Practical Application of 2018 Lipid Guidelines

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Description

During this presentation we will discuss how to utilize risk calculators and the updated guidelines to reduce risk of cardiovascular events and practical application of pharmacologic therapy for dyslipidemia.

Objectives

Discuss the major changes in the 2018 lipid guidelines

Determine risk categories for ASCVD using a risk stratification tool

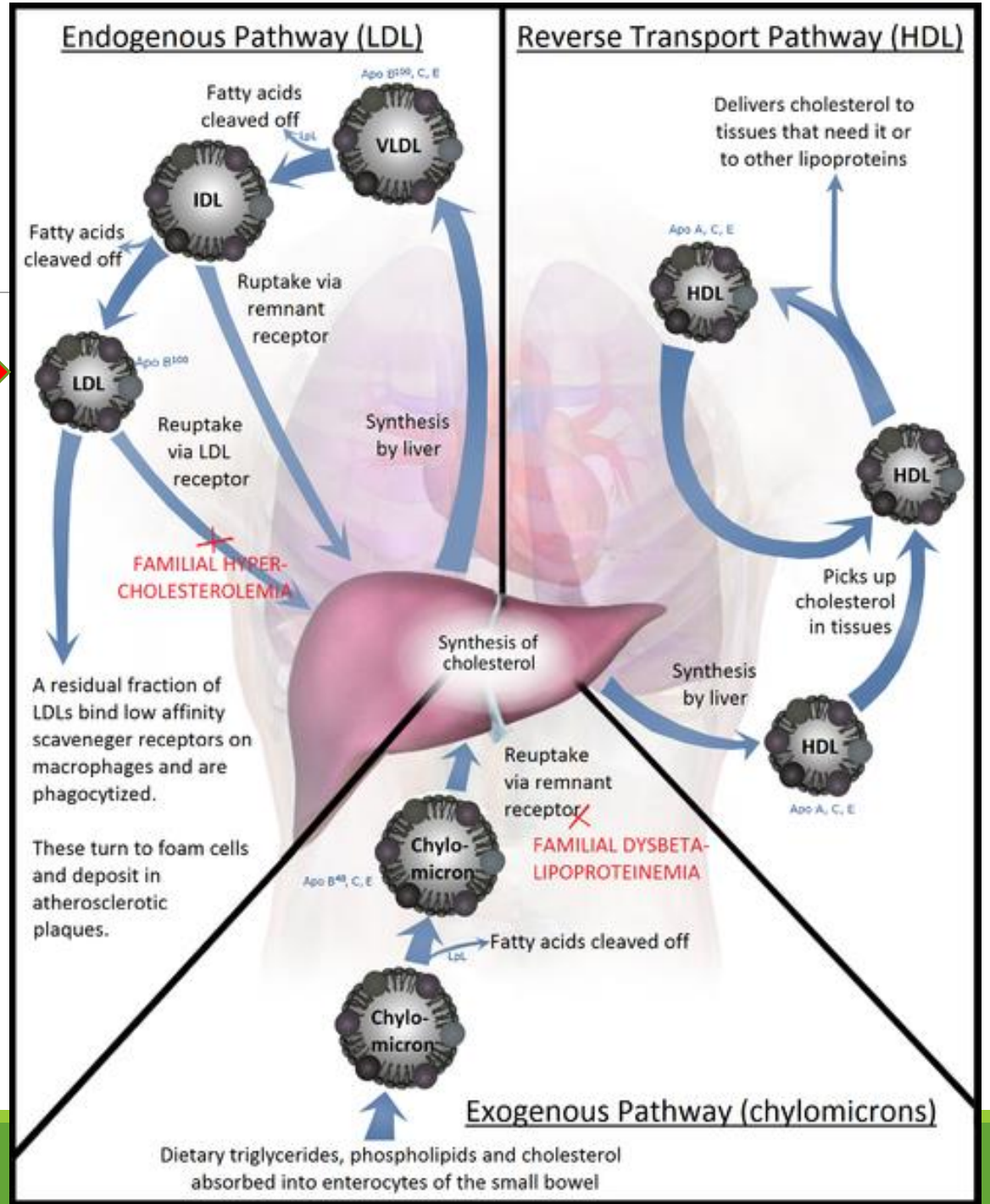
Describe strategies for addressing adverse effects associated with statins.

Integrate guidelines into practice through case study application

Lipid metabolism

Lowering

LDL



10 Key points

1. Promote heart healthy lifestyle choices across all age groups over a lifetime.

2. If clinical ASCVD present, focus is on reducing LDL-C with high intensity statin at the maximally tolerated dose.

3. High risk patients with ASCVD should have LDL-C threshold of 70 mg/dl

10 Key Points

4. For patients with LDL-C ≥ 190mg/dl (severe primary hypercholesterolemia) start a high-intensity statin without calculating risk.

5. Age 40-75 with diabetes and LDL-C ≥ 70 mg/dl start moderate intensity statin without calculating risk.

6. In patients age 40-75 evaluated for primary ASCVD prevention, engage in patient-provider risk discussion prior to starting a statin.

7. Age 40-75 without diabetes and ≥ 7.5% risk with LDL-C ≥ 70 mg/dl start moderate intensity statin.

Risk Enhancing Factors

Persistent elevations of triglycerides ≥ 175mg/dl

Persistently elevated LDL-C ≥ 160 mg/dl

Metabolic syndrome

CKD (not on dialysis)

Chronic inflammatory disorders

High risk ethnic groups (South Asian)

Family history of premature ASCVD

History of preeclampsia or menopause before age 40

10 Key Points

8. Age 40-75 without diabetes and 10 yr ASCVD risk between 7.5%-19.9% , risk enhancing factors favor statin initiation.

9. Age 40-75 without diabetes and 10 yr ASCVD risk 7.5%-19.9% with LDL-C ≥ 70-189 mg/dl and uncertain about statin, consider measuring a coronary artery calcium score (CAC).

10. Assess adherence and percentage LDL-C lowering medications and lifestyle changes 4-12 weeks after statin initiation or dose change. Repeat every 3-12 months as needed.

Determining Cardiovascular Risk

ASCVD Risk Estimator Plus

Pooled Cohort Equations-
Can over or under estimate risk

<u>Over estimate</u>

- Healthy women, high SES

<u>Underestimate</u>

- Low SES, inflammatory disease

ASCVD Estimator Plus use in age 40-79

- Age
- Gender
- Race

Total Cholesterol

HDL Cholesterol

Systolic and diastolic BP

Yes/No- Diabetes, Smoker, treatment for Hypertension

Yes/No- On aspirin and/or statin

Example

Age 56

BP 148/86 (no treatment for Htn)

Diabetes

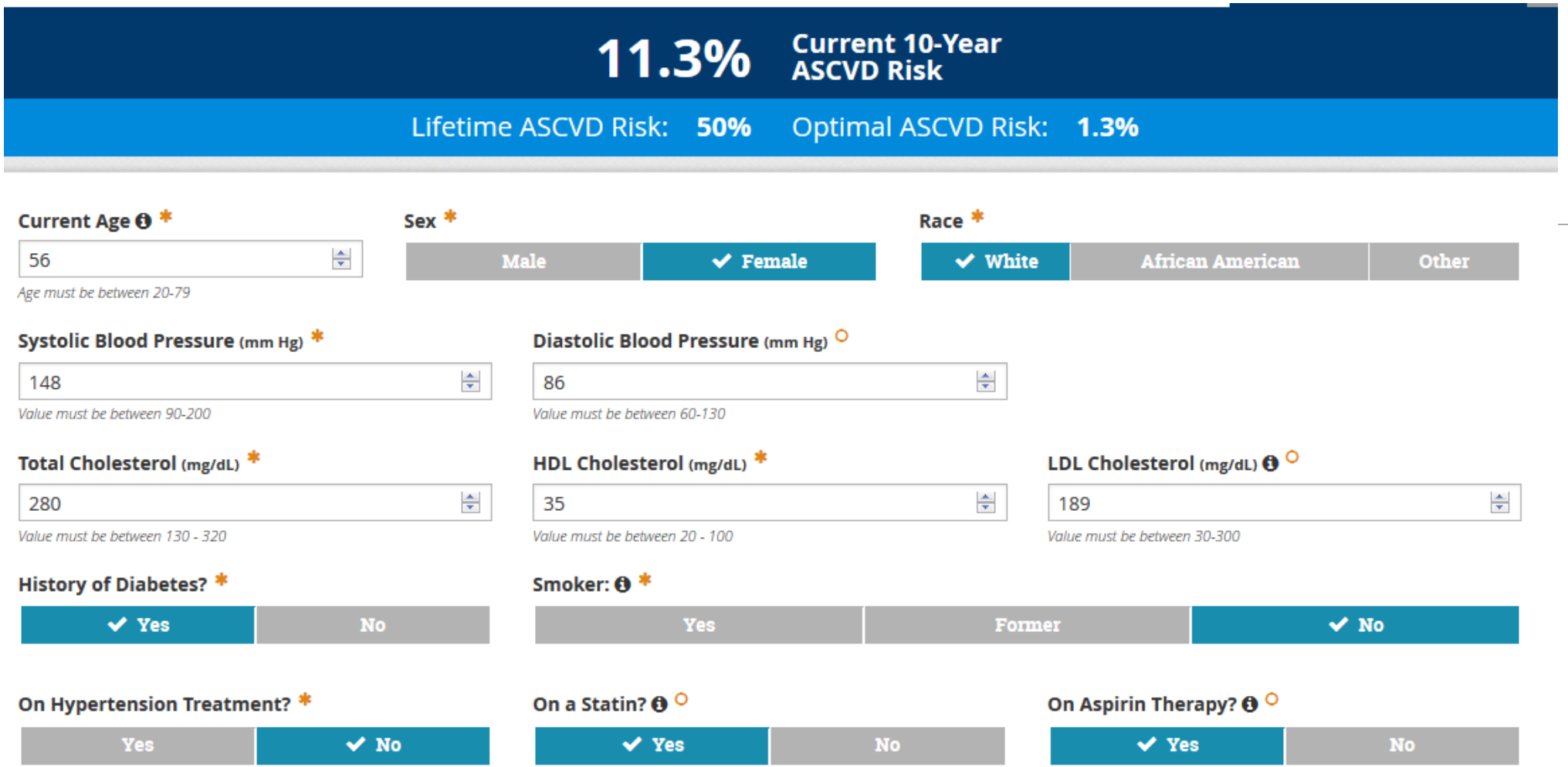
Nonsmoker

Total 280

LDL 189

HDL 35

On Aspirin and statin

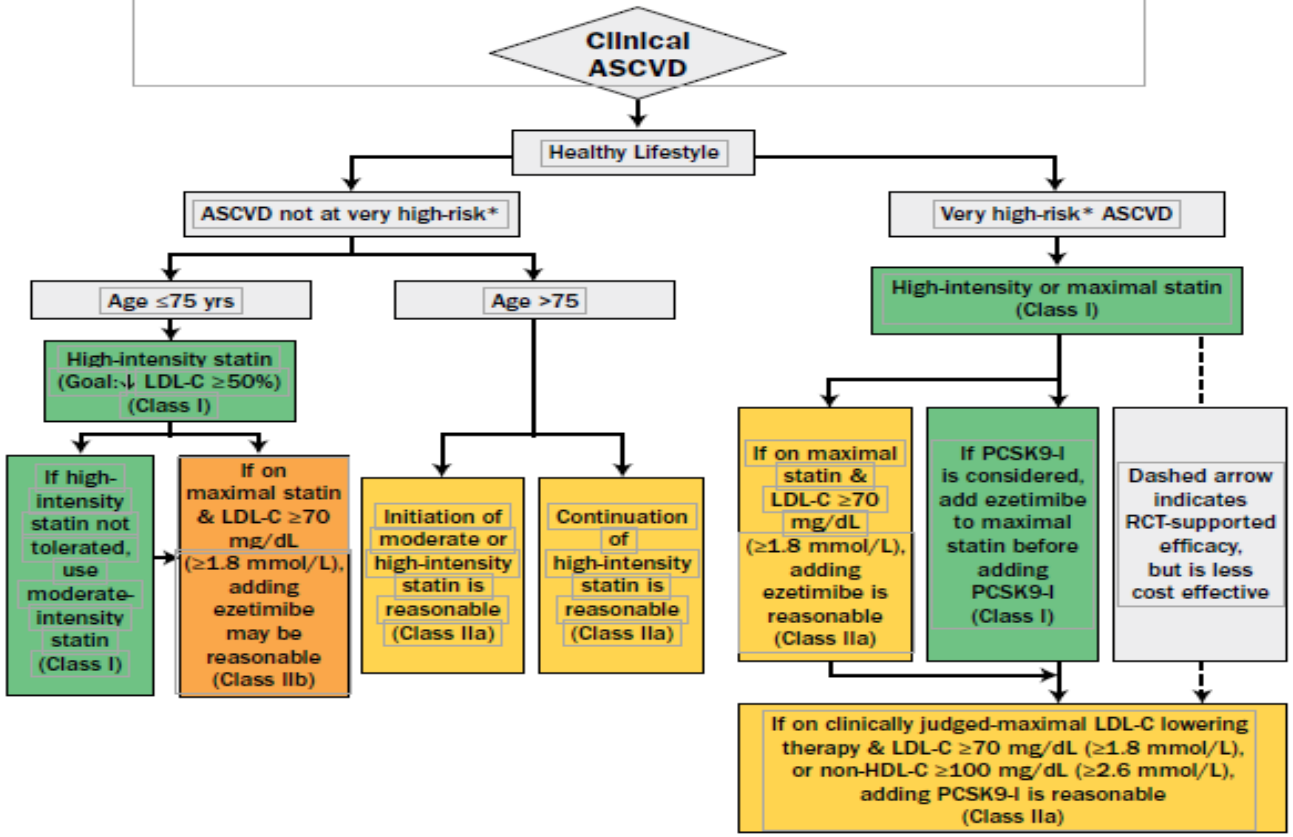


https://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/

Secondary ASCVD Prevention

First Statin Benefit Group

Figure 1:
Secondary Prevention in Patients with Clinical ASCVD



*Very high-risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions (Table 4 on following page).

Figure 1

AMERICAN COLLEGE of CARDIOLOGY

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Secondary ASCVD Prevention

First Statin Benefit Group

Very High-Risk for Future ASCVD Events*

Table 4

Major ASCVD Events
Recent acute coronary syndrome (within the past 12 months)
History of myocardial infarction (other than recent acute coronary syndrome event listed above)
History of ischemic stroke
Symptomatic peripheral arterial disease (history of claudication with ankle brachial index <0.85, or previous revascularization or amputation)
High-Risk Conditions
Age ≥65 years
Heterozygous familial hypercholesterolemia
History of prior coronary artery bypass surgery or PCI outside of the major ASCVD event(s)
Diabetes Mellitus
Hypertension
Chronic kidney disease (eGFR 15-59 mL/min/1.73 m²)
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 heart failure

*Very High Risk includes a history of multiple major ASCVD events or one major ASCVD event and multiple high-risk conditions.

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Primary Prevention Groups

Diabetes Mellitus

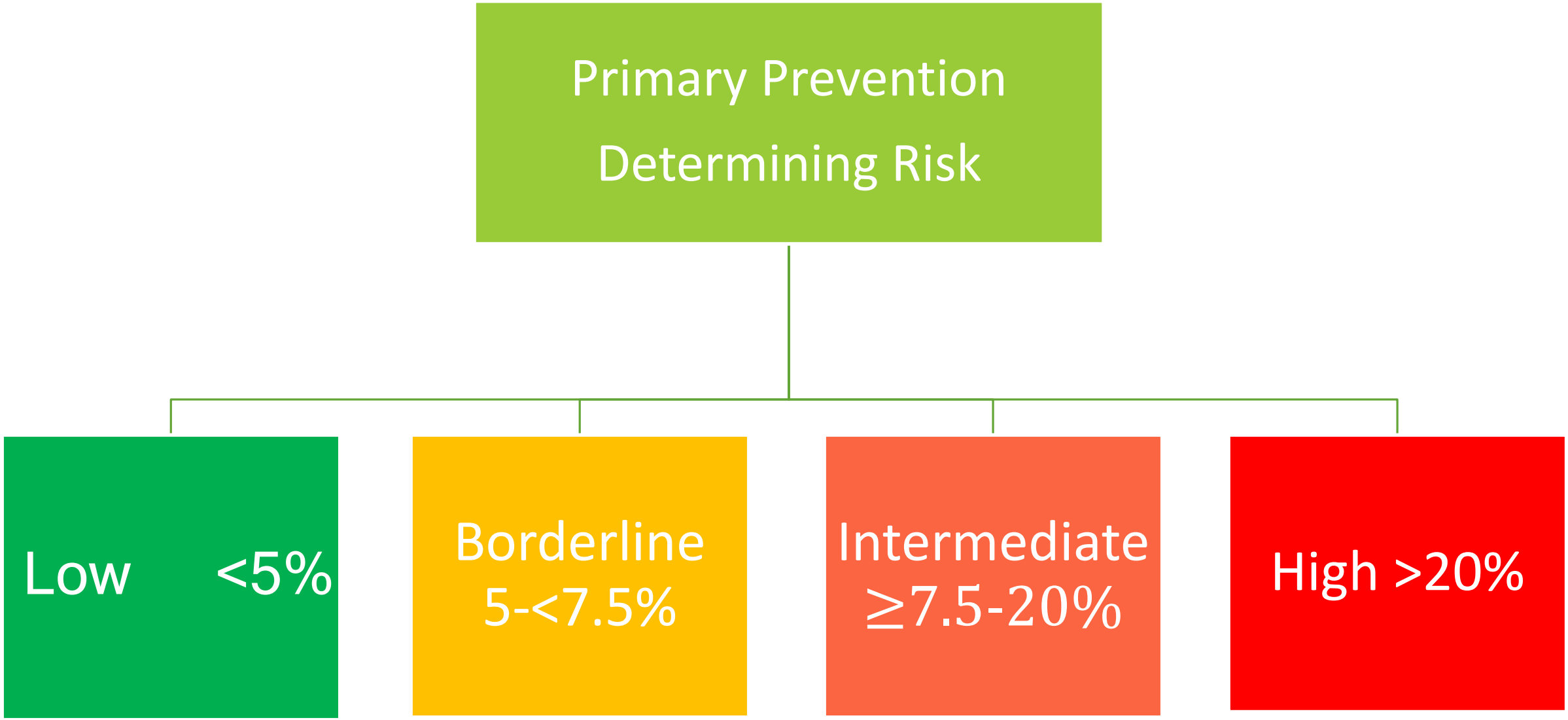
LDL-C ≥ 190 mg/dl

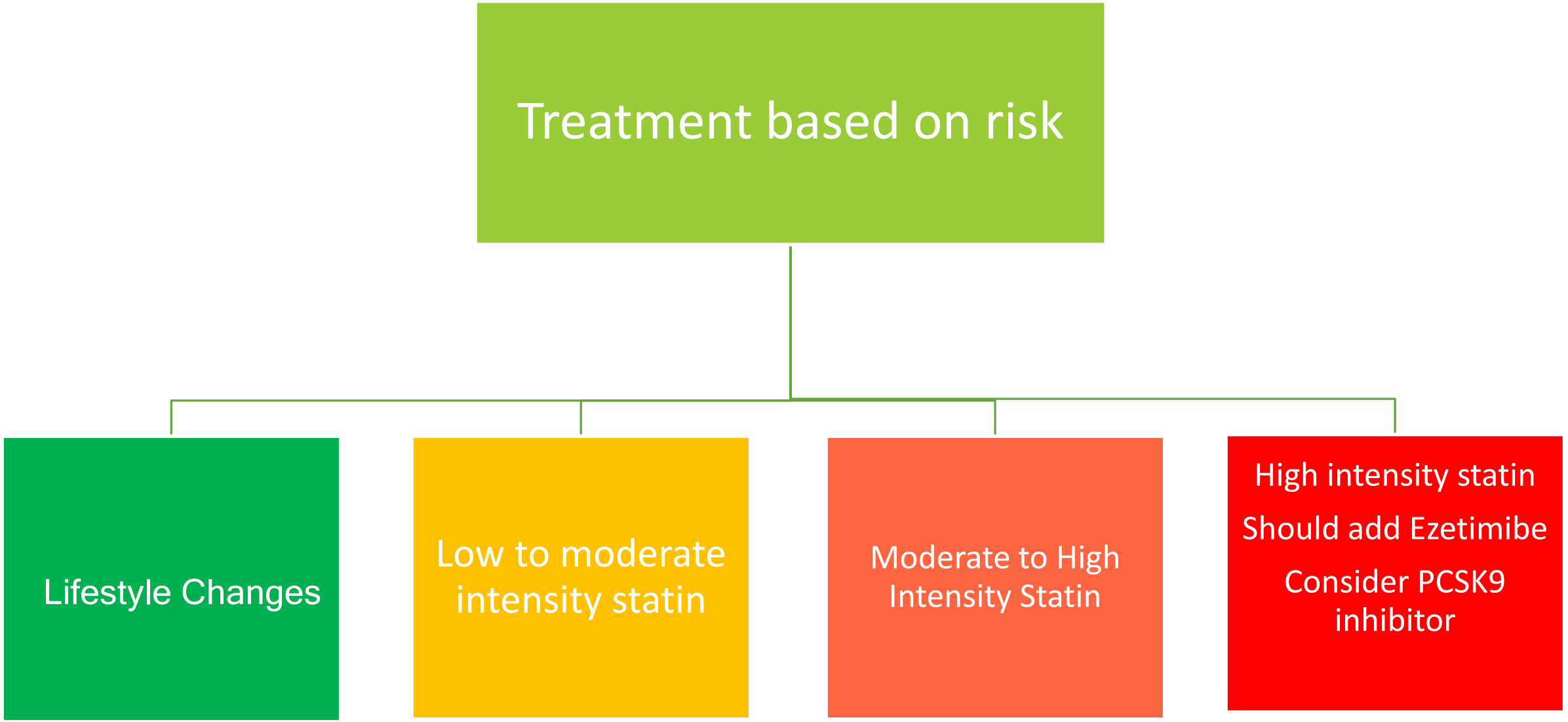
Age:

0-19- Lifestyle changes, use statin if familial hypercholesterolemia

20-39- Lifestyle changes, consider statin for LDL-C >160 mg/dl or + family history of early ASCVD

40-75- LDL-C 70-190 mg/dl without diabetes estimate 10 yr risk and treat as directed


Primary Prevention
Determining Risk
Low <5%
Borderline
5-<7.5%
Intermediate
≥7.5-20%
High >20%


Treatment based on risk
Lifestyle Changes
Low to moderate intensity statin
Moderate to High Intensity Statin
High intensity statin
Should add Ezetimibe
Consider PCSK9 inhibitor

Heart Healthy Lifestyle

New Definition of High Blood Pressure

2017 ACC/AHA Hypertension in adults over age 65 redefined:

Target is a BP <130/80

Under age 65 target is BP < 120/80

Elevated Blood pressure 120-129/80 mmHg

Stage 1 Hypertension: 130-139/80-89 mmHg

Stage 2 Hypertension: 140-159/90-99 mmHg

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018;71:e127-e248.

HMG-CoA reductase inhibitors - STATIN

Decrease LDL

Reduce triglycerides

Increase HDL production

Low vs. Moderate vs. High Intensity Statin Therapy

High Intensity	Moderate Intensity	Low Intensity
Daily dose lowers LDL-C on average, approximately ≥ 50%	Daily dose lowers LDL-C on average, approximately 30 to >50%	Daily dose lowers LDL-C by 30%
Atorvastatin 40-80mg Rosuvastatin 20-(40)mg	Atorvastatin 10-20mg Rosuvastatin 5-10mg Simvastatin 20-40mg Lovastatin 40mg Pravastatin 40-80mg Fluvastatin 40mg BID Pitavastsatin 2-4mg	Simvastatin 10mg Pravastatin 10-20mg Lovastatin 20mg Fluvastatin 20-40mg Pitavastatin 1mg

Effect	Lovastatin	Pravastatin	Simvastatin	Atorvastatin	Fluvastatin	Rosuvastatin	Pitavastatin
LDL %	-34	-34	-41	-50	-24	-63	-45
TG %	-16	-24	-18	-29	-10	-28	-19
HDL	+9	+12	+12	+6	+8	+10	+5
½ life (hrs)	2	1-2	1-2	14	1-2	18-20	12
CYP450	3A4	None	3A4	3A4	2C9	2C9, 2C19	2C9
Lipophilic	Yes	No	Yes	Yes	No	N0	Yes
Protein BInding	95%	50%	95%	98%	98%	88%	99%
Renal excretion	10%	20%	13%	2%	<6%	10%	15%

Statins: Contraindications

Contraindications

- Active Liver disease
- Cholestasis
- Pregnancy or lactation (pregnancy category X)

Precautions

- Heavy alcohol use
- Grapefruit juice
- Drug interactions-increase risk of liver damage/myopathy
  - 3A4 Inhibitors-erythromycin, cyclosporine, fibrates, azole antifungals, diltiazem, verapamil, grapefruit juice
  - Warfarin

Symptoms	Evidence	Predisposing factors	Frequency
Myalgias	RCTs Cohorts/observational	Age, low BMI, female sex, high-risk medications, comorbidities, Asian ancestry, excess alcohol, high levels of physical activity, and trauma	Infrequent
Myositis/myopathy	RCTs Cohorts/observational		Rare
Rhabdomyolysis	RCTs Cohorts/observational		Rare
Autoimmune myopathy	Case Reports		Rare

Symptoms	Evidence	Predisposing factors	Frequency
Transaminase elevation 3 × ULN	RCTs/ cohorts/observational Case reports		Infrequent
Hepatic failure			Rare
Memory/cognition	Case reports; no increase in memory/cognition problems in 3 large-scale RCTs		Rare/Unclear
New Onset Diabetes Mellitus	RCT and meta-analysis	High intensity statin treatment, metabolic syndrome	More common if: BMI≥30, fasting blood glucose ≥100 mg/dL; metabolic syndrome, or A1c ≥6%.

PCSK9 inhibitor

PCSK9 inhibitor is monoclonal antibody which blocks endogenous PCSK9.

Prevents degradation of LDL-C receptors

Results in reduced amount of circulating LDL.

Increases the clearance of LDL by 43 to 58%

PCSK9 inhibitor

Alirocumab and Evolocumab- not to be used as monotherapy

Administered by injection every 2-4 weeks.

Prior authorization

Cost

PCSK9 inhibitor

Clinical Trial Results

ODYSSEY- Alirocumab + atorvastatin compared to others

- Lowered LDL by 54%

LAPLACE-2- Evolocumab + ezetimibe or placebo

- Lowered LDL by 66%

FOURIER- Evolocumab + statin

- 15% reduction in composite endpoints of MI, CVA and hospitalizations for cardiac or death.

Palmer, C. 2018. New Directions in Managing Dyslipidemia. The Journal for Nurse Practitioners. 73-79e2. doi.org/10.1016/j.nurpra.2018.08.033

Alirocumab and Evolucumab

Alirocumab

½ life is 17-20 days

when given with statin, ½ life 12 days

Evolocumab

½ life 11 to 17 days

Safety Profile of PCSK9 inhibitors

Mortality profile:

- Lower rates of MI, stroke and coronary revascularization
- No difference in heart failure hospitalizations

Adverse effects:

- Injection site irritation
- Hypersensitivity reactions
- No Muscle toxicity, neurocognitive changes, liver toxicity

Ezetimibe

Inhibits absorption of cholesterol by 54% at brush border of small intestine

- **Increased** expression of hepatic LDL receptors
- **Reduced** cholesterol content of atherogenic particles
- **Decreased** intestinal delivery of cholesterol to the liver

- Monotherapy 18% LDL reduction
- Combined with statin 25% and may be higher

Hypertriglyceridemia

In adults age 20 or older fasting or non-fasting 175-499 mg/dl

- Address lifestyle
- Secondary factors
  - Diabetes, chronic liver or kidney disease, hypothyroidism
  - Medications that affect triglycerides.

In adults 40-75 with moderate or severe hypertriglyceridemia and ASCVD risk 7.5% or higher

- Consider statin

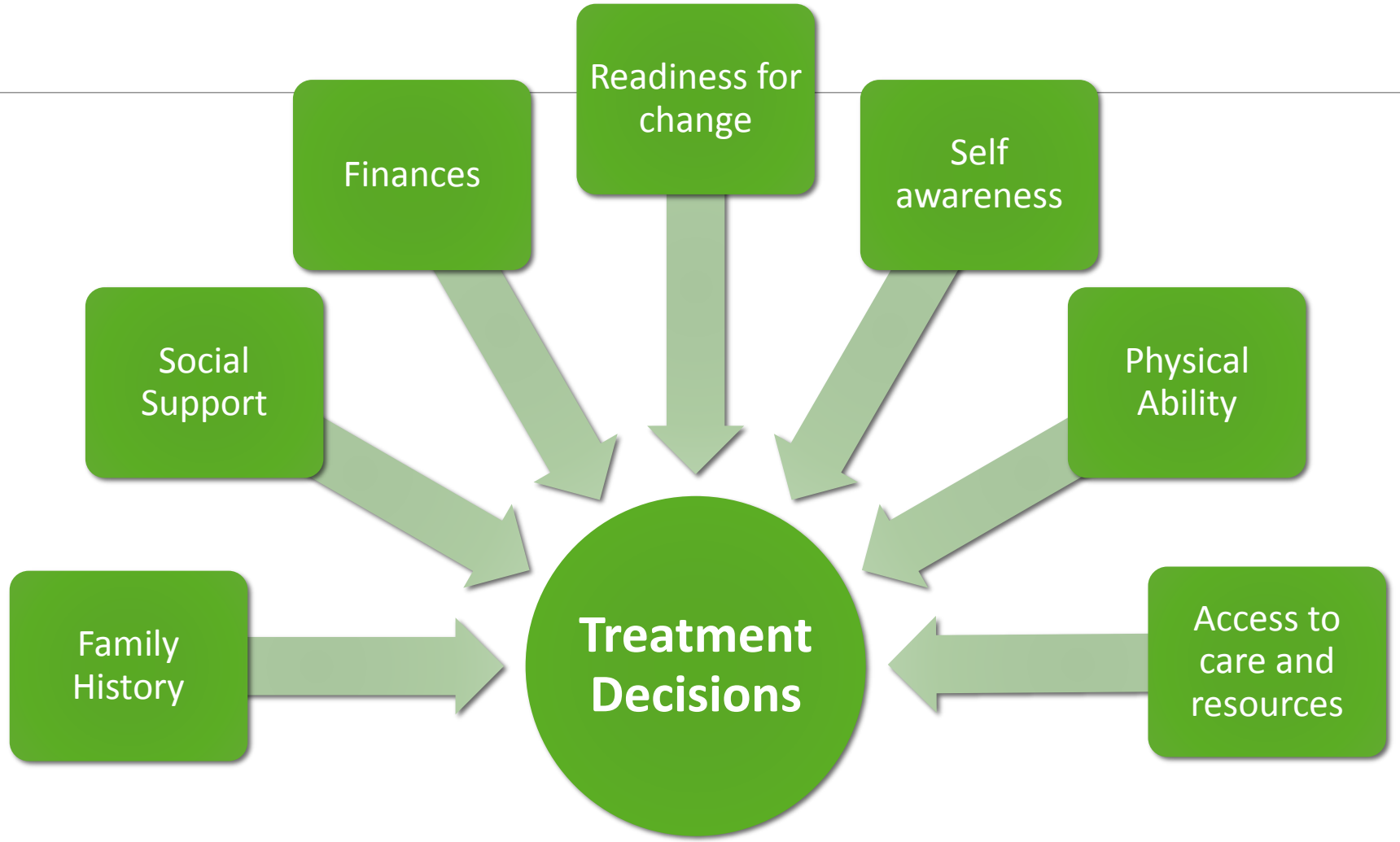
In adults 40-75 with triglycerides≥ 500mg/dl

- Address other causes
- Advise very-low fat, avoid carbs and alcohol
- Increase omega-3 fatty acid intake
- Add fenofibrate

Shared Decision Making

- Patient's priorities for health care
- Perceived risk of ASCVD
- Discussion of actual risk and risk enhancers
- Risk/benefit of pharmacotherapy
- Cost of therapy
- Discuss "realistic" opportunities for lifestyle modifications.

Factors affecting Treatment Adherence



47 year-old male with hypertension, smoker and dyslipidemia

BP 144/90 HR 84 SpO2 98% RA Wt. 210 lbs. Ht. 69 in. BMI 31.0

ASCVD Risk 13.2% 10 yr

Lifetime 69%

Total Cholesterol	254 mg/dl
Triglycerides	107 mg/dl
HDL	69m/dl
LDL	180mg/dl

Medications

Lisinopril 10 mg daily

55 year-old female with obesity, diabetes and dyslipidemia

BP 120/68 HR 73 SpO2 100% RA Wt. 184 lbs. Ht. 64 in. BMI 33.3

ASCVD Risk 7.6% 10 yr

39%

Total Cholesterol	280 mg/dl
Triglycerides	122 mg/dl
HDL	44m/dl
LDL	180mg/dl

Medications

Metformin 850 mg daily

ASA 81 mg daily

55 year-old female with obesity, diabetes and dyslipidemia

First visit

Focus on lifestyle changes

Based on intermediate risk

Pravastatin 40 mg daily

4 weeks later

Tot Chol	210 mg/dl
Trig	100 mg/dl
HDL	47m/dl
LDL	120mg/dl

She c/o myalgias. What is your next step?

What are your options for treatment?

Pearls for prescribing Statins

No routine CK monitoring, but consider if muscle symptoms or concomitant drug therapy that would increase risk for myopathy

If muscle pain, stop statin, evaluate symptoms, re-challenge with original or lower dose of statin

Cognitive SE: switch from lipid soluble to water soluble statin, lower dose

Summary

- For very high risk patients the threshold for LDL-C is 70 mg/dl
- Goal of therapy is not a number but a percentage reduction in LDL
- Consider ASCVD risk enhancers in discussion.
- In intermediate risk patient, if statin therapy uncertain, consider measuring CAC.
- Lifestyle changes are foundation for prevention of ASCVD and should be introduced early in life.
- Shared decision making is a hallmark of implementation of guideline.