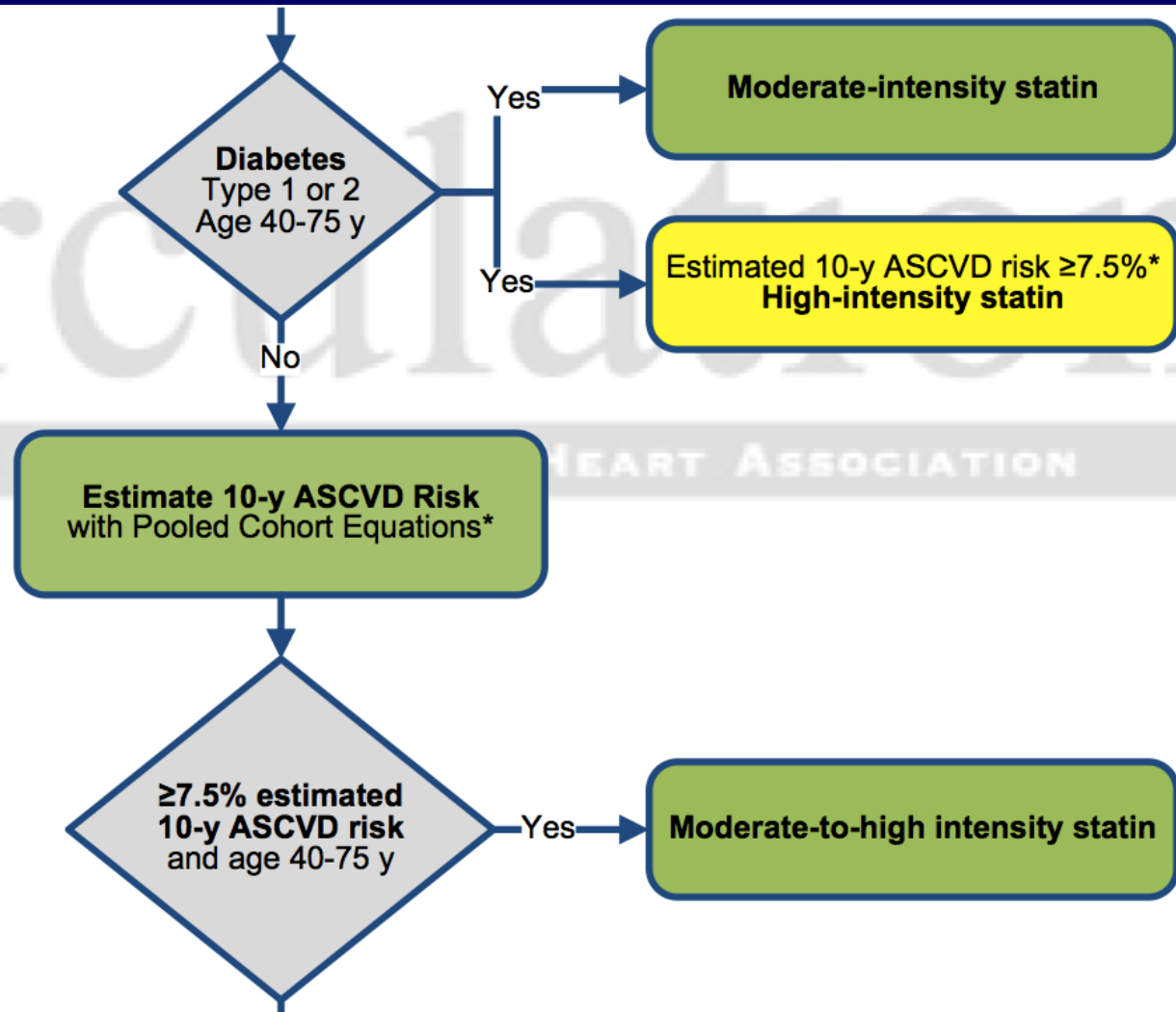
Yes

High-intensity statin
(Moderate-intensity statin if not candidate for high-intensity statin)

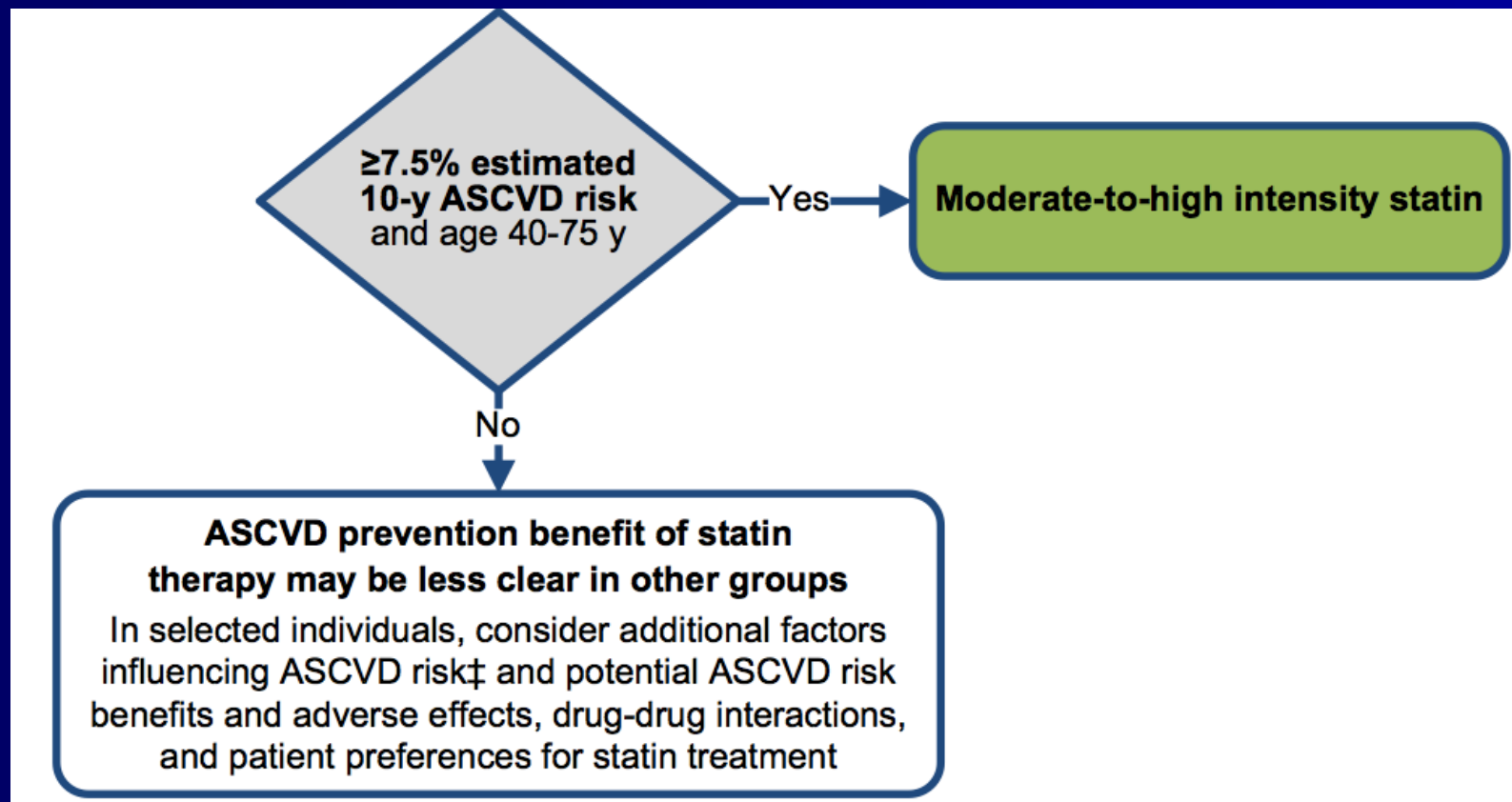
No



Major Recommendations: Statins



Major Recommendations: Statins



ATP III vs ATP IV

■ ATP III

- Target LDL
- Titration of statin dose
- Framingham Risk Assessment (validated)
- Treat elevated triglycerides

■ "ATP IV"

- No target LDL
- Fixed statin doses
- Pooled Cohort Equation (not validated)
- No specific recommendation on hypertriglyceridemia

Guideline Limitations

- Guidelines focus on patient populations represented in RCTs
 - Clinical judgment is key
- Evidence from post-hoc analyses of included RCTs, poor quality RCTs, or from observational studies not included
 - Limitation?

Guideline Conclusions

- Goal of treatment to reduce blood cholesterol for preventing ASCVD:
 - Intensity of statin therapy
 - NOT LDL-C or non-HDL-C targets
- Classification of four statin benefit groups
- Quite different from ATP III!

Test Your Knowledge

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“An aspirin a day will help prevent a heart attack if you have it for lunch instead of a cheeseburger.”

Question 1

- Which of the following patients may be evaluated by the Pooled Cohort equation risk calculator?
 - A) 83 year old African American female
 - B) 37 year old Caucasian male
 - C) 50 year old Hispanic female
 - D) 63 year old African American male

Question 2

- A 75 year old male just underwent CABG surgery s/p STEMI. Which of the following medications is most appropriate for his cholesterol management?
 - A) Niacin 500 mg
 - B) Lipitor 40 mg
 - C) Lipitor 20 mg
 - D) Crestor 10 mg

Question 3

- A 58 yo male is diagnosed with new onset T2DM. Which of the following medications is most appropriate for his ASCVD risk reduction?
 - A) Lipitor 10 mg
 - B) Lipitor 80 mg
 - C) Pravachol 20 mg
 - D) Lovastatin 20 mg

Question 4

- A 29 yo female visits her PCP for her annual wellness check-up. A fasting lipid panel demonstrates an LDL of 202. All of the following are appropriate initially in this patient, *except*:
 - A) Evaluate secondary causes of elevated LDL
 - B) Initiate a moderate intensity statin plus fenofibrate
 - C) Initiate a high intensity statin
 - D) Counsel on lifestyle management

Question 5

- Which is a tenet of the "ATP IV" guidelines?
 - A) Intensity of statin therapy
 - B) Target LDL levels
 - C) Target non-HDL levels
 - D) Appropriate titration of statin dose

Question 6

- A 64 year old male with no past medical history is assessed by the Pooled Cohort equation with a 12.5% 10-year risk of ASCVD events. Which of the following is the most appropriate statin to initiate in this patient?
 - A) Lipitor 20 mg
 - B) Zocor 40 mg
 - C) Crestor 20 mg
 - D) Pravachol 40 mg

References

- Stone NJ, Robinson J, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;00:000–000.
- Stone NJ, Robinson JG, Lichtenstein AH, et al. Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Disease Risk in Adults: Synopsis of the 2013 American College of Cardiology/American Heart Association Cholesterol Guideline. *Ann Intern Med*. 2014;160:339-343.

Questions?

