Cardiac Prevention in 2020

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Cardiology Fellow, PGY5

BUMCP IM Academic Half Day

10 March 2020

Objectives

- Review the 2019 ACC/AHA Guidelines for Primary Cardiovascular Prevention
- Discuss the appropriate use of statins in primary and secondary cardiovascular prevention
- Recognize when PCSK-9 inhibitors should be offered to our patients
- Identify anti-glycemic agents with cardiovascular benefit including the role of the new SGLT-2 inhibitors

Case of Mrs. Jones

- 56 y/o female with PMHX of DM2, HTN, and fibromyalgia presents to the clinic for routine cardiovascular examination.
- FMHX: mother with CAD/MI at 45 y/o, brother with CAD/MI at 63 y/o
- SocHX: social alcohol, denies tobacco or illicit drugs, works as architect, no formal exercise but states she is active at work
- Rx: Metformin 500 mg BID, Lisinopril 20 mg, Aspirin 81 mg daily, OTC supplements

Case of Mrs. Jones

- ROS: denies fevers/chills, chest pain, orthopnea, PND, LE edema, fatigue, myalgias

- Physical Exam

  Vitals: 98.2 F, 128/91, 78, 16, 95% on RA, BMI 30

  Obese female, NAD, RRR with normal S1/S2, no murmurs,gallops

  JVP 10 cmH2O

Case of Mrs. Jones

My mother is on a statin, do I need to be on one too?

My blood sugar is decently controlled, but I've heard there's new medications on the market…should I be taking one of them?

Should I continue taking a daily Aspirin?

Do I exercise enough?

Keto, Paleo, Atkins, DASH, Mediterranean…which diet is best?

Is a little alcohol cardioprotective? How much is too much?

I've read about coronary Ca2+ scores online, should I have one of these done?

What can I do to minimize my risk of a heart attack?

What's the meaning of life???

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 74, NO. 10, 2019

PUBLISHED BY ELSEVIER

CLINICAL PRACTICE GUIDELINE

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, the American Geriatrics Society, the American Society of Preventive Cardiology, and the Preventive Cardiovascular Nurses Association

Life ‘Simple’ 7

1. Control cholesterol
2. Reduce blood sugar
3. Manage blood pressure
4. Exercise
5. Diet
6. Lose weight
7. Stop smoking

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Question 1

What should you recommend first to maximize Mrs. Jones ASCVD risk reduction?

A. Prescribe Atorvastatin 20 mg
B. Increase Metformin to 1000 mg BID
C. Order coronary Ca2+ score
D. Exercise 5-7 days out of the week
E. Order pharmacologic SPECT stress test

Question 1

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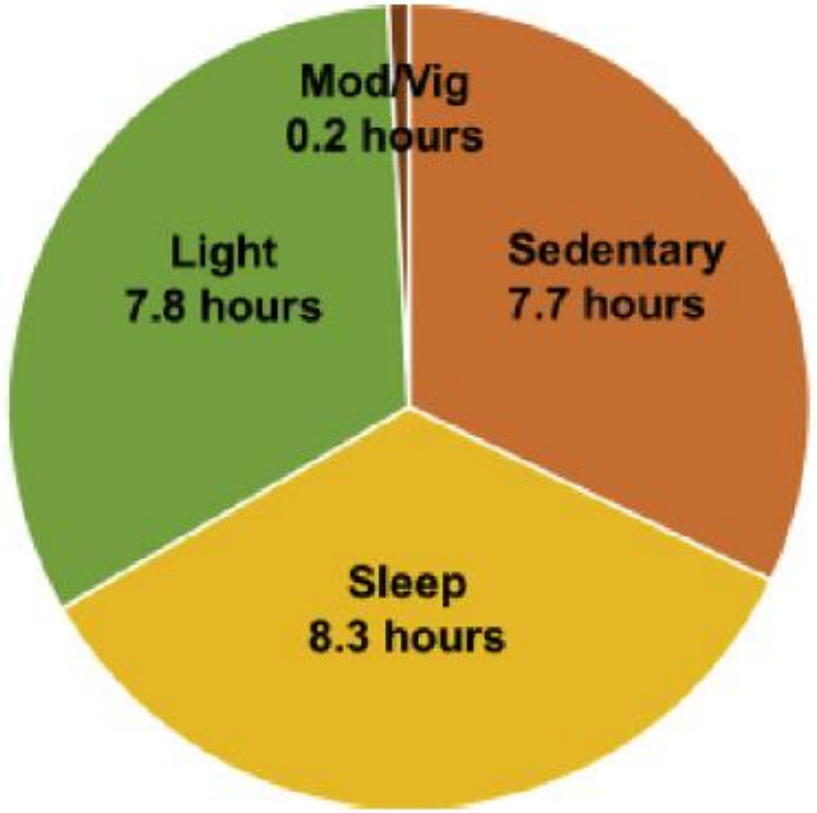
TABLE 4 Definitions and Examples of Different Intensities of Physical Activity

Intensity	METs	Examples
Sedentary behavior*	1-1.5	Sitting, reclining, or lying; watching television
Light	1.6-2.9	Walking slowly, cooking, light housework
Moderate	3.0-5.9	Brisk walking (2.4-4 mph), biking (5-9 mph), ballroom dancing, active yoga, recreational swimming
Vigorous	≥6	Jogging/running, biking (≥10 mph), singles tennis, swimming laps

FIGURE 1 Hours Per Day Spent in Various States of Activity



U.S. adults spend >7 h/d on average in sedentary activities. Replacing sedentary time with other physical activity involves increasing either moderate- to vigorous-intensity physical activity or light-intensity physical activity. Data modified from Young et al. (S3.2-30).

ACC/AHA Guidelines

COR	LOE	RECOMMENDATIONS
I	B-R	1. Adults should be routinely counseled in healthcare visits to optimize a physically active lifestyle (S3.2-1, S3.2-2).
I	B-NR	2. Adults should engage in at least 150 minutes per week of accumulated moderate-intensity or 75 minutes per week of vigorous-intensity aerobic physical activity (or an equivalent combination of moderate and vigorous activity) to reduce ASCVD risk (S3.2-3–S3.2-8).
IIa	B-NR	3. For adults unable to meet the minimum physical activity recommendations (at least 150 minutes per week of accumulated moderate-intensity or 75 minutes per week of vigorous-intensity aerobic physical activity), engaging in some moderate- or vigorous-intensity physical activity, even if less than this recommended amount, can be beneficial to reduce ASCVD risk (S3.2-5, S3.2-6).
IIb	C-LD	4. Decreasing sedentary behavior in adults may be reasonable to reduce ASCVD risk (S3.2-3, S3.2-9–S3.2-11).

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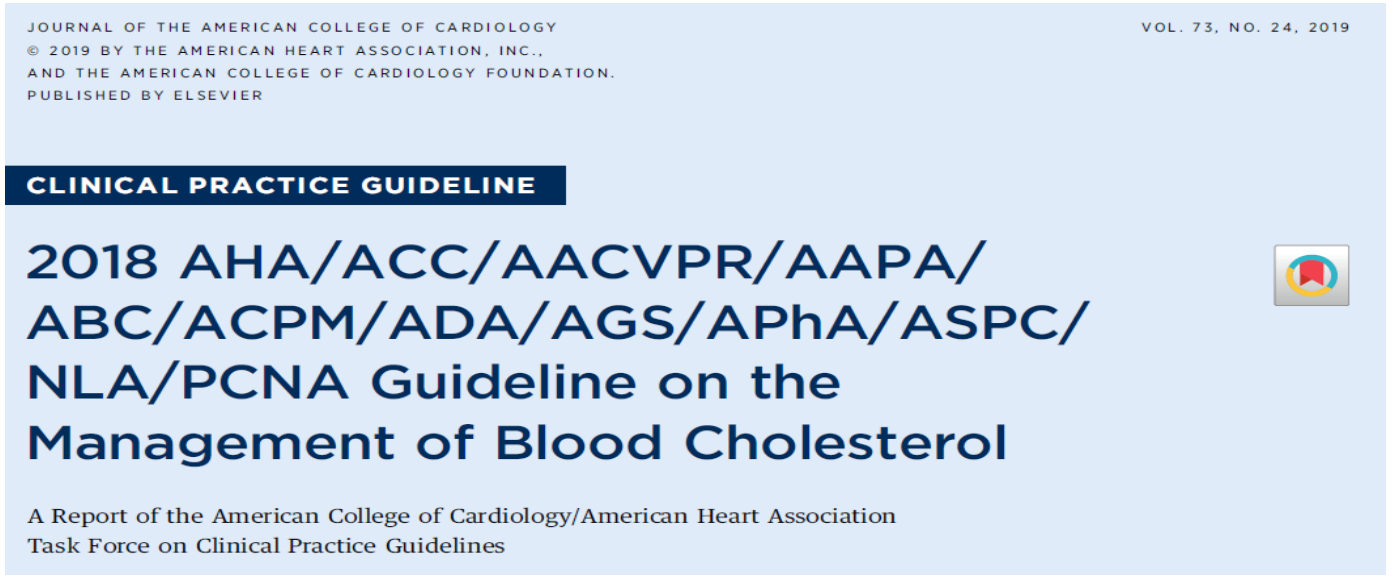
Primary Prevention

- Primary Prevention
  - Old School
    - The Framingham Heart Study – 1948
    - WHO Cooperative Trial – 1978
    - Lipid Research Clinical Trial – 1984
    - Multiple Risk Factor Intervention Trial (MRFIT) – 1986
    - Helsinki Heart Study – 1987
  - New School
    - PROVE IT –TIMI Trial – 2004
    - SATURN Trial – 2011
    - JUPITER Trial – 2008



4 Statin Benefit Groups

1. Clinical ASCVD (Grade A)

2. 40-75 y/o diabetics, with no clinical ASCVD and LDL-C 70-189 mg/dL (Grade A)

3. 40-75 y/o without diabetes, clinical ASCVD, LDL-C 70-189 mg/dL, and estimated 10 year ASCVD risk score ≥7.5% (Grade A)

4. Primary elevations of LDL-C ≥190 mg/dL (Grade B)

Question 2

Which Rx would you electronically send to the pharmacy?

A. Atorvastatin 20 mg daily
B. Rosuvastatin 40 mg daily
C. Simvastatin 10 mg daily
D. Pravastatin 80 mg daily

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ACC/AHA Guidelines

COR	LOE	RECOMMENDATIONS
I	A	1. In adults at intermediate risk (≥7.5% to <20% 10-year ASCVD risk), statin therapy reduces risk of ASCVD, and in the context of a risk discussion, if a decision is made for statin therapy, a moderate-intensity statin should be recommended (S4.3-2–S4.3-9). Adapted from recommendations in the 2018 Cholesterol Clinical Practice Guidelines (S4.3-1).
I	A	2. In intermediate risk (≥7.5% to <20% 10-year ASCVD risk) patients, LDL-C levels should be reduced by 30% or more, and for optimal ASCVD risk reduction, especially in patients at high risk (≥20% 10-year ASCVD risk), levels should be reduced by 50% or more (S4.3-2, S4.3-5–S4.3-10). Adapted from recommendations in the 2018 Cholesterol Clinical Practice Guidelines (S4.3-1).
I	A	3. In adults 40 to 75 years of age with diabetes, regardless of estimated 10-year ASCVD risk, moderate-intensity statin therapy is indicated (S4.3-11–S4.3-19). Included from recommendations in the 2018 Cholesterol Clinical Practice Guidelines (S4.3-1).
I	B-R	4. In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL (≥4.9 mmol/L) or higher, maximally tolerated statin therapy is recommended (S4.3-2, S4.3-20–S4.3-25). Included from recommendations in the 2018 Cholesterol Clinical Practice Guidelines (S4.3-1).

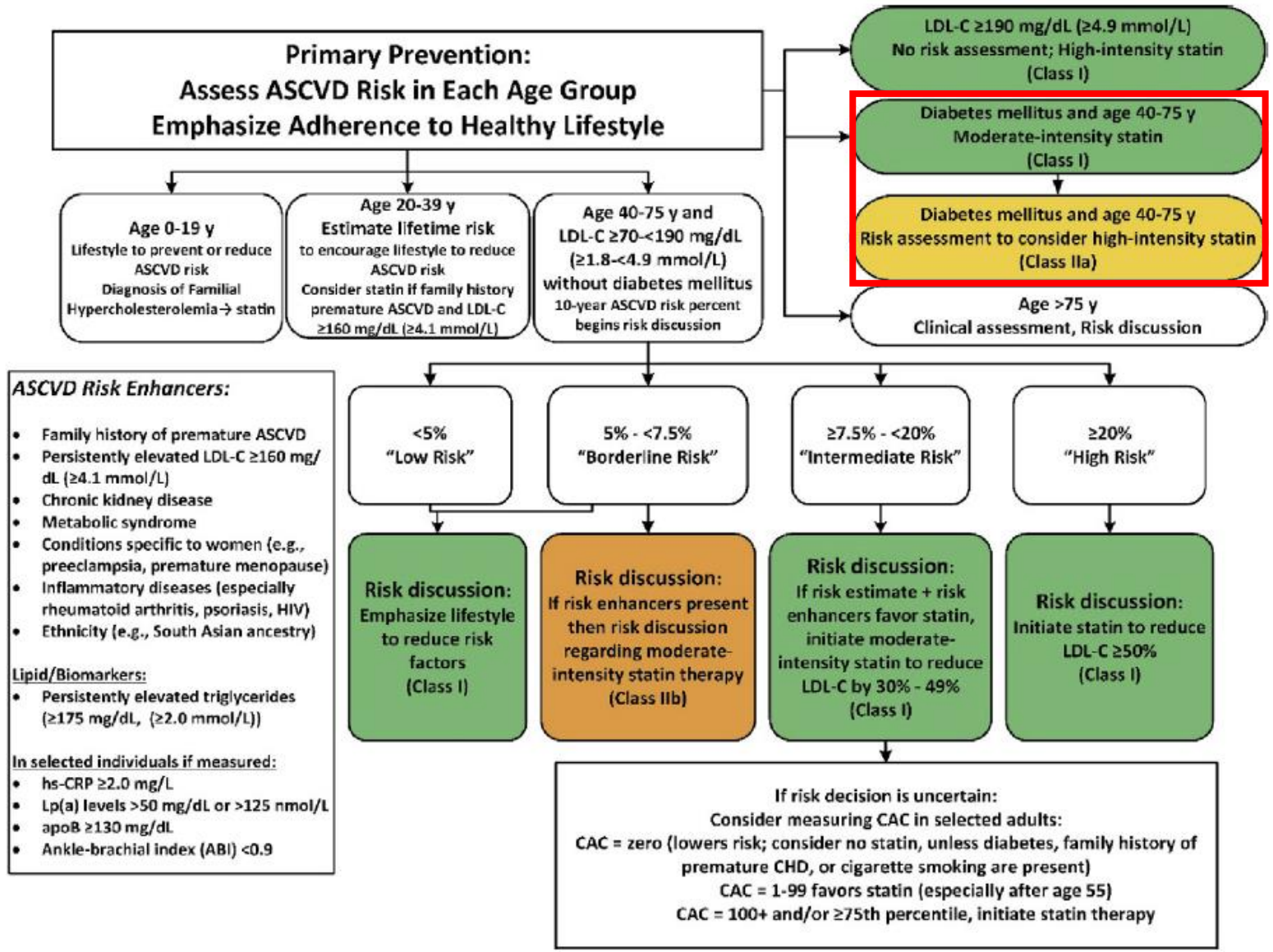
Statin Intensity

- Atorvastatin, Lovastatin, and Simvastatin are *lipophilic*
- Rosuvastatin, Pravastatin, and Fluvastatin are *hydrophilic*
- Pravastatin and Rosuvastatin have *limited CYP450 metabolism*
- Simvastatin has most *drug-drug interactions!!!*

TABLE 3 High-, Moderate-, and Low-Intensity Statin Therapy*

	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

FIGURE 3 Primary Prevention



Clinical ASCVD Risk Calculator

Gender

Age

Race

Total cholesterol

HDL cholesterol

LDL cholesterol

Blood pressure

Treatment for hypertension

Diabetes

Smoker

American Heart Association.

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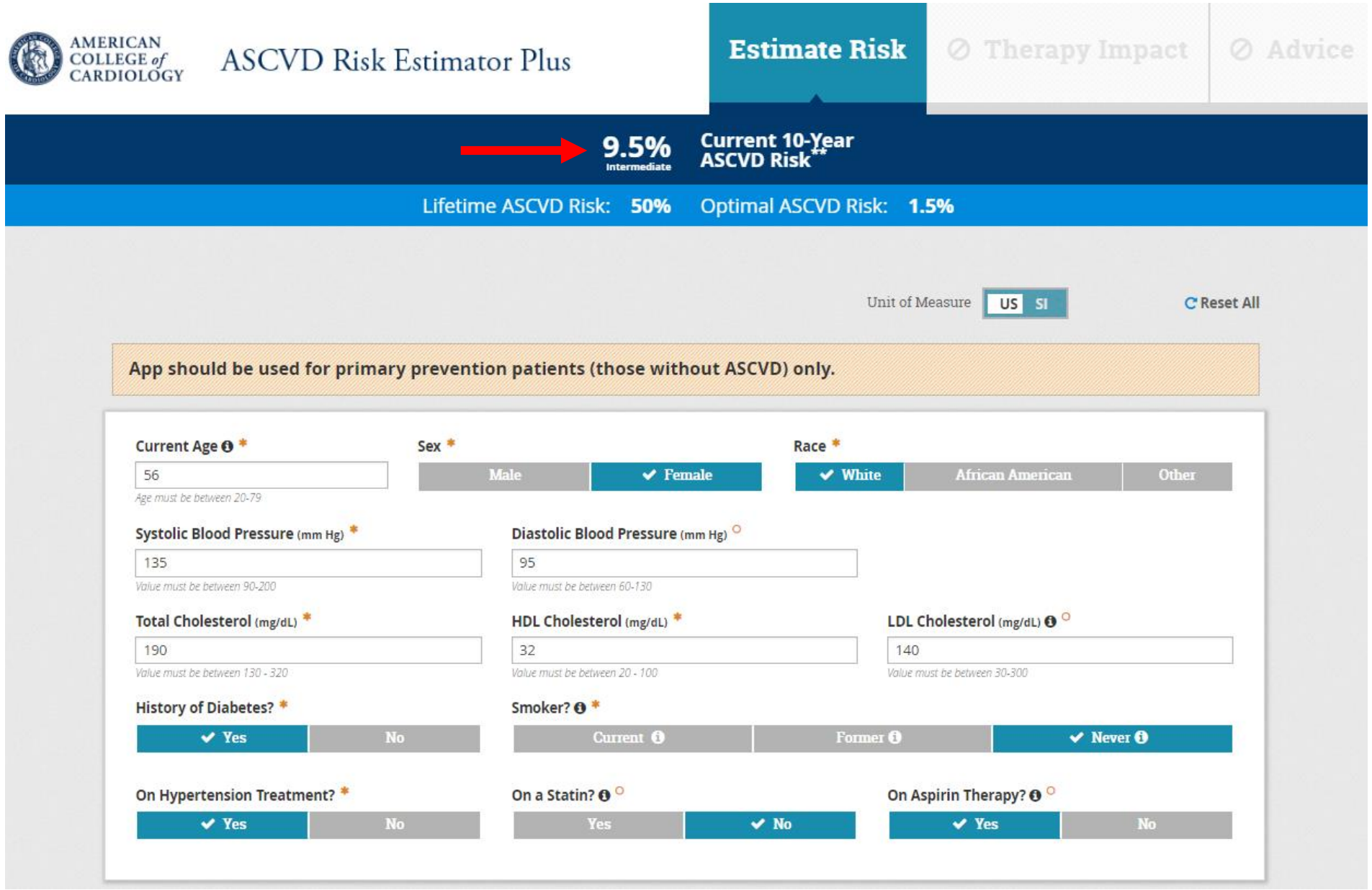
2013 Prevention Guidelines Tools

CV RISK CALCULATOR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ASCVD Risk Estimator Plus
Estimate Risk
Therapy Impact
Advice
9.5%
Intermediate
Current 10-Year ASCVD Risk**
Lifetime ASCVD Risk: 50%
Optimal ASCVD Risk: 1.5%
Unit of Measure US SI
Reset All
App should be used for primary prevention patients (those without ASCVD) only.
Current Age *
56
Age must be between 20-79
Sex *
Male
Female
Race *
White
African American
Other
Systolic Blood Pressure (mm Hg) *
135
Value must be between 90-200
Diastolic Blood Pressure (mm Hg)
95
Value must be between 60-130
Total Cholesterol (mg/dL) *
190
Value must be between 130 - 320
HDL Cholesterol (mg/dL) *
32
Value must be between 20 - 100
LDL Cholesterol (mg/dL)
140
Value must be between 30-300
History of Diabetes? *
Yes
No
Smoker? *
Current
Former
Never
On Hypertension Treatment? *
Yes
No
On a Statin?
Yes
No
On Aspirin Therapy?
Yes
No

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

Risk Enhancers in Diabetic Patients

- Long duration (≥10 years for T2DM (S4.3-61) or ≥20 years for type 1 diabetes mellitus (S4.3-16))
- Albuminuria ≥30 mcg albumin/mg creatinine (S4.3-62)
- eGFR <60 mL/min/1.73 m^2 (S4.3-62)
- Retinopathy (S4.3-63)
- Neuropathy (S4.3-64)
- ABI <0.9 (S4.3-65, S4.3-66)

TABLE 3 Risk-Enhancing Factors for Clinician–Patient Risk Discussion

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 [by ethnically appropriate cutpoints], elevated triglycerides [>150 mg/dL, nonfasting], elevated blood pressure, elevated glucose, and low HDL-C [<40 mg/dL in men; <50 mg/dL in women] are factors; a 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, lupus, 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/ethnicity** (e.g., South Asian ancestry)
- **Lipids/biomarkers**: associated with increased ASCVD risk
  - Persistently elevated* primary hypertriglyceridemia (≥175 mg/dL, nonfasting)
  - 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 triglyceride ≥200 mg/dL. A level ≥130 mg/dL corresponds to an LDL-C >160 mg/dL and constitutes a risk-enhancing factor
    - **ABI** (<0.9)

*Optimally, 3 determinations.

ABI indicates 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); and RA, rheumatoid arthritis.

Risk Enhancers

Case of Mrs. Jones

ASCVD risk score intermediate range ≥7.5 to <20%

+ FMHX of premature CAD – mother at age 45, brother at age 63

ACC/AHA Guidelines

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-NR	2. In adults 40 to 75 years of age with diabetes mellitus and an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), it is reasonable to assess the 10-year risk of a first ASCVD event by using the race and sex-specific PCE to help stratify ASCVD risk (S4.3-10, S4.3-11).
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).
IIa	B-NR	4. In adults older than 75 years of age with diabetes mellitus and who are already on statin therapy, it is reasonable to continue statin therapy (S4.3-5, S4.3-8, S4.3-13).
IIb	C-LD	5. In adults with diabetes mellitus and 10-year ASCVD risk of 20% or higher, it may be reasonable to add ezetimibe to maximally tolerated statin therapy to reduce LDL-C levels by 50% or more (S4.3-14, S4.3-15).

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ASCVD Risk Estimator Plus

Estimate Risk | Therapy Impact | Advice

5.0% Borderline — **Current 10-Year ASCVD Risk****

Lifetime ASCVD Risk: **39%** Optimal ASCVD Risk: **1.5%**

Current Age * 56
Age must be between 20-79

Sex * Male | ✔ Female

Race * ✔ White | African American | Other

Systolic Blood Pressure (mm Hg) * 135
Value must be between 90-200

Diastolic Blood Pressure (mm Hg) 95
Value must be between 60-130

Total Cholesterol (mg/dL) * 190
Value must be between 130 - 320

HDL Cholesterol (mg/dL) * 32
Value must be between 20 - 100

LDL Cholesterol (mg/dL) 140
Value must be between 30-300

History of Diabetes? * Yes | ✔ No

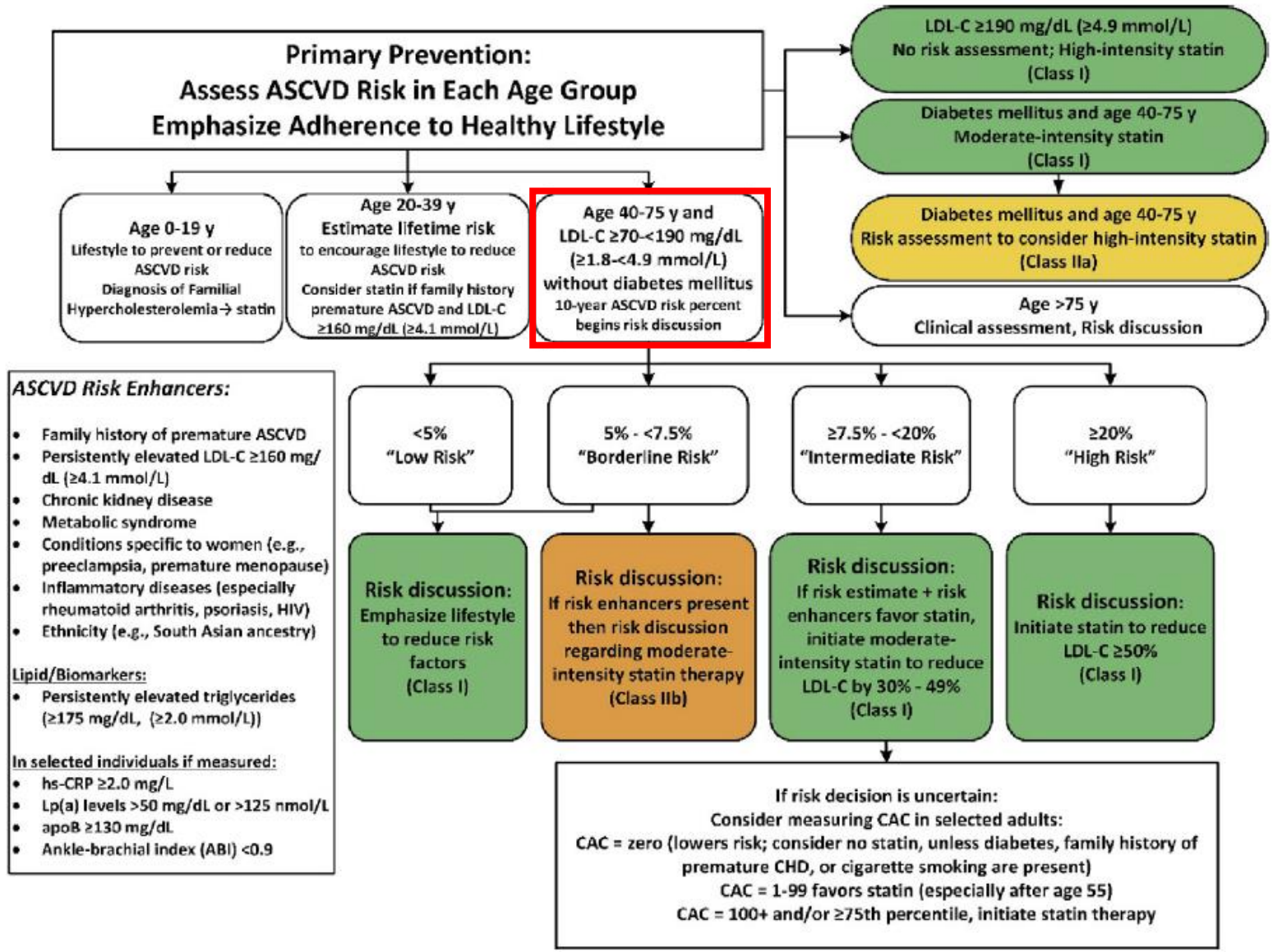
Smoker? * Current | Former | ✔ Never

On Hypertension Treatment? * ✔ Yes | No

On a Statin? Yes | ✔ No

On Aspirin Therapy? ✔ Yes | No

FIGURE 3 Primary Prevention



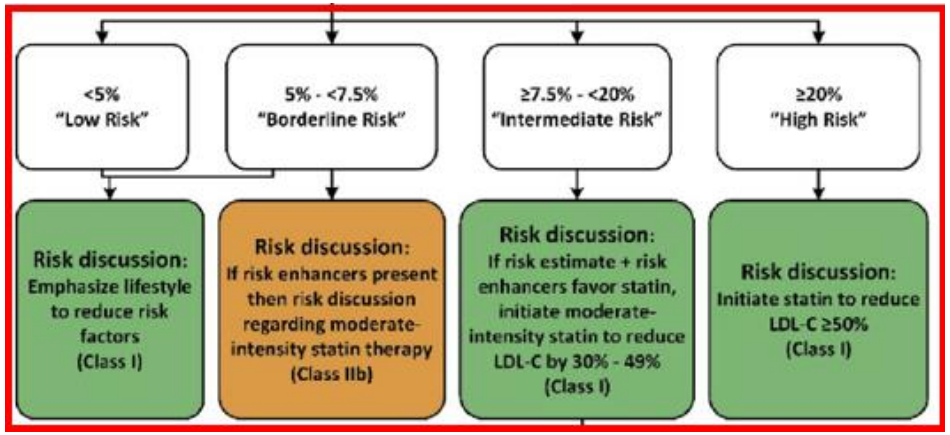
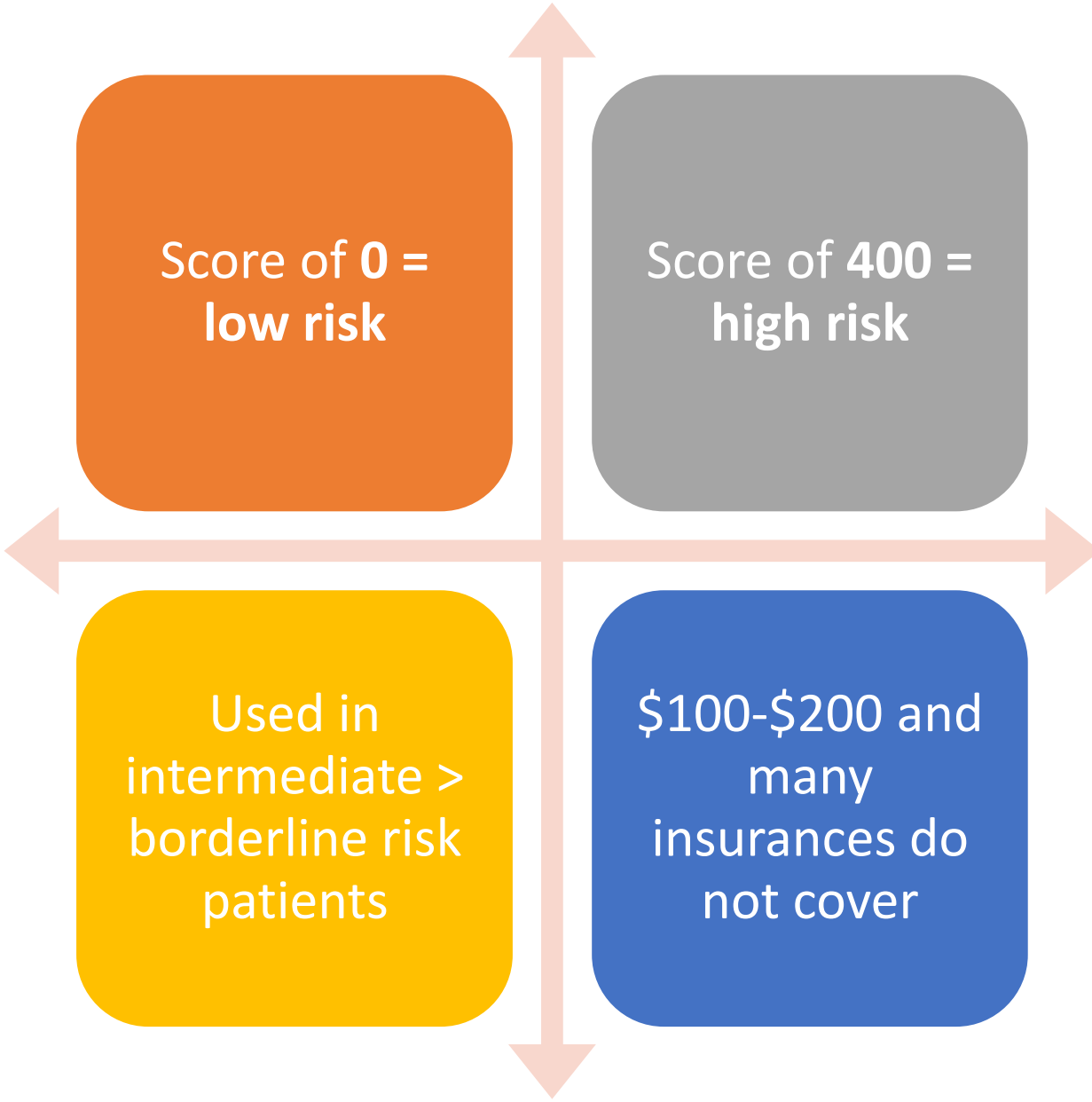


TABLE 6 Selected Examples of Candidates for Coronary Artery Calcium Measurement Who Might Benefit From Knowing Their Coronary Artery Calcium Score Is Zero

Coronary Artery Calcium Measurement Candidates Who Might Benefit from Knowing Their Coronary Artery Calcium Score Is Zero
■ Patients reluctant to initiate statin who wish to understand their risk and potential for benefit more precisely
■ Patients concerned about need to reinstitute statin therapy after discontinuation for statin-associated symptoms
■ Older patients (men 55–80 y of age; women 60–80 y of age) with low burden of risk factors (S4.3-53) who question whether they would benefit from statin therapy
■ Middle-aged adults (40–55 y of age) with PCE-calculated 10-year risk of ASCVD 5% to <7.5% with factors that increase their ASCVD risk, although they are in a borderline risk group.

Coronary Artery Calcium Score (CAC)



Question 3

Mrs. Jones returns to your office with repeat fasting lipid profile shown below:

TC - 160 TG - 151 LDL - 92
HDL - 42

What would be your next step in management?

A. Start PCSK9 inhibitor

B. Change to Fenofibrate

C. Add Zetia

D. Add Niacin

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Statin Intolerance

- Myalgias most common side effect with prevalence of 1-10%
- Avoid unnecessary discontinuation of statin
- If high suspicion…
  1. *Discontinue statin* until symptoms can be evaluated
  2. *Rule out* other conditions
  3. *Re-trial* original statin lower dose to establish causal relationship
  4. *Trial* low dose of a different statin once symptoms resolve
  5. *Gradually increase* the dose as tolerated

Question 4

Does Mrs. Jones qualify for Icosapant Ethyl therapy?

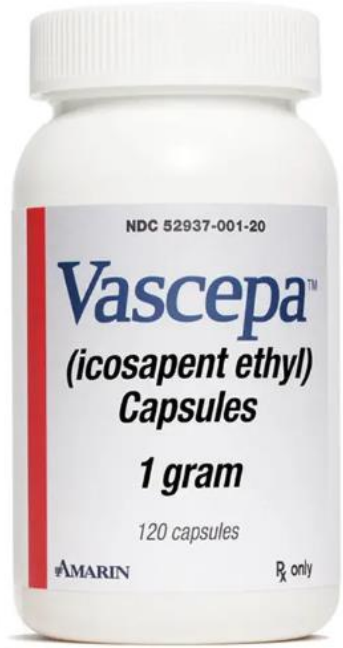
A. Yes
B. No
C. What is Icosapant Ethyl

Question 4

Does Mrs. Jones qualify for Icosapant Ethyl therapy?

A. Yes
B. No
C. What is Icosapant Ethyl

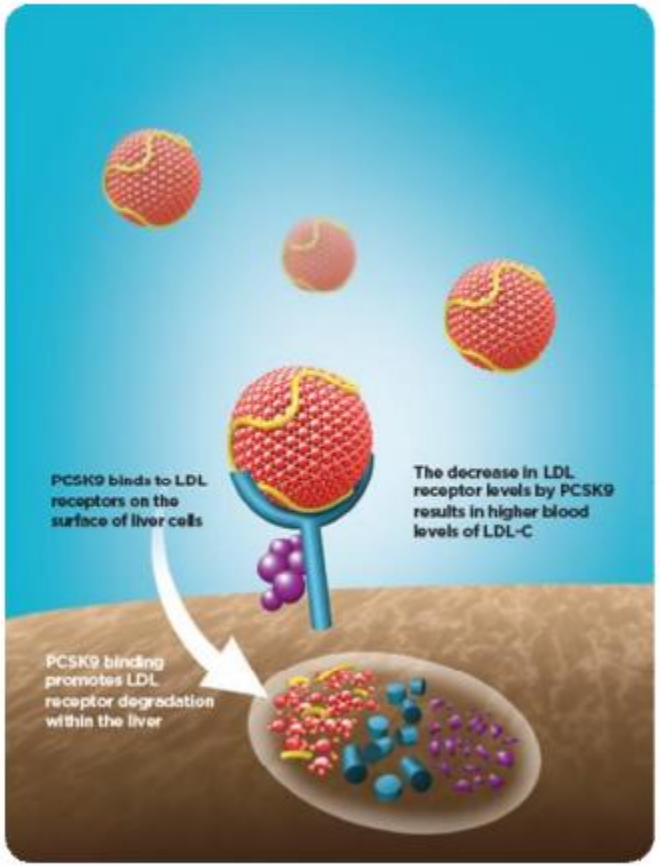
Icosapant Ethyl (Vascepa)

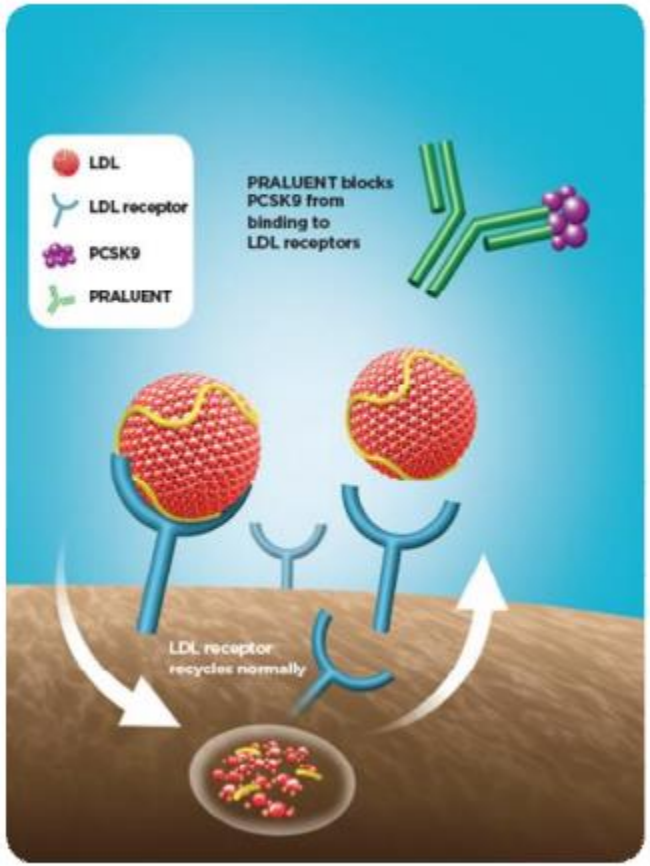


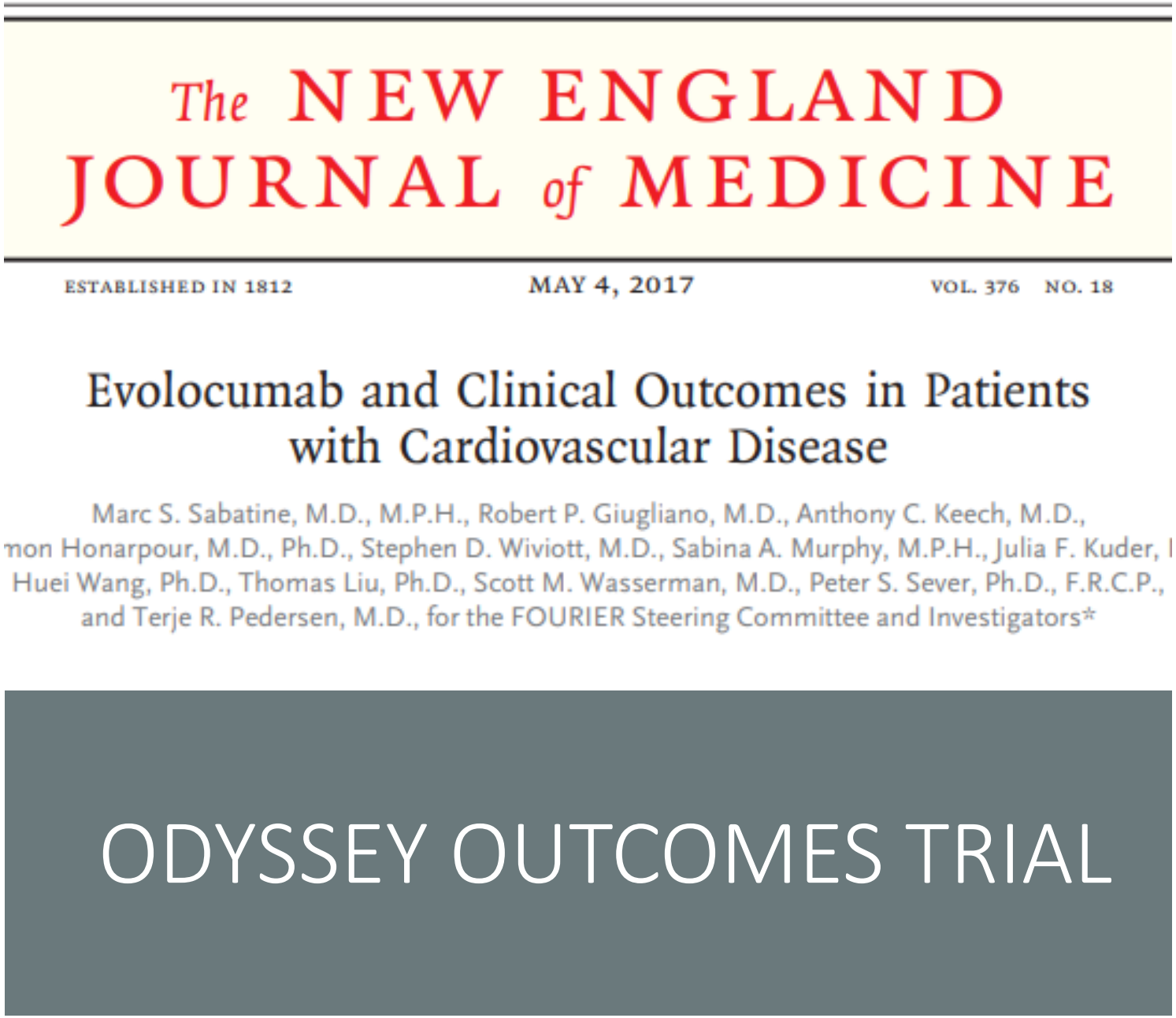
- Highly purified and stable EPA ethyl ester = fish oil
- REDUCE-IT Trial by Bhatt et al. in NEJM. January 2019
- N 8,179 patients with established CVDx or DM + additional RF on pre-existing statin therapy with residual hyperTG (135-499 mg/dL)
- Outcome: Vascepa was associated with an absolute 4.8% reduction in cardiovascular events (cardiovascular death, nonfatal MI, nonfatal stroke, coronary revascularization, or unstable angina), with a 0.9% absolute reduction in cardiovascular death, at 4.9 years.

PCSK9 Inhibitors

- *Proprotein convertase subtilisin/kexin type 9* (PCSK9) inhibition







The NEW ENGLAND JOURNAL of MEDICINE

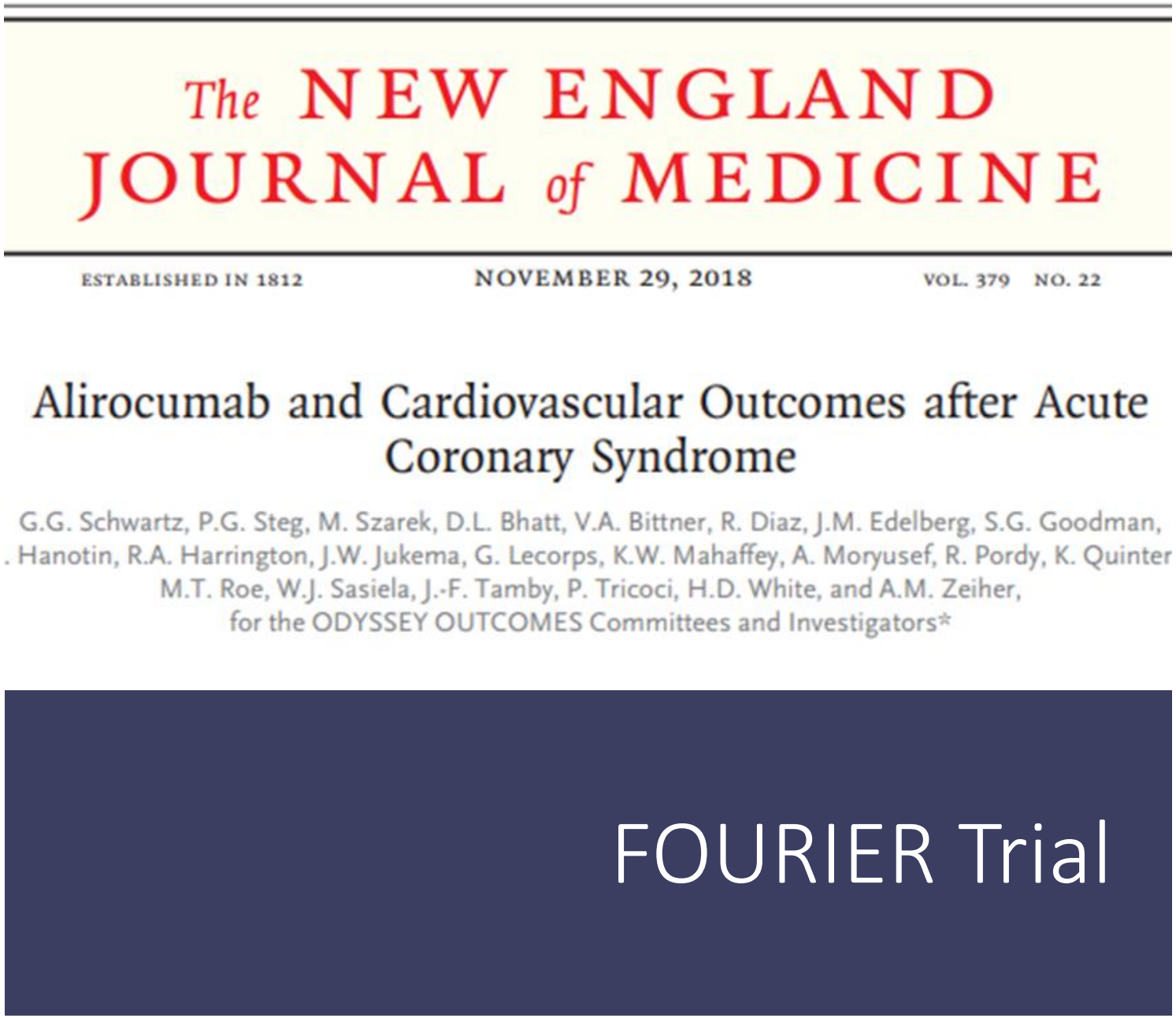
ESTABLISHED IN 1812 MAY 4, 2017 VOL. 376 NO. 18

Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease

Marc S. Sabatine, M.D., M.P.H., Robert P. Giugliano, M.D., Anthony C. Keech, M.D., mon Honarpour, M.D., Ph.D., Stephen D. Wiviott, M.D., Sabina A. Murphy, M.P.H., Julia F. Kuder, Huei Wang, Ph.D., Thomas Liu, Ph.D., Scott M. Wasserman, M.D., Peter S. Sever, Ph.D., F.R.C.P., and Terje R. Pedersen, M.D., for the FOURIER Steering Committee and Investigators*

ODYSSEY OUTCOMES TRIAL

- N 8,924 (DM 29%)
- Inclusion: >40 y/o, ACS within previous 1-12 months, acute MI or unstable angina, on HI statin therapy 90% (or documented intolerance to statins), Inadequate control of lipids (LDL >70, non-HDL >100, or apolipoprotein B >80 mg/dL
- Conclusion: primary outcome, MACE, 9.5% vs 11.1% with HR 0.85 ($p < 0.001$ mainly driven by lower MI, UA, and ischemic CVA ($p= 0.006, 0.02, 0.01$)
- Patients with LDL-C >100 seemed to derive the greatest benefit



The NEW ENGLAND JOURNAL of MEDICINE

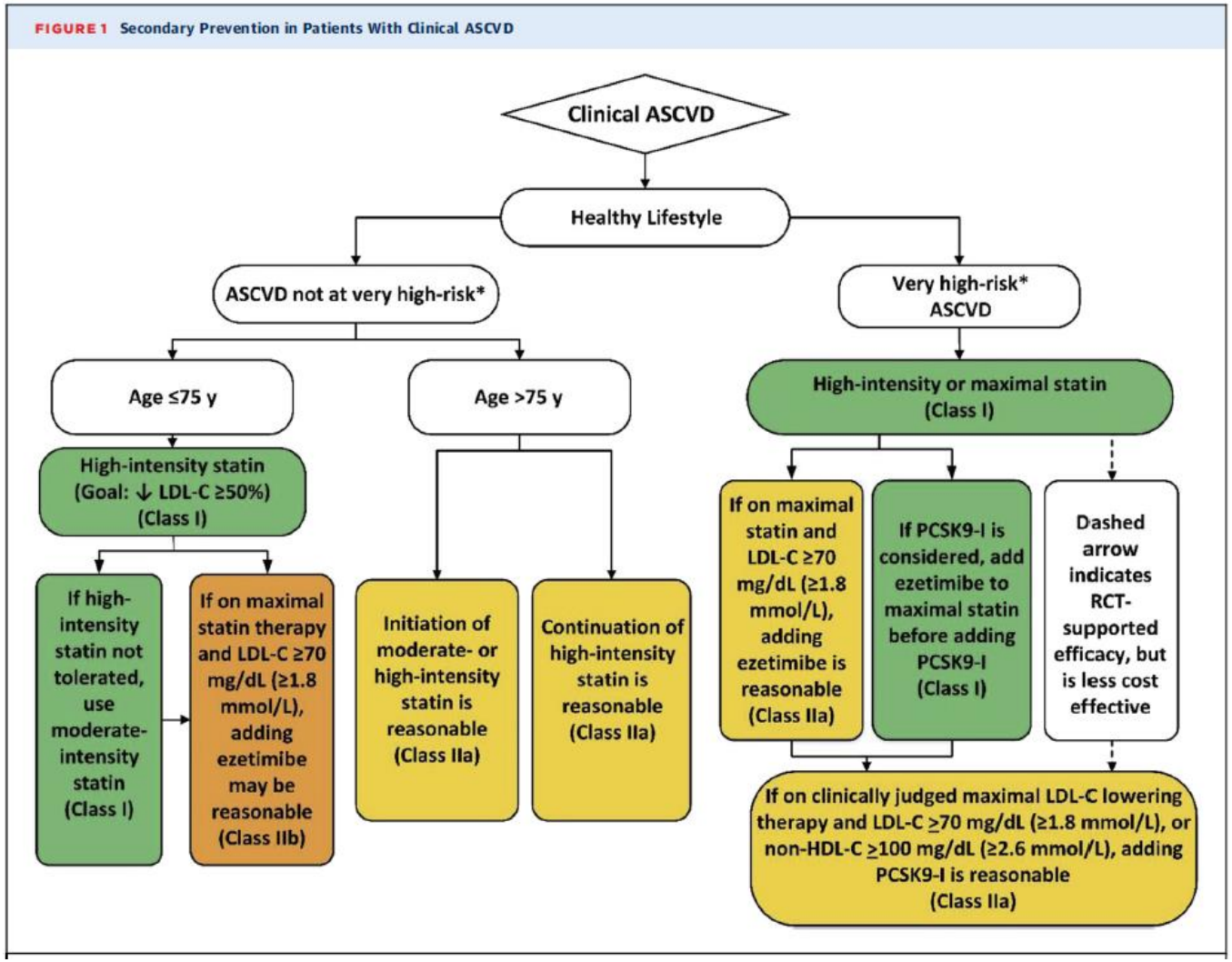
ESTABLISHED IN 1812 NOVEMBER 29, 2018 VOL. 379 NO. 22

Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome

G.G. Schwartz, P.G. Steg, M. Szarek, D.L. Bhatt, V.A. Bittner, R. Diaz, J.M. Edelberg, S.G. Goodman, . Hanotin, R.A. Harrington, J.W. Jukema, G. Lecorps, K.W. Mahaffey, A. Moryusef, R. Pordy, K. Quinter M.T. Roe, W.J. Sasiela, J.-F. Tamby, P. Tricoci, H.D. White, and A.M. Zeiher, for the ODYSSEY OUTCOMES Committees and Investigators*

FOURIER Trial

- N: 27,564 (DM 37%)
- Inclusion: established cardiovascular disease, mean age 63, on statin therapy (69% high intensity, 30% moderate intensity) with LDL >70, median LDL 92
- Findings: primary outcome incidence of CV death, MI, CVA, hospitalization for UA, or coronary revascularization (12.6% vs. 14.6% with p <0.0001) benefit enhanced among higher risk groups (recent MI, multiple prior MI's, residual MV CAD), reduction in total CV events with HR 0.82, p <0.001
- Patients with LDL-C >100 seemed to derive the greatest benefit



Conclusion is that there is no role for PCSK9 inhibitors for primary prevention at this time!!!

Question 5

Which of the following is not considered a very high risk patient per the 2018 high cholesterol guidelines?

A. Recent ACS (within past 12 months)
B. Symptomatic PAD (h/o claudication with ABI <0.85)
C. Diabetes mellitus
D. Heterozygous familial hypercholesterolemia
E. All of the above are very high risk

Very High Risk* of Future ASCVD Events

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 (S4.1-39))
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 m²) (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

Which of the following is not considered a very high risk patient per the 2018 high cholesterol guidelines?

A. Recent ACS (within past 12 months)
B. Symptomatic PAD (h/o claudication with ABI <0.85)
C. Diabetes mellitus
D. Heterozygous familial hypercholesterolemia
E. All of the above are very high risk

Case of Mrs. Jones

My mother is on a statin, do I need to be on one too?

My blood sugar is decently controlled, but I've heard there's new medications on the market…should I be taking one of them?

Should I continue taking a daily Aspirin?

Do I exercise enough?

Keto, Paleo, Atkins, DASH, Mediterranean…which diet is best?

Is a little alcohol cardioprotective? How much is too much?

I've read about coronary Ca2+ scores online, should I have one of these done?

What can I do to minimize my risk of a heart attack?

What's the meaning of life???

EMPA-REG Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Bernard Zinman, M.D., Christoph Wanner, M.D., John M. Lachin, Sc.D., David Fitchett, M.D., Erich Bluhmki, Ph.D., Stefan Hantel, Ph.D., Michaela Mattheus, Dipl. Biomath., Theresa Devins, Dr.P.H., Odd Erik Johansen, M.D., Ph.D., Hans J. Woerle, M.D., Uli C. Broedl, M.D., and Silvio E. Inzucchi, M.D., for the EMPA-REG OUTCOME Investigators

- N: 7,028
- 63 y/o with DM, HbA1c >7 but <10%, >10 yrs (57%), 29% monotherapy with Metformin (36% and insulin 46%), 43% Metformin + sulfonylurea, 45% Metformin + insulin, 77% were on statins
- Primary outcome: CV death, nonfatal MI, CVA occurred in 10.5% vs 12.1% (HR 0.86, P 0.04 superiority, <0.001 for non-inferiority)
- Conclusion: SGLT2 inhibitors were superior to placebo in improving glycemic control and reducing CV events in pts with DM2 and established CVD

CANVAS Trial

The NEW ENGLAND JOURNAL of MEDICINE

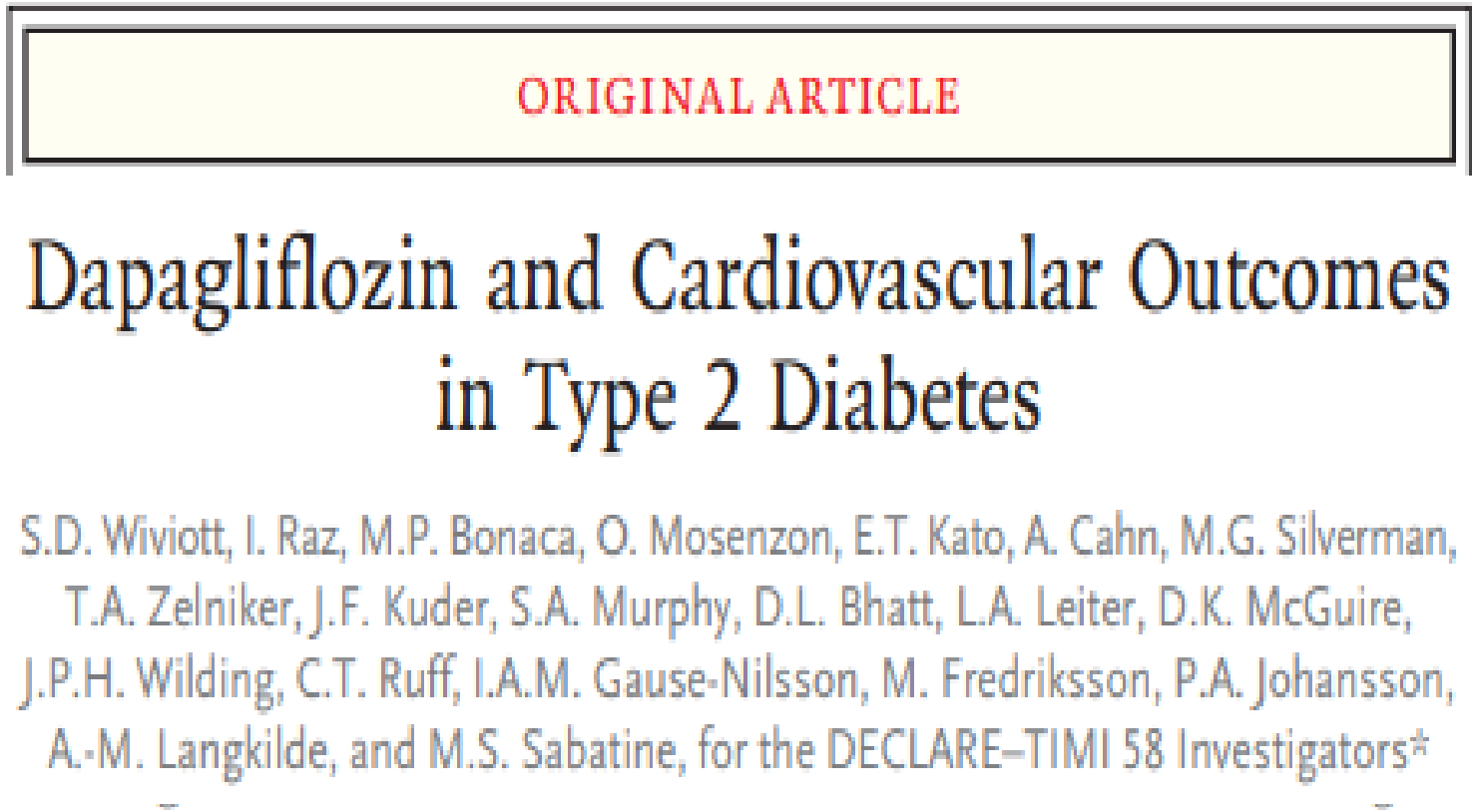
ORIGINAL ARTICLE

Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes

Bruce Neal, M.B., Ch.B., Ph.D., Vlado Perkovic, M.B., B.S., Ph.D., Kenneth W. Mahaffey, M.D., Dick de Zeeuw, M.D., Ph.D., Greg Fulcher, M.D., Ngozi Erondu, M.D., Ph.D., Wayne Shaw, D.S.L., Gordon Law, Ph.D., Mehul Desai, M.D., and David R. Matthews, D.Phil., B.M., B.Ch., for the CANVAS Program Collaborative Group*

- N: 10,142
- 63 y/o with DM ~13 years, 65% had history of CVDx, 34% enrolled for primary prevention (>50 y/o, at lest 2 RF's)
- Primary outcome: incidence of CV death, MI, or CVA occurred in 26.9 per 1000 pt-yrs versus 31.5 per 1000 pt-yrs (p=0.02 for superiority, P <0.001 for non-inferiority)
- Conclusion: among pts with DM2, Canagliflozin was beneficial at reducing primary outcome, including less adverse cardiovascular events; also with greater benefit among HF pts

DECLARE-TIMI 58 Trial



ORIGINAL ARTICLE

Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes

S.D. Wiviott, I. Raz, M.P. Bonaca, O. Mosenzon, E.T. Kato, A. Cahn, M.G. Silverman, T.A. Zelniker, J.F. Kuder, S.A. Murphy, D.L. Bhatt, L.A. Leiter, D.K. McGuire, J.P.H. Wilding, C.T. Ruff, I.A.M. Gause-Nilsson, M. Fredriksson, P.A. Johansson, A.-M. Langkilde, and M.S. Sabatine, for the DECLARE–TIMI 58 Investigators*

- N: 17,160
- 64 y/o with DM, HbA1c >6.5% but <12% (~8.3%), duration of DM 10.5 yrs, 60% without established CVDx, 75% on statins, 41% on insulin, 82% on Metformin, multiple RF's including mean >55 or women >60 with HTN, HLD, or tobacco use
- Primary outcomes: MACE was 8.8% vs 9.4% (HR 0.93, $p<0.001$ for non-inferiority but $p=0.17$ for superiority)
- Conclusions: superior to placebo in improving glycemic control and noninferior but not superior for reducing MACE in pts with DM2 and high CV risk

Question 6

You review Mrs. Jones labs and see that her HbA1c is 7.6%. What would be your next step in management of her diabetes?

A. Start Lantus/Lispro therapy
B. Start Liraglutide 0.6 mg SC daily
C. Increase Metformin to 1000 mg BID
D. Start Empagliflozin 10 mg QAM
E. Start Glipizide 5 mg daily

Question 6

You review Mrs. Jones labs and see that her HbA1c is 7.6%. What would be your next step in management of her diabetes?

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B. Start Liraglutide 0.6 mg SC daily

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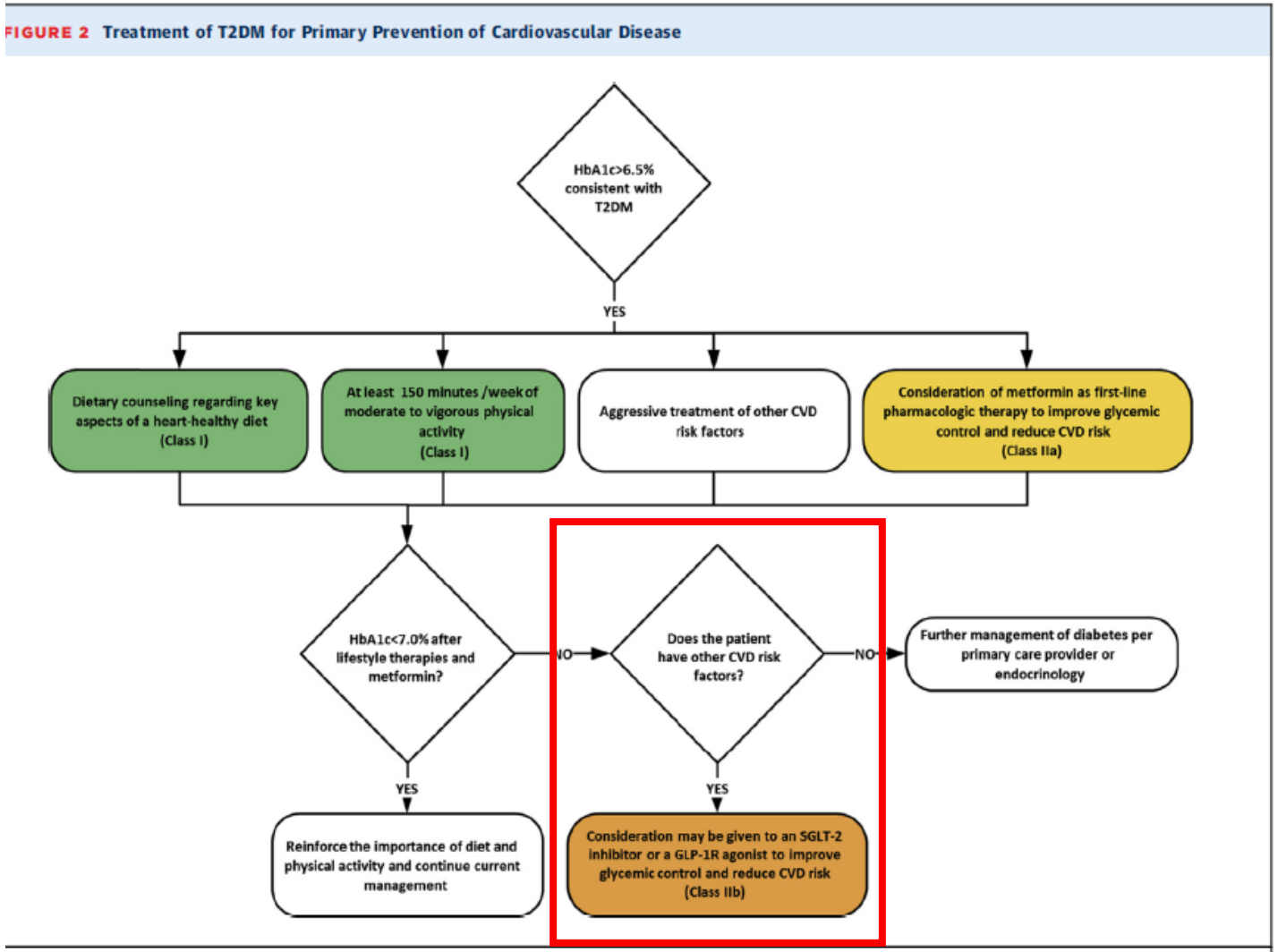


ACC/AHA Guidelines

COR	LOE	RECOMMENDATIONS
I	A	1. For all adults with T2DM, a tailored nutrition plan focusing on a heart-healthy dietary pattern is recommended to improve glycemic control, achieve weight loss if needed, and improve other ASCVD risk factors (S4.2-1, S4.2-2).
I	A	2. Adults with T2DM should perform at least 150 minutes per week of moderate-intensity physical activity or 75 minutes of vigorous-intensity physical activity to improve glycemic control, achieve weight loss if needed, and improve other ASCVD risk factors (S4.2-3, S4.2-4).
IIa	B-R	3. For adults with T2DM, it is reasonable to initiate metformin as first-line therapy along with lifestyle therapies at the time of diagnosis to improve glycemic control and reduce ASCVD risk (S4.2-5–S4.2-8).
IIb	B-R	4. For adults with T2DM and additional ASCVD risk factors who require glucose-lowering therapy despite initial lifestyle modifications and metformin, it may be reasonable to initiate a sodium-glucose cotransporter 2 (SGLT-2) inhibitor or a glucagon-like peptide-1 receptor (GLP-1R) agonist to improve glycemic control and reduce CVD risk (S4.2-9–S4.2-14).

Objectives

- Review the 2019 ACC/AHA Guidelines for Primary Cardiovascular Prevention
- Discuss the appropriate use of statins in primary and secondary cardiovascular prevention
- Recognize when PCSK-9 inhibitors should be offered to our patients
- Identify anti-glycemic agents with cardiovascular benefit including the role of the new SGLT-2 inhibitors

Thank You

Hypertension – won’t have time to cover

COR	LOE	RECOMMENDATIONS
I	A	1. In adults with elevated blood pressure (BP) or hypertension, including those requiring antihypertensive medications nonpharmacological interventions are recommended to reduce BP. These include: ■ weight loss (S4.4-2-S4.4-5); ■ a heart-healthy dietary pattern (S4.4-6-S4.4-8); ■ sodium reduction (S4.4-9-S4.4-13); ■ dietary potassium supplementation (S4.4-14-S4.4-18); ■ increased physical activity with a structured exercise program (S4.4-3, S4.4-5, S4.4-11, S4.4-19-S4.4-23); and ■ limited alcohol (S4.4-24-S4.4-29). Adapted from recommendations in the 2017 Hypertension Clinical Practice Guidelines (S4.4-1).
I	SBP:A DBP: C-EO	2. In adults with an estimated 10-year ASCVD risk* of 10% or higher and an average systolic BP (SBP) of 130 mm Hg or higher or an average diastolic BP (DBP) of 80 mm Hg or higher, use of BP-lowering medications is recommended for primary prevention of CVD (S4.4-30-S4.4-38). Adapted from recommendations in the 2017 Hypertension Clinical Practice Guidelines (S4.4-1).
I	SBP: B-R[SR] DBP: C-EO	3. In adults with confirmed hypertension and a 10-year ASCVD event risk of 10% or higher, a BP target of less than 130/80 mm Hg is recommended (S4.4-33, S4.4-39-S4.4-42). Adapted from recommendations in the 2017 Hypertension Clinical Practice Guidelines (S4.4-1).
I	SBP: B-R[SR] DBP: C-EO	4. In adults with hypertension and chronic kidney disease, treatment to a BP goal of less than 130/80 mm Hg is recommended (S4.4-43-S4.4-48). Adapted from recommendations in the 2017 Hypertension Clinical Practice Guidelines (S4.4-1).
I	SBP: B-R[SR] DBP: C-EO	5. In adults with T2DM and hypertension, antihypertensive drug treatment should be initiated at a BP of 130/80 mm Hg or higher, with a treatment goal of less than 130/80 mm Hg (S4.4-33, S4.4-47, S4.4-49-S4.4-54). Adapted from recommendations in the 2017 Hypertension Clinical Practice Guidelines (S4.4-1).
I	C-LD	6. In adults with an estimated 10-year ASCVD risk <10% and an SBP of 140 mm Hg or higher or a DBP of 90 mm Hg or higher, initiation and use of BP-lowering medication are recommended (S4.4-36, S4.4-55-S4.4-58). Adapted from recommendations in the 2017 Hypertension Clinical Practice Guidelines (S4.4-1).
IIb	SBP: B-NR DBP: C-EO	7. In adults with confirmed hypertension without additional markers of increased ASCVD risk, a BP target of less than 130/80 mm Hg may be reasonable (S4.4-59-S4.4-62). Adapted from recommendations in the 2017 Hypertension Clinical Practice Guidelines (S4.4-1).

FIGURE 4 BP Thresholds and Recommendations for Treatment

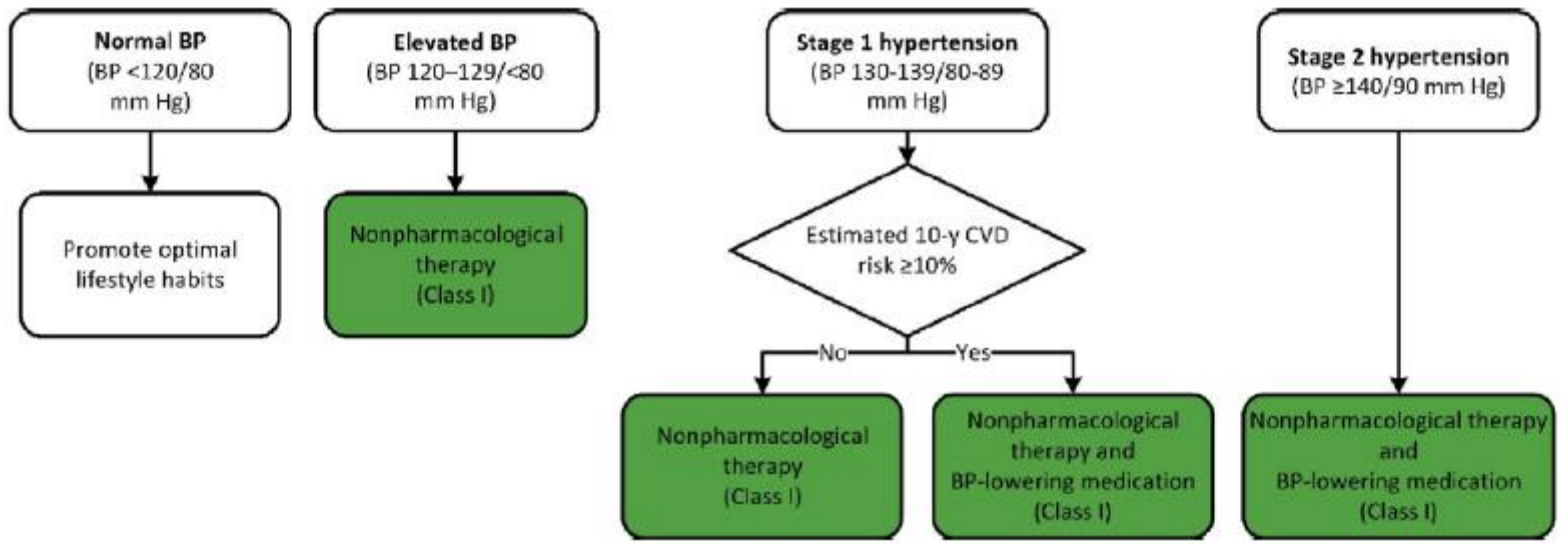


TABLE 6 Selected Examples of Candidates for Coronary Artery Calcium Measurement Who Might Benefit From Knowing Their Coronary Artery Calcium Score Is Zero

Coronary Artery Calcium Measurement Candidates Who Might Benefit from Knowing Their Coronary Artery Calcium Score Is Zero
■ Patients reluctant to initiate statin who wish to understand their risk and potential for benefit more precisely
■ Patients concerned about need to reinstitute statin therapy after discontinuation for statin-associated symptoms
■ Older patients (men 55–80 y of age; women 60–80 y of age) with low burden of risk factors (S4.3-53) who question whether they would benefit from statin therapy
■ Middle-aged adults (40–55 y of age) with PCE-calculated 10-year risk of ASCVD 5% to <7.5% with factors that increase their ASCVD risk, although they are in a borderline risk group.

Caveats: If patient is at intermediate risk and if a risk decision is uncertain and a coronary artery calcium score is obtained, it is reasonable to withhold statin therapy unless higher-risk conditions, such as cigarette smoking, family history of premature ASCVD, or diabetes mellitus, are present and to reassess coronary artery calcium score in 5 to 10 years. Moreover, if coronary artery calcium scoring is recommended, it should be performed in facilities that have current technology and expertise to deliver the lowest radiation possible.

ASCVD indicates atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; and PCE, pooled cohort equations.

TABLE 7 Best Proven Nonpharmacological Interventions for Prevention and Treatment of Hypertension*

	Nonpharmacological Intervention	Goal	Approximate Impact on SBP		
			Hypertension	Normotension	Reference
Weight loss	Weight/body fat	Best goal is ideal body weight, but aim for at least a 1-kg reduction in body weight for most adults who are overweight. Expect about 1 mm Hg for every 1-kg reduction in body weight.	-5 mm Hg	-2/3 mm Hg	(S4.4-2)
Healthy diet	DASH dietary pattern†	Consume a diet rich in fruits, vegetables, whole grains, and low-fat dairy products, with reduced content of saturated and total fat.	-11 mm Hg	-3 mm Hg	(S4.4-7, S4.4-8)
Reduced intake of dietary sodium	Dietary sodium	Optimal goal is <1500 mg/d, but aim for at least a 1000-mg/d reduction in most adults.	-5/6 mm Hg	-2/3 mm Hg	(S4.4-10, S4.4-12)
Enhanced intake of dietary potassium	Dietary potassium	Aim for 3500–5000 mg/d, preferably by consumption of a diet rich in potassium.	-4/5 mm Hg	-2 mm Hg	(S4.4-14)
Physical activity	Aerobic	■ 90–150 min/wk ■ 65%–75% heart rate reserve	-5/8 mm Hg	-2/4 mm Hg	(S4.4-19, S4.4-20)
	Dynamic resistance	■ 90–150 min/wk ■ 50%–80% 1 rep maximum ■ 6 exercises, 3 sets/exercise, 10 repetitions/set	-4 mm Hg	-2 mm Hg	(S4.4-19)
	Isometric resistance	■ 4 × 2 min (hand grip), 1 min rest between exercises, 30%–40% maximum voluntary contraction, 3 sessions/wk ■ 8–10 wk	-5 mm Hg	-4 mm Hg	(S4.4-21, S4.4-78)
Moderation in alcohol intake	Alcohol consumption	In individuals who drink alcohol, reduce alcohol‡ to: ■ Men: ≤2 drinks daily ■ Women: ≤1 drink daily	-4 mm Hg	-3 mm Hg	(S4.4-20, S4.4-24, S4.4-25)

COR	LOE	RECOMMENDATIONS
I	A	1. All adults should be assessed at every healthcare visit for tobacco use and their tobacco use status recorded as a vital sign to facilitate tobacco cessation (S4.5-1).
I	A	2. To achieve tobacco abstinence, all adults who use tobacco should be firmly advised to quit (S4.5-2).
I	A	3. In adults who use tobacco, a combination of behavioral interventions plus pharmacotherapy is recommended to maximize quit rates (S4.5-2, S4.5-3).
I	B-NR	4. In adults who use tobacco, tobacco abstinence is recommended to reduce ASCVD risk (S4.5-4, S4.5-5).
IIa	B-R	5. To facilitate tobacco cessation, it is reasonable to dedicate trained staff to tobacco treatment in every healthcare system (S4.5-1).
III: Harm	B-NR	6. All adults and adolescents should avoid secondhand smoke exposure to reduce ASCVD risk (S4.5-6).

COR	LOE	RECOMMENDATIONS
IIb	A	1. Low-dose aspirin (75-100 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk (S4.6-1-S4.6-8).
III: Harm	B-R	2. Low-dose aspirin (75-100 mg orally daily) should not be administered on a routine basis for the primary prevention of ASCVD among adults >70 years of age (S4.6-9).
III: Harm	C-LD	3. Low-dose aspirin (75-100 mg orally daily) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding (S4.6-10).

- 1. The most important way to prevent atherosclerotic vascular disease, heart failure, and atrial fibrillation is to promote a healthy lifestyle throughout life.
- 2. A team-based care approach is an effective strategy for the prevention of cardiovascular disease. Clinicians should evaluate the social determinants of health that affect individuals to inform treatment decisions.
- 3. Adults who are 40 to 75 years of age and are being evaluated for cardiovascular disease prevention should undergo 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimation and have a clinician–patient risk discussion before starting on pharmacological therapy, such as antihypertensive therapy, a statin, or aspirin. In addition, assessing for other risk-enhancing factors can help guide decisions about preventive interventions in select individuals, as can coronary artery calcium scanning.
- 4. All adults should consume a healthy diet that emphasizes the intake of vegetables, fruits, nuts, whole grains, lean vegetable or animal protein, and fish and minimizes the intake of *trans* fats, red meat and processed red meats, refined carbohydrates, and sweetened beverages. For adults with overweight and obesity, counseling and caloric restriction are recommended for achieving and maintaining weight loss.
- 5. Adults should engage in at least 150 minutes per week of accumulated moderate-intensity physical activity or 75 minutes per week of vigorous-intensity physical activity.
- 6. For adults with type 2 diabetes mellitus, lifestyle changes, such as improving dietary habits and achieving exercise recommendations, are crucial. If medication is indicated, metformin is first-line therapy, followed by consideration of a sodium-glucose cotransporter 2 inhibitor or a glucagon-like peptide-1 receptor agonist.
- 7. All adults should be assessed at every healthcare visit for tobacco use, and those who use tobacco should be assisted and strongly advised to quit.
- 8. Aspirin should be used infrequently in the routine primary prevention of ASCVD because of lack of net benefit.
- 9. Statin therapy is first-line treatment for primary prevention of ASCVD in patients with elevated low-density lipoprotein cholesterol levels (≥190 mg/dL), those with diabetes mellitus, who are 40 to 75 years of age, and those determined to be at sufficient ASCVD risk after a clinician–patient risk discussion.
- 10. Nonpharmacological interventions are recommended for all adults with elevated blood pressure or hypertension. For those requiring pharmacological therapy, the target blood pressure should generally be <130/80 mm Hg.

COR	LOE	RECOMMENDATIONS
I	B-NR	1. For adults 40 to 75 years of age, clinicians should routinely assess traditional cardiovascular risk factors and calculate 10-year risk of ASCVD by using the pooled cohort equations (PCE) (S2.2-1, S2.2-2).
IIa	B-NR	2. For adults 20 to 39 years of age, it is reasonable to assess traditional ASCVD risk factors at least every 4 to 6 years (S2.2-1–S2.2-3).
IIa	B-NR	3. In adults at borderline risk (5% to <7.5% 10-year ASCVD risk) or intermediate risk (≥7.5% to <20% 10-year ASCVD risk), it is reasonable to use additional risk-enhancing factors to guide decisions about preventive interventions (e.g., statin therapy) (S2.2-4–S2.2-14).
IIa	B-NR	4. In adults at intermediate risk (≥7.5% to <20% 10-year ASCVD risk) or selected adults at borderline risk (5% to <7.5% 10-year ASCVD risk), if risk-based decisions for preventive interventions (e.g., statin therapy) remain uncertain, it is reasonable to measure a coronary artery calcium score to guide clinician–patient risk discussion (S2.2-15–S2.2-31).
IIb	B-NR	5. For adults 20 to 39 years of age and for those 40 to 59 years of age who have <7.5% 10-year ASCVD risk, estimating lifetime or 30-year ASCVD risk may be considered (S2.2-1, S2.2-2, S2.2-32–S2.2-35).

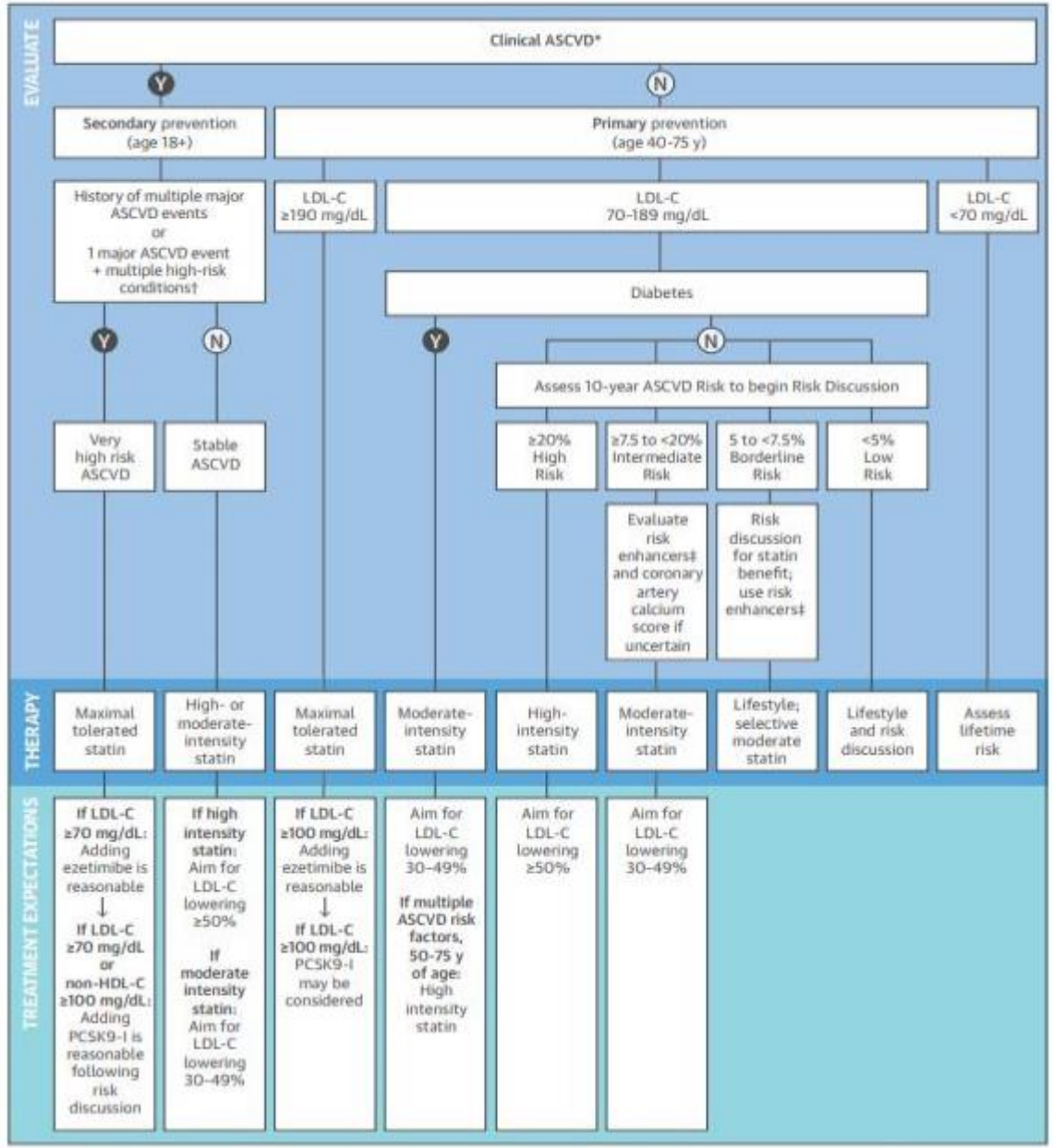
COR	LOE	RECOMMENDATIONS
I	B-R	1. A diet emphasizing intake of vegetables, fruits, legumes, nuts, whole grains, and fish is recommended to decrease ASCVD risk factors (S3.1-1–S3.1-11).
IIa	B-NR	2. Replacement of saturated fat with dietary monounsaturated and polyunsaturated fats can be beneficial to reduce ASCVD risk (S3.1-12, S3.1-13).
IIa	B-NR	3. A diet containing reduced amounts of cholesterol and sodium can be beneficial to decrease ASCVD risk (S3.1-9, S3.1-14–S3.1-16).
IIa	B-NR	4. As a part of a healthy diet, it is reasonable to minimize the intake of processed meats, refined carbohydrates, and sweetened beverages to reduce ASCVD risk (S3.1-17–S3.1-24).
III: Harm	B-NR	5. As a part of a healthy diet, the intake of *trans* fats should be avoided to reduce ASCVD risk (S3.1-12, S3.1-17, S3.1-25–S3.1-27).

COR	LOE	RECOMMENDATIONS
I	B-R	1. Adults should be routinely counseled in healthcare visits to optimize a physically active lifestyle (S3.2-1, S3.2-2).
I	B-NR	2. Adults should engage in at least 150 minutes per week of accumulated moderate-intensity or 75 minutes per week of vigorous-intensity aerobic physical activity (or an equivalent combination of moderate and vigorous activity) to reduce ASCVD risk (S3.2-3–S3.2-8).
IIa	B-NR	3. For adults unable to meet the minimum physical activity recommendations (at least 150 minutes per week of accumulated moderate-intensity or 75 minutes per week of vigorous-intensity aerobic physical activity), engaging in some moderate- or vigorous-intensity physical activity, even if less than this recommended amount, can be beneficial to reduce ASCVD risk (S3.2-5, S3.2-6).
IIb	C-LD	4. Decreasing sedentary behavior in adults may be reasonable to reduce ASCVD risk (S3.2-3, S3.2-9–S3.2-11).

COR	LOE	RECOMMENDATIONS
I	B-R	1. In individuals with overweight and obesity, weight loss is recommended to improve the ASCVD risk factor profile (S4.1-1).
I	B-R	2. Counseling and comprehensive lifestyle interventions, including calorie restriction, are recommended for achieving and maintaining weight loss in adults with overweight and obesity (S4.1-1, S4.1-2).
I	C-EO	3. Calculating body mass index (BMI) is recommended annually or more frequently to identify adults with overweight and obesity for weight loss considerations.
IIa	B-NR	4. It is reasonable to measure waist circumference to identify those at higher cardiometabolic risk (S4.1-3–S4.1-6).

Overview of Primary and Secondary ASCVD Prevention

This tool provides a broad overview of the 2018 Cholesterol Guideline.
Please refer to the full guideline document for specific recommendations.



IIa	B-R	5. 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 (S4.3-2, S4.3-7). Included from recommendations in the 2018 Cholesterol Clinical Practice Guidelines (S4.3-1).
IIa	B-R	6. In intermediate-risk (≥7.5% to <20% 10-year ASCVD risk) adults, risk-enhancing factors favor initiation or intensification of statin therapy (S4.3-7, S4.3-26–S4.3-33). Adapted from recommendations in the 2018 Cholesterol Clinical Practice Guidelines (S4.3-1).
IIa	B-NR	7. In intermediate-risk (≥7.5% to <20% 10-year ASCVD risk) adults or selected borderline-risk (5% to <7.5% 10-year ASCVD risk) adults in whom a coronary artery calcium score is measured for the purpose of making a treatment decision, AND ▪ If the coronary artery 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 (e.g., diabetes, family history of premature CHD, cigarette smoking); ▪ If coronary artery calcium score is 1 to 99, it is reasonable to initiate statin therapy for patients ≥55 years of age; ▪ If coronary artery calcium score is 100 or higher or in the 75th percentile or higher, it is reasonable to initiate statin therapy (S4.3-28, S4.3-34). Adapted from recommendations in the 2018 Cholesterol Clinical Practice Guidelines (S4.3-1).
IIb	B-R	8. In patients at borderline risk (5% to <7.5% 10-year ASCVD risk), in risk discussion, the presence of risk-enhancing factors may justify initiation of moderate-intensity statin therapy (S4.3-28, S4.3-35). Adapted from recommendations in the 2018 Cholesterol Clinical Practice Guidelines (S4.3-1).

Safety

Recommendations	NHLBI Grade	NHLBI Evidence Statements	ACC/AHA COR	ACC/AHA LOE
1. To maximize the safety of statins, selection of the appropriate statin and dose in men and nonpregnant/nonnursing women should be based on patient characteristics, level of ASCVD* risk, and potential for adverse effects. Moderate-intensity statin therapy should be used in individuals in whom high-intensity statin therapy would otherwise be recommended when characteristics predisposing them to statin-associated adverse effects are present. Characteristics predisposing individuals to statin adverse effects include but are not limited to: • Multiple or serious comorbidities, including impaired renal or hepatic function. • History of previous statin intolerance or muscle disorders. • Unexplained ALT elevations ≥3 times ULN. • Patient characteristics or concomitant use of drugs affecting statin metabolism. • Age >75 years. Additional characteristics that could modify the decision to use higher statin intensities might include but are not limited to: • History of hemorrhagic stroke. • Asian ancestry.	A (Strong)	46–55	I	B
2a. CK should not be routinely measured in individuals receiving statin therapy.	A (Strong)	45,49–51,54,55	III: No Benefit	A
2b. Baseline measurement of CK is reasonable for individuals believed to be at increased risk for adverse muscle events because of a personal or family history of statin intolerance or muscle disease, clinical presentation, or concomitant drug therapy that might increase the risk of myopathy.	E (Expert Opinion)	—	IIa	C[88]
2c. During statin therapy, it is reasonable to measure CK in individuals with muscle symptoms, including pain, tenderness, stiffness, cramping, weakness, or generalized fatigue.	E (Expert Opinion)	—	IIa	C[88]
3a. Baseline measurement of hepatic transaminase levels (ALT) should be performed before initiation of statin therapy.	B (Moderate)	46,52,53	I†	B
3b. During statin therapy, it is reasonable to measure hepatic function if symptoms suggesting hepatotoxicity arise (eg, unusual fatigue or weakness, loss of appetite, abdominal pain, dark-colored urine, or yellowing of the skin or sclera).	E (Expert Opinion)	—	IIa	C[89]
4. Decreasing the statin dose may be considered when 2 consecutive values of LDL-C levels are <40 mg/dL.	C (Weak)	45	IIb	C
5. It may be harmful to initiate simvastatin at 80 mg daily or increase the dose of simvastatin to 80 mg daily.	B (Moderate)	6,54	III: Harm	A[87,90]
6. Individuals receiving statin therapy should be evaluated for new-onset diabetes according to the current diabetes screening guidelines.[91] Those who develop diabetes during statin therapy should be encouraged to adhere to a heart-healthy dietary pattern, engage in physical activity, achieve and maintain a healthy body weight, cease tobacco use, and continue statin therapy to reduce their risk of ASCVD events.	B (Moderate)	44	I‡	B
7. For individuals taking any dose of statins, it is reasonable to use caution in individuals >75 years of age, as well as in individuals who are taking concomitant medications that alter drug metabolism, taking multiple drugs, or taking drugs for conditions that require complex medication regimens (eg, those who have undergone solid organ transplantation or are receiving treatment for HIV). A review of the manufacturer's prescribing information may be useful before initiation of any cholesterol-lowering drug.	E (Expert Opinion)	—	IIa	C[16,64–70,89,92–94]

(Continued)

Table 8. Continued

Recommendations	NHLBI Grade	NHLBI Evidence Statements	ACC/AHA COR	ACC/AHA LOE
8. It is reasonable to evaluate and treat muscle symptoms, including pain, tenderness, stiffness, cramping, weakness, or fatigue, in statin-treated patients according to the following management algorithm: • To avoid unnecessary discontinuation of statins, obtain a history of prior or current muscle symptoms to establish a baseline before initiation of statin therapy. • If unexplained *severe* muscle symptoms or fatigue develop during statin therapy, promptly discontinue the statin and address the possibility of rhabdomyolysis by evaluating CK and creatinine and performing urinalysis for myoglobinuria. • If *mild to moderate* muscle symptoms develop during statin therapy: – Discontinue the statin until the symptoms can be evaluated. – Evaluate the patient for other conditions that might increase the risk for muscle symptoms (eg, hypothyroidism, reduced renal or hepatic function, rheumatologic disorders such as polymyalgia rheumatica, steroid myopathy, vitamin D deficiency, or primary muscle diseases). – If muscle symptoms resolve, and if no contraindication exists, give the patient the original or a lower dose of the same statin to establish a causal relationship between the muscle symptoms and statin therapy. – If a causal relationship exists, discontinue the original statin. Once muscle symptoms resolve, use a low dose of a different statin. – Once a low dose of a statin is tolerated, gradually increase the dose as tolerated. – If, after 2 months without statin treatment, muscle symptoms or elevated CK levels do not resolve completely, consider other causes of muscle symptoms listed above. – If persistent muscle symptoms are determined to arise from a condition unrelated to statin therapy, or if the predisposing condition has been treated, resume statin therapy at the original dose.	E (Expert Opinion)	—	IIa	B[15,88,96–98]
9. For individuals presenting with a confusional state or memory impairment while on statin therapy, it may be reasonable to evaluate the patient for nonstatin causes, such as exposure to other drugs, as well as for systemic and neuropsychiatric causes, in addition to the possibility of adverse effects associated with statin drug therapy.	E (Expert Opinion)	—	IIb	C[38,89,99,100]
C. Regularly monitor adherence to lifestyle and drug therapy with lipid and safety assessments				
1. Assess adherence, response to therapy, and adverse effects within 4–12 wk following statin initiation or change in therapy			I	
a. Measure a fasting lipid panel			I	
b. Do not routinely monitor ALT or CK unless symptomatic			IIa	
c. Screen and treat type 2 diabetes according to current practice guidelines. Heart-healthy lifestyle habits should be encouraged to prevent progression to diabetes			I	
d. Anticipated therapeutic response: approximately ≥50% reduction in LDL-C from baseline for high-intensity statin and 30% to <50% for moderate-intensity statin			IIa	
i. Insufficient evidence for LDL-C or non–HDL-C treatment targets from RCTs				
ii. For those with unknown baseline LDL-C, an LDL-C <100 mg/dL was observed in RCTs of high-intensity statin therapy				
e. Less than anticipated therapeutic response:				
i. Reinforce improved adherence to lifestyle and drug therapy			I	
ii. Evaluate for secondary causes of hyperlipidemia if indicated (Table 6)			I	
iii. Increase statin intensity, or if on maximally-tolerated statin intensity, consider addition of nonstatin therapy in selected high-risk individuals§			IIb	
f. Regularly monitor adherence to lifestyle and drug therapy every 3–12 mo once adherence has been established. Continue assessment of adherence for optimal ASCVD risk reduction and safety			I	

Statin Associated Side Effects (SASE)

Table 11 *(1 of 2)*

Statin Associated Side Effects	Frequency	Predisposing Factors	Quality of Evidence
Statin Associated Muscle Symptoms (SAMS) • Myalgias (CK normal)	Infrequent (1%–5%) in RCTs/frequent (5%–10%) in observational studies and clinical setting	Age, female, low BMI, high- risk medications (CYP3A4 inhibitors, OATP1B1 inhibitors), comorbidities (HIV, renal, liver, thyroid, pre-existing myopathy), Asian descent, excess alcohol, high levels of physical activity and trauma.	RCTs cohorts/observational
• Myositis/Myopathy (CK >ULN) with concerning symptoms/objective weakness	Rare		RCTs cohorts/observational
• Rhabdomyolysis (CK >10xULN + renal injury)	Rare		RCTs Cohorts/observational
• Statin-associated autoimmune myopathy (SAAM) (HMGCR Ab's, incomplete resolution)	Rare		Case reports
New onset Diabetes Mellitus	Depends on population; more frequent if diabetes mellitus risk factors such as BMI ≥30, fasting blood sugar ≥100 mg/dL; metabolic syndrome or A1c ≥6% are present	Diabetes risk factors/ metabolic syndrome High-intensity statin therapy	RCTs/Meta-analyses

Table 11 *is continued in the next page. For references please see page 18.*

Statin Associated Side Effects (SASE)
(2 of 2)

Table 11 *(continued from previous page)*

Statin Associated Side Effects	Frequency	Predisposing Factors	Quality of Evidence
Liver • Transaminase elevation 3xULN	Infrequent		RCTs/cohorts/observational Case reports
• Hepatic Failure	Rare		
CNS • Memory/Cognition	Rare/Unclear		Case reports; no increase in memory/cognition problems in three large scale RCTs
Cancer	No definite association		RCTs/meta-analyses
Other • Renal Function • Cataracts • Tendon Rupture • Hemorrhagic Stroke • Interstitial Lung Disease • Low Testosterone	 Unclear/unfounded Unclear Unclear/unfounded Unclear Unclear/unfounded Unclear/unfounded		