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Understanding Genetic Lipid Abnormalities, Screening, and Treatments

Seth S. Martin, MD, MHS, FACC, FAHA, FASPC
Professor of Medicine, Division of Cardiology
Barker Firm Faculty Leader, Osler Medical Residency
Director, Ciccarone Advanced Lipid Disorders Clinic
Director, Digital Health Lab & mTECH Center

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Disclosures

- Partial to the Barker Firm
- I do not intend to reference unlabeled/unapproved uses of drugs or products
- Johns Hopkins University previously filed a patent for the Martin/Hopkins LDL-C calculation and has since abandoned the patent to enable widespread adoption
- Co-Founder, Corrie Health
- Philanthropic support from David & June Trone Foundation, Pollin Digital Innovation Fund, PJ Schafer Cardiovascular Research Fund, Sandra and Larry Small
- Research support from the American Heart Association (20SFRN35380046, 20SFRN35490003, COVID19-811000, AHA878924, AHA882415, AHA946222), PCORI (ME-2019C1-15328, IHS-2021C3-24147), NIH (P01 HL108800, R01AG071032), Aetna Foundation, Maryland Innovation Initiative, Amgen, Google, Apple, and Merck
- Consulting for Amgen, AstraZeneca, BMS, Chroma, HeartFlow, Sanofi, Premier, Merck, NewAmsterdam, Novo Nordisk, Novartis, iHealth, Kaneka, Verve Therapeutics

Learning Objectives

1) Discuss the role of genetic testing in screening for lipid abnormalities in individuals and families
2) Review lipid treatment considerations including when to start lipid lowering therapies and how to apply additional screening tools such as genetic testing or coronary artery calcium (CAC).
3) Examine the impact of Lp(a) on CVD risk and treatment
4) Explore the future of cardiovascular risk management and the role of the interdisciplinary team

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What is Precision Medicine?

Precision medicine:

- Is based on you as an individual
- Takes into account your environment (where you live), lifestyle (what you do), and your family health history and genetic makeup
- Gives health care providers the information they need to make customized recommendations for people of different backgrounds, ages, and regions
- Helps you get better information about how to be healthier
- Reduces health care costs by matching the right person with the right treatment the first time

Precision medicine tools include genetics, biomarkers, imaging, big data, digital health, AI, and machine learning.

Precision Medicine Initiative (PMI) Working Group
Report to the Advisory Committee to the Director, NIH

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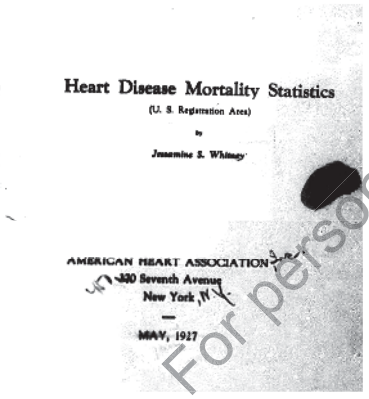
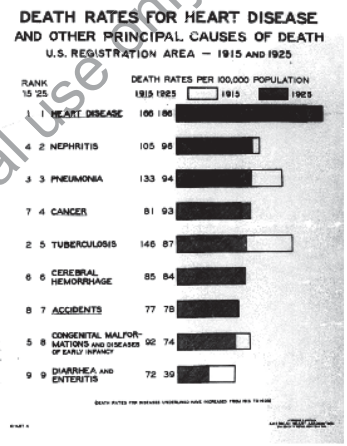
Heart Disease: A Stubborn Problem





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CVD Persists as the Leading Cause of Death in the US and Globally

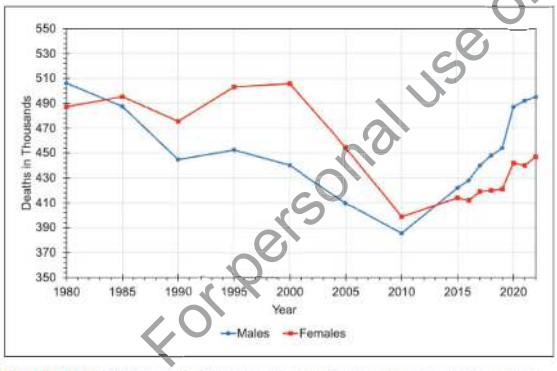
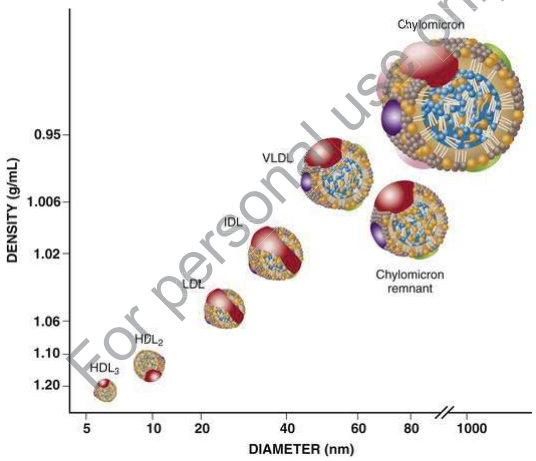


Chart 14-9. CVD mortality trends for US males and females, 1980 to 2022.

Martin SS et al. Circulation 2025;151(8):e41-e660.

The Major Lipoproteins



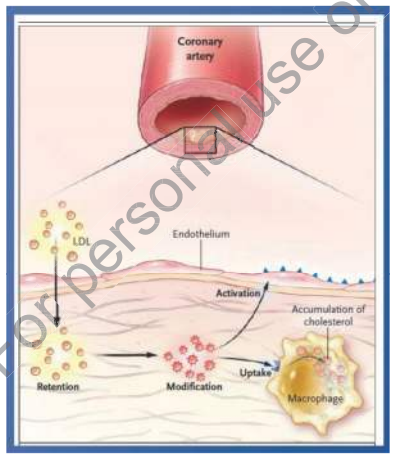
Genest J, Libby P. Lipoprotein Disorders and Cardiovascular Disease.

NLA Lipid Measurement Recommendations

Laboratory Measurement and Reporting		
LDL-C measurement is recommended for screening	I	B-NR
LDL-C measurement is recommended on lipid therapy	I	B-NR
Non-HDL-C measurement is recommended for screening	I	B-NR
Non-HDL-C measurement is recommended on lipid therapy	I	B-NR
Apolipoprotein B measurement may be reasonable for initial evaluation	IIb	B-NR
Apolipoprotein B measurement is reasonable on lipid therapy	IIa	B-NR
Apolipoprotein B measurement is recommended to facilitate diagnosis of Familial Dysbetalipoproteinemia and Familial Combined Hyperlipidemia	IIa	B-NR
Lipoprotein (a) measurement is reasonable for initial evaluation in those with premature ASCVD, family history of premature ASCVD or of elevated Lp(a), history of LDL-C >190 mg/dL or suspected FH, or those with very high ASCVD risk.	IIa	B-NR

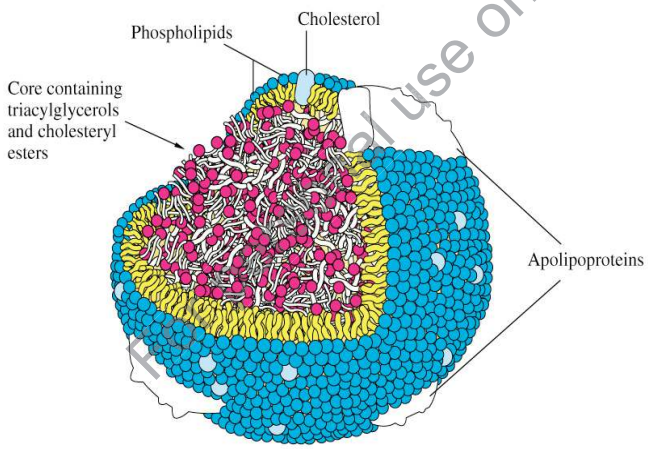
J Clin Lipidol. 2021;15(5):629-648.

Central Role of LDL in Atherosclerosis



N Engl J Med 1999;340:115-126

Structure of Lipoproteins



http://apbrwww5.apsu.edu/thompsonj/Anatomy%20&%20Physiology/2020/2020%20Exam%20Reviews/Exam%201/CH18%20Lipoproteins.htm

Composition of Lipoproteins

Lipoprotein class	Density (g mL^{-1})	Diameter (nm)	% Protein	% Cholesterol	% Phospholipid	% Triglycerides
HDL	1.063–1.210	5–15	33	30	29	8
LDL	1.019–1.063	18–28	25	50	21	4
IDL	1.006–1.019	25–50	18	29	22	31
VLDL	0.95–1.006	30–80	10	22	18	50
Chylomicrons	<0.95	100–1000	<2	8	7	84

http://www.learn.ppdictionary.com/exercise_and_lipoproteins3.htm

Classical Dyslipidemias

Fredrickson-Levy-Lees Classification

- Type I: Chylomicrons
- Type IIa: LDL
- Type IIb: LDL + VLDL
- Type III: VLDL + Chylomicron remnants
- Type IV: VLDL
- Type V: VLDL and Chylomicrons

Scientific Statement

Genetic testing in dyslipidemia: A scientific statement from the National Lipid Association

Emily E. Brown, MGC, CGC, Amy C. Sturm, MS, CGC, Marina Cuchel, MD, PhD, Lynne T. Braun, PhD, FNLA, P. Barton Duell, MD, FNLA, James A. Underberg, MD, MS, FACP, FNLA, Terry A. Jacobson, MD, FNLA, Robert A. Hegele, MD, FRCPC, FACP*

Table 2 Potential indications for genetic testing in dyslipidemias

- Strong clinical suspicion of a genetic dyslipidemia.
- Strong family history of dyslipidemia or its complications.
- Presence of related syndromic features (see Table 1).
- Evidence that testing might change management.
- Available and effective early interventions exist.
- Eligibility for new or investigational drugs.
- Patient preference.
- Family planning.

Genetic Testing in Dyslipidemia

Table 3 Clinical impact of genetic diagnosis in selected monogenic dyslipidemias

Condition	Causative gene(s)	Management effect
Familial hypercholesterolemia	*LDLR, APOB, PCSK9* heterozygous FH: single pathogenic variants; homozygous FH: biallelic pathogenic variants in the above and *LDLRAP1*	Cascade screening May influence insurance eligibility for inhibitors of PCSK9 eg, evolocumab (Repatha) or alirocumab (Praluent) or lomitapide (Juxtapid—inhibitor of microsomal triglyceride transfer protein) Treatment selection: eg, in homozygous FH, a genetic diagnosis may support the need for apheresis; also in homozygous FH having at least one LDL receptor allele with retained function predicts response to PCSK9 inhibition.
Familial chylomicronemia	*LPL, APOC2, APOA5, LMF1, GPIHBP1* biallelic pathogenic variants	Volanesorsen (Waylivra—antisense inhibitor of apolipoprotein C-III) available in Europe.
Sitosterolemia	*ABCG5/ABCG8* biallelic pathogenic variants	Reduced dietary sterol intake plus ezetimibe to prevent ASCVD
Cerebrotendinous xanthomatosis	*CYP27A1* biallelic pathogenic variants	Chenodeoxycholic acid to prevent multiple progressive neurological symptoms.
Cholesterol ester storage disease (Wolman syndrome; lysosomal acid lipase deficiency)	*LIPA* biallelic pathogenic variants	Sebelipase alfa therapy (Kanuma—intravenous enzyme replacement for lysosomal acid lipase).
Abetalipoproteinemia or homozygous familial hypobetalipoproteinemia	*MTTP* or *APOB* biallelic pathogenic variants, respectively	Can help confirm a clinical diagnosis and provides justification for lifelong reduction in dietary fat intake plus high dose fat soluble vitamins.

Genetic Testing Recommendations

Table 4 Recommendations for genetic testing in patients with dyslipidemia

Recommendation	Class (strength)	Level of evidence
Principles of genetic testing—counseling		
1. Before ordering a genetic test, it **is recommended** to obtain informed consent and counsel the patient about the benefits and risks of genetic testing.	I	C-EO
2. After a positive genetic test result, it **is reasonable** to provide genetic counseling to patients and their family through either a skilled clinician or a certified genetic counselor.	IIa	C-EO
3. After a negative genetic test result, it still **may be reasonable** to provide genetic counseling to a patient through either a skilled clinician or a certified genetic counselor.	IIb	C-EO
Genetic testing in patients with dyslipidemia		
4. Direct-to-consumer genetic tests are **not recommended** or appropriate for clinical use in dyslipidemia.	III (No benefit)	C-EO
5. Polygenic scores for dyslipidemias are not yet standardized and are currently **not recommended** or appropriate for clinical use in dyslipidemia.	III	C-EO
Genetic testing for monogenic lipid disorders		
6. Genetic testing **is reasonable** when heterozygous familial hypercholesterolemia is suspected but not definitively diagnosed based on clinical criteria alone.	IIa	B-NR
7. Cascade screening for FH either by lipid profile or genetic testing **is recommended** in all first-degree relatives (children and siblings) of an individual who has tested genetically positive for FH.	I	C-EO
8. Genetic testing for other monogenic lipid disorders (Table 3) **is reasonable** when an accurate diagnosis may affect treatment choice or outcomes.	IIa	C-LD
9. Genetic testing in severe hypertriglyceridemia (SHTG) is generally **not indicated** because most SHTG is polygenic or multifactorial.	III	C-EO
10. Genetic testing in severe hypertriglyceridemia **may be reasonable** if a monogenic disorder is suspected clinically such as familial chylomicronemia syndrome (eg, young age, failure to thrive, relapsing pancreatitis, and absence of secondary causes).	IIb	C-EO

EO, expert opinion; NR, nonrandomized; LD, limited data.

Hopkins Experience in Genetic Testing for FH

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Incorporation of genetic testing significantly increases the number of individuals diagnosed with familial hypercholesterolemia

Emily E. Brown, MGC, CGC*, Kathleen H. Byrne, CRNP,
Dorothy M. Davis, PMC, MSN, RN, Rebecca McClellan, MGC, CGC,
Thorsten Leucker, MD, PhD, Steven R. Jones, MD, Seth S. Martin, MD, MHS

Emily Brown
(Genetic Counselor)

Scientific Statement

Genetic testing in dyslipidemia: A scientific statement from the National Lipid Association

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James A. Underberg, MD, MS, FACP, FNLA, Terry A. Jacobson, MD, FNLA,
Robert A. Hegele, MD, FRCPC, FACP*

Case: T.A.

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History

- 48-year-old African American woman hospitalized at JHH, then following up in cardiology clinic
- MI s/p single-vessel PCI 5 years ago
- Recent Type 1 NSTEMI - multivessel disease s/p CABG
- Risk factor profile: hyperlipidemia*, diabetes mellitus, hypertension, stage 3 CKD, rheumatoid arthritis

- **Family history**
  - Father had MI at age 57 and hyperlipidemia
  - Brother died from an MI at age 50; had hyperlipidemia
  - Paternal uncle died of an MI in his 40s and had hyperlipidemia
- **Physical Exam**
  - Notable for bilateral corneal arcus and thickened Achilles tendons

*Untreated lipids: TC 368, TG 90, HDL-C 43, LDL-C 304 mg/dL → (Atorva 80 / Ezetimibe + cardiac rehab) → LDL-C 127 → (Lipid Clinic) → PCSK9i → LDL-C 46

Familial Hypercholesterolemia (FH)

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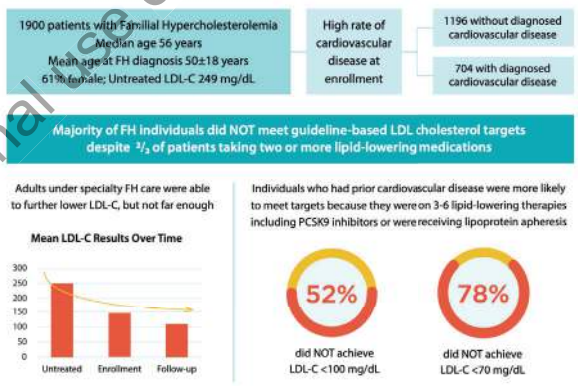
- Approximately 1 in 250 people has definite/probable FH
- Autosomal dominant
- 20-fold increased CVD risk
- FH phenotype (LDL-C ≥190 mg/dL) accelerates CHD risk by decades
- Underdiagnosed (3 in 10) and undertreated

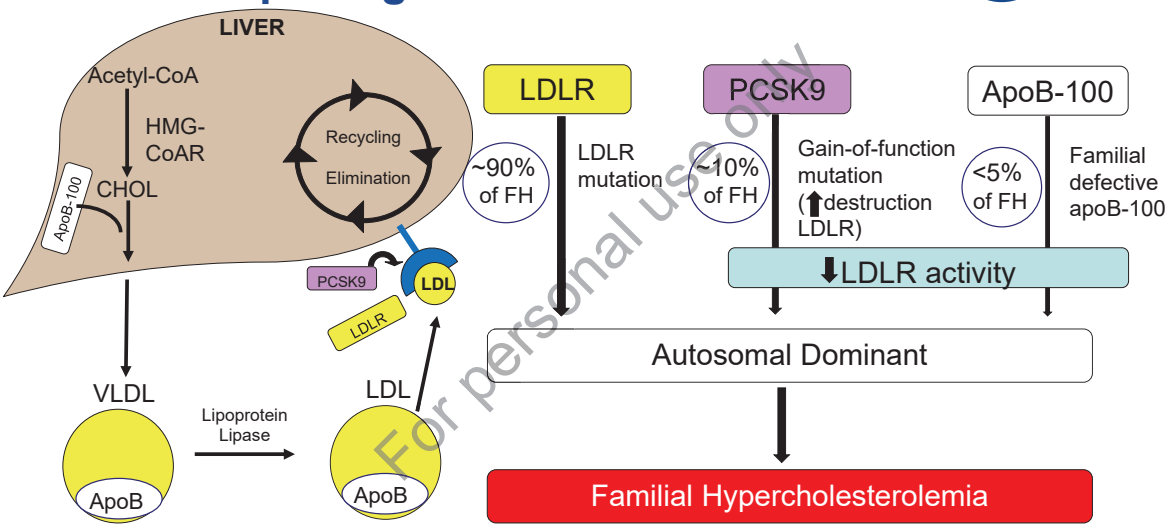
CASCADE FH Registry



Singh A et al. *J Am Coll Cardiol*. 2019;73(19):2439-2450.
Virani SS, et al. *Circulation*. 2020;141(9):139-596.

Atherosclerosis. 2019 Oct;289:85-93.

Molecular pathogenesis of FH



Clinical Schema for FH Diagnosis

US MedPed Criteria

Dutch Lipid Clinic Criteria

British Simon Broome

Table 3. North American and European Clinical Schema for Diagnosis of FH[a]

US MedPed Program Diagnostic Criteria for Probable Heterozygous FH[5,6]

Age	First-Degree Relative with FH	Second-Degree Relative with FH	Third-Degree relative with FH	General Population
	Total Cholesterol Level (mg/dL)			
<20	220	230	240	270
20-29	240	250	260	290
30-39	270	280	290	340
≥40	290	300	310	360

Dutch Lipid Clinic Network Diagnostic Criteria for FH (Points)[5,6]

Criteria	Points	
First-degree relative with premature CHD defined as men <55-year-old and women <60-year-old, or first-degree relative with LDL-C ≥190 mg/dL	1	*Definite FH:* >8 points *Probable FH:* 6-8 points *Possible FH:* 3-5 points
Any patient with premature CHD	2	
Any patient with premature cerebrovascular disease or PVD	1	
Tendon Xanthomas	6	
Arcus cornealis before 45 years of age	4	
LDL-C ≥330 mg/dL	8	
LDL-C 250-329 mg/dL	5	
LDL-C 190-249 mg/dL	3	
LDL-C 155-189 mg/dL	1	
Positive Genetic Test Result (*LDLR, PCSK9, APOB*)	8	

British Simon Broome FH Register Diagnostic Criteria (Letter Grading)[5,6]

Criteria	Grade	
Total cholesterol >290 mg/dL in adults or >260 mg/dL in children aged <16yo, or LDL-C >190 mg/dL in adults or LDL-C >155 mg/dL in children<16yo.	A	*Definite FH:* A and B *or* C *Probable FH:* A and D *or* A and E
Tendon xanthoma in the patient or first-degree relative	B	
Positive DNA testing	C	
Family history of premature myocardial infarction defined as before age 50 in a second-degree relative or before age 60 in a first-degree relative	D	
Family history of total cholesterol >290 mg/dL in a first-degree or second-degree relative or >260 mg/dL in a child or sibling aged <16 years old	E	

ASCVD risk from high LDL-C is a function of cumulative exposure

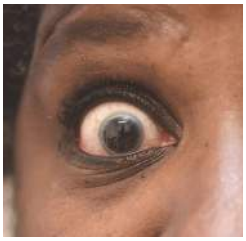
LDL-C x Years = LDL-Years

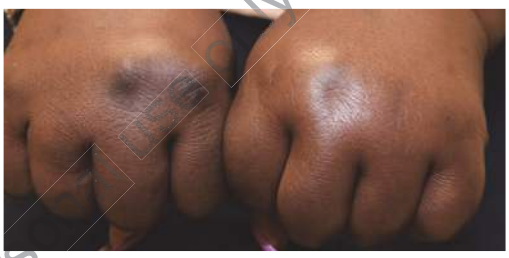
like with smoking…

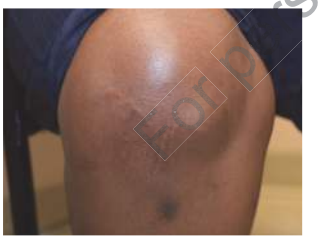
Packs per day x Years = Pack-Years

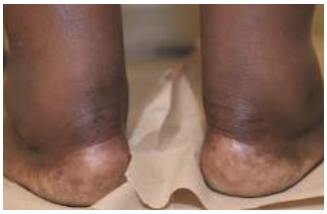
Patricia's Story

Physical Exam Findings





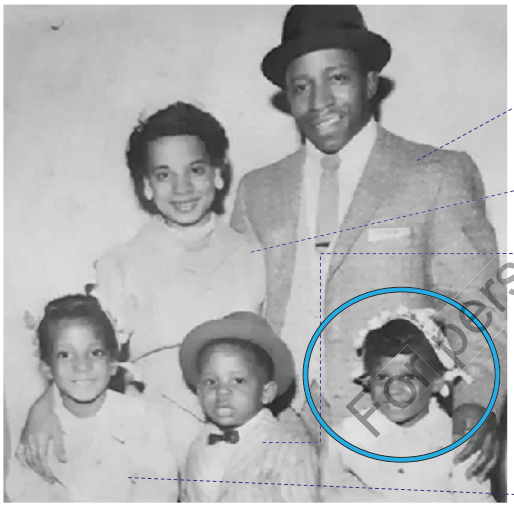




Early Onset of Hypercholesterolemia

Patient
Age 11
Total Cholesterol > 1000 mg/dL

Family History of Hypercholesterolemia



Father
hypercholesterolemia, arcus, myocardial infarction age 60 years old, hypertension

Mother
hypercholesterolemia, hypertension

Brother
hypercholesterolemia

Patient
Age 11
Total Cholesterol > 1000 mg/dL

Sister
hypercholesterolemia

Challenges Living With HoFH

- **Physical Appearance and Disfigurement**
  - Xanthomas
  - Surgical resection of xanthomas at age 12 y.o.
- **Lack of Family and Social Support**
  - Parental abuse due to her illness
  - Limited dietary support
- **Mental Health Conditions**
  - Suicidal ideation as a teenager
  - Anxiety

Patricia became a ward of state at age 13, and grew up at boarding schools

LDL-C Lowering Therapies in 1960s: Surgery

Ten Years Clinical Experience with Partial Ileal Bypass in Management of the Hyperlipidemias

ANNALS OF SURGERY
A Monthly Review of Surgical Science Since 1885

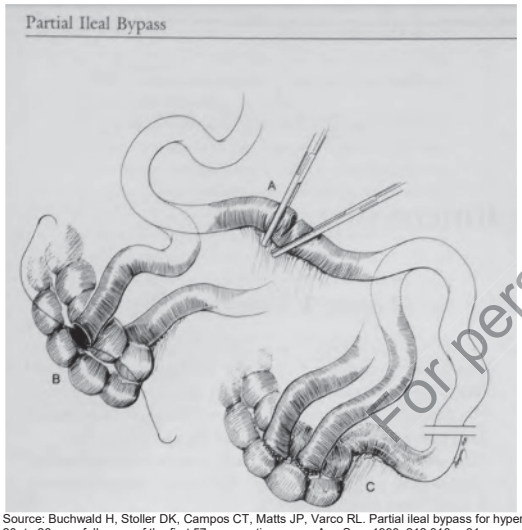
HENRY BUCHWALD, M.D., Ph.D., RICHARD B. MOORE, M.D., RICHARD L. VARCO, M.D., Ph.D.

"It is concluded that partial ileal bypass is the **most effective means for lipid reduction available today**; it is obligatory in its actions, safe, and associated with minimal side effects."

-1974, Surgeon Dr. Henry Buchwald

Ann Surg. 1974 Oct; 180(4): 384–392.Ten Years Clinical Experience with Partial Ileal Bypass in Management of the Hyperlipidemias. doi: 10.1097/00000658-197410000-00002

Partial ileal bypass at age 12 years old



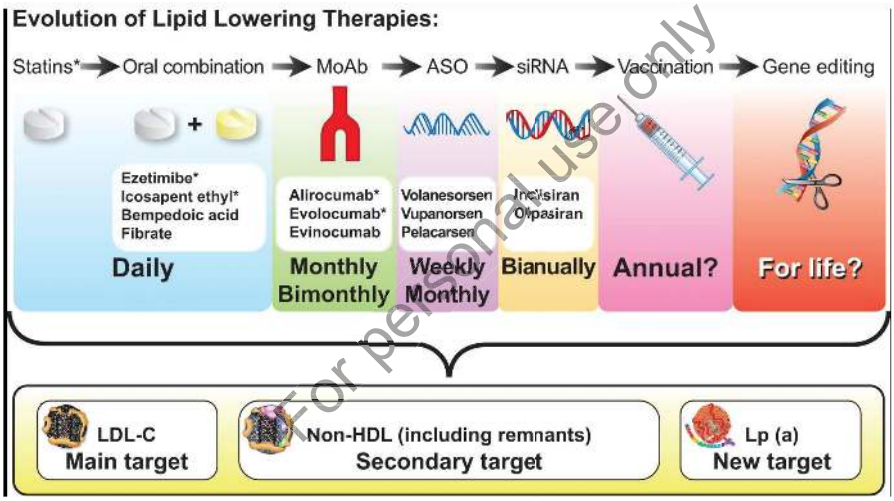
Partial ileal bypass surgical procedure for Hyperlipemia management
1963

Post-Op Results

Total Cholesterol:
- **608 mg/dL**

Source: Buchwald H, Stoller DK, Campos CT, Matts JP, Varco RL. Partial ileal bypass for hypercholesterolemia: 20- to 26-year follow-up of the first 57 consecutive cases. Ann Surg 1990; 212:318— 31.

Evolution of Lipid Lowering Therapies



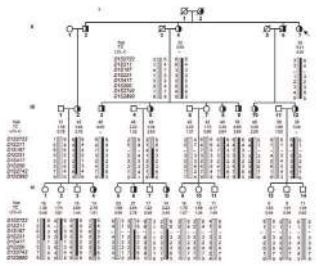
Source: The dawn of a new era of targeted lipid-lowering therapies. *European Heart Journal*, Volume 43, Issue 34, 7 September 2022

Mutations in *PCSK9* cause autosomal dominant hypercholesterolemia

Marianne Abifadel[1,2], Mathilde Varret[1], Jean-Pierre Rabès[1,3], Delphine Allard[1], Khadija Ouguerram[4], Martine Devillers[1], Corinne Cruaud[5], Suzanne Benjannet[6], Louise Wickham[6], Danièle Erlich[1], Aurélie Derré[1], Ludovic Villéger[1], Michel Farnier[7], Isabel Beucler[8], Eric Bruckert[9], Jean Chambaz[10], Bernard Chanu[11], Jean-Michel Lecerf[12], Gerald Luc[12], Philippe Moulin[13], Jean Weissenbach[5], Annick Prat[6], Michel Krempf[4], Claudine Junien[1,3], Nabil G Seidah[6] & Catherine Boileau[1,3]

Autosomal dominant hypercholesterolemia (ADH; OMIM144400), a risk factor for coronary heart disease, is characterized by an increase in low-density lipoprotein cholesterol levels that is associated with mutations in the genes *LDLR* (encoding low-density lipoprotein receptor) or *APOB* (encoding apolipoprotein B). We mapped a third locus associated with ADH, *HCHOLA3* at 1p32, and now report two mutations in the gene *PCSK9* (encoding proprotein convertase subtilisin/kexin type 9) that cause ADH. *PCSK9* encodes NARC-1 (neural apoptosis regulated convertase), a newly identified human subtilase that is highly expressed in the liver and contributes to cholesterol homeostasis.

Pedigree in French family with xanthomas, premature CVD, and PCSK9 mutation



[redacted]

Major Trial Evidence for PCSK9i

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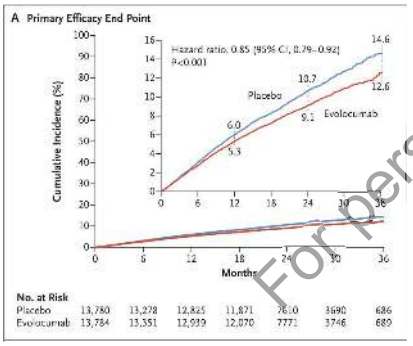
FOURIER

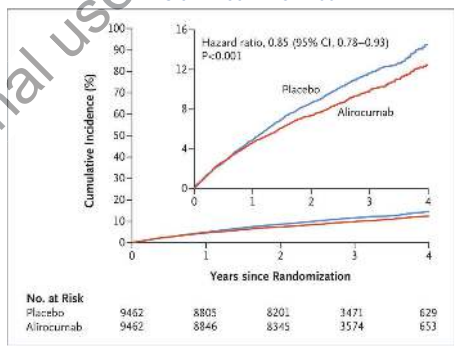
27,564 pts w/ ASCVD
median 2.2yr
LDL-C 92 → 30



N Engl J Med 2017; 376:1713-22

ODYSSEY OUTCOMES

18,924 pts w/ ACS
median 2.8yr
LDL-C 92 → 30 → 48 → 66



N Engl J Med 2018; 379:2097-2107

Inclisiran Safety & Efficacy

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Wright, R.S. et al. J Am Coll Cardiol. 2021;77(9):1182-93.

How low can we go?

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"Thanks for all your help with him. It seems that the Repatha is doing a great job.

I had a question...is the LDL now too low? Is he on any other lipid lowering drugs the dose of which can be modified? 23 seems to low. What are your thoughts"

"Patient familiar to you, w/ CAD… was started on Repatha

His last LDL could not be calculated, lab stated it was -9

Should patient continue with Repatha?"

Big Data to Precision in LDL-C Calculation

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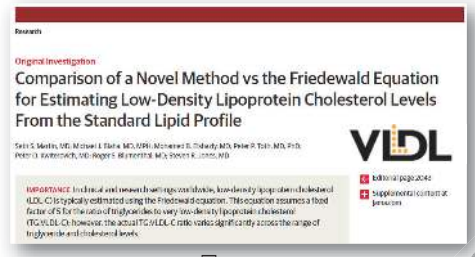
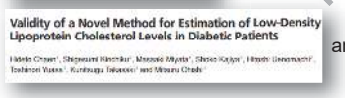


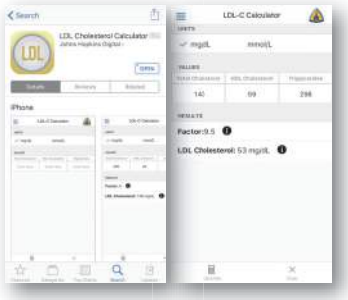
Externally validated around the globe



and more

Endorsed by guidelines and adopted in practice via:

- Lab IT integration
- ldlcalculator.com
- Apple iOS and Android mobile apps



For personal use only

Missed Opportunities for Treatment Intensification due to LDL-C Underestimation

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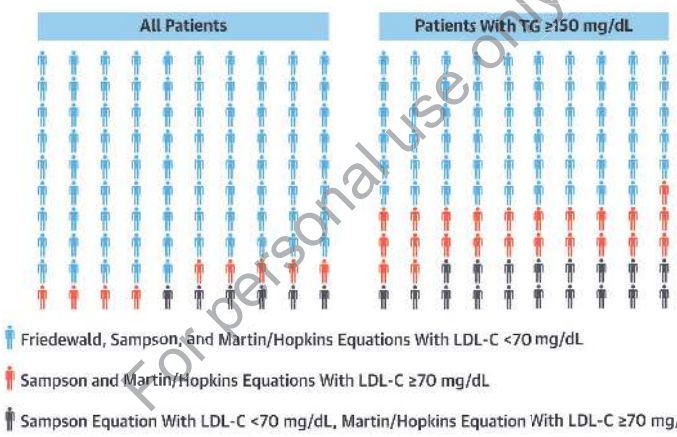

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Sajja, A. et al. J Am Coll Cardiol. 2022;79(6):530–541

Expert Recommendations Around the Globe

Circulation

American Heart Association.

CHOLESTEROL CLINICAL PRACTICE GUIDELINES

2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol

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

AMERICAN COLLEGE of CARDIOLOGY.

2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk

NATIONAL LIPID ASSOCIATION

Lipid measurements in the management of cardiovascular diseases: Practical recommendations a scientific statement from the national lipid association writing group

EFLM Consensus Paper

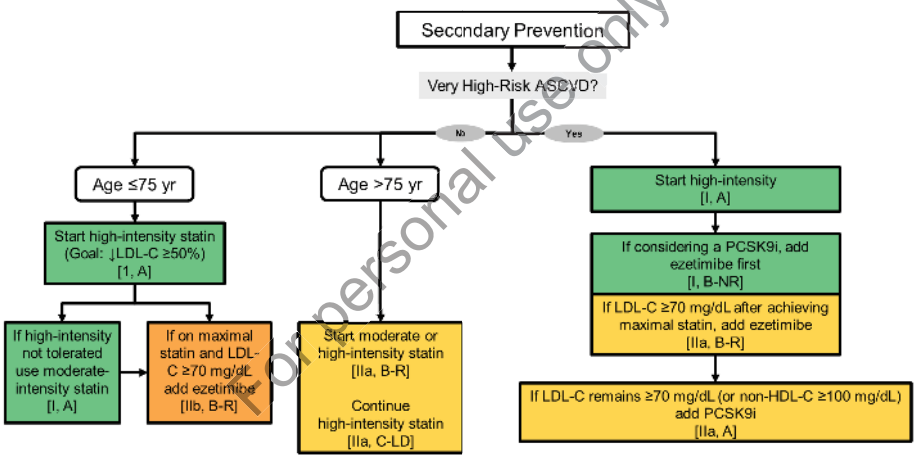
Quantifying atherogenic lipoproteins for lipid-lowering strategies: consensus-based recommendations from EAS and EFLM

Special Article

Positioning about the Flexibility of Fasting for Lipid Profiling

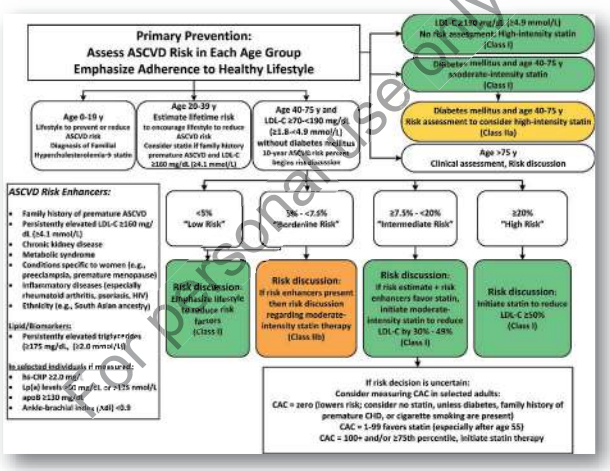
PoLA/CFPiP/PCS/PSLD/PSD/PSH guidelines on diagnosis and therapy of lipid disorders in Poland 2021

2018 AHA/ACC Cholesterol Guideline



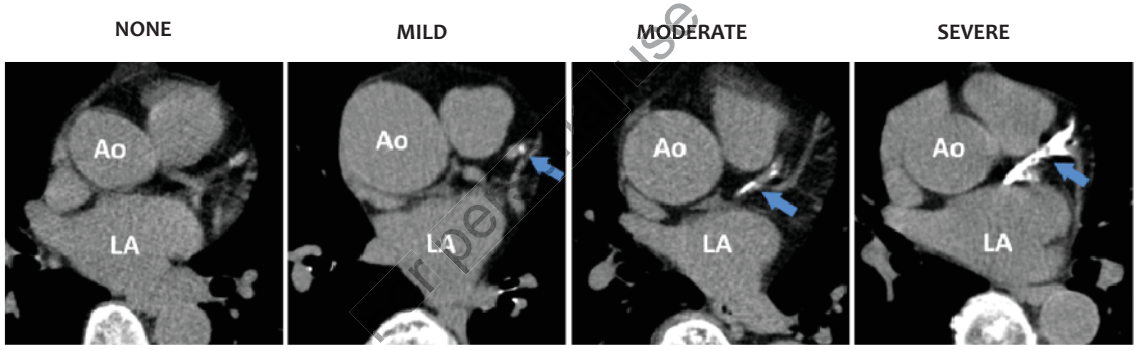
Grundy SM, et al. *J Am Coll Cardiol.* 2019;73(24):e285-e350.

Primary Prevention



Grundy SM, et al. *J Am Coll Cardiol.* 2019;73(24):e285-e350.

Visual Assessment of Incidental CAC



Slide courtesy of Dr. Jelani Grant

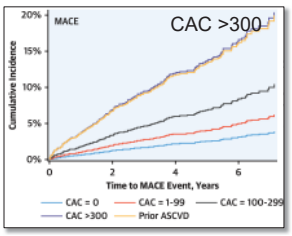
Guideline Recommendations for Reporting Incidental CAC

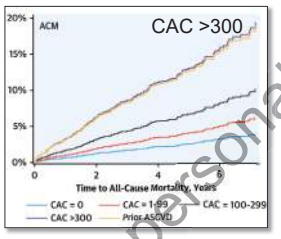
Radiology or Cardiology Society	Recommendation
2016 Society of Cardiovascular Computed Tomography/ Society of Thoracic Radiology guidelines	Report moderate/severe CAC on all patients undergoing LSCT
2019 American College of Cardiology/American Heart Association special report on risk assessment	Findings of moderate or more CAC suggest a CAC score of ≥ 100
2018 American College of Radiology incidental findings committee	• Incidental CAC should be reported when likely to affect management • CAC can be reported using either the Agatston scoring system or the visual method
2021 National Lipid Association scientific statement	• A qualitative indication of CAC severity (mild, moderate, heavy/severe) should be reported on all thoracic CTs • For those with mild calcification, a dedicated CAC score is useful to aid in clinical decision making • Moderate or severe CAC generally correlates with a CAC score of ≥ 100, a guideline-based indication for statin benefit

Slide courtesy of Dr. Jelani Grant

Hecht et al. J Cardiovasc Comput Tomogr, 11 (2) (2017), pp. 157-168; Jones DL et al. J Am Coll Cardiol 2019;73:3153-67; Munden, RF et al. J Am Coll Radiol, 15 (8) (2018), pp. 1087-1096; Orringer CE et al. J Clin Lipidol 2021 doi.org/10.1016/j.jacl.2020.12.005

When does high CAC equate to secondary prevention?



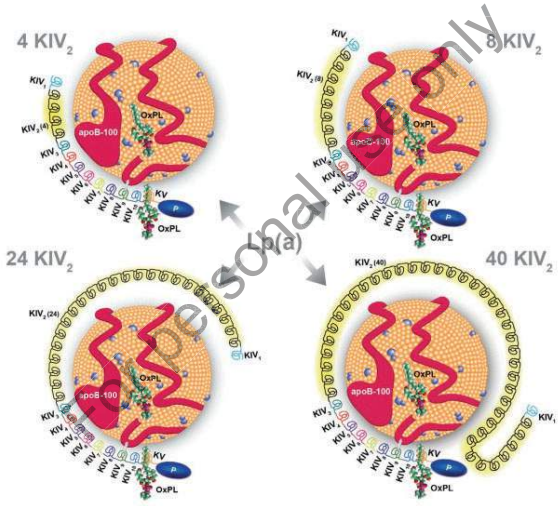


		Adjusted*		
Risk Category	Outcome	HR	95% CI	P Value
Prior ASCVD	MACE	Ref.	NA	NA
CAC = 0		0.31	0.22-0.45	<0.001
CAC 1-99		0.41	0.30-0.57	<0.001
CAC 100-299		0.59	0.42-0.84	0.003
CAC >300		0.94	0.72-1.24	0.683

- CONFIRM registry: 4,511 individuals without ASCVD compared to those with known ASCVD with CAC on CCTA
- CAC > 300 associated with similar risk to having prior ASCVD event, those with CAC < 300 had significantly lower risk of ASCVD

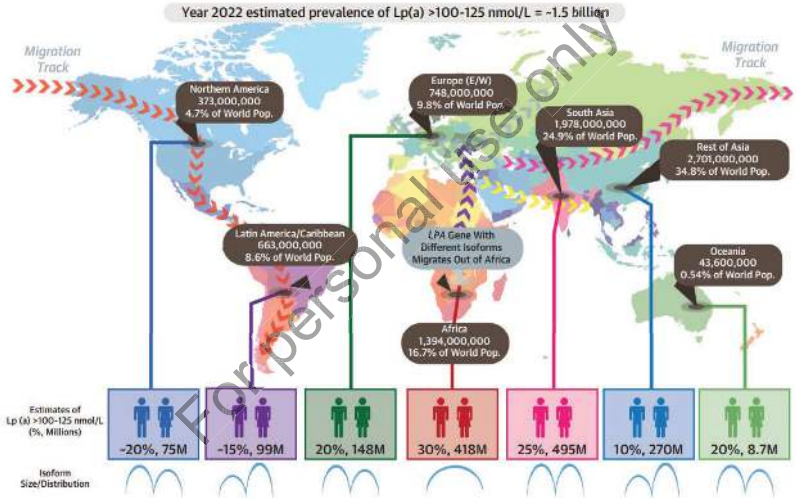
Budoff et al, 2023. *JACC: Imaging*. 16 (9):1181 – 1189.

Composition of Lipoprotein(a)



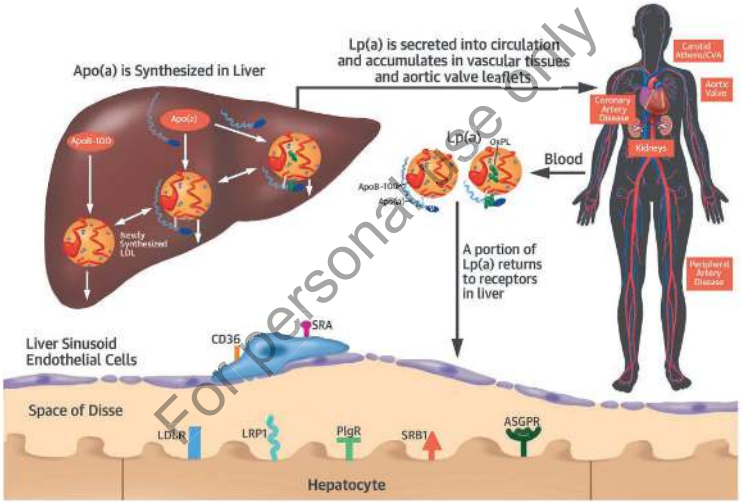
Tsimikas S. J Am Coll Cardiol. 2017;69(6):692-711.

Global Prevalence of Elevated Lp(a)



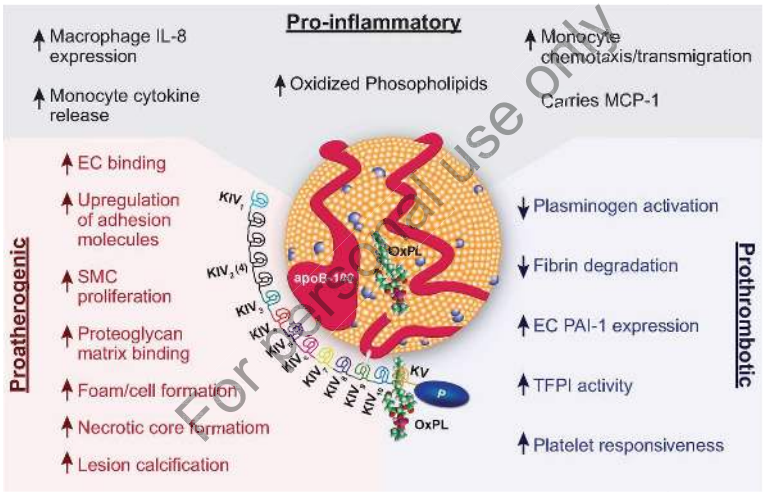
Tsimikas S, Marcovina SM. J Am Coll Cardiol. 2022;80(9):934-946.

Lp(a) Metabolism



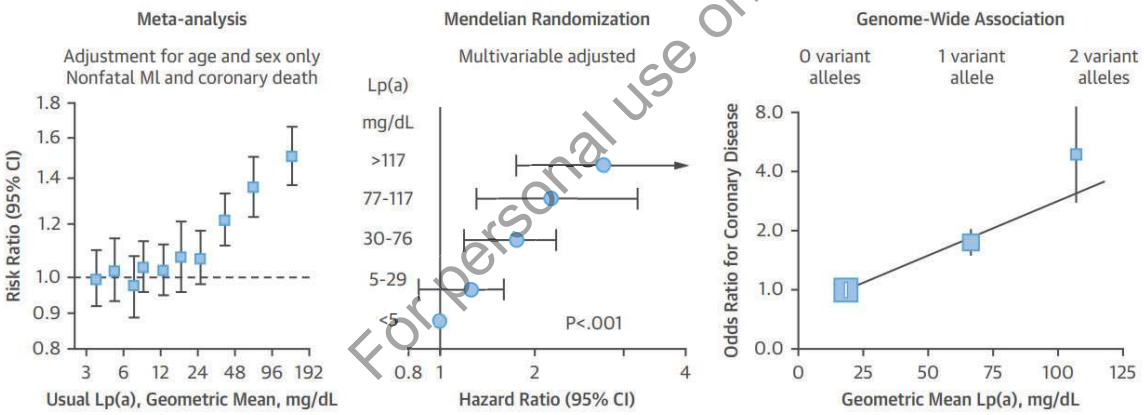
Tsimikas S, et al. J Am Coll Cardiol. 2018;71(2):177-192.

Mechanisms of Lp(a) Mediated CVD Risk



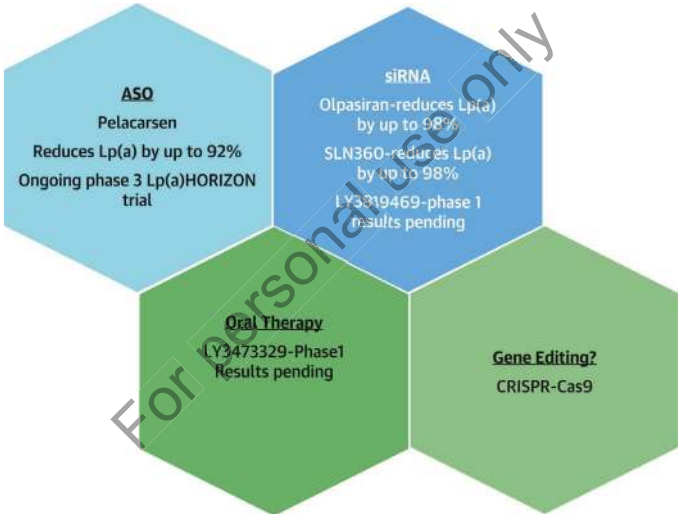
Tsimikas S. J Am Coll Cardiol. 2017;69(6):692-711.

Lp(a): An Independent, Causal, Genetic Factor in CVD



Tsimikas S. J Am Coll Cardiol. 2017;69(6):692-711.

Emerging Lp(a) Therapeutics

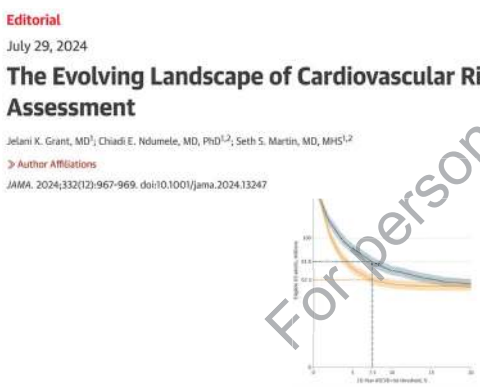


Malick WA et al. J Am Coll Cardiol. 2023;81(16):1633-1645.

As We Await Lp(a) Directed Therapy

- Use Lp(a) as a risk-enhancing factor
- Drive down LDL-C and mitigate risk from other cardiovascular risk factors
- Enroll patients in Lp(a) trials when possible
- Cascade test Lp(a) in family members

Recent Developments in Risk Assessment


Editorial

July 29, 2024

The Evolving Landscape of Cardiovascular Risk Assessment

Jelani K. Grant, MD[1]; Chiadi E. Ndumele, MD, PhD[1,2]; Seth S. Martin, MD, MHS[1,2]

Author Affiliations

JAMA. 2024;332(12):967-969. doi:10.1001/jama.2024.13247

JAMA. 2024;332(12):989-1000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EDITORIAL

Prevention of Cardiovascular Disease — Don't Stop Thinking about Tomorrow

Authors: Roger S. Blumenthal, M.D., and Seth S. Martin, M.D., M.H.S. Author Info & Affiliations

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Corrie Health Lipids Program

Enrolling Soon

1000 Patients

- Known ASCVD or high risk ASCVD

3 US Study Sites

- Johns Hopkins, Yale, Pennsylvania State University

Corrie Lipids Program

- Enrollment with Corrie App
- LLT intensified to reach guideline-based thresholds

Outcomes

- LDL-C control at the end 6 months
- RE-AIM findings (Reach, Effectiveness, Adoption, Implementation, and Maintenance)

Yale University School of Medicine

Johns Hopkins Medicine

PennState Health

LATTICE
Leading Awareness To action Through Implementation of CardioMetabolic Efforts

Take Home Points

- Atherosclerotic cardiovascular disease is the leading cause of death and atherogenic lipids, predominantly LDL, play a central role
- The primary role of genetic testing in screening for lipid abnormalities is in individuals and familiesin which familial hypercholesterolemia is suspected
  - Know FH, look for FH – common, yet severely underdiagnosed and undertreated
- Start lipid lowering therapies as recommended by AHA/ACC/multisociety guidelines for both primary and secondary prevention of ASCVD
- Primary prevention – PCE for now, PREVENT equations pending guideline adoption
  - Use risk enhancing factors and CAC; shared decision making key; get LDL-C <100 at a minimum
- Secondary prevention – get LDL-C <70 at a minimum and ideally <55, especially if VHR
- Cardiovascular risk is related to long-term cumulative exposure to LDL / ApoB
  - Lower LDL-C for longer is better

Take Home Points (Cont.)

- Lifestyle and statins remain 1st line, with expanding set of non-statin lipid therapies
  - Combination Rx common and enables achievement of low LDL-C even when starting high
  - PCSK9 inhibitors have been a game changer
- Measure lipids at baseline,1-3 mo after Rx changes, and q6-12 mo thereafter
  - Beware of LDL-C underestimation from outside labs; avoid undertreatment
  - There is no apparent lower safety limit for LDL-C levels
- Lp(a) is a causal factor in ASCVD and emerging target of therapy, with multiple drugs in the pipeline
- Interdisciplinary teamwork is essential in lipid and CVD risk management; digital health is a promising implementation tool