Diabetes and Hypertension Project ECHO* Clinic

*ECHO: Extension of Community Healthcare Outcomes

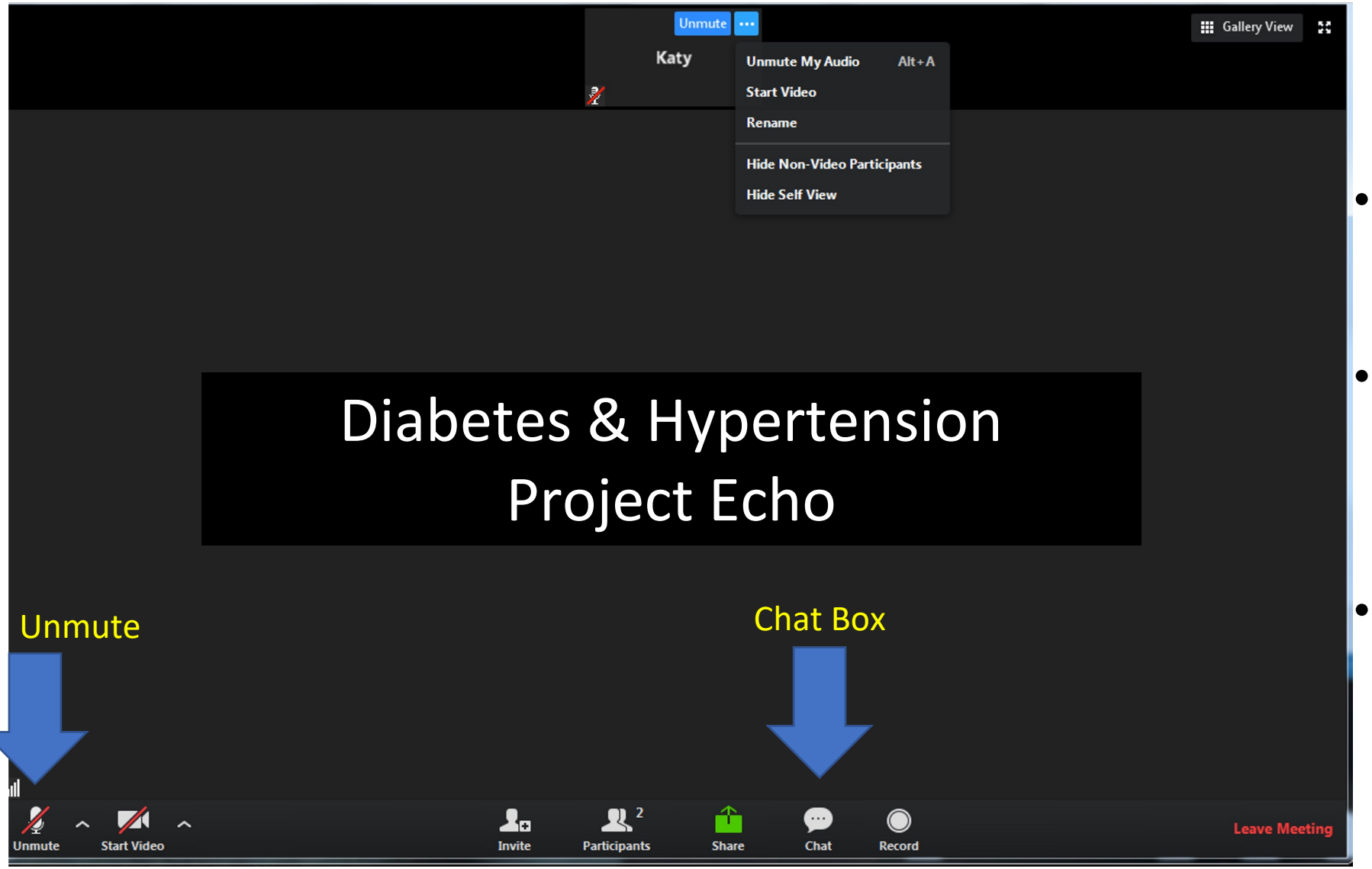
May 11, 2023

Before we begin:

- Rename your Zoom screen with your name and organization
- Claim CE: text 29388 - 28189 to 804-625-4041
  - Go to **vcuhealth.org/echodmhtn** for instructions on creating your account

The Diabetes and Hypertension ECHO is made possible by funding through CDC Cooperative Agreement NU58DP006620-InnoVAte.

Zoom Reminders



- You are all on mute. Please unmute to talk.
- If joining by telephone audio only, press *6 to mute and unmute.
- Use the chat function to speak with our team or ask questions.

Helpful Reminders

- Please feel free to eat your lunch or step away briefly if needed
- We are recording and can share sessions upon request
  - Each session's slides are available on www.vcuhealth.org/echodmhtn
- Please **do not share any protected health information** in your discussion or the chat box
- Project ECHO operates on the "All Teach, All Learn" model
  - Feel free to ask questions in the chat or unmute to ask questions at designated times
  - We're all here to learn from each other and value each person's input and expertise!

VCU Health Diabetes & Hypertension ECHO Clinics

VCU Hub Team	
Principal Investigator	Dave Dixon, PharmD
Administrative Medical Director ECHO Hub	Vimal Mishra, MD, MMCi
Clinical Experts	Niraj Kothari, MD Trang Le, MD
Project Coordinator/IT Support	Sydney Weber

- One-hour ECHO clinics on 2nd Thursdays
- Every ECHO clinic includes a didactic presentation followed by case discussions
- Website: www.vcuhealth.org/echodmhtn
  - Directions for claiming CE can be found here
  - You have up to six days after our session to claim CE by texting **29388 - 28189** to **804-625-4041**

How to Manage Elevated Triglycerides in Patients with Diabetes Mellitus (DM) or Chronic Kidney Disease (CKD)

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Disclosures

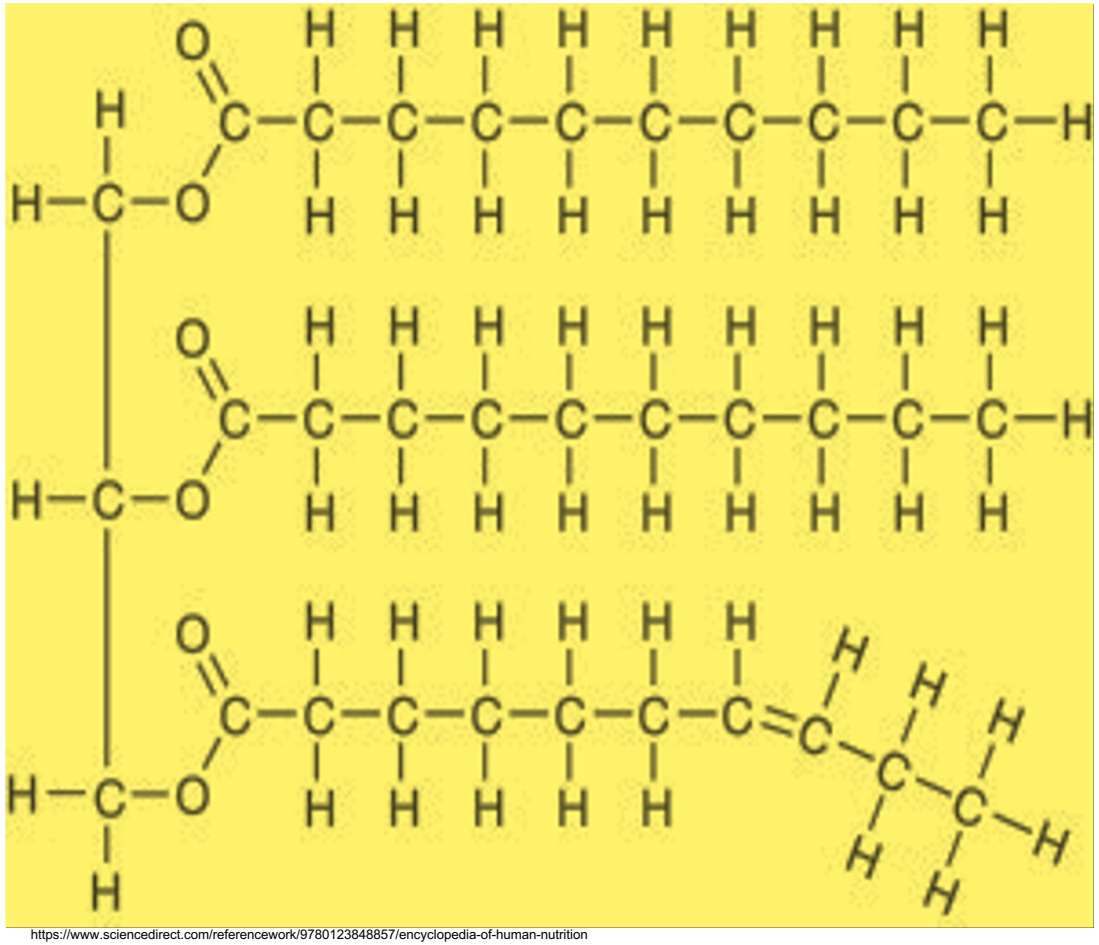
Ibrahim Alhomoud, has no financial conflicts of interest to disclose.

There is no commercial or in-kind support for this activity.

Learning Objectives

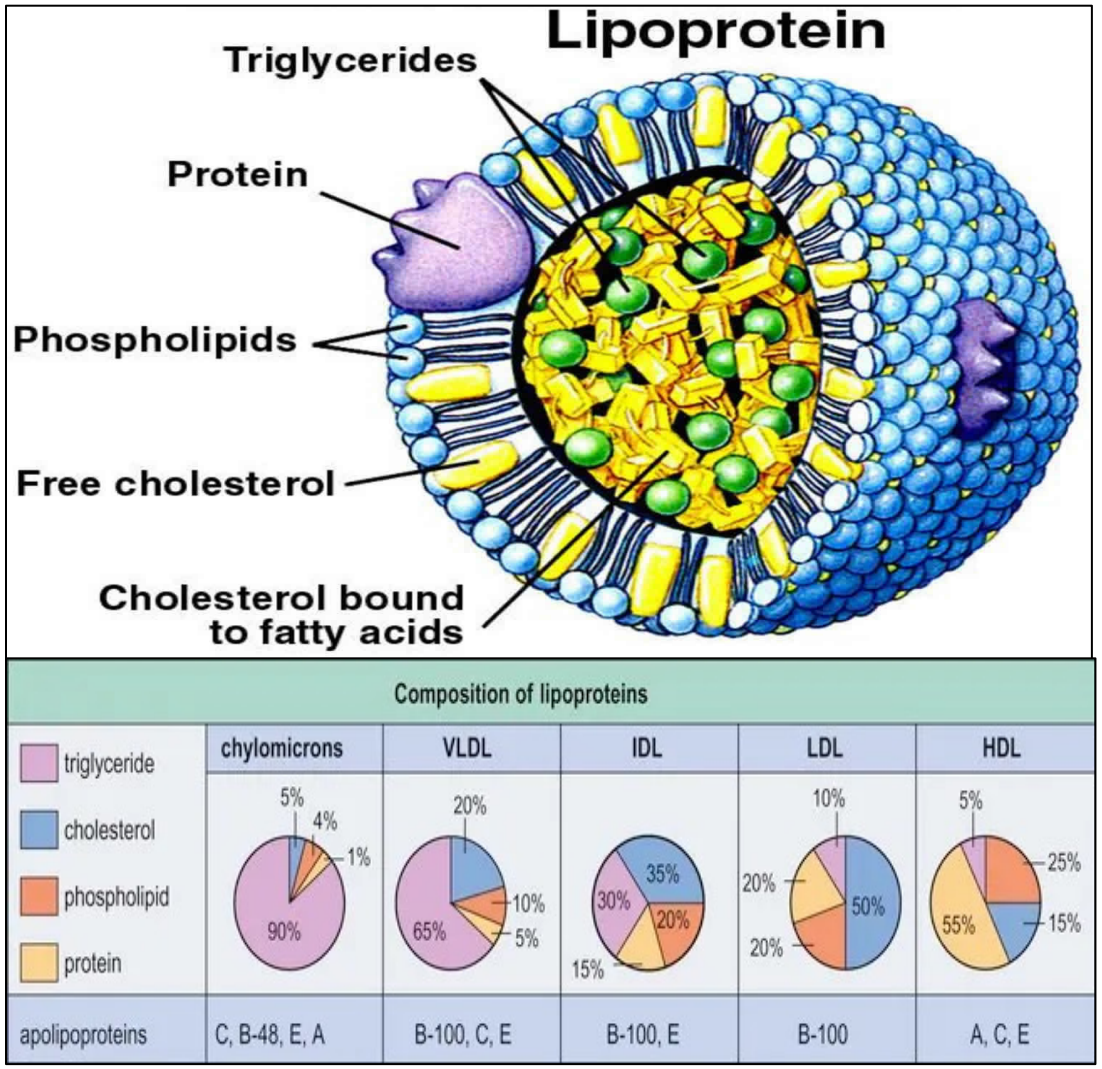
- Describe the prevalence and diagnostic criteria for hypertriglyceridemia
- Explain the link between elevated triglyceride levels and increased cardiovascular risk
- Discuss the role of lifestyle changes and when medication may be necessary in managing hypertriglyceridemia

TG Molecules & Lipoprotein Structures



https://www.sciencedirect.com/referencework/9780123848857/encyclopedia-of-human-nutrition

Triglycerides



Grundy et al. *J Am Coll Cardiol*. 2019;73(24):e285-350.
JAMA. 2012;307(12):1302-1309

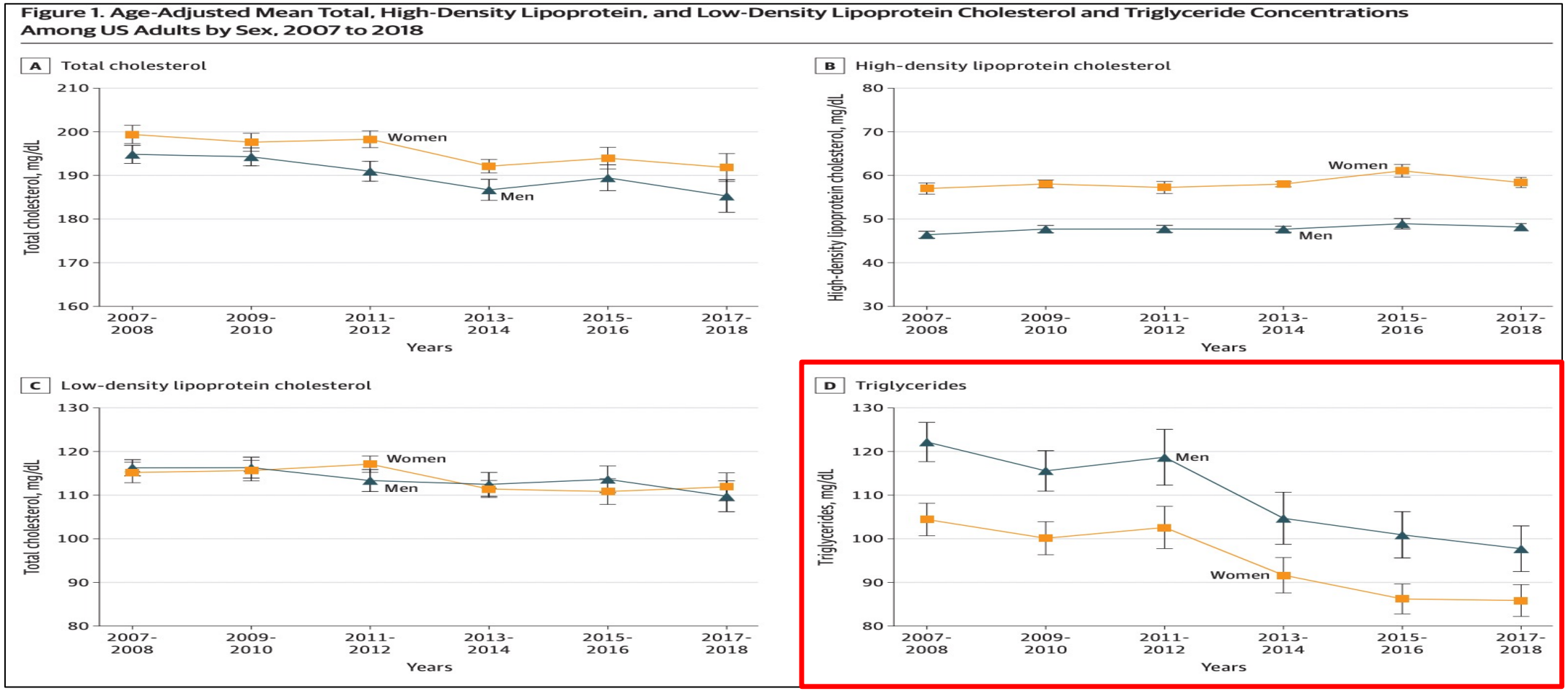
Overall Prevalence of Hypertriglyceridemia

- Data from the National Health and Nutrition Examination Survey, 2001–2012

Demographic	TG ≥150 mg/dL
Overall (age ≥20 years)	**25.1%**
Men	28.7%
Women	21.5%

Carroll MD, et al. NCHS data brief, no 198. Hyattsville, MD: National Center for Health Statistics. 2015.

Triglyceride Trends



Aggarwal R, et al. *JAMA*. 2022;328(8):737-745

Major guidelines classifying level of hypertriglyceridemia

ESC/EAS Guidelines for the Management of Dyslipidemia, 2019		
Severe	>10 mmol/L	
AHA/ACC/Multi-Society Guideline on the Management of Blood Cholesterol, 2018		
Normal	≤2.0 mmol/L	≤175 mg/dL
Mild-Moderate	2.0-5.6 mmol/L	175-499 mg/dL
Severe	≥5.7 mmol/L	≥500 mg/dL
The Endocrine Society Clinical Practice Guideline on the Evaluation and Treatment of Hypertriglyceridemia, 2012		
Normal	<1.7 mmol/L	<150 mg/dL
Mild Hypertriglyceridemia	1.7-2.3 mmol/L	150-199 mg/dL
Moderate Hypertriglyceridemia	2.3-11.2 mmol/L	200-999 mg/dL
Severe Hypertriglyceridemia	11.2-22.4 mmol/L	1000-1999 mg/dL
Very severe hypertriglyceridemia	≥22.4 mmol/L	≥2000 mg/dL

Curr Atheroscler Rep. 2021 Sep 13;23(11):72

Persistent HyperTG

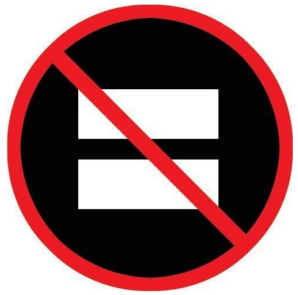
- **Persistent Hypertriglyceridemia:**
  - **Defined as fasting TG ≥150 mg/dL or non-fasting TG ≥175 mg/dL**
  - Following a minimum of 4 to 12 weeks of lifestyle intervention
    - Stable dose of maximally tolerated statin therapy when indicated
    - Evaluation and management of secondary causes of Hypertriglyceridemia

- **Before initiating of TG risk-based nonstatin therapies, a fasting lipid panel should be obtained**
  - At least 2 measurements of fasting lipids, preferably at least 2 weeks apart

J Am Coll Cardiol. 2021;78(9):960-993

HyperTriglyceridemia: Treatment Strategies

Triglyceride lowering

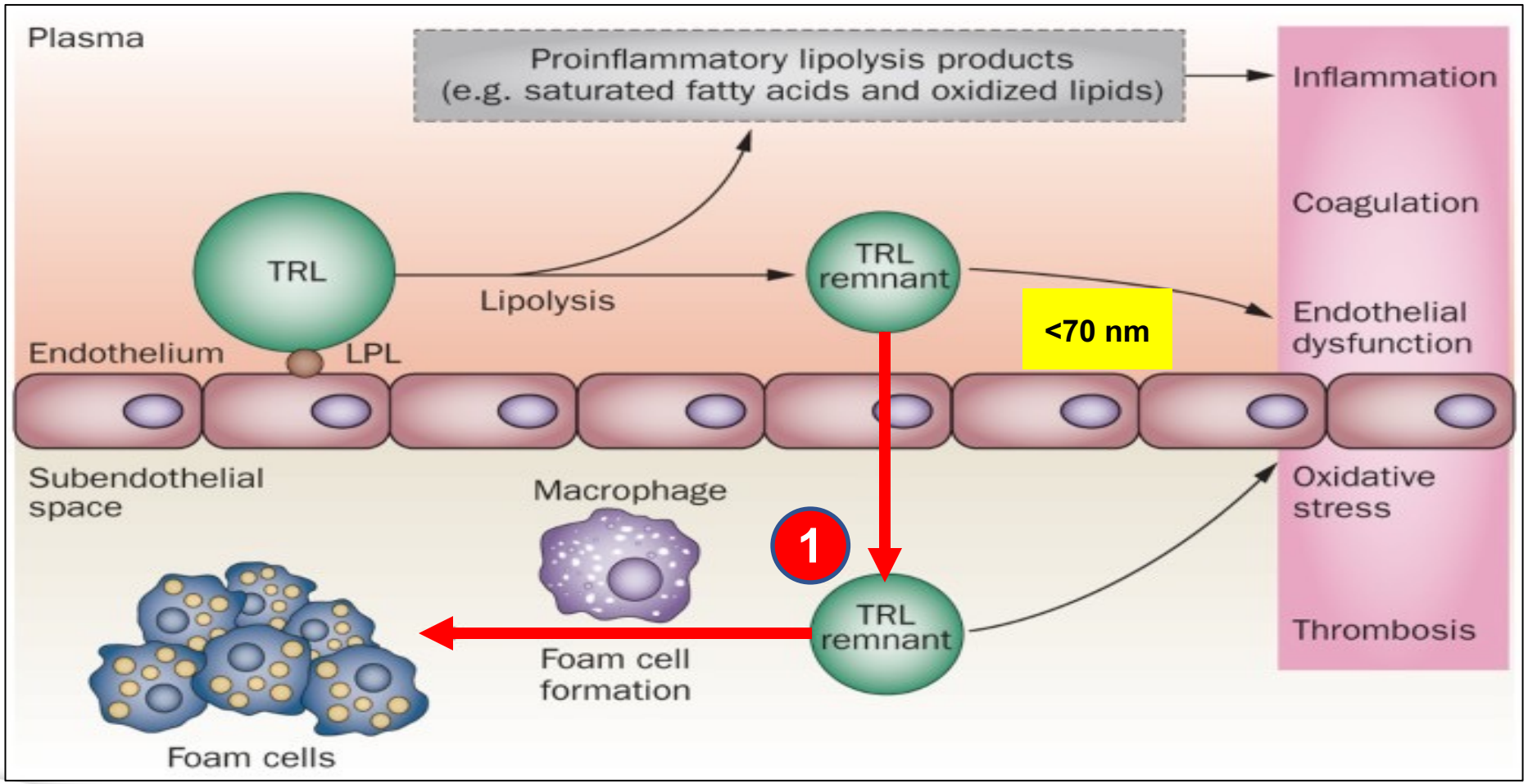


Therapies to lower triglycerides level to reduce the risk of acute pancreatitis

Triglyceride risk-based

Therapies to reduce ASCVD risk in individuals with elevated TG levels as a marker of residual risk

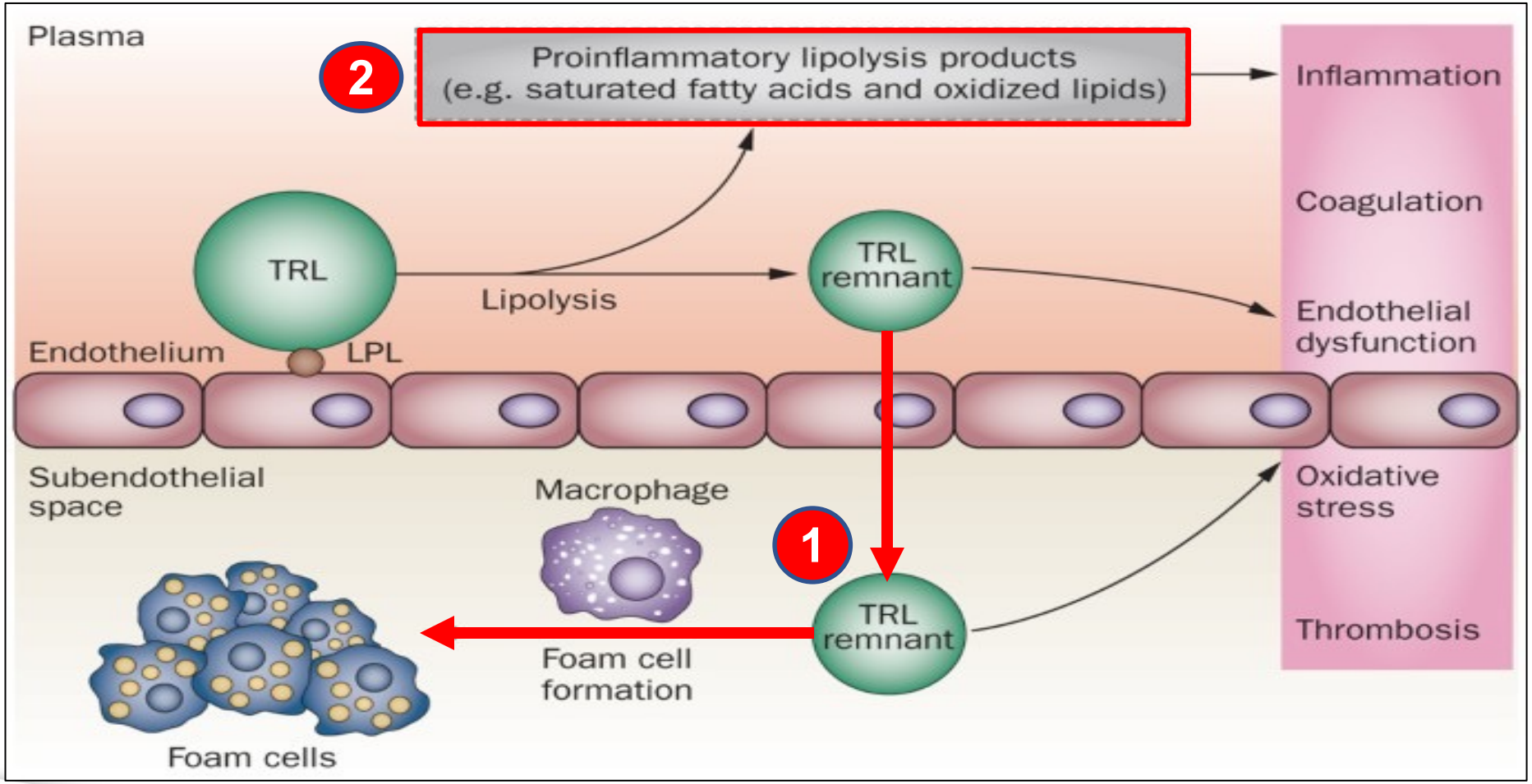
The Atherogenic Role of Triglyceride-rich Lipoproteins (TRL)



1- Direct

Watts GF, at al. *Nat Rev Cardiol*. 2013;10(11):648-661

The Atherogenic Role of Triglyceride-rich Lipoproteins

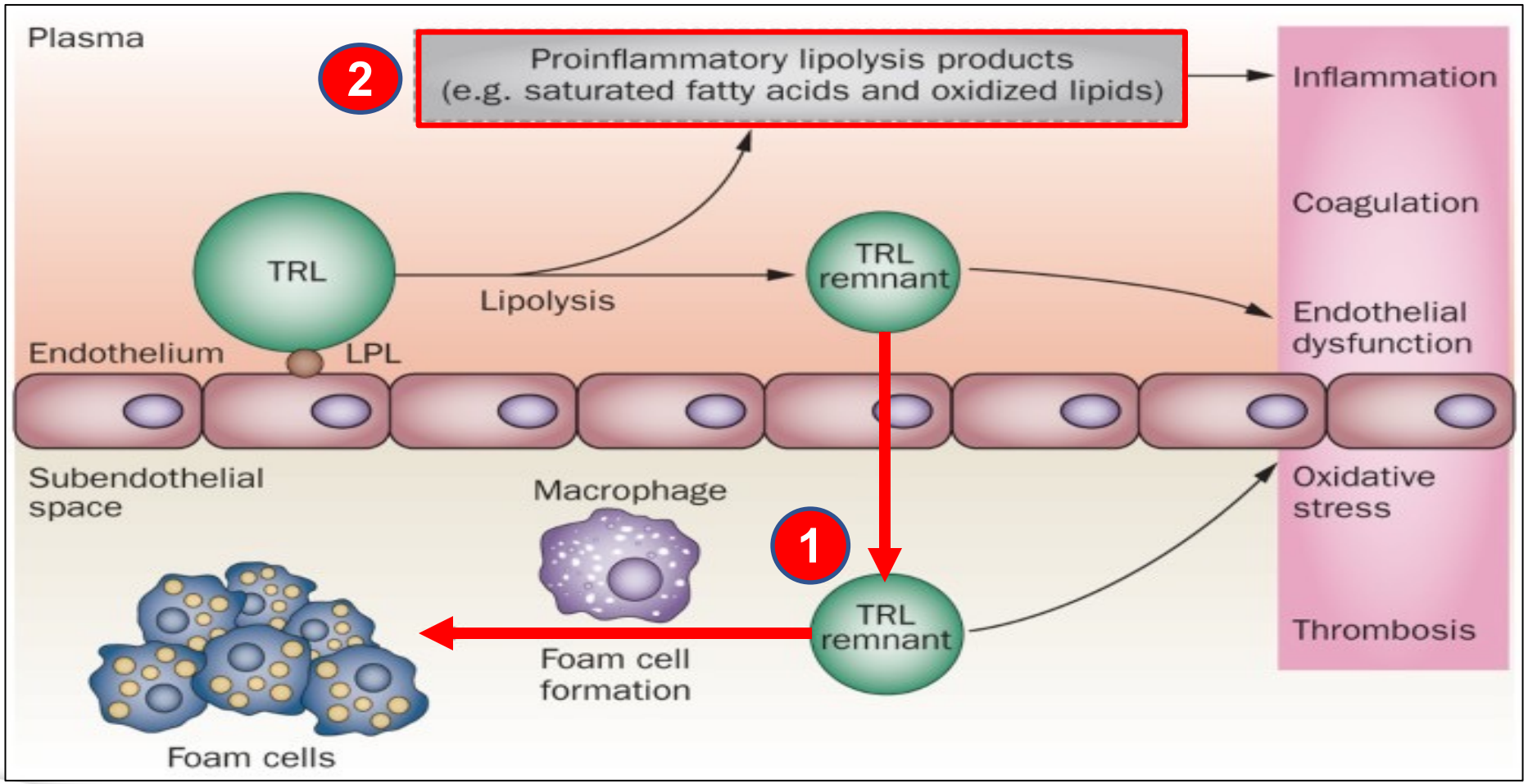


1- Direct

2- Indirect

Watts GF, at al. *Nat Rev Cardiol*. 2013;10(11):648-661

The Atherogenic Role of Triglyceride-rich Lipoproteins



1- Direct

2- Indirect

3- Bystander

Watts GF, at al. *Nat Rev Cardiol*. 2013;10(11):648-661

- **Which ONE of the following is NOT a diagnostic component of the Metabolic Syndrome?**
  - A. Waist circumference for a women > 35 inches
  - B. Blood pressure ≥130/≥85 mmHg
  - C. Triglycerides levels ≥ 500 mg/dL
  - D. HDL-cholesterol > 50 mg/dL in men
  - E. Fasting blood glucose ≥100 mg/dL

- **Which ONE of the following is NOT a diagnostic component of the Metabolic Syndrome?**
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  - C. Triglycerides levels ≥ 500 mg/dL
  - D. HDL-cholesterol > 50 mg/dL in men
  - E. Fasting blood glucose ≥100 mg/dL

Metabolic Syndrome: The NCEP ATP III

- In order to make a diagnosis of the metabolic syndrome, a patient must present with **three or more** of the following five risk factors:

Risk factor	Define Level
Abdominal obesity • Men • Women	Waist circumference • >102 cm (>40 in) • >88 cm (>35 in)
Triglycerides	≥150 mg/dL (1.7 mmol/L)
HDL Cholesterol • Men • Women	 <40 mg/dL (1.04 mmol/L) <50 mg/dL (1.30 mmol/L)
Blood pressure	≥130/≥85 mmHg
Fasting glucose	≥100 mg/dL (5.6 mmol/L)

Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *Circulation. 2002;106;3143.*

HyperTriglyceridemia: Treatment Strategies

1984

2014

Publication	Organization	Region	Recommendation to Treat With Lifestyle Modification and Medication: To Prevent Atherosclerotic Cardiovascular Disease: Mild-to-Moderately Elevated Triglycerides* (or Elevated Non-HDL Cholesterol)	To Prevent Atherosclerotic Cardiovascular Disease: Elevated LDL and Total Cholesterol	To Prevent Atherosclerotic Cardiovascular Disease: Reduced HDL Cholesterol	To Prevent Pancreatitis: Severely Elevated Triglycerides*
1984, Grundy et al[1]	AHA recommendation	US	Yes	Yes	No	Yes
1987, Lewis et al[2]	EAS strategies	Europe	Yes	Yes	No	Yes
1988, Lewis et al[3]	EAS policy statement	Europe	Yes	Yes	No	Yes
1988, Goodman et al[4]	ATP-I-NCEP	US	No	Yes	No	Yes
1993, Grundy et al[5]	ATP-II-NCEP	US	(Yes)	Yes	(Yes)	Yes
1994, Pyörälä et al[6]	ESC, EAS, and ESH recommendation	Europe	No	Yes	No	Yes
1998, Wood et al[7]	ESC, EAS, and ESH recommendation II	Europe	No	Yes	No	†
2001, Grundy et al[8]	ATP-III-NCEP	US	(Yes)	Yes	(Yes)	Yes
2003, De Backer et al[9]	ESC, EAS, ESH, and others guidelines	Europe	No	Yes	No	†
2007, Graham et al[10]	ESC, EAS, ESH, and others guidelines	Europe	No	Yes	No	†
2011, Chapman et al[11]	EAS consensus	Europe	Yes	Yes	(Yes)	Yes
2011, Reiner et al[12]	ESC/EAS guidelines	Europe	(Yes)	Yes	No	Yes
2011, Miller et al[13]	AHA scientific statement	US	No	†	†	Yes
2012, Berglund et al[14]	Endocrine Society guidelines	US	Yes	†	†	Yes
2012, Perk et al[15]	ESC, EAS, ESH, and others guidelines	Europe	No	Yes	No	†
2014, Stone et al[16]	ACC/AHA guidelines	US	No	Yes	No	†
2014, Hegele et al[17]	EAS consensus	Europe	Yes	Yes	No	Yes

Nordestgaard BG. *Circ Res*. 2016;118(4):547-563.

Evaluation and Management of Hypertriglyceridemia

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VOL. 78, NO. 9, 2021

EXPERT CONSENSUS DECISION PATHWAY

2021 ACC Expert Consensus Decision Pathway on the Management of ASCVD Risk Reduction in Patients With Persistent Hypertriglyceridemia

A Report of the American College of Cardiology Solution Set Oversight Committee

Endorsed by the National Lipid Association

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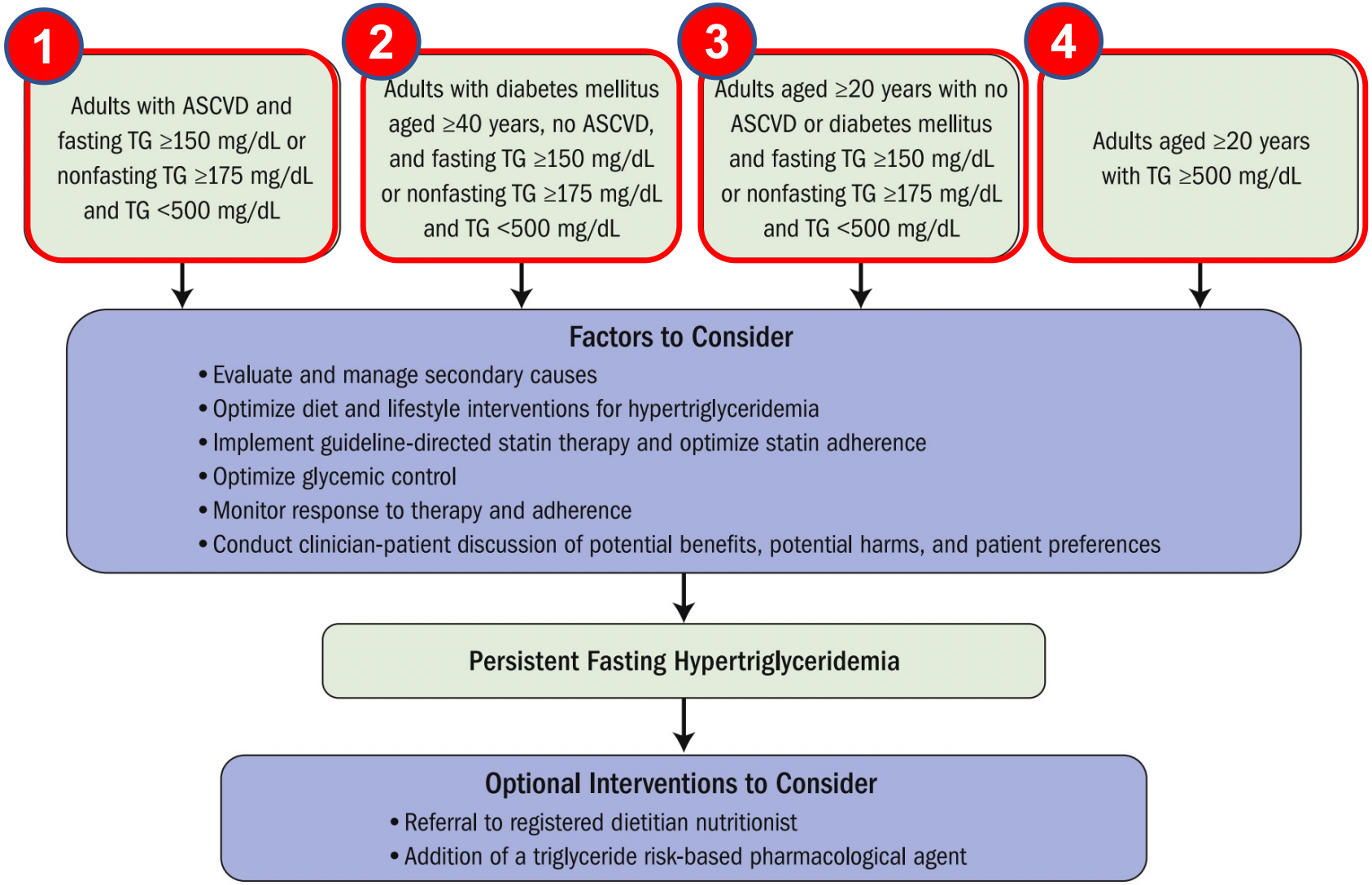
J Am Coll Cardiol. 2021;78(9):960-993

Patient Population and Factors to Consider

Adults with hyperTG

1- ASCVD
2- DM
3- Moderate HyperTG
4- Severe HyperTG



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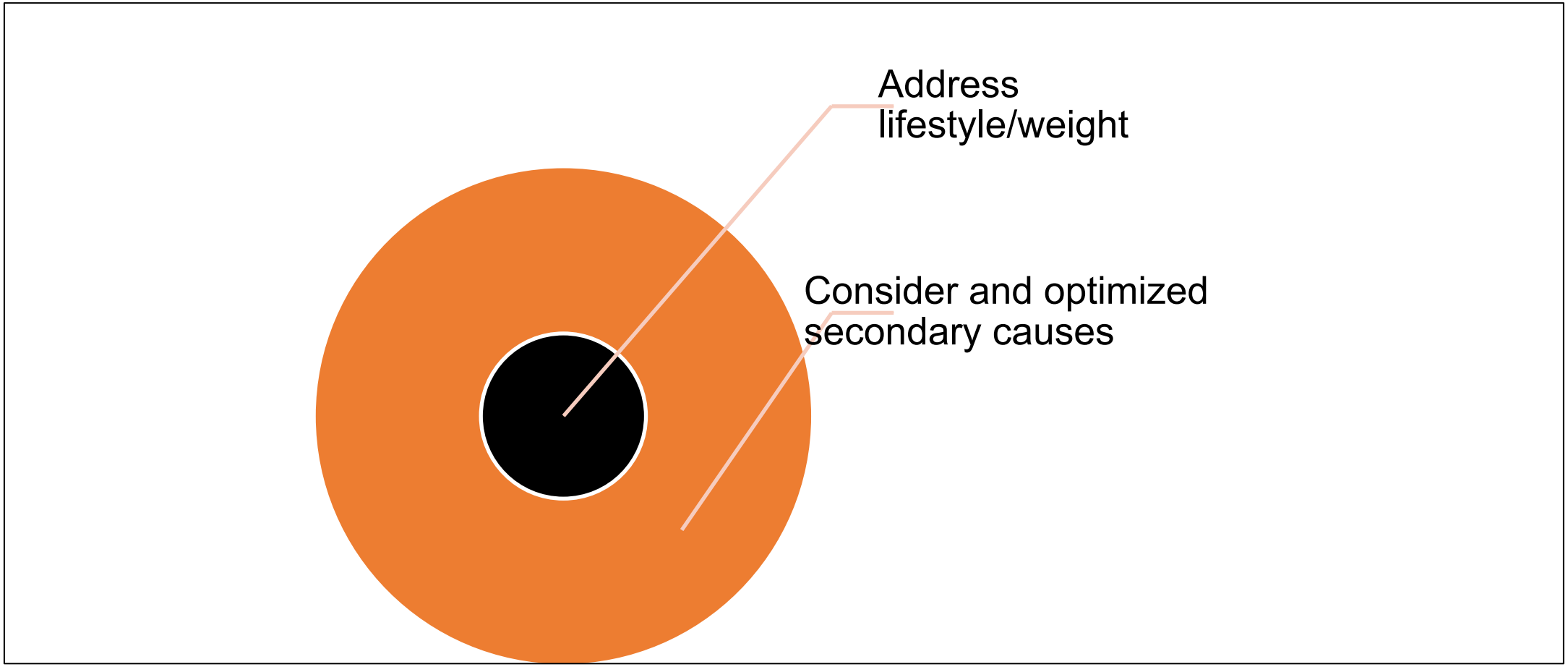
Case 1: office worker with hyperTG

- **36-year-old Caucasian female presents for annual check-up**
  - No prior gestational diabetes or HTN
  - Family hx: no ASCVD or diabetes
  - Meds:
    - oral contraceptive pills
    - Isotretinoin
  - BMI: 33
  - Lifestyle:
    - Active at work, but no regular exercise
    - Frequently eats at fast food restaurants for convenience
    - Three 20-ounce bottles of Mountain Dew during the day and 4 beers evening

Parameters	Results (mg/dL)
TC	200
TG	**750**
LDL-C	-
HDL-C	35
nonHDL-C	135
Glu/A1c	80/5.5%
AST/ALT, TSH, uric acid	normal

Initial Treatment for Hypertriglyceridemia



Grundy SM, et al. *Circulation*. 2019;139(25):e1082-e1143
J Am Coll Cardiol. 2021;78(9):960-993

Lifestyle Interventions

Implement shared decision-making intervention	TG <500 mg/dL†	TG 500-999 mg/dL†	TG ≥1000 mg/dL‡
Added sugars (percent calories)	<6%	<5%	Eliminate
Total fat (percent calories)	30%-35%	20%-25%§	10%-15%
Alcohol	Restrict	Abstain completely	Abstain completely
Aerobic activity	At least 150 min/wk of accumulated moderate-intensity or 75 min/wk of vigorous-intensity aerobic physical activity (or equivalent combination of both)‖		
Weight loss (percent body weight)	Recommended weight loss goal is 5%-10% for all patients with elevated TG		

- Monitor response to intervention
- Consider referral to RDN, exercise trainer, or other supportive services
- Continue intervention or adjust as indicated

J Am Coll Cardiol. 2021;78(9):960-993

Lifestyle Interventions in HyperTG

Lifestyle Intervention	Reduction in Triglycerides (%)	Qualifier
Weight loss	Up to 70%	Although **most patients** will likely experience reductions in TG levels of **10%-20%** with weight loss, evidence suggests that in some patients, a reduction in TG levels of up to 70% may be achieved
Dietary modifications (including alcohol—restrict or abstain completely)	>70%	Response may vary depending on the baseline triglyceride level and how strictly dietary recommendations are followed
Physical activity and exercise	Up to 30%	Response may vary depending on the type, duration, and intensity of activity

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Conditions Contributing to HyperTG

Diseases

- **Poorly controlled diabetes**
- Hypothyroidism
- **Chronic Kidney Disease**
- Cushing syndrome
- Rheumatoid arthritis (RA)
- Psoriasis
- Systemic lupus erythematosus
- Myeloma
- Sepsis
- Familial lipodystrophy

Diet/lifestyle

- **Alcohol** excess/abuse
- Diet high in saturated fat/**sugar**/high glycemia index foods
- **Sedentary** lifestyle
- TPN with fat emulsions

Disorders of metabolism

- **Overweight and obesity** (esp. BMI >40 kg/m2)
- Weight gain after weight loss
- **Pregnancy** (esp. 3rd trimester)

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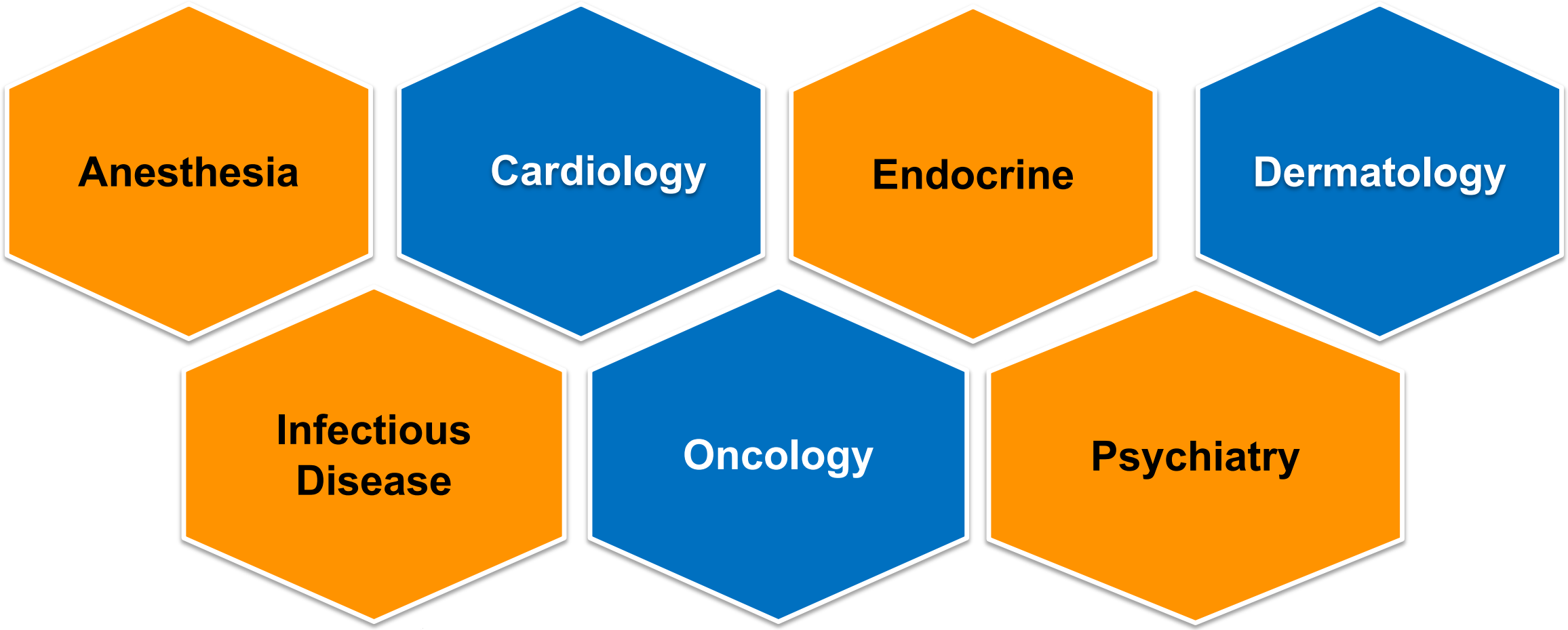
Medications Contributing to HyperTG



Case 2: severe hyperTG

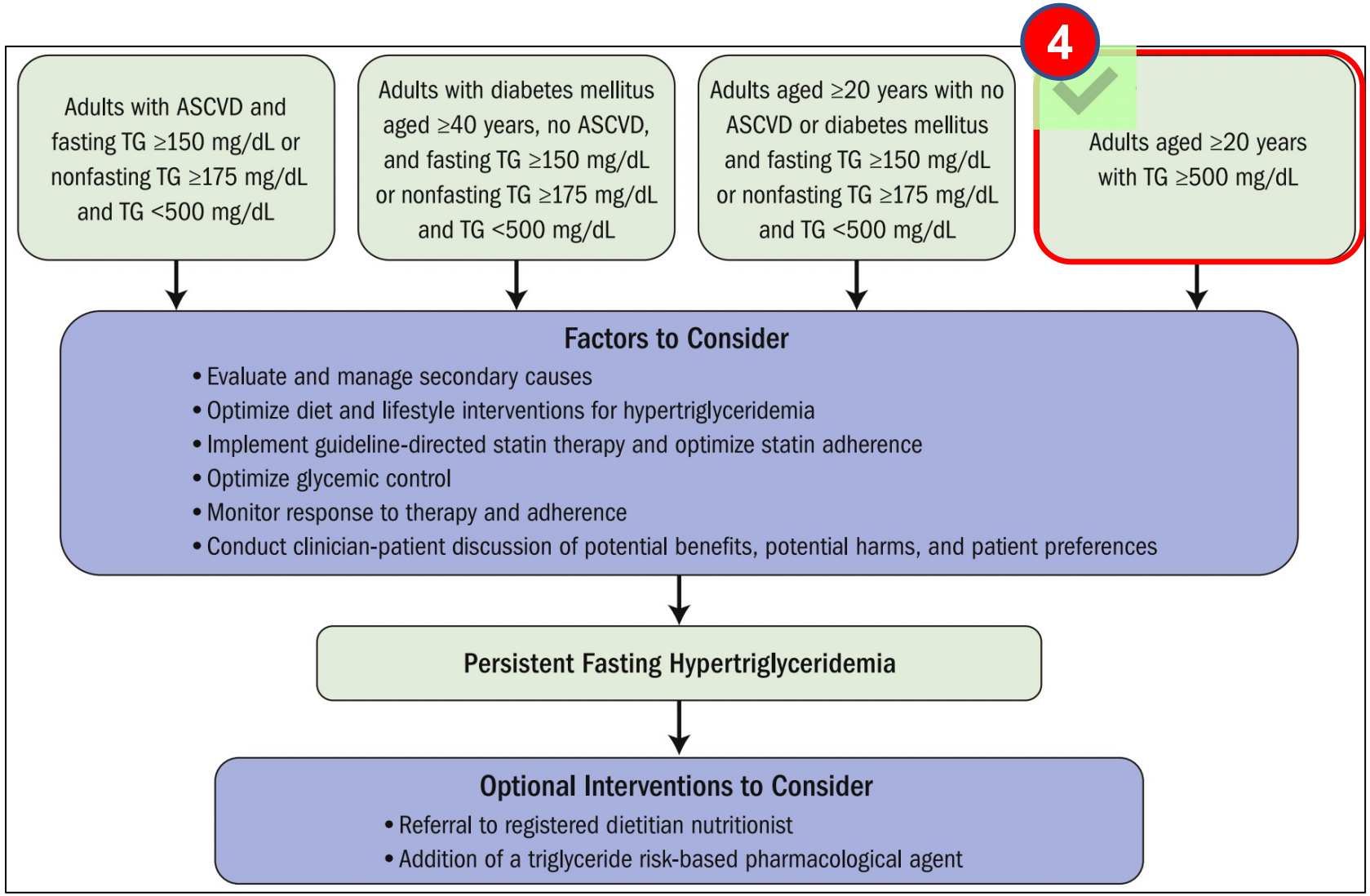
- 50-year-old Caucasian male presents for f/u
  - **PMH:** pancreatitis, fatty liver, uncontrolled T2DM, CKD (G3a/A3), and HTN
  - **Lifestyle:**
    - Drinking significant amounts of alcohol due to recent job loss
  - **Family history:**
    - Father had “high cholesterol” and s/p NSTEMI with PCI at 52 yr
    - Brother had high triglycerides, and s/p PCI for angina at age 54 yr
  - **Medications:**
    - HTN: Carvedilol 6.25mg twice daily, and HCTZ 25mg daily
    - T2DM: dulaglutide 3mg weekly, empagliflozin 10mg daily
    - Hyperlipidemia: rosuvastatin 10mg daily
  - **Physical exam:** BP 145/95 mmHg, BMI 31

Parameters	Results (mg/dL)
TC	310 mg/dL
TG	**1350 mg/dL**
HDL-C	35 mg/dL
nonHDL-C	160 mg/dL
eGFR/ACR	50 / 65
Glu/A1c	175/8.5%
AST/ALT	60 U/L, 95 U/L
TSH, uric acid	normal

Patient Population and Factors to Consider

Adults with hyperTG

1- ASCVD
2- DM
3- Moderate HyperTG
4- Severe HyperTG



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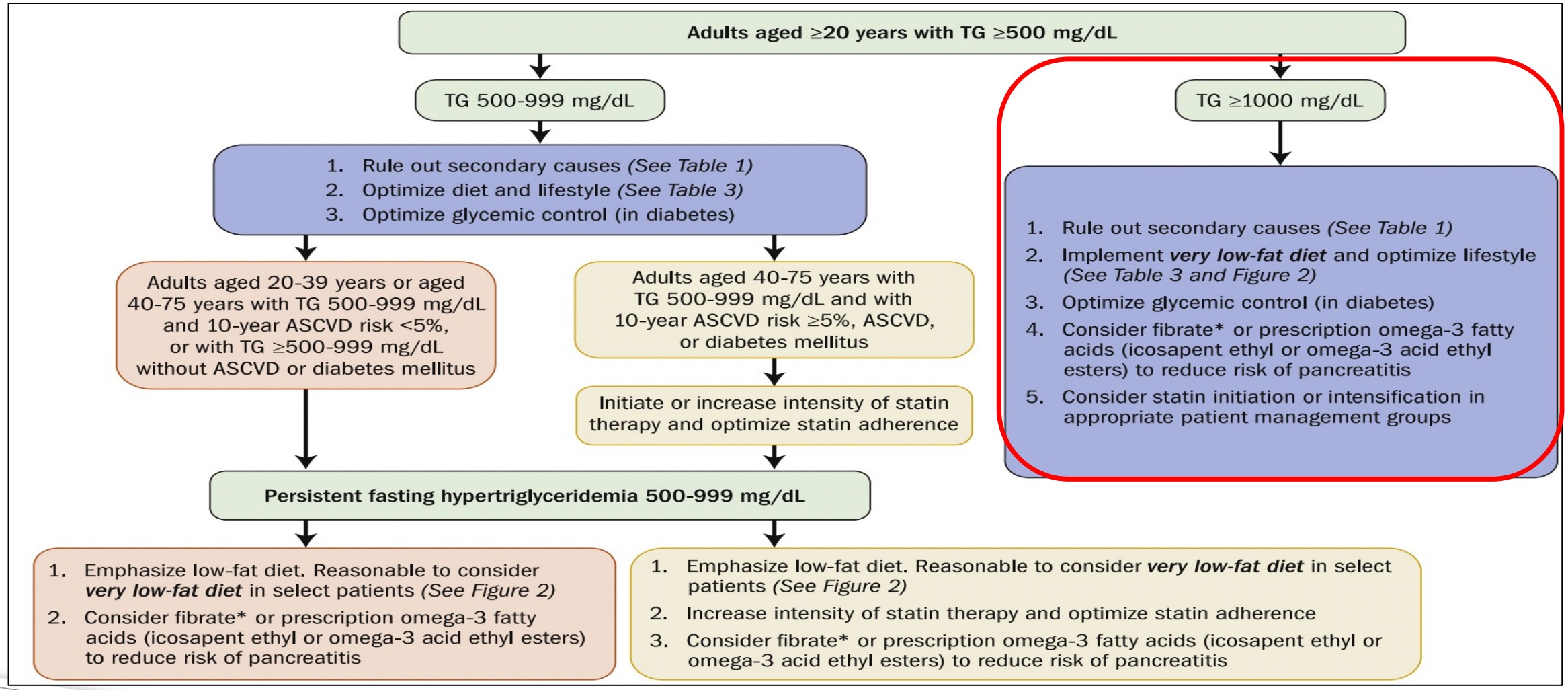
Adults Aged ≥20 Years With Severe HyperTG (≥500 mg/dL)



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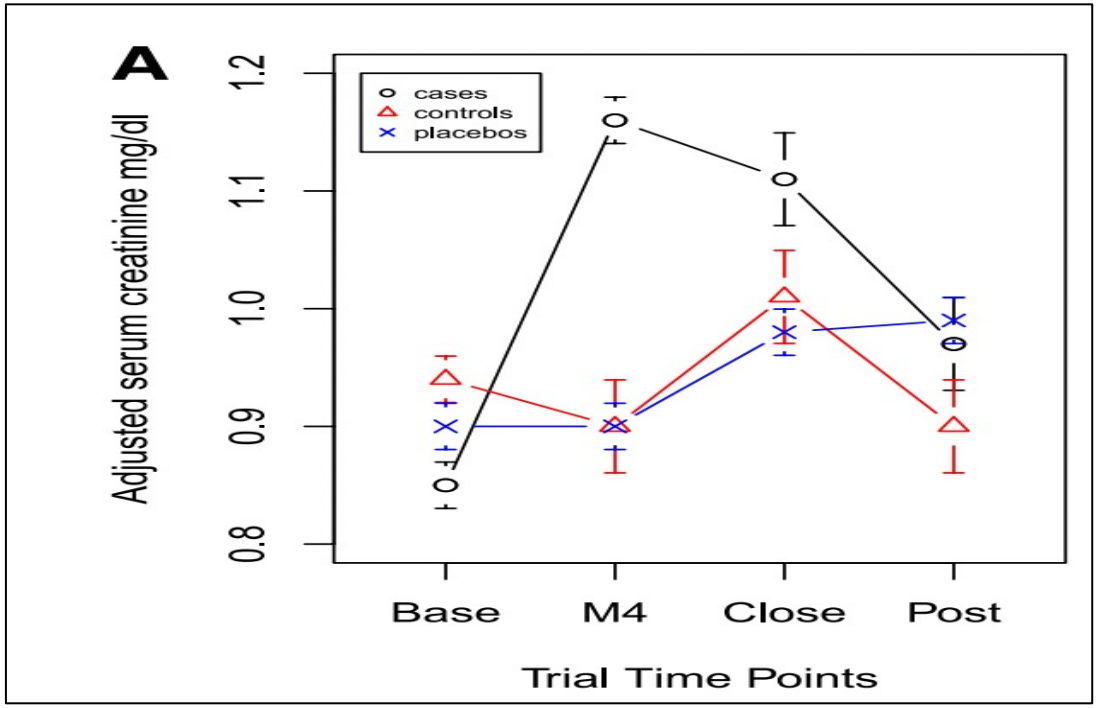
Lipid Rx

	LDL-C	HDL-C	TG
★**Statins**	↓ 18–55%	↑ 5-15%	↓ 7–30%
Cholesterol absorption inhibitor (ezetimibe)			
Nicotinic acid	↓ 5-25%	↑ 15-35%	↓20-50%
★**Fibric acid derivatives** (fenofibrate)	↓ 5-20% or	↑ 10-20%	↓20-50%
★**Omega-3 fatty acids** (prescription strength only)	↓/↑	↑ 9%	↓ 45%
Bile acid sequestrants (cholestyramine, colesevelam, colestipol)	↓ 15-30%	↑ 3-5%	0 or ↑
Non-statin cholesterol synthesis (bempedoic acid)	↓ 17-25%	-	-
PCSK9 mAbs (alirocumab, evolocumab)	↓ 50-70%	N	↓
PCSK9 siRNA (inclisiran)	↓ 50%	N	↓

Nissen SE, et al. *N Engl J Med*. 2023;388(15):1353-1364
Shimada YJ, et al. *Eur Heart J*. 2015;36(36):2415-2424
Jacobson TA, et al. *Clin Lipidol*. 2014;8(5):473-488

Reversibility of renal function changes with fenofibrate

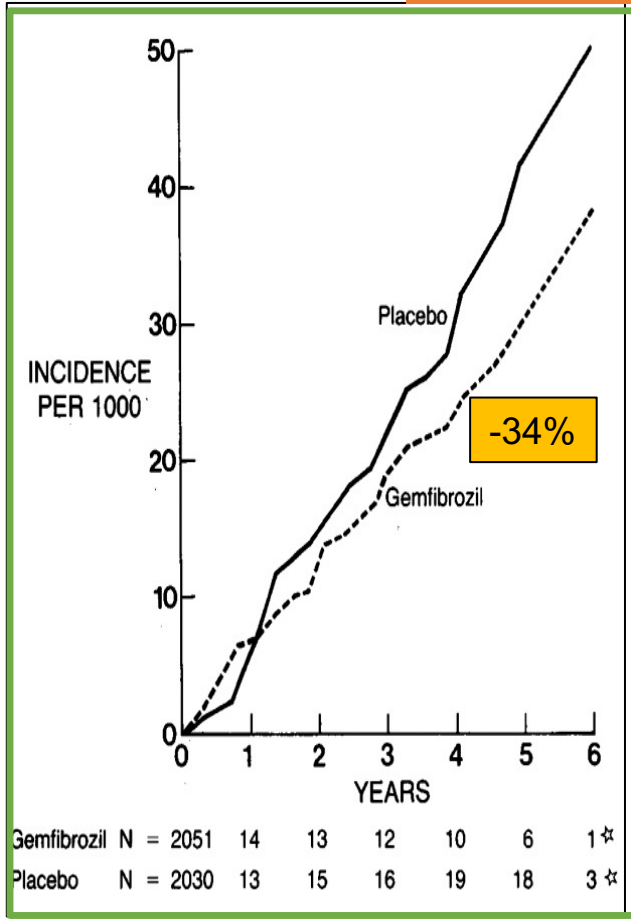


Fenofibrate has been reported to worsen renal function, although this is usually transient and self-limiting

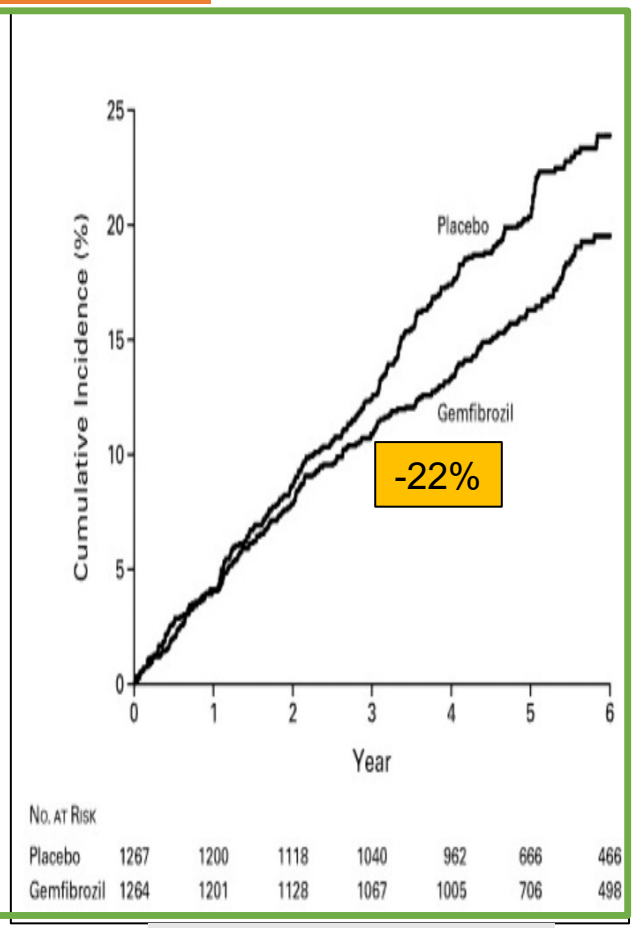
Mychaleckyj JC, et al. *Diabetes Care*. 2012;35(5):1008-1014

Fibrate Trials

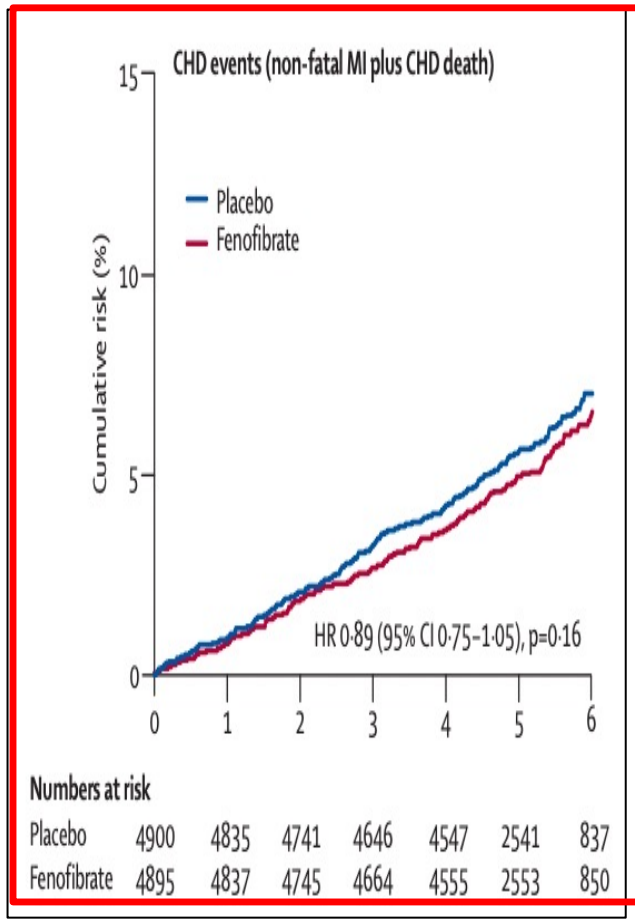
W/Statins



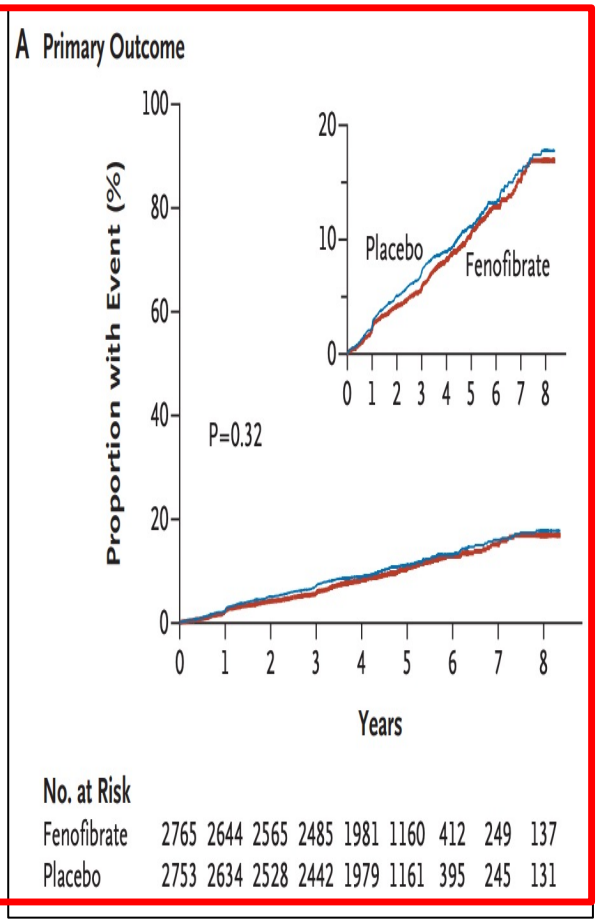
Helsinki Heart Study
(Primary Prevention)



VA-HIT
(Secondary Prevention)



FIELD
Primary & Secondary Prevention



ACCORD Lipid

Case 2: severe hyperTG

Diabetes Mellitus

- Start metformin
- D/C GLP-1 RA
- Consider pioglitazone
- Continue SGLT2i

HTN/CKD

- START to ACEi or ARB
- Continue SGLT2i

Case 2: severe hyperTG

- Laboratories studies:

Current therapies:

- Rosuvastatin 20mg daily
- Fenofibrate 160mg daily
- Metformin 1000mg BID
- Empagliflozin 10mg daily
- Pioglitazone 30mg daily
- Losartan 50mg daily
- Amlodipine 5mg

Parameters	Baseline	12 weeks
TC	310 mg/dL	225 mg/dL
TG	**1350 mg/dL**	**480 mg/dL**
HDL-C	35 mg/dL	40 mg/dL
nonHDL-C	160 mg/dL	100 mg/dL
LDL-C	-	95 mg/dL
eGFR/ACR	50 / 65	55 / 22
Glu/A1c	175/8.5%	102 /7.3%
AST/ALT	60 U/L, 95 U/L	45 / 50
TSH, uric acid	normal	-

- **According to the 2018 AHA/ACC Multi-society cholesterol guidelines and Hypertriglyceridemia Management Expert Consensus, which of the following is the most appropriate next therapy(ies)?**
  - A. Add prescription omega 3 fatty acid (4g)
  - B. Add niacin extended release 2 g
  - C. Add bedtime insulin
  - D. Add ezetimibe 10 mg
  - E. Add bile acid resin

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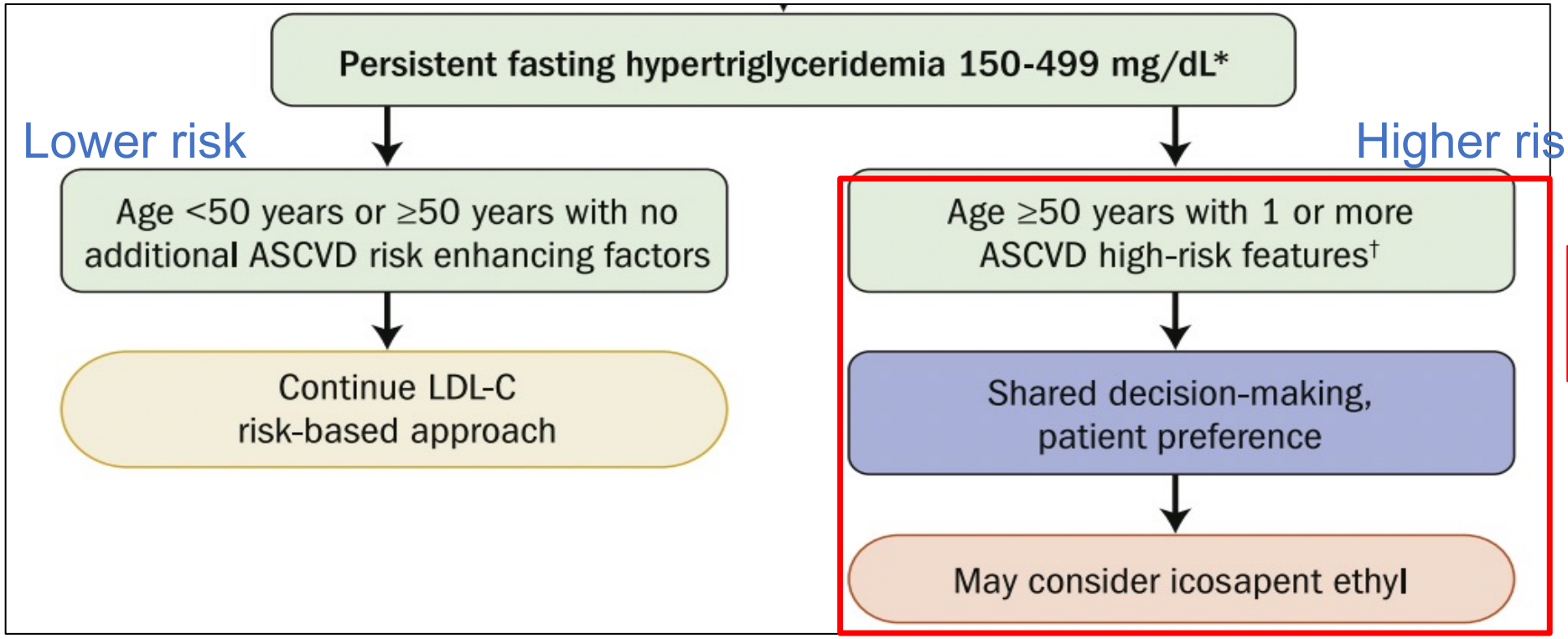
  - B. Add niacin extended release 2 g
  - C. Add bedtime insulin
  - D. Add ezetimibe 10 mg
  - E. Add bile acid resin

Adults Age ≥50 years with Diabetes, TG (150-499)



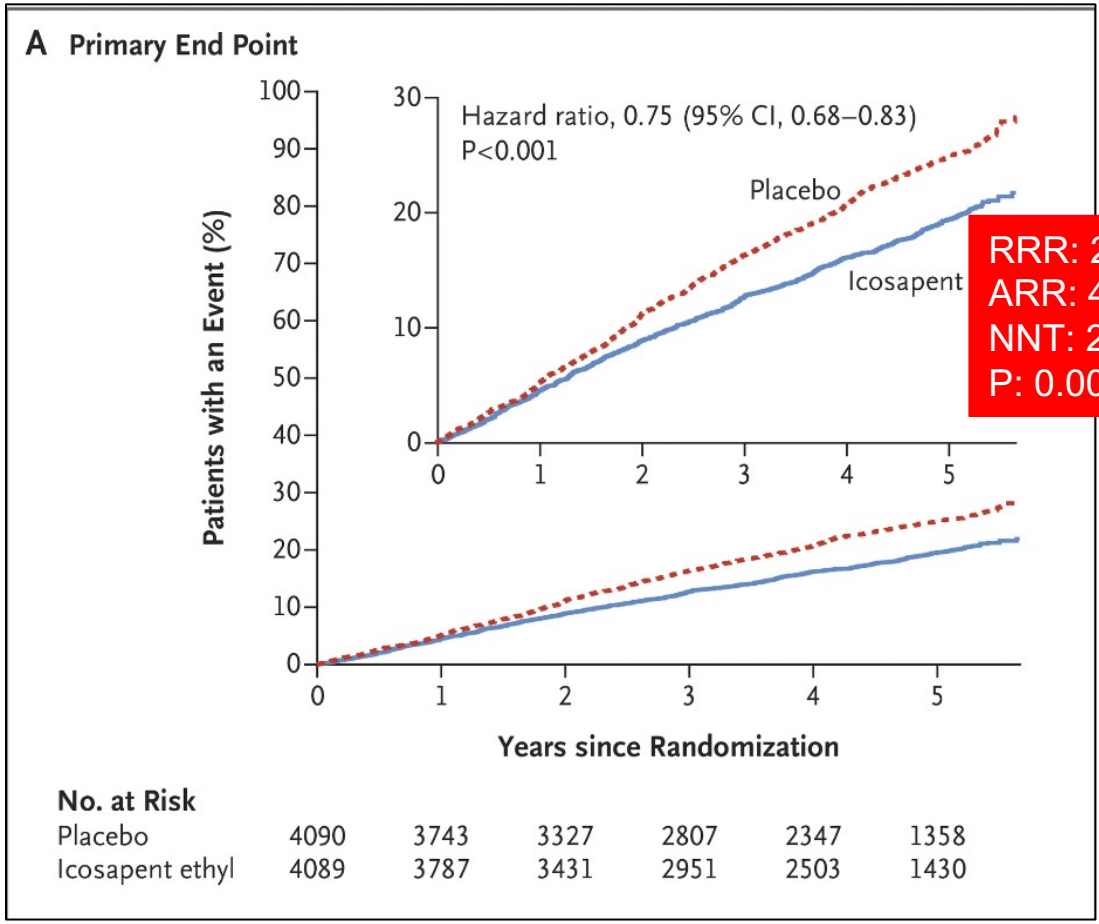
Optimize LDL-C, then add IPE

J Am Coll Cardiol. 2021;78(9):960-993

REDUCE-IT

- Patients with ASCVD or T2DM (w/ASCVD risk factor) and TG >135 to 499 mg/dL
- N=8179
- 4.9 years median follow-up
- 94% on moderate or high statins

- **Primary end point:** a composite of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or unstable angina.



RRR: 24.8%
ARR: 4.8%
NNT: 21
P: 0.00000001

Bhatt D, et al. NEJM 2019. doi:10.1056/NEJMoa1812792

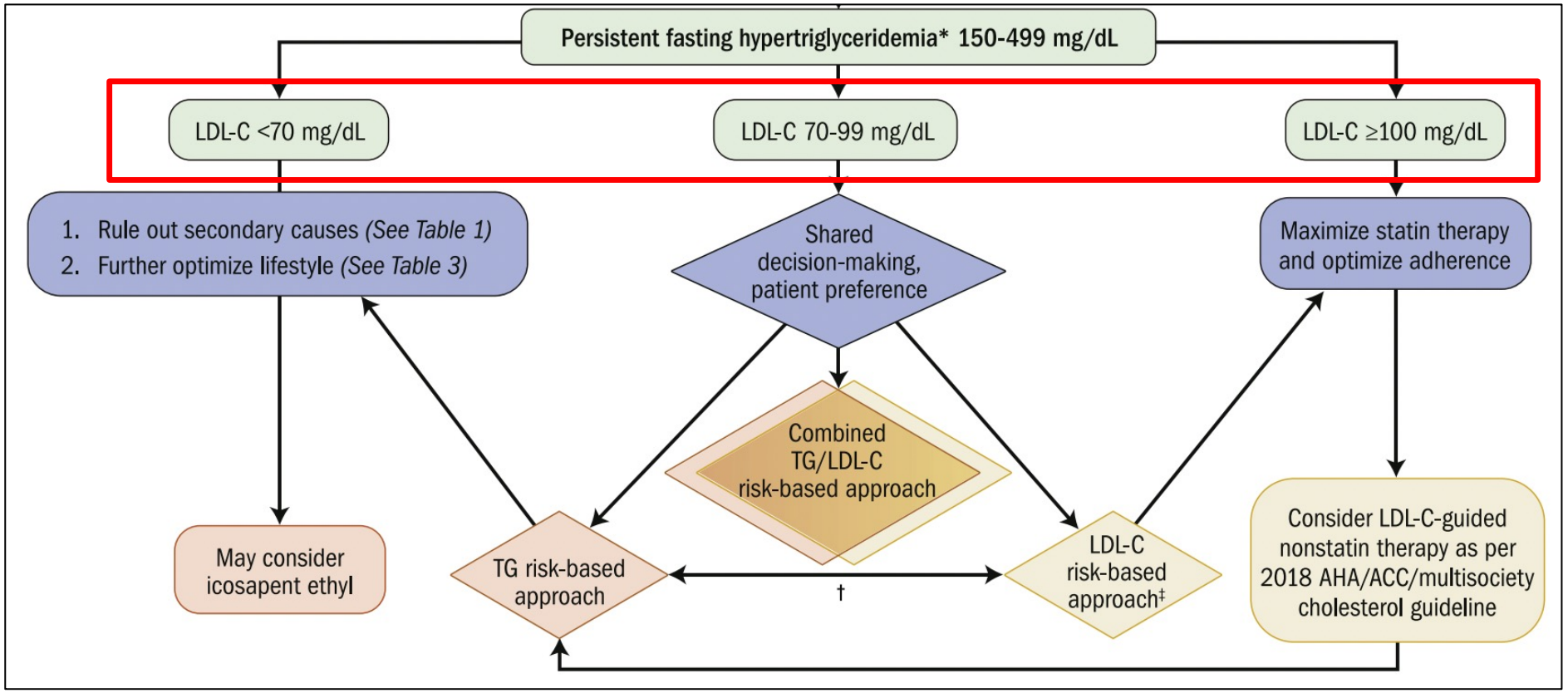
Comparison between REDUCE-IT and ongoing outcomes trials in patients with HTG

	REDUCE-IT	STRENGTH*	PROMINENT*
Agent Dose	EPA (EE) 4 g/d	EPA+DHA (FFA) 4 g/d	SPPARMα – Pemafibrate 0.2 mg bid
N	8179	Estimated 13,000	Estimated 10,000
Age	≥45 years	≥18 years	≥18 years
Risk Profile	CVD (70%) or ↑CVD risk (30%)	CVD (50% ↑CVD risk (5	2DM only CVD (2/3) or CVD risk (1/3)
Follow-up	4.9 year median followup	3–5 years (planne	5 years (planned)
Statin Use	100% (at LDL-C goal)	100% (at LDL-C goal	Moderate- / high-intensity or LDL <70 mg/dL
Primary Endpoint	Expanded MACE	Expanded MA	xpanded MACE
Entry TG Entry HDL-C	150–499 mg/dL N/A	200–499 m <40 mg/dL M, < g/dL W	499 mg/dL 0 mg/dL

*Locations: International sites; Statistics: Powered for 15% RRR. REDUCE-IT http://www.clinicaltrials.gov; REDUCE-IT: NCT01492361; STRENGTH: NCT02104817; PROMINENT: NCT03071692.

Park, J.E. et al. *Curr Cardiovasc Risk Rep* **13**, 6 (2019).

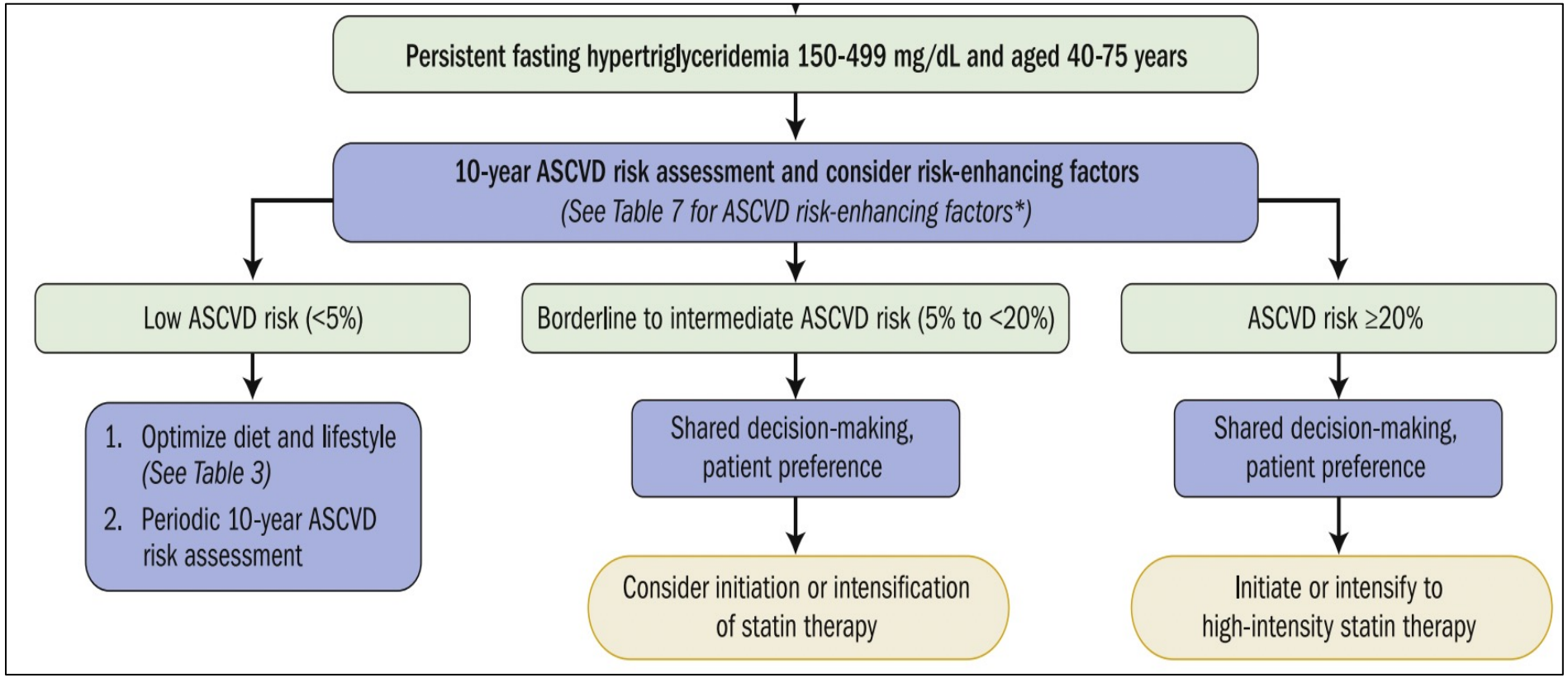
Adults With ASCVD and TG (150-500 mg/dL)



Optimize LDL-C, then add IPE

J Am Coll Cardiol. 2021;78(9):960-993

No DM or ASCVD, TG 150-499 mg/dL (Adults ≥20 years)



1- Estimate ASCVD risk
2- +/- statins

J Am Coll Cardiol. 2021;78(9):960-993

Questions?

Case Studies

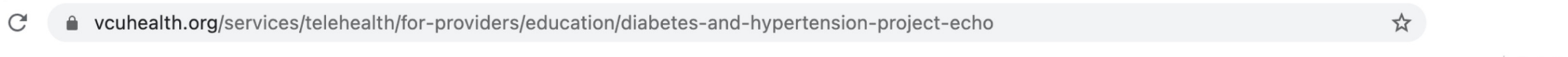
- Anyone can submit cases: www.vcuhealth.org/echodmhtn
- Receive feedback from participants and content experts
- Earn **$150** for submitting and presenting

Provide Feedback

www.vcuhealth.org/echodmhtn

- Feedback
  - Overall feedback related to session content and flow?
  - Ideas for guest speakers?

Access Your Evaluation



For Providers

- Education −
  - **Diabetes and Hypertension Project ECHO** −
    - Our Team
    - Curriculum
    - Claiming CE Credit
    - Contact Us
  - VCU Nursing Home ECHO +
  - VCU Health Palliative Care ECHO +
  - Virginia Opioid Addiction ECHO +
  - Virginia Sickle Cell Disease ECHO +

Diabetes and Hypertension Project ECHO

Welcome to the Diabetes and Hypertension Extension for Community Health Outcomes or ECHO, a virtual network of multidisciplinary diabetes and hypertension experts. An ECHO model connects professionals with each other in real-time collaborative virtual sessions on Zoom. Participants present de-identified cases to one another, share resources, connect to each other, and grow in their expertise. This ECHO will address practice level issues and solutions related to managing complex patients with difficult to control diabetes and hypertension. Register now for an ECHO Session!

Network, Participate and Present

- Engage in a collaborative community with your peers.
- Listen, learn and discuss informational and case presentations in real-time.
- Take the opportunity to submit your de-identified case study for feedback from a team of specialists for diabetes and hypertension.
- Provide valuable feedback.
- Claim CE credit by texting in attendance.

Benefits

VCU Diabetes & Hypertension Project ECHO Clinics

2nd Thursdays — 12 p.m. to 1 p.m.

Mark Your Calendars — Upcoming Sessions

June 8, 2023 - Lightning Round - submit your topics

Please register at www.vcuhealth.org/echodmhtn

Thank you for coming!

Text **29388 - 28189** to **804-625-4041** for CE credit

Reminder: Mute and Unmute to talk
Press *6 for phone audio
Use chat function for questions