


A Practical Approach to Integrating the New Dyslipidemia Guidelines for People with Diabetes

AADE American Association of Diabetes Educators

AADE19



1



John Bucheit
PharmD, CDE, BCACP
Ambulatory Care Pharmacist

Assistant Professor
VCU School of Pharmacy
Richmond VA

#AADE19

2



Michael S. Kelly
PharmD, CDE, CLS
Assistant Professor

Chapman University School of Pharmacy
Irvine, CA

#AADE19

3

Disclosure to Participants

- Notice of Requirements For Successful Completion
 - Please refer to learning goals and objectives
 - Learners must attend the full activity and complete the evaluation in order to claim continuing education credit/hours
- Conflict of Interest (COI) and Financial Relationship Disclosures:
 - Presenter: Michael Kelly, PharmD, CDE, CLS – Consulting: Medisure Inc.
- Non-Endorsement of Products:
 - Accredited status does not imply endorsement by AADE, ANCC, ACPE or CDR of any commercial products displayed in conjunction with this educational activity
- Off-Label Use:
 - Participants will be notified by speakers to any product used for a purpose other than for which it was approved by the Food and Drug Administration.

#AADE19

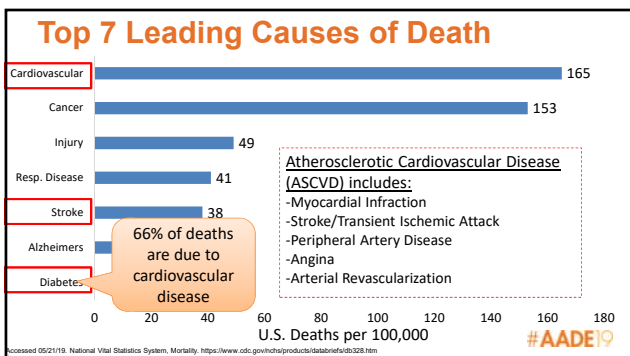
4

Objectives

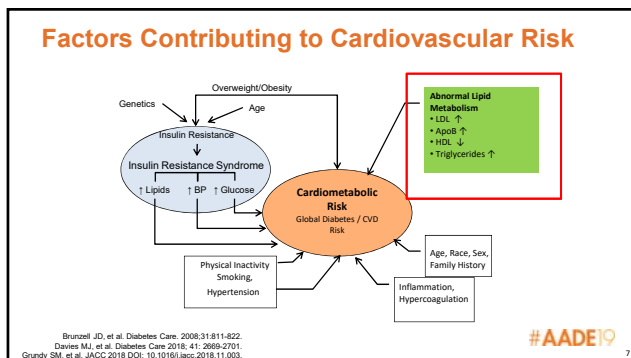
1. Compare current dyslipidemia guideline recommendations as they apply to people with diabetes
2. Develop a risk assessment approach to determine management strategies for dyslipidemia
3. Apply the 2018 ACC/AHA treatment recommendations to participant case examples

#AADE19

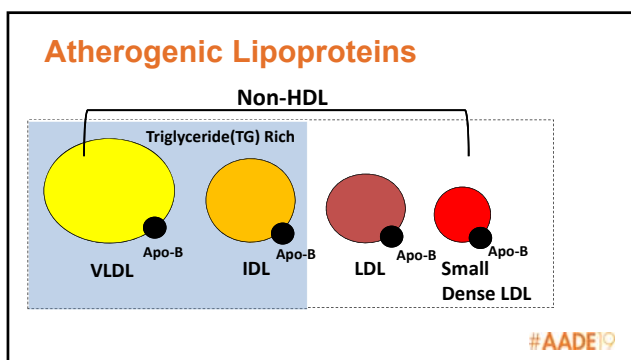
5



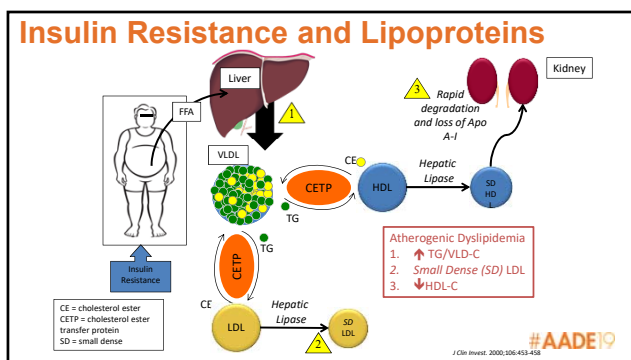
6



7



8



9

Friedewald Equation for LDL-C

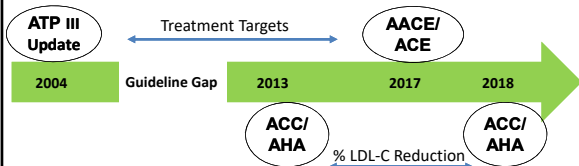
- Calculated LDL-C** = Total Cholesterol – TG/5-HDL-C
- Elevated Triglycerides (TGs) falsely lowers LDL-C
 - Ignore low calculated LDL-C in the presence of high TGs
 - Inaccurate calculation starting at TGs \geq 200 mg/dL
 - Invalid calculation once TGs reach 400 mg/dL
 - Persistently elevated TGs is a **risk enhancing feature** commonly founds in people with diabetes (PWD)
 - Consider using Non-HDL-C for risk assessment
 - Non-HDL-C= total cholesterol – HDL-C

#AADE19

10

Cholesterol Treatment Guidelines

Goals: Treatment Targets or Percent LDL-C Reduction?



ATP III= Adult Treatment Panel III update
ACC/AHA= American College of Cardiology/American Heart Association
AACE/ACE= American Association of Clinical Endocrinologists/American College of Endocrinology

#AADE19

11

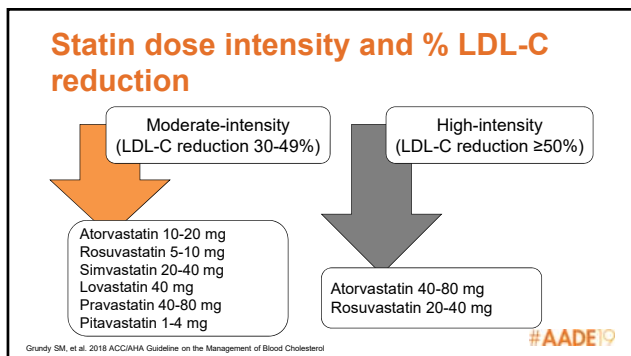
2013 ACC/AHA "Statin Guidelines"

- Clinical ASCVD**
 - Moderate-intensity statin (Age >75)
 - High-intensity statin (Age \leq 75)
- LDL-C \geq 190 mg/dL**
 - High-intensity statin
- Diabetes (Age 40-75) (LDL-C 70-189mg/dL)**
 - Moderate-intensity statin
 - High-intensity statin if 10-y risk \geq 7.5%
- 10-y risk \geq 7.5% (Age 40-75) (LDL-C 70-189mg/dL)**
 - Moderate-to-high intensity statin

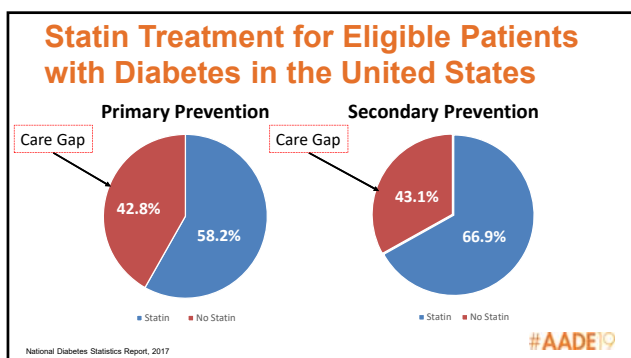
Stone NJ, et al. 2013 ACC/AHA Blood Cholesterol Guideline

#AADE19

12



13



14

AAACE/ACE 2017 ASCVD Risk Factors

Risk Assessment includes:

- 10-year Risk Calculation and Assessment of Risk Factors

Major risk factors	Additional risk factors	Nontraditional risk factors
Advancing age	Obesity, abdominal obesity	↑ Lipoprotein (a)
↑ Total serum cholesterol level	Family history of hyperlipidemia	↑ Clotting factors
↑ Non-HDL-C	↑ Small, dense LDL-C	↑ Inflammation markers
↑ LDL-C	↑ Apo B	(hsCRP, Lp-PLA ₂)
Low HDL-C	↑ LDL particle concentration	↑ Homocysteine levels
Diabetes mellitus	Fasting/postprandial hypertriglyceridemia	Apo E4 isoform
Hypertension	PCOS	↑ Uric acid
Stage 3 or 4 chronic kidney disease	Dyslipidemic triad (High TGs + Low HDL + small dense LDL)	↑ TG-rich remnants
Cigarette smoking		
Family history of ASCVD		

Abbreviations: apo, apolipoprotein; ASCVD, atherosclerotic cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; hsCRP, highly sensitive C-reactive protein; LDL, low-density lipoprotein; LDL-C, low-density lipoprotein cholesterol; Lp-PLA₂, lipoprotein-associated phospholipase; PCOS, polycystic ovary syndrome. #AADE19

15

AAACE/ACE 2017 "Lower is Better"

Risk category	Risk factors/10-year risk	Treatment goal		
		LDL-C (mg/dL)	Non-HDL-C (mg/dL)	Apo B (mg/dL)
Extreme risk	- Progressive ASCVD including unstable angina in individuals after achieving an LDL-C <70 mg/dL - Established clinical cardiovascular disease in individuals with DM, stage 3 or 4 CKD, or HeFH - History of premature ASCVD (<55 male, <65 female)	<55	<80	<70
Very high risk	- Established or recent hospitalization for ACS, coronary, carotid or peripheral vascular disease, 10-year risk >20% - DM or stage 3 or 4 CKD with 1 or more risk factor(s) - Heterozygous Familial Hypercholesterolemia	<70	<100	<80
High risk	- ≥2 risk factors and 10-year risk 10%-20% - DM or stage 3 or 4 CKD with no other risk factors	<100	<130	<90
Moderate risk	≤2 risk factors and 10-year risk <10%	<100	<130	<90
Low risk	0 risk factors	<130	<160	NR

Endocr Practice. 2017;23(4):479-497. #AADE19

Non-HDL is usually 30 mg/dL above the LDL goal

16

Comparing Past Guidelines

ACC/AHA 2013	AAACE/ACE 2017
<ul style="list-style-type: none"> • Statin focused • No guidance for non-statin agents • Treatment goal: % LDL-C reduction based on statin intensity • Recommended lipid monitoring <ul style="list-style-type: none"> - 4-12 weeks for change in therapy - 4-12 months for stable patients 	<ul style="list-style-type: none"> • Comprehensive guideline • Statin and non-statin recommendations • Treatment goal: Targets <ul style="list-style-type: none"> - LDL-C, Non-HDL, Apo-B • Recommended lipid monitoring <ul style="list-style-type: none"> - 6 weeks for change in therapy - 6-12 months for stable patients

Storie NJ, et al. 2013 ACC/AHA Blood Cholesterol Guideline
Endocr Practice. 2017;23(4):479-497 #AADE19

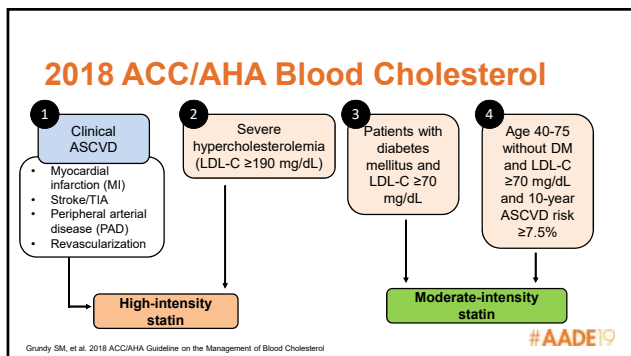
17

2018 ACC/AHA Blood Cholesterol

- Lifestyle Therapies
 - Heart healthy diet
 - Physical activity
- Four (4) Statin Benefit Groups
 - Moderate- or high-intensity statins

Grundy SM, et al. 2018 ACC/AHA Guideline on the Management of Blood Cholesterol #AADE19

18



19

2018 ACC/AHA Blood Cholesterol

- Monitoring
 - Adherence to lifestyle and LDL-C lowering therapies
 - 4 to 12 weeks after statin initiation or dose adjustment
 - 3 to 12 months thereafter

Grundy SM, et al. 2018 ACC/AHA Guideline on the Management of Blood Cholesterol

#AADE19

20

Case 1:

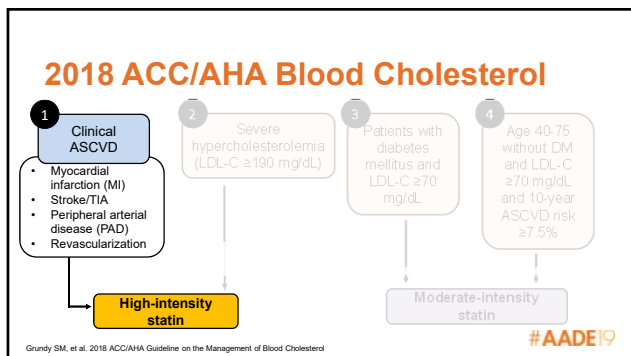
What changes would you make to HB's lipid therapy?

- HB is a 67-year-old African American male here for diabetes management
- PMH: T2DM, HTN, previous MI (2016)
- Meds:
 - lisinopril 40 mg/d
 - carvedilol 12.5 mg BID
 - aspirin 81 mg/d
 - metformin 1000 mg BID
 - empagliflozin 10 mg/d
 - rosuvastatin 40 mg/d
- Vitals
 - BP= 126/68 mm Hg
 - HR= 67 bpm
 - Weight= 193 lbs.
 - BMI= 27.6 kg/m²
 - FBG= 113 mg/dL

Lipid panel	
Total Chol.	171 mg/dL
TG	133 mg/dL
HDL-C	42 mg/dL
LDL-C	84 mg/dL

#AADE19

21



22

2018 ACC/AHA: Secondary Prevention

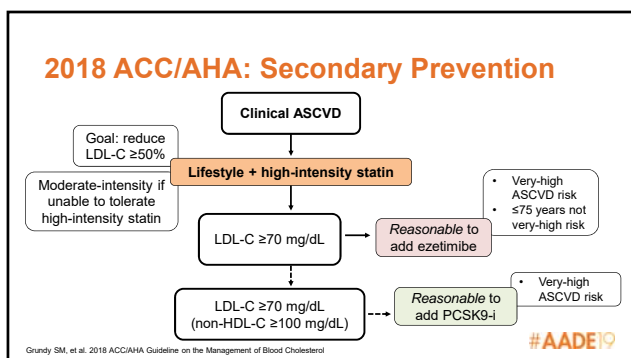
• “Very-high risk” group

Very-high risk includes: \geq 2 major ASCVD events **or** major ASCVD event + multiple high-risk conditions

Major ASCVD events	High-risk Conditions
<ul style="list-style-type: none"> ACS within previous 12 months Previous MI or ischemic stroke Symptomatic PAD, previous peripheral revascularization/amputation, or claudication with ABI $<$ 0.85 	<ul style="list-style-type: none"> Prior revascularization (CABG; PCI) outside of ASCVD event Diabetes mellitus Hypertension Current smoking eGFR 15-59 ml/min/1.73m² LDL-C \geq 100 mg/dL (despite maximally tolerated statin + ezetimibe) Age \geq 65 years Heterozygous Familial Hypercholesterolemia Congestive heart failure

Grundy SM, et al. 2018 ACC/AHA Guideline on the Management of Blood Cholesterol #AADE19

23



24

Non-statins for Secondary Prevention

Ezetimibe

- ↓ LDL-C 20-25%
- Once-daily oral pill
- Generic available

PCSK9-inhibitors

- ↓ LDL-C 45-65%
- Bi-weekly SQ injection
- Brand only
 - ~\$14,000/yr (2018)
 - ~\$6,000/yr (2019)

#AADE19

25

Case 1:

- HB is a 67-year-old African American male with hypertension management
- PMH: T2DM, HTN, previous MI (2016)
- Meds:
 - lisinopril 40 mg/d
 - carvedilol 12.5 mg BID
 - aspirin 81 mg/d
 - metformin 1000 mg BID
 - empagliflozin 10 mg/d
 - rosuvastatin 40 mg/d
- Vitals
 - BP= 126/68 mm Hg
 - HR= 67 bpm
 - Weight= 193 lbs.
 - BMI= 27.6 kg/m²
 - FBG= 113 mg/dL

Total Cholesterol	171 mg/dL
TG	133 mg/dL
HDL-C	42 mg/dL
LDL-C	84 mg/dL

What changes would you make to HB's lipid therapy?

Reasonable to add ezetimibe 10 mg daily to current therapy

#AADE19

26

ADA 2019: Lipids

- Lifestyle modifications (diet & physical activity) should be recommended to improve the lipid profile and **reduce the risk of ASCVD** in patients with diabetes (A)

Diabetes Care 2019;42(Suppl. 1):S103-S123

#AADE19

27

ADA 2019: Reducing ASCVD Risk

Age	ASCVD or 10-year ASCVD risk >20%	Recommended treatment
<40 years	Yes	High-intensity statin*
	No	None^
≥40 years	Yes	High-intensity statin*
	No	Moderate-intensity statin^

Maximally tolerated statin dose if unable to tolerate recommended intensity

*moderate-/high-intensity may be considered if additional ASCVD risk factors present: (LDL-C ≥100 mg/dL; high blood pressure, smoking, family history of premature ASCVD, CKD, or albuminuria).
^If LDL-C ≥70 mg/dL on max-tolerated statin, consider additional LDL-C lowering therapy (ezetimibe/PCSK9-I)

Diabetes Care 2019;42(Suppl. 1):S103-S123

#AADE19

28

Case 2:

Would you recommend statin therapy for GN?

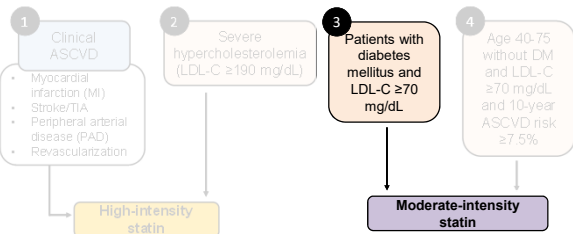
- GN is a 63-year-old non-Hispanic female here for initial visit.
- PMH: T2DM, HTN, CKD
- SH: Smokes 8-12 cig/d
- Meds:
 - amlodipine 5 mg/d
 - losartan 100 mg/d
 - metformin 1000 mg BID
- Vitals
 - BP= 132/78 mm Hg
 - HR= 82 bpm
 - BMI= 28.6 kg/m²

Labs			
eGFR	56 ml/min/1.73m ²	Total Chol.	194 mg/dL
UACR	69 mcg/mg	TG	156 mg/dL
FBG	124 mg/dL	HDL-C	44 mg/dL
HgbA1C	7.2%	LDL-C	116 mg/dL

#AADE19

29

2018 ACC/AHA Blood Cholesterol



Grundy SM, et al. 2018 ACC/AHA Guideline on the Management of Blood Cholesterol

#AADE19

30

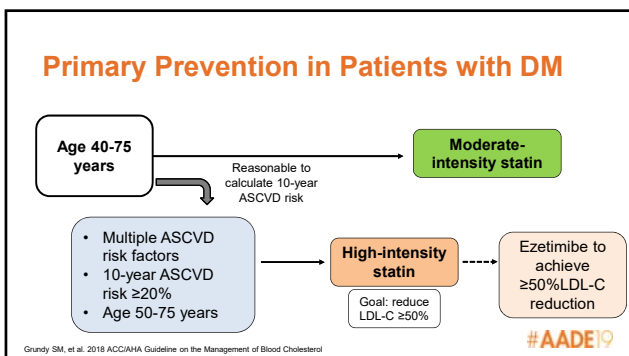
Primary Prevention in Patients with Diabetes Mellitus (DM)

- Recommendations for adult patients with diabetes mellitus and LDL-C 70-189 mg/dL
 - 20-39 years
 - 40-75 years
 - >75 years

Grundy SM, et al. 2018 ACC/AHA Guideline on the Management of Blood Cholesterol

#AADE19

31



32

ADA 2019: Reducing ASCVD Risk

Age	ASCVD or 10-year ASCVD risk >20%	Recommended treatment
<40 years	Yes	High-intensity statin*
	No	None^
≥40 years	Yes	High-intensity statin*
	No	Moderate-intensity statin^

Maximally tolerated statin dose if unable to tolerate recommended intensity

*moderate-/high-intensity may be considered if additional ASCVD risk factors present: (LDL-C ≥100 mg/dL; high blood pressure, smoking, family history of premature ASCVD, CKD, or albuminuria).
^If LDL-C ≥70 mg/dL on max-tolerated statin, consider additional LDL-C lowering therapy (ezetimibe/PCSK9-I)

Diabetes Care 2019;42(Suppl. 1):S103-S123

#AADE19

33

34

10-year ASCVD Risk Calculator

- 57 y/o AAF with diabetes
 - BP =138/78 mmHg (treated)
 - TC=234 mg/dL; HDL-C=48 mg/dL
- 51 y/o Hispanic male with diabetes and current smoking
 - BP =126/68 mmHg (treated)
 - TC=208 mg/dL; HDL-C=44 mg/dL
- 61 y/o non-Hispanic male with diabetes
 - BP =144/90 mmHg (untreated)
 - TC=185 mg/dL; HDL-C=46 mg/dL

10-year ASCVD risk >20%

#AADE19

35

Case 2:

Is lipid-lowering medication recommended for GN?

High-intensity statin

- GN is a 63-year-old non-Hispanic female here for initial visit.
- PMH: T2DM, HTN, CKD
- SH: Smokes 8-12 cig/d
- Meds:
 - amlodipine 5 mg/d
 - losartan 100 mg/d
 - metformin 1000 mg BID
- Vitals
 - BP= 132/78 mm Hg
 - HR= 82 bpm
 - BMI= 28.6 kg/m²

10-year ASCVD risk = 24.3%

Labs			
eGFR	56 ml/min/1.73m ²	Total Chol.	194 mg/dL
UACR	69 mcg/mg	TG	156 mg/dL
FBG	124 mg/dL	HDL-C	44 mg/dL
HgbA1C	7.2%	LDL-C	116 mg/dL

#AADE19

36

Primary Prevention in Patients with DM

Age 20-39 years

Assess Diabetes-Specific Risk Enhancers

- Long duration of DM
 - ≥20 years T1DM
 - ≥10 years T2DM
- Retinopathy
- Neuropathy
- Albuminuria ≥30 mcg of albumin/mg creatinine
- eGFR <60 mL/min/1.73 m²
- ABI <0.9

Moderate-intensity statin

Age >75 years

Already on statin

Reasonable to continue

Not on statin

Clinician-patient discussion (Benefits vs Risks)

Grundy SM, et al. 2018 ACC/AHA Guideline on the Management of Blood Cholesterol #AADE19

37

Case 3:

Is lipid-lowering medication recommended for HL?

- HL is a 48-year-old African American male here for pre-diabetes education
- PMH: HTN, pre-diabetes
- Meds: amlodipine 5 mg/d
- Vitals
 - BP= 137/74 mm Hg
 - HR= 72 bpm
 - BMI= 33.8 kg/m²
 - Waist circumference= 42.3"

Labs			
eGFR	115 ml/min/1.73m ²	Total Chol.	214 mg/dL
UACR	3 mcg/mg	TG	234 mg/dL
FBG	118 mg/dL	HDL-C	36 mg/dL
HgbA1C	6.4%	LDL-C	113 mg/dL

#AADE19

38

Primary Prevention in Patients without DM

Age 0-19 years

Lipid screening for FH

Promote lifestyle to reduce ASCVD risk

Age 20-39 years

Assess lifetime ASCVD risk + risk factors

Promote lifestyle to reduce ASCVD risk

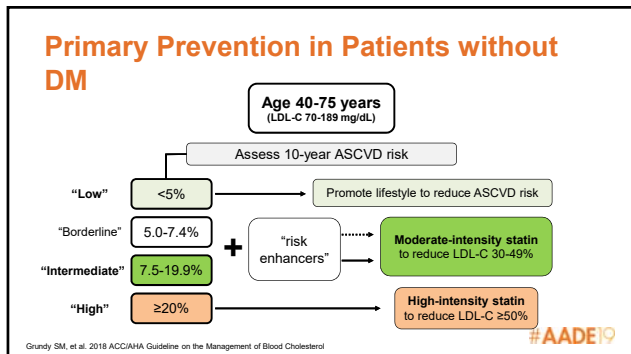
Consider statin if premature family history of ASCVD and LDL-C ≥160 mg/dL

Age 40-75 years
(70-189 mg/dL)

Assess 10-year ASCVD risk

Grundy SM, et al. 2018 ACC/AHA Guideline on the Management of Blood Cholesterol #AADE19

39



40

Risk Enhancing Factors

	Lipid/biomarkers
Family history of premature ASCVD	
Chronic kidney disease	
Metabolic syndrome	Persistently elevated LDL-C (≥160 mg/dL)
Ethnicity (South Asian)	Persistently elevated TG (≥175 mg/dL)
Inflammatory diseases (RA, HIV, psoriasis)	hs-CRP ≥2.0 mg/L
Preeclampsia & premature menopause	Lp(a) ≥50 mg/dL or >125 nmol/L
Ankle-brachial index <0.9	apoB ≥130 mg/dL

*to guide decision to initiate statin therapy in "borderline" and "intermediate-risk" individuals age 40-75 with LDL-C ≥70 mg/dL

Grundy SM, et al. 2018 ACC/AHA Guideline on the Management of Blood Cholesterol #AADE19

41

Case 3:

Is lipid-lowering medication recommended for HL? → **Moderate-intensity statin to reduce LDL-C 30-49%**

Intermediate-risk + MetS → **10-year ASCVD risk = 10.3%**

- HL is a 48-year-old male here for pre-diabetes
- PMH: HTN, pre-diabetes
- Meds: amlodipine 5 mg/d
- Vitals
 - BP= 137/74 mm Hg
 - HR= 72 bpm
 - BMI= 33.8 kg/m²
 - Waist circumference= 42.3"

Labs			
eGFR	115 ml/min/1.73m ²	Total Chol.	214 mg/dL
UACR	3 mcg/mg	TG	234 mg/dL
FBG	118 mg/dL	HDL-C	36 mg/dL
HgbA1C	6.4%	LDL-C	113 mg/dL

Grundy SM, et al. 2018 ACC/AHA Guideline on the Management of Blood Cholesterol #AADE19

42

Hypertriglyceridemia

- VLDL particles = Increase ASCVD risk
- Persistent TG ≥ 175 mg/dL is a risk-enhancing factor

Grundy SM, et al. 2018 ACC/AHA Guideline on the Management of Blood Cholesterol

#AADE19

43

Approach to Hypertriglyceridemia (HTG)

Moderate HTG
175-499 mg/dL

Severe HTG
 ≥ 500 mg/dL

Address Underlying Causes

- Secondary disorders
 - Diabetes mellitus
 - Chronic liver disease
 - Chronic kidney disease and/or nephrotic syndrome
- Hypothyroidism
- Triglyceride-raising drugs
- Lifestyle (obesity and metabolic syndrome)

ASCVD $\geq 7.5\%$
→ moderate-intensity statin or intensify therapy

ASCVD $\geq 7.5\%$
→ moderate-intensity statin or intensify therapy

Prevention of Pancreatitis

- Especially if fasting TG ≥ 1000 mg/dL
- Very low-fat diet
- Avoid of refined carbohydrates and alcohol
- Consume omega-3 fatty acids
- Add fibrate therapy (avoid gemfibrozil if concurrent use of statin)

Grundy SM, et al. 2018 ACC/AHA Guideline on the Management of Blood Cholesterol

#AADE19

44

Case 4:

- AD is a 66-year-old Hispanic female here for follow-up on diabetes and dyslipidemia.
- PMH: T2DM, elevated TG, HTN, prior MI (2015).
- Meds:
 - Benazepril/HCTZ 20/25 mg/d
 - Atorvastatin 80 mg/d
 - Metformin ER 2g/d
 - Canagliflozin 300 mg/d
 - Liraglutide 1.8 mg/d
 - Aspirin 81 mg/d

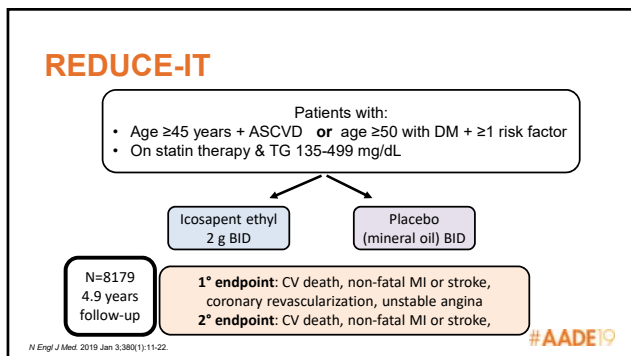
What changes would you make to AD's lipid lowering meds?

Labs					
	Lipid panel				
	TC	TG	HDL-C	LDL-C	A1C
Aug. '19	176	213	44	68	6.9%
May '19	168	198	42	71	7.1%
Jan. '19	182	226	43	75	7.5%

Grundy SM, et al. 2018 ACC/AHA Guideline on the Management of Blood Cholesterol

#AADE19

45



46

REDUCE-IT

Patient characteristic	IE (n=4089)	Placebo (n=4090)
Age (median) years	64.0	64.0
Male sex	71.6%	70.8%
History of ASCVD	70.7%	70.7%
Statin intensity (moderate or high)	93.4%	93.0%
Median LDL-C (mg/dL)	74.0	76.0
Median TG (mg/dL)	216.5	216.0
Distribution of TG		
<150 mg/dL	10.1%	10.5%
150-199 mg/dL	29.2%	29.1%
≥200 mg/dL	60.7%	60.4%

#AADE19

N Engl J Med. 2019; Jan 3;380(1):11-22.

47

REDUCE-IT

Outcome	IE (n=4089)	Placebo (n=4090)	Hazard Ratio (95% CI)
1° composite	17.2%	22.0%	0.75 (0.68-0.83)
2° composite	11.2%	14.8%	0.74 (0.65-0.83)
CV death or non-fatal MI	9.6%	12.4%	0.75 (0.66-0.86)
Fatal/non-fatal MI	6.1%	8.7%	0.69 (0.58-0.81)
Fatal/non-fatal stroke	2.4%	3.3%	0.72 (0.55-0.93)
CV death	4.3%	5.2%	0.80 (0.66-0.98)
All cause mortality	6.7%	7.6%	0.87 (0.74-1.02)
1° composite = 4.8% ARR (NNT=21)			

#AADE19

N Engl J Med. 2019; Jan 3;380(1):11-22.

48

ADA 2109 Recommendations

- In patients with ASCVD or other cardiac risk factors on a statin with *controlled* LDL-C, but elevated triglycerides (135-499 mg/dL), the addition of **icosapent ethyl** *should* be considered to reduce cardiovascular risk. (A)

ADA Standards of Medical Care in Diabetes 2019 [web annotation]. Diabetes Care 2019;42(Suppl. 1):S103-S123.

#AADE19

49

Agents in development

- Bempedoic acid
 - LDL-C lowering
- EPA/DHA carboxylic acids
 - TG-lowering in moderate hypertriglyceridemia
- Pemafibrate
 - TG-lowering in moderate hypertriglyceridemia

#AADE19

50