Importance of Lipoprotein(a) Screening and Testing

Lipoprotein(a) Discovery Initiative
American Heart Association
June 18, 2024

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SCHOOL OF MEDICINE

American Heart Association.

Disclosures

- *Speaker's Bureau*- None
- *Consultant*-
  Novartis, Medtronic, Eli Lilly, Boehringer Ingelheim, Johnson and Johnson
- *Stocks*- None
- *Patents*- None

Disclaimer

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Learning Objectives

- Understand the evidence for Lp(a) as an independent and causal risk factor for cardiovascular disease
- Understand the worsening disparities in US Life Expectancy
- Appreciate clinical considerations for Lp(a) screening and testing

Susan B.: 47-year-old female referred to cardiac clinic for chest pain evaluation

- Ms. B. recently presented to the ED one week prior with recurrent, new onset chest tightness.
- ECG: nonspecific changes, normal troponin x 3 and discharged home with a diagnosis of possible anxiety attack.
- She denies prior cardiac disease and BP has been well controlled.
- Chest discomfort now often noted with minimal activity.

Susan B.: A 47-year-old female referred to cardiac clinic for chest pain evaluation

- Concerned because of her family history of premature ASCVD. Mother had CABG at 62 y/o.
- A hospital nurse and she consumes occasional alcohol but does not smoke or use illicit drugs.
- Physical exam of systems is unremarkable, but she appears anxious.

47-year-old F: new onset chest pain

Lipid Profile

- CHOL 180 mg/dL
- TRIG 54 mg/dL
- HDL-C 71 mg/dL
- LDL-C 108 mg/dL
- BP 125/76 mmHg
- No diabetes: A1C 5.4; FBS 72
- BMI 24.6

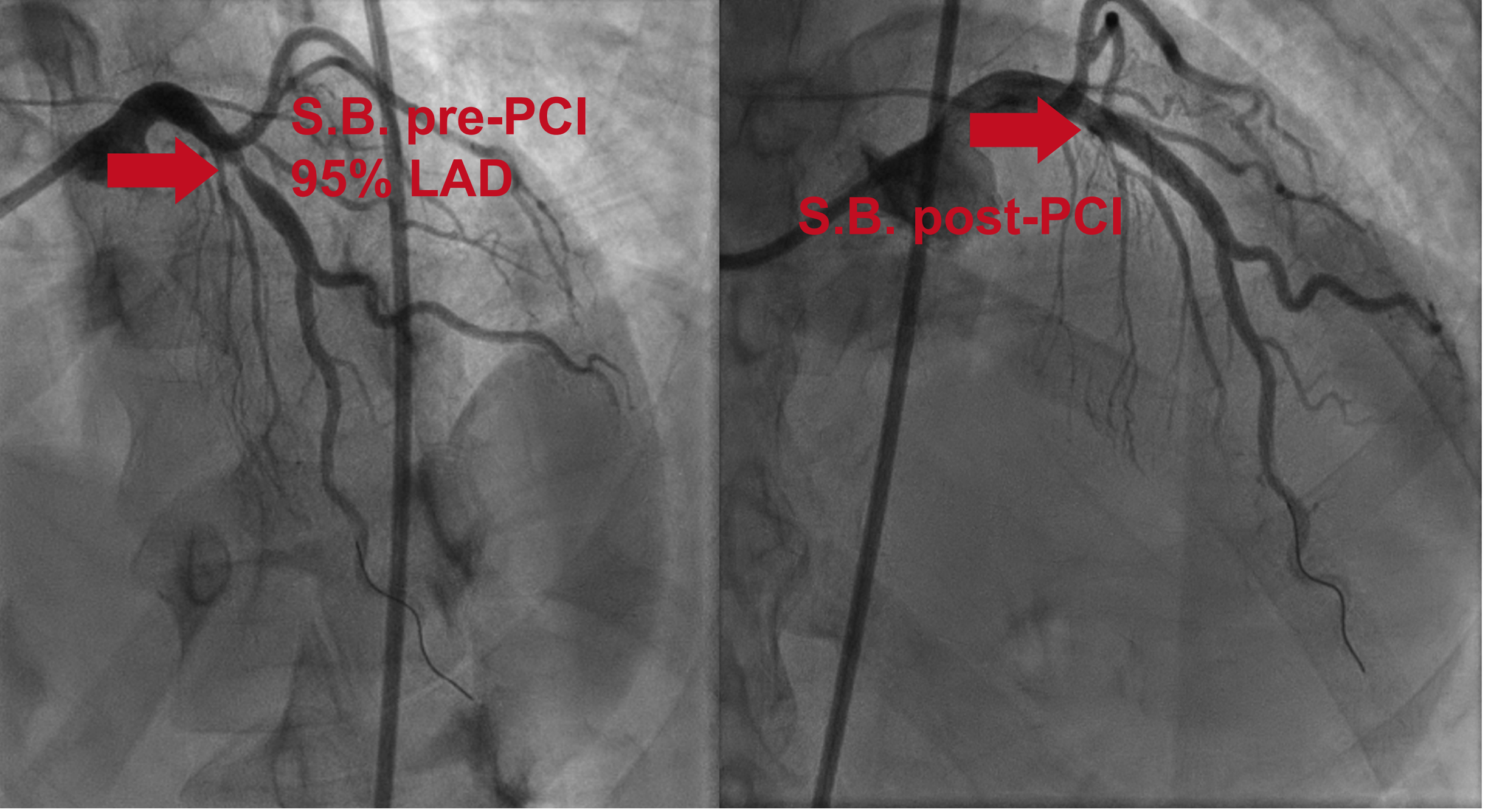
47-year-old F: new onset chest pain

Lipid Profile

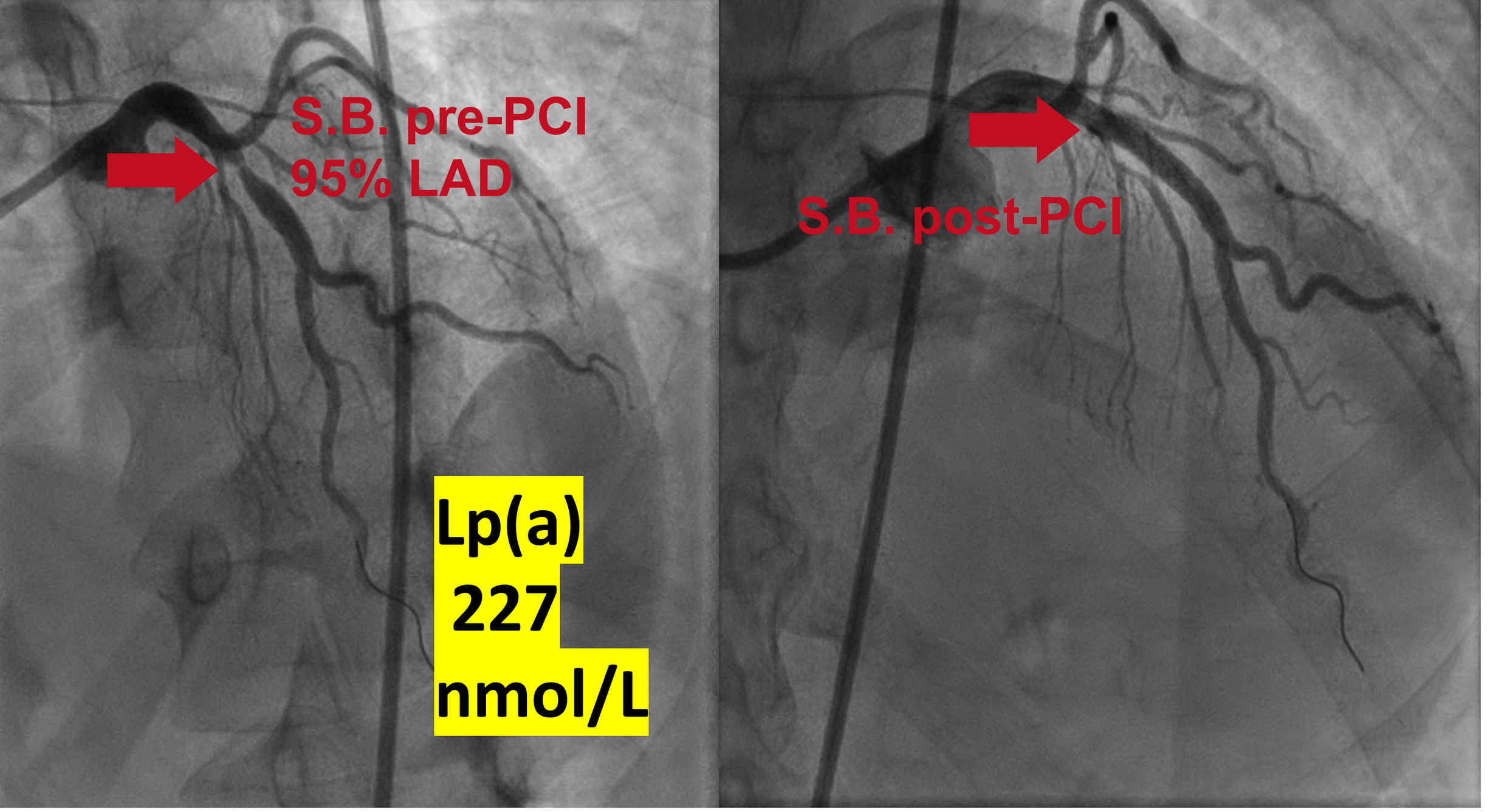
- CHOL 180 mg/dL
- TRIG 54 mg/dL
- HDL-C 71 mg/dL
- LDL-C 108 mg/dL

Current 10-year ASCVD risk 1.0%

She eventually underwent nuclear stress test- positive anterior wall



Coronary Angiography, Tulane University Medical Center, NOLA

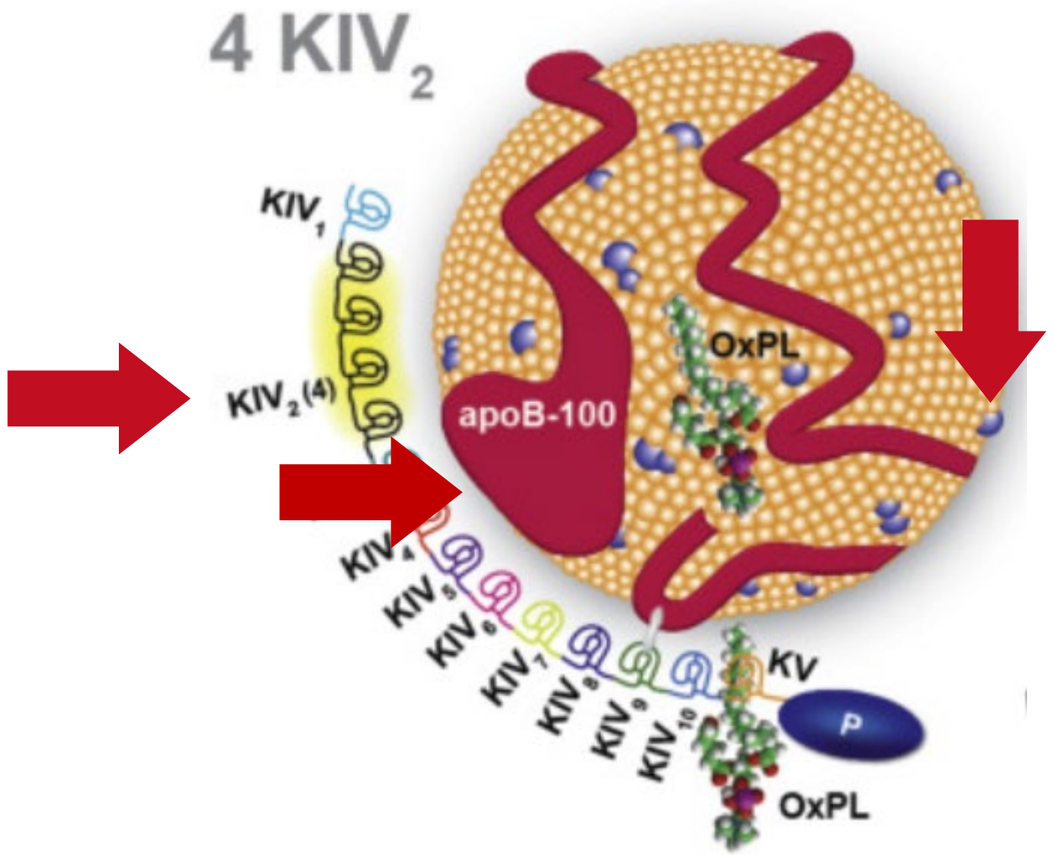


Coronary Angiography, Tulane University Medical Center, NOLA

Access 12/21/22: https://www.delish.com/cooking/recipe-ideas/a42006213/danish-kringle-recipe/
Photo Credit: LUCY SCHAEFFER; FOOD STYLING: ERIKA JOYCE

Lp(a): atherogenic LDL-like lipoprotein

Single molecule of apo(a), unique Lp(a) covalently bound to apoB. Presence of apo(a) distinguishes Lp(a) from LDL

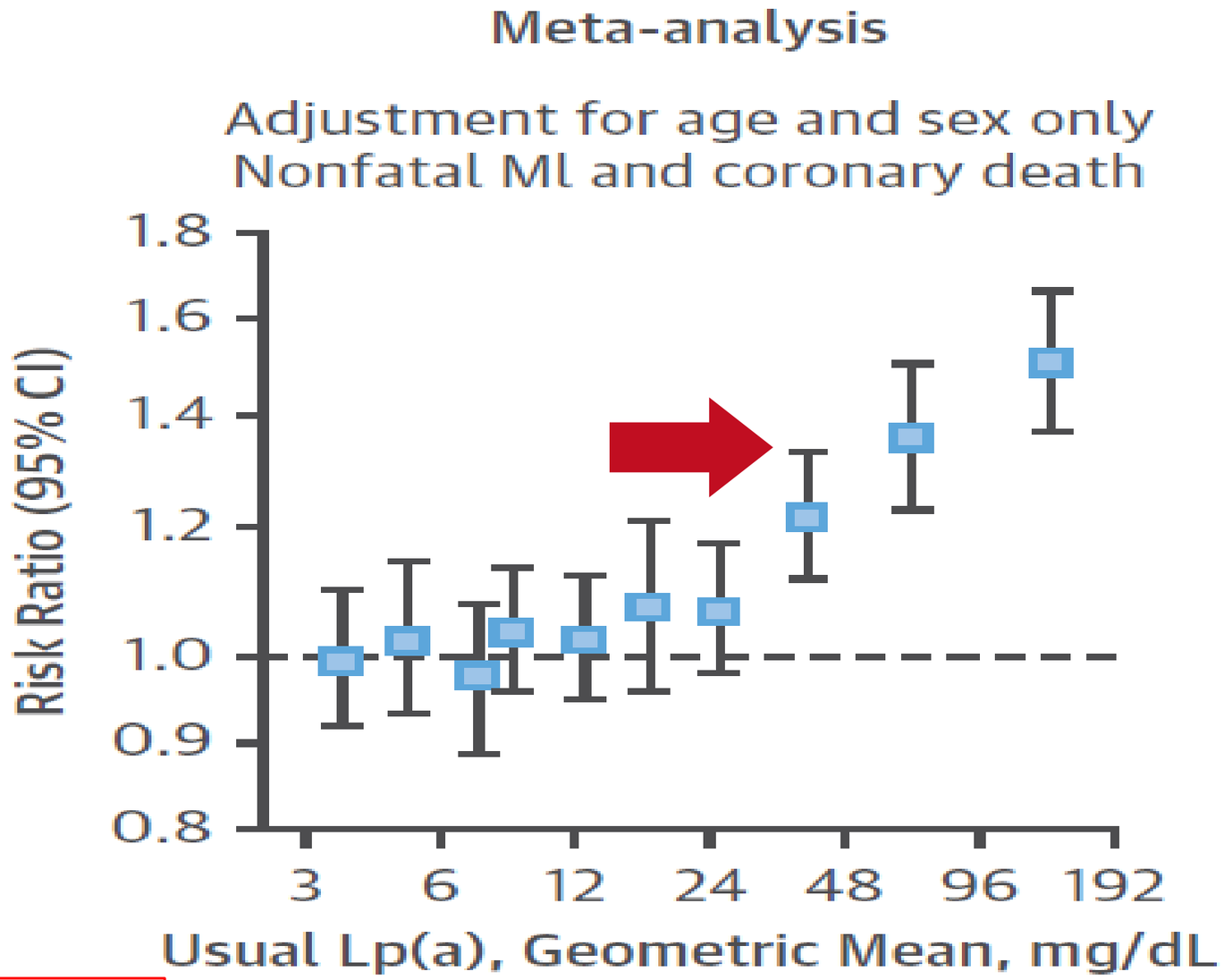


Feingold KR, Grunfeld Cl. *Endotext.* South Dartmouth (MA); 2018.
Cegla J et al. *Atherosclerosis.* 2019;291:62-70;
Tsimikas S. *J Am Coll Cardiol.* 2017;69:692-711.
Boffa M, Koschinsky M. *Nature Reviews cardiology.* 2019; 16:305-318.

apo, apolipoprotein; CE, cholesterol ester; FC, free cholesterol; KIV1-KIV10 / KV, kringle domains; LDL, low-density lipoprotein; Lp(a), lipoprotein(a); OxPL, oxidized phospholipid; PL, phospholipid; TG, triglyceride.

Lp(a): Independent, Causal, Genetic CVD Risk Factor

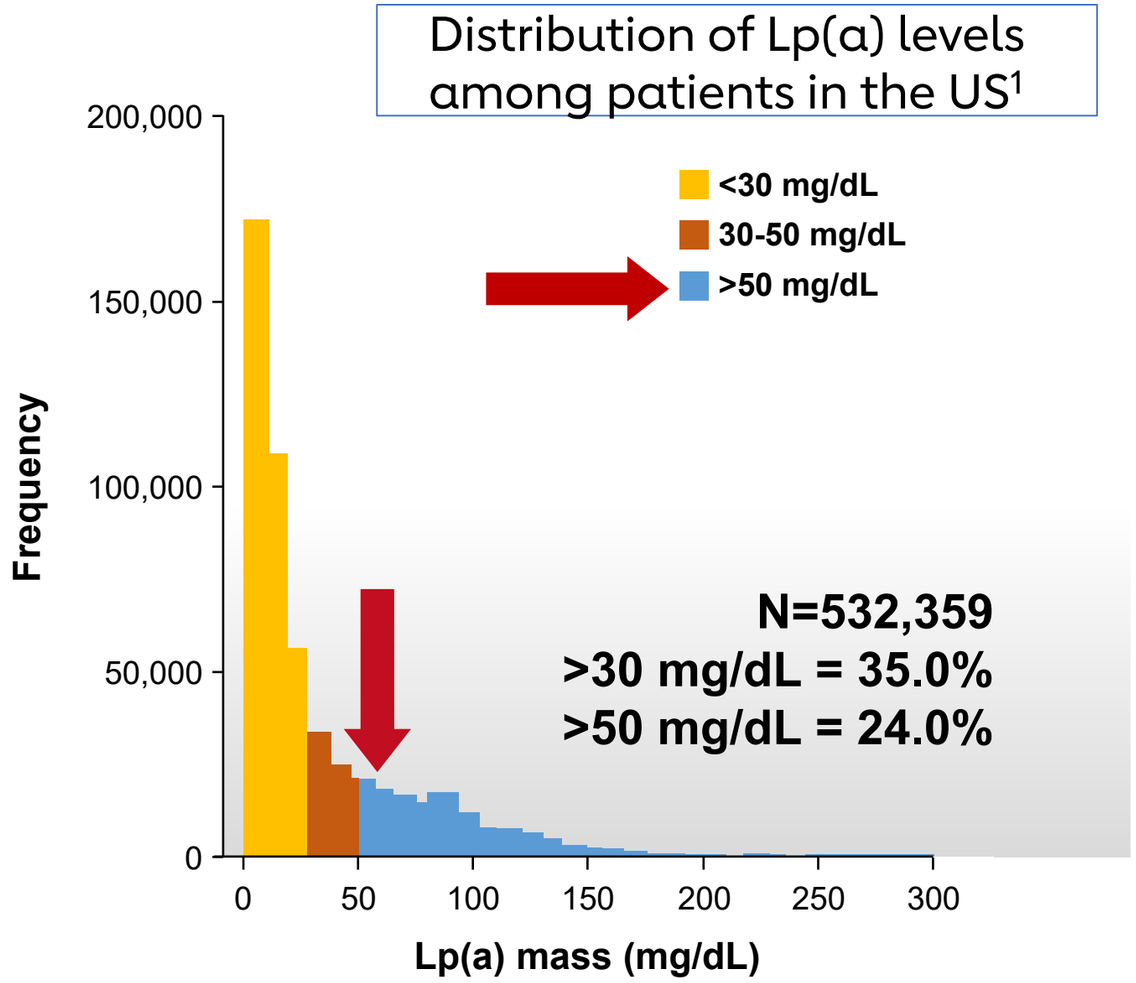
n=9,318



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

The Emerging Risk Factors Collaboration

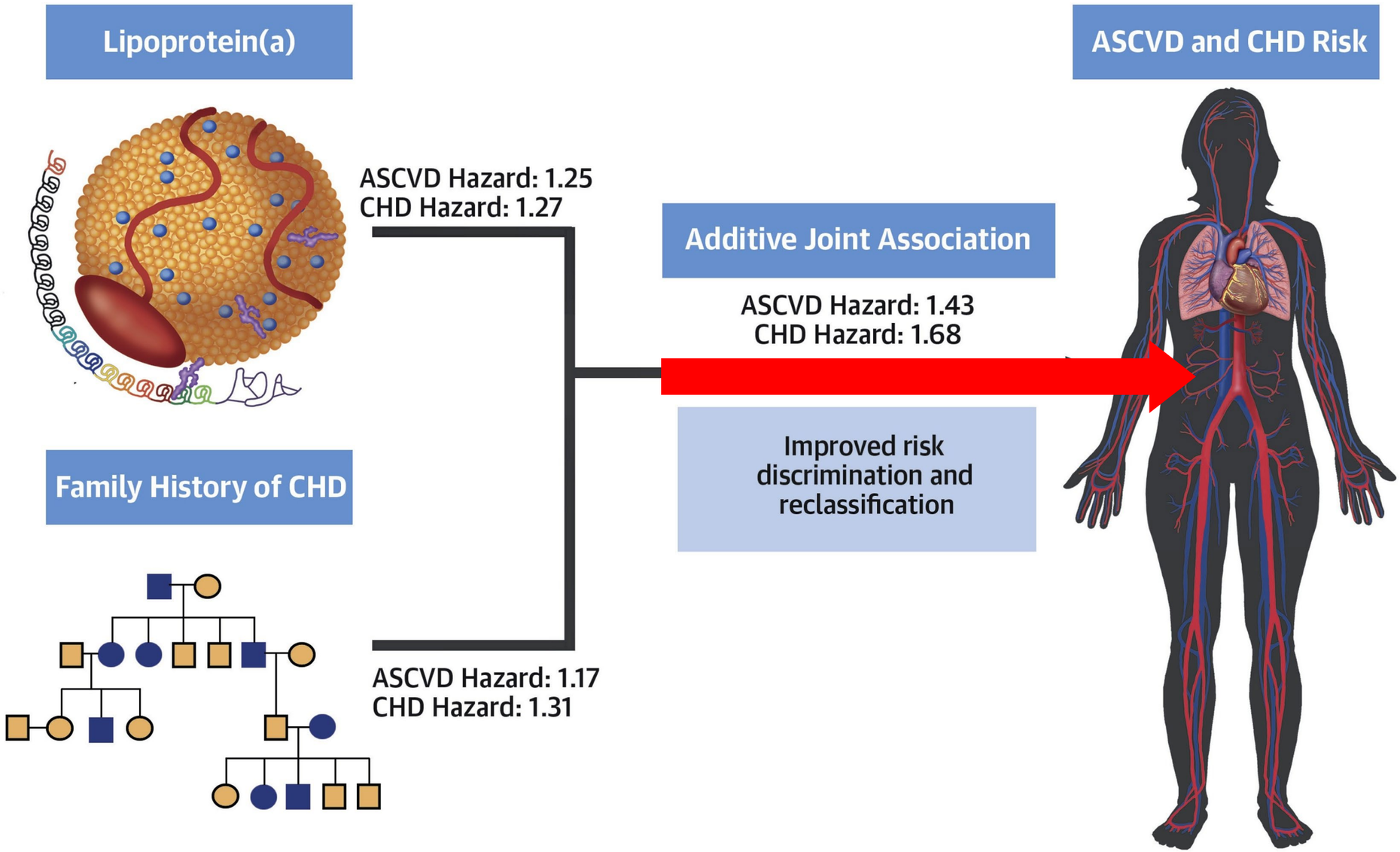
Plasma Lp(a) follows a skewed distribution



- Unlike LDL-C normal distribution, Lp(a) skewed towards highest level
- Majority individuals (~70%) exhibit normal Lp(a) (<30 mg/dL)

Varvel S et al. Arterioscler Thromb Vasc Biol. 2016;36:2239-2245
Nordestgaard BG, Langsted A. J Lipid Res. 2016;57:1953-1975.

CENTRAL ILLUSTRATION: Independent and Joint Association of Lipoprotein(a) and Family History With Cardiovascular Risk



Mehta, A. et al. J Am Coll Cardiol. 2020;76(7):781-93.

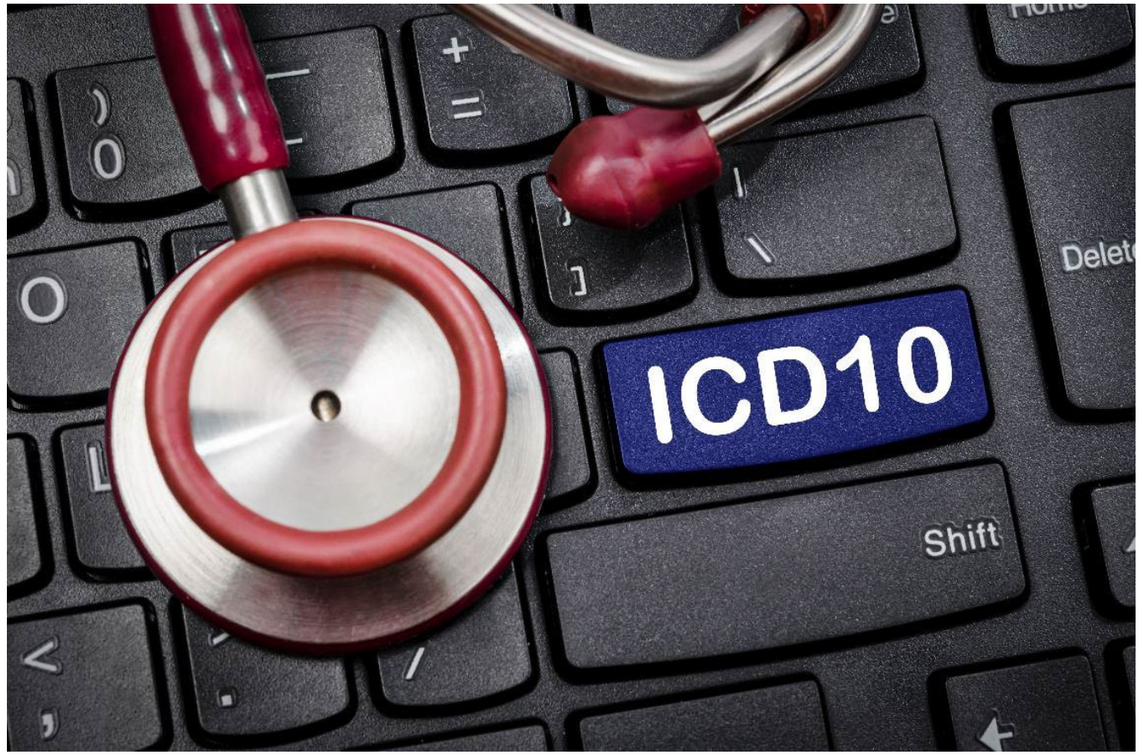
How is Lp(a) measured? Concentration assays and mass assays

- Concentration assays: key features
- nmol/L
- Number of apo(a) particles
- Unaffected by size heterogeneity
- Assay calibrators traceable to WHO / IFCCLM secondary reference

- Mass assays: key features
- mg/dL
- Mass of entire Lp(a) particle
- Includes apo(a) and associated lipids
- Lack of traceability of various calibrators to any established reference material
- Low #K-IV repeats ~small apo(a) isoforms and markedly higher Lp(a) vs. large isoforms

Tsimikas S. *J Am Coll Cardiol.* 2017;69:692-711
Tsimikas S et al. *J Am Coll Cardiol.* 2018;71:177-192
Wilson DP et al. *J Clin Lipidol.* 2019;13:374-392

apo, apolipoprotein; CE, cholesterol ester; IFCCLM, International Federation of Clinical Chemistry and Laboratory Medicine; PL, phospholipid; TG, triglyceride; WHO, World Health Organization



Lp(a) ICD-10-CM* coded clinical diagnosis with codes:

- E78.41 (Elevated Lp[a])
- Z83.430 (Family history of elevated Lp[a])

*International Classification of Diseases, 10th Revision, Clinical Modification. https://www.cdc.gov/nchs/icd/icd10cm.htm
Engler RJM et al. *Fed Pract.* 2019;36(Suppl 7):S19-S31.

Lp(a) levels predominantly genetically determined

Lp(a) predominantly under genetic control

Lp(a) concentration 70% to >90% genetic control

Major locus controlling LPA gene

reverse strand of chromosome 6q27

LPA encodes apo(a) of Lp(a)

Non-genetic factors influences

CKD:
↑ Lp(a) with ↓ GFR and severe proteinuria (nephrotic syndrome)

Liver disease: ↓ Lp(a)

Pregnancy/ GH/Hypothyroidism: ↑ Lp(a)

Hormone replacement post-menopausal women: ↓ Lp(a)

Lifestyle changes no impact on Lp(a)

Low-saturated fat diet

Physical exercise

Cegla J et al. Atherosclerosis. 2019;291:62-70
Schmidt K et al. J Lipid Res. 2016;57:1339-1359
Wilson DP et al. J Clin Lipidol. 2019;13:374-392.

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THE PRESENT AND FUTURE

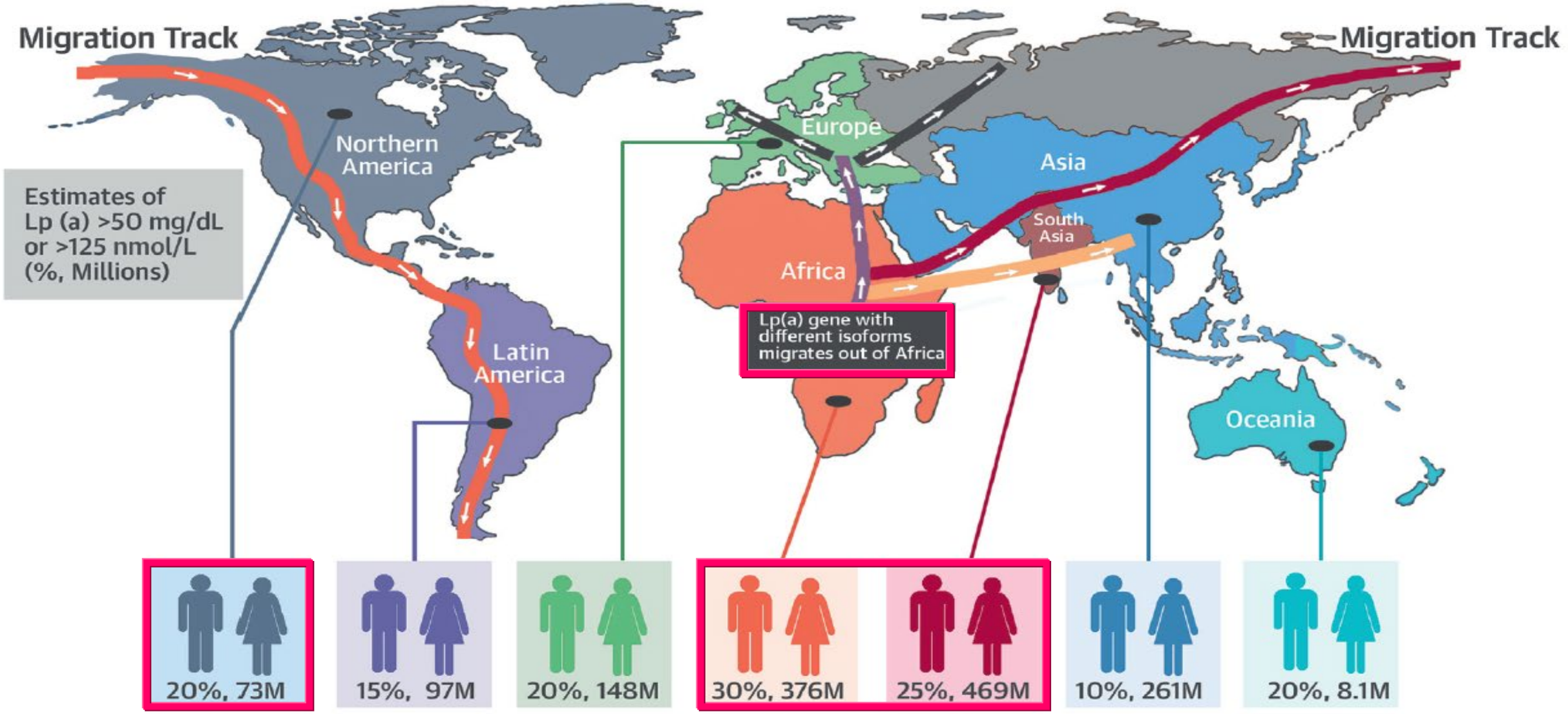
STATE-OF-THE-ART REVIEW

NHLBI Working Group Recommendations to Reduce Lipoprotein(a)-Mediated Risk of Cardiovascular Disease and Aortic Stenosis

Sotirios Tsimikas, MD,[a] Sergio Fazio, MD, PhD,[b] Keith C. Ferdinand, MD,[c] Henry N. Ginsberg, MD,[d] Marlys L. Koschinsky, PhD,[e] Santica M. Marcovina, PhD, ScD,[f] Patrick M. Moriarty, MD,[g] Daniel J. Rader, MD,[h] Alan T. Remaley, MD, PhD,[i] Gissette Reyes-Soffer, MD,[d] Raul D. Santos, MD, PhD,[j] George Thanassoulis, MD,[k] Joseph L. Witztum, MD,[l] Simhan Danthi, PhD,[i] Michelle Olive, PhD,[i] Lijuan Liu, PhD[i]

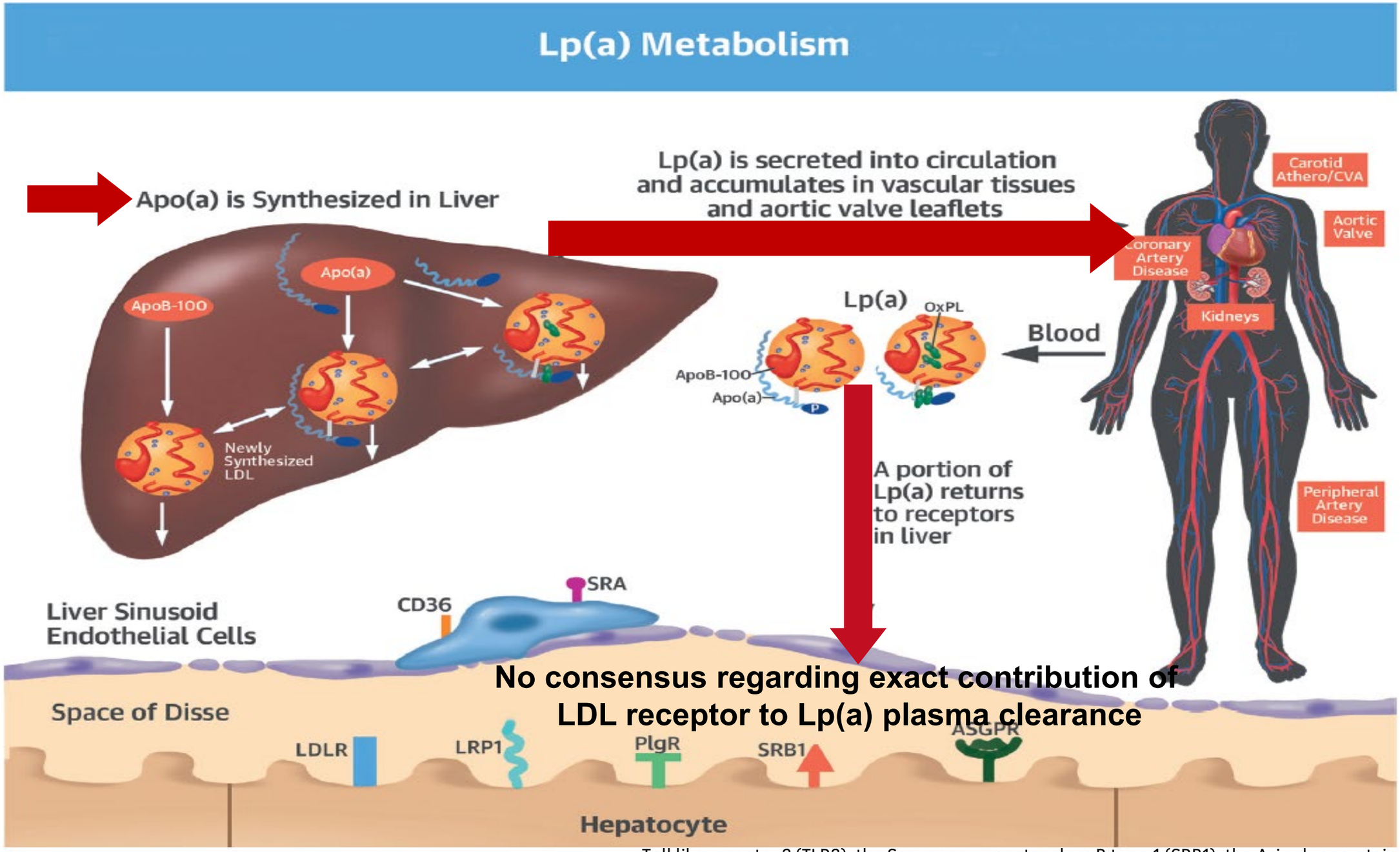
Tsimikas S, et al. J Am Coll Cardiol. 2018 Jan 16;71(2):177-192.

Estimated World Population With Elevated Lp(a) > 50mg/dL = 1.43 Billion



Tsimikas, S. et al. JACC. 2018;71(2):177–92xc

Lp(a) Metabolism



No consensus regarding exact contribution of LDL receptor to Lp(a) plasma clearance

Tsimikas, S. et al. JACC. 2018;71(2):177–92xc

Toll like receptor 2 (TLR2), the Scavenger receptor class B type 1 (SRB1), the Asiaglycoprotein receptor (ASGPR), the Plasminogen receptor ($PLGR_{KT}$), the VLDL receptor (VLDLR), the Lipoprotein receptor related proteins 1, 2 and 8 and the LDL receptor (LDLR).

Conclusive evidence: Lp(a) and Higher CVD and CAVS Risk

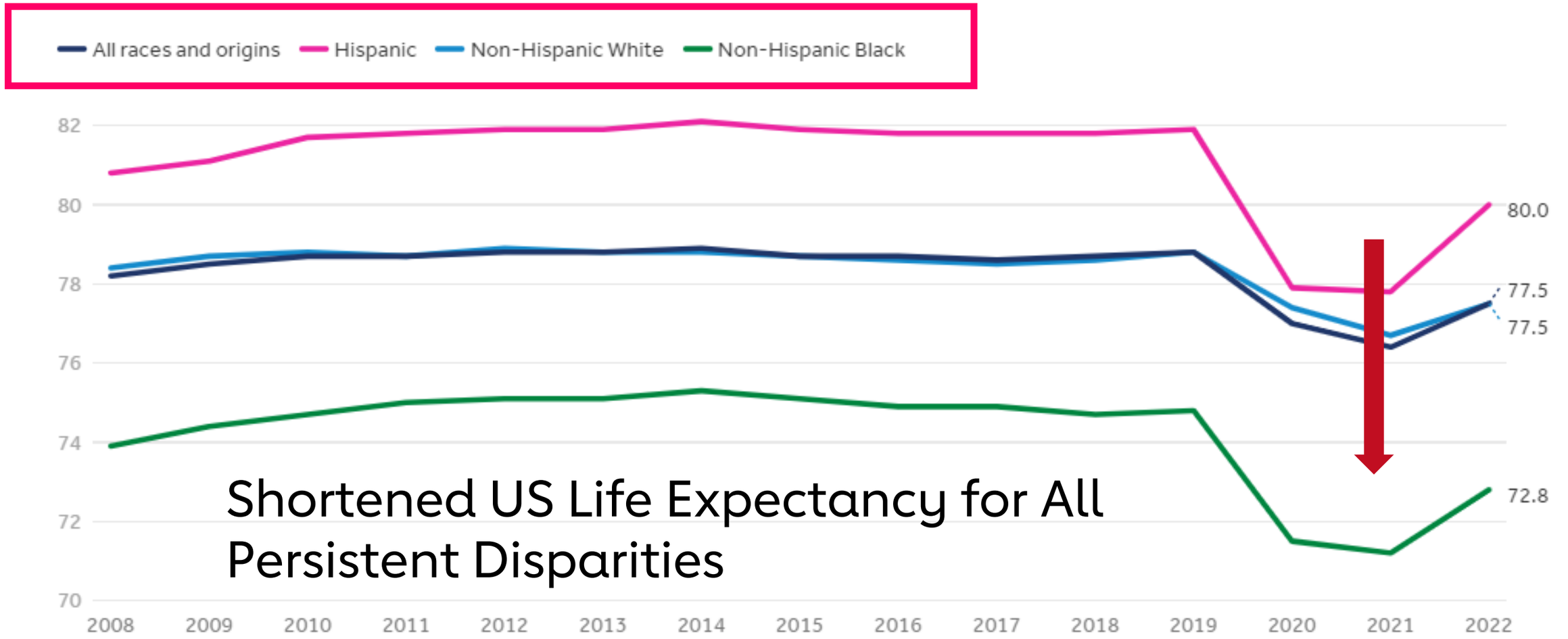
Genetically Lp(a) → higher risk: particularly acute MI, CVD stroke, PAD, HF, and CAVS, and all-cause mortality

- Epidemiological studies and meta-analyses
- Genome-wide association studies
- Mendelian randomization studies

ASCVD=atherosclerotic cardiovascular disease, CVD=cardiovascular disease, PAD=peripheral arterial disease, HF=heart failure, and CAVS=calcified aortic valve stenosis

Tsimikas, S. et al. JACC. 2018;71(2):177–92xc

Lp(a) and ASCVD Risk : Focus on Women, South Asian, African American Populations



Shortened US Life Expectancy for All Persistent Disparities

Note: Starting with 2018 data, race is presented as single-race estimates (only one race was reported on the death certificate). Persons of Hispanic origin may be of any race but are categorized as Hispanic for this analysis; other groups are non-Hispanic. See Methods section of "How does U.S. life expectancy compare to other countries?" Data for 2022 are provisional.

KFF health system tracker. https://www.healthsystemtracker.org/indicator/health-well-being/life-expectancy. Accessed Feb 27, 2024.

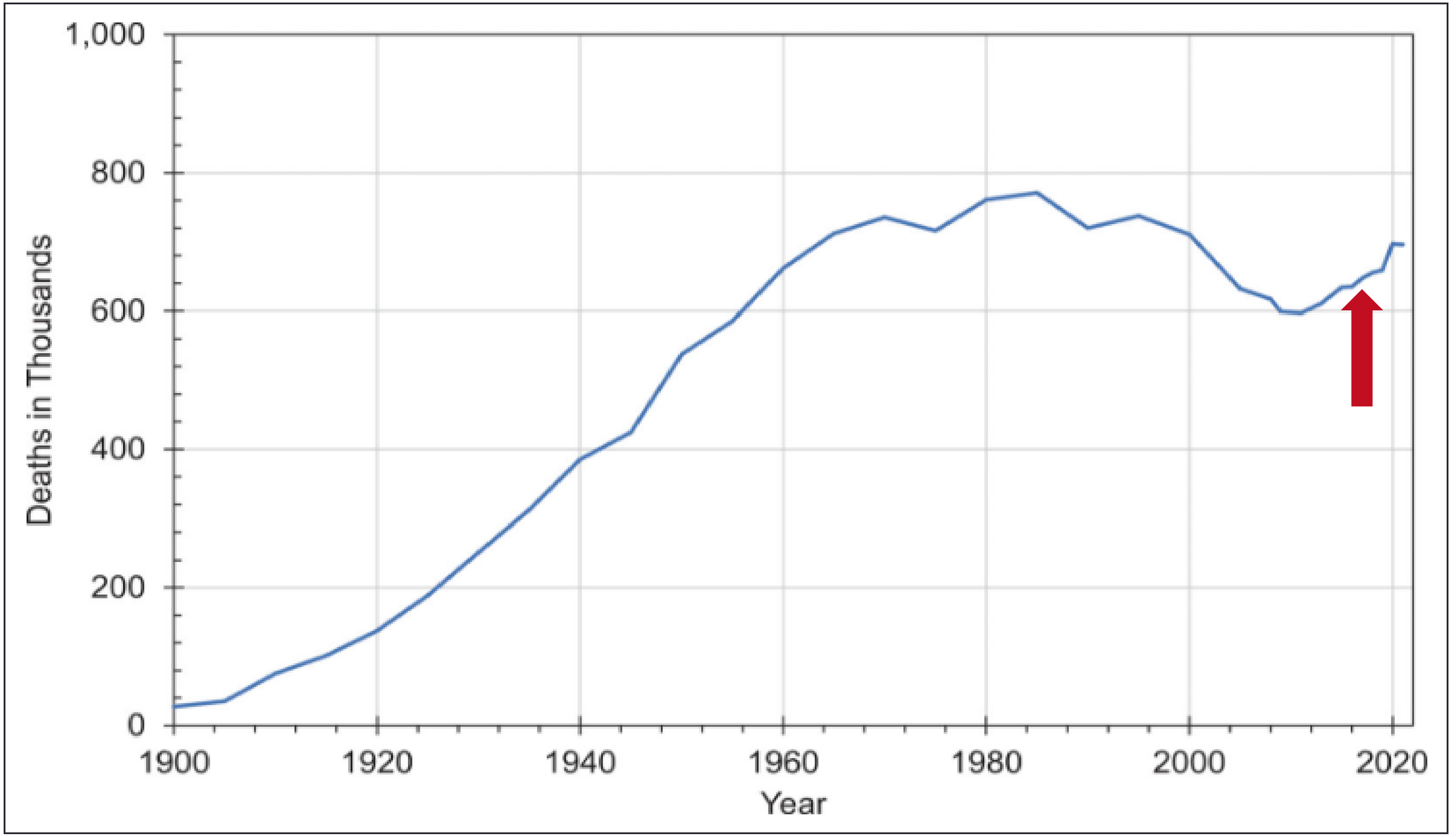


Chart 14-2. Deaths attributable to diseases of the heart, United States, 1900 to 2020.

Martin SS, Aday AW, Almarzooq ZI, et al. 2024 heart disease and stroke statistics: A report of US and Global Data from the American Heart Association. *Circulation*. Published online January 24, 2024.

Race/Ethnicity and Lp(a) Mass Concentrations

Table 1. Characteristics of Multi-Ethnic Study of Atherosclerosis (MESA) Participants in 4 Ethnic Groups at Visit 1

	Blacks	Whites	Chinese Americans	Hispanics
n	1323	1677	548	1044
Age, y	61 (52–70)	62 (54–71)	62 (53–71)	61 (52–69)
Sex (men)	621 (46.1%)	813 (47.6%)	217 (38.8%)	517 (48.6%)
Smoker	726 (53.9%)	929 (54.4%)	137 (24.5%)	504 (47.4%)
Diabetes mellitus	196 (14.6%)	86 (5.0%)	55 (9.8%)	171 (16.1%)
Hypertensive	428 (31.8%)	325 (19.0%)	126 (22.5%)	257 (24.2%)
On hypertension medicine	613 (45.5%)	493 (28.8%)	138 (24.7%)	305 (28.7%)
Non-Lp(a) LDL-C, mg/dL	113 (92–133)	115 (97–136)	114 (96–132)	116 (97–137)
HDL-C, mg/dL	50 (41–61)	50 (41–62)	48 (40–58)*	45 (38–54)*
Triglycerides, mg/dL	89 (66–122)*	110 (75–160)*	121 (85–169)*	133 (94–189)*
Lp(a), mg/dL	35.1 (20.4–61.6)*	12.9 (5.8–29.6)	12.9 (7.7–23.4)	13.1 (6.3–28.8)

Guan, W. et al. Arteriosclerosis, Thrombosis, and Vascular Biology. 2015;35:996-1001

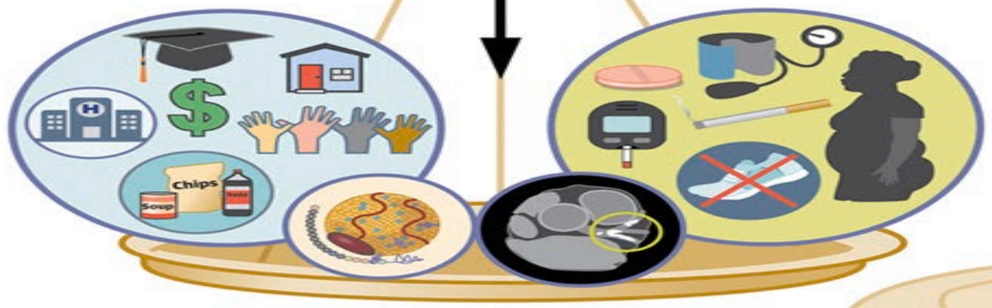
Weighing Factors That Impact Higher ASCVD Risk in Black Adults

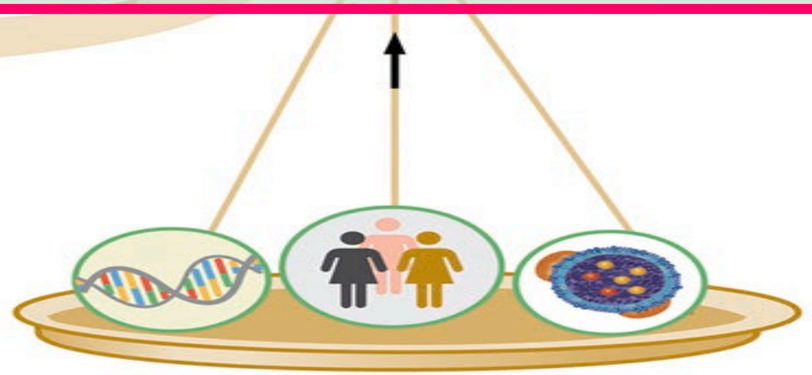
Factors to Maximize

1. **SDOH**
   - Adverse environments
   - Inadequate health access
   - Low SES
   - Limited educational attainment
   - Food desserts
   - Structural inequities
   - Intrinsic bias
2. **Uncontrolled major risk factors**
   - HTN
   - Obesity (especially Black females)
   - T2DM
   - Smoking
   - Physical inactivity
   - Suboptimal LDL goal attainment and statin intensity
3. **CAC scoring with intermediate risk score**
4. **Elevated Lp(a)**

Factors to Minimize

1. Skin color or self-identified race
2. Unmeasured genetic factors
3. Low HDL-C as increased risk
4. High HDL-C and low triglycerides as indicating lower risk





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EDITORIAL COMMENT

HDL-C in Black Adults for ASCVD Risk Calculation

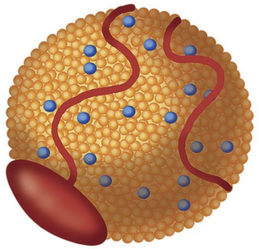
Benefit or Barrier to Achieving Health Equity?*

Keith C. Ferdinand, MD

Ferdinand, K. JACC VOL. 80, NO. 22, 2022

American Heart Association.

CENTRAL ILLUSTRATION: Lipoprotein(a) and Long-Term Incidence of Atherosclerotic Cardiovascular Disease in a Multi-Ethnic Pooled Cohort in the United States



Pooled Community-Based Cohorts in the U.S. (n = 27,756)

- MESA: n = 5,892
- CARDIA: n = 4,001
- JACKSON: n = 2,098
- FHS-OS: n = 2,587
- ARIC: n = 13,178

Baseline Lp(a) (Median)	Adjusted Relative Risks (95% CI) of Incident ASCVD
<50th percentile (3.6 mg/dL) (n = 13,835)	Reference
50th-<75th percentile (13.5 mg/dL) (n = 6,960)	HR: 1.06 (95% CI: 0.99-1.14)
75th-<90th percentile (25.9 mg/dL) (n = 4,177)	HR: 1.18 (95% CI: 1.09-1.28)
≥90th percentile (52.6 mg/dL) (n = 2,784)	HR: 1.46 (95% CI: 1.33-1.59)

Mean Follow-Up 21.1 Years

Lp(a) ≥90th vs <50th Percentile

- Myocardial Infarction: HR: 1.66 (95% CI: 1.44-1.90)
- Revascularization: HR: 1.68 (95% CI: 1.48-1.91)
- Stroke: HR: 1.26 (95% CI: 1.08-1.47)
- CHD Death: HR: 1.32 (95% CI: 1.06-1.64)
- All-Cause Mortality: HR: 1.01 (95% CI: 0.93-1.08)

The relation of Lp(a) with incident ASCVD was similar by:

- Risk group (low-intermediate vs high)
- Sex (female vs male)
- Race/ethnicity (Asian, Black, Hispanic, and White)
- LDL-C category (<70, 70-<100, 100-<130, and ≥130 mg/dL)

The relation of Lp(a) (≥90th vs <50th percentile) with incident ASCVD was stronger in those with:

- Diabetes: HR: 1.92 (95% CI: 1.50-2.45) vs
- No diabetes: HR: 1.41 (95% CI: 1.28-1.55)

Overall interaction $P < 0.01$

Wong ND, et al. J Am Coll Cardiol. 2024;83(16):1511-1525.

Putting Lp(a) Data into Practice

Access 5/13/24: https://www.healio.com/

American Heart Association

Arteriosclerosis, Thrombosis, and Vascular Biology

AHA SCIENTIFIC STATEMENT

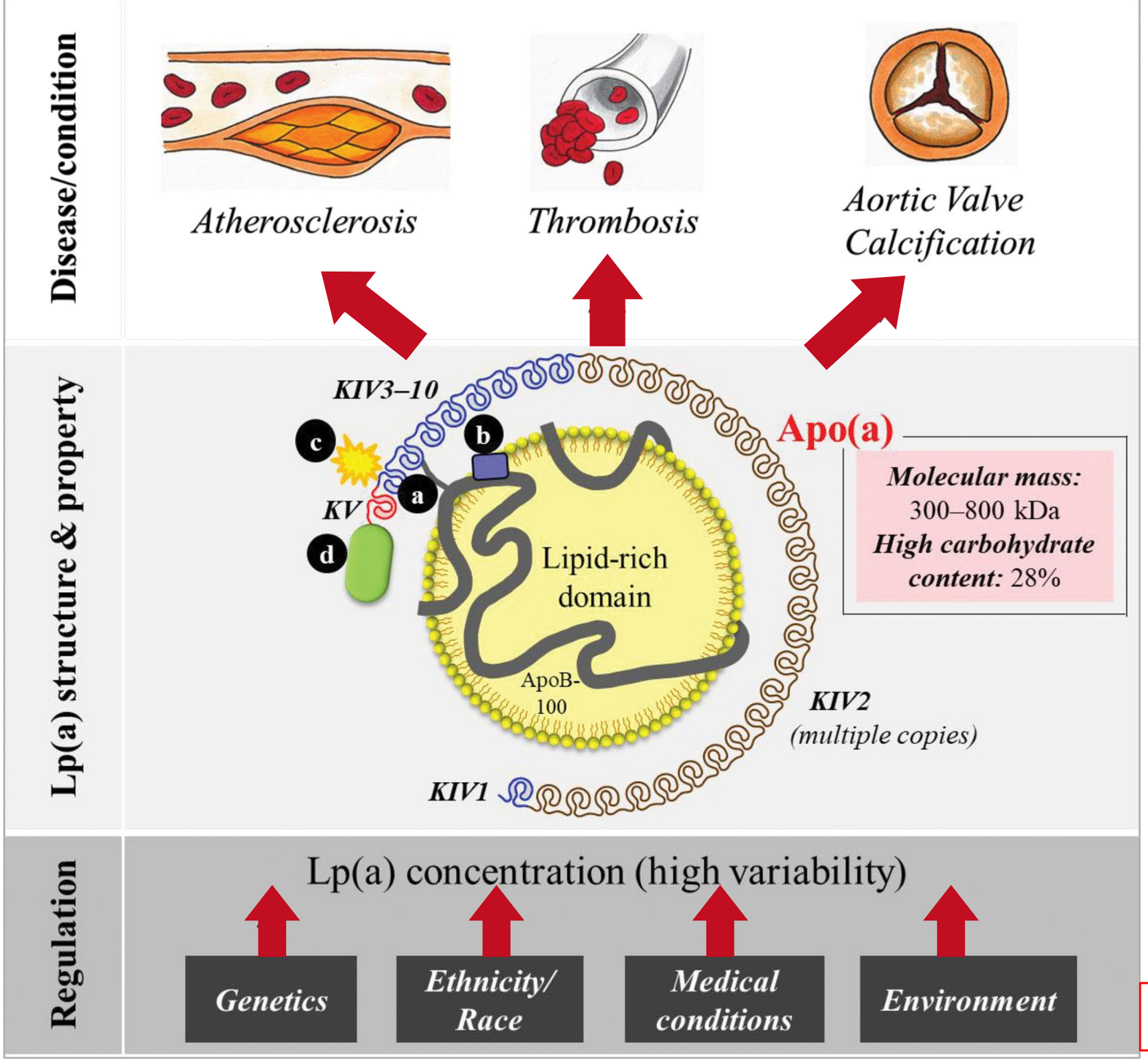
Lipoprotein(a): A Genetically Determined, Causal, and Prevalent Risk Factor for Atherosclerotic Cardiovascular Disease: A Scientific Statement From the American Heart Association

The International Atherosclerosis Society endorses this statement.

Gissette Reyes-Soffer, MD, FAHA, Chair; Henry N. Ginsberg, MD, FAHA; Lars Berglund MD, PhD; P. Barton Duell, MD, FAHA; Sean P. Heffron, MD, MS, MSc; Pia R. Kamstrup, MD, PhD; Donald M. Lloyd-Jones, MD, ScM, FAHA; Santica M. Marcovina, PhD, ScD, FAHA; Calvin Yeang, MD, PhD; Marlys L. Koschinsky PhD, FAHA, Co-Chair; on behalf of the American Heart Association Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular Radiology and Intervention; and Council on Peripheral Vascular Disease

Reyes-Soffer G, et al. Arterioscler Thromb Vasc Biol. 2022 Jan;42(1):e48-e60.

Lp(a) structure, properties, regulation, and relation to disease



Apo(a) binds apolipoprotein B100 (apoB) via single disulfide bond (a)

Apo(a) repeated kringle (K) like plasminogen(b)

Proinflammatory & proatherogenic oxidized phospholipids bind to KIV type 10 (c)

Protease domain (d) lacks enzymatic activity

Reyes-Soffer G, et al. Arterioscler Thromb Vasc Biol. 2022 Jan;42(1):e48-e60.

Lipoprotein(a): A Genetically Determined, Causal, and Prevalent Risk Factor for Atherosclerotic Cardiovascular Disease: A Scientific Statement From the American Heart Association

- Evidence in favor of screening for Lp(a) is strongest for those w/ family or personal history of ASCVD
- Various organizations have proposed to obtain a level once in every adult.
- Once issues w/ Lp(a) measurement are resolved, reassessment of broader population-based screening should be considered.
- Current best approach to lower overall ASCVD risk in patients w/ high Lp(a) is to target LDL-C/apoB w/ statin & adjunctive medications as initial therapy
- Additional information needed on newer therapies for apoB lowering to reduce ASCVD risk in part through effects on Lp(a).
- Novel therapeutics that directly target apo(a) production are in clinical development.

Reyes-Soffer G, et al. Arterioscler Thromb Vasc Biol. 2022 Jan;42(1):e48-e60.

ESC European Society of Cardiology

European Heart Journal (2022) **43**, 3925–3946
https://doi.org/10.1093/eurheartj/ehac361

SPECIAL ARTICLE
Miscellaneous

Lipoprotein(a) in atherosclerotic cardiovascular disease and aortic stenosis: a European Atherosclerosis Society consensus statement

Florian Kronenberg [1], Samia Mora [2], Erik S.G. Stroes [3], Brian A. Ference [4], Benoit J. Arsenault [5], Lars Berglund [6], Marc R. Dweck [7], Marlys Koschinsky [8], Gilles Lambert [9], François Mach [10], Catherine J. McNeal [11], Patrick M. Moriarty [12], Pradeep Natarajan [13], Børge G. Nordestgaard [14,15], Klaus G. Parhofer [16], Salim S. Virani [17], Arnold von Eckardstein [18], Gerald F. Watts [19], Jane K. Stock [20], Kausik K. Ray [21], Lale S. Tokgözoğlu [22], and Alberico L. Catapano [23,24]

Kronenberg F, et al. Eur Heart J. 2022 Oct 14;43(39):3925-3946.

Key Points 2022 EAS Consensus Statement: Testing

1. Test Lp(a) ≧1 in adults
2. Cascade: FH, or family or personal Hx of (very) high Lp(a) or premature ASCVD
3. Lp(a) 100 mg/dL (250 nmol/L) ≈2.5X risk of ASCVD irrespective of baseline absolute risk
4. ↑ risk of major CV events caused lifetime exposure to ≈120 nmol/L (50 mg/dL) higher Lp(a) mitigated by lifetime exposure to ≈21 mg/dL lower LDL-C

Kronenberg F, et al. Eur Heart J. 2022 Oct 14;43(39):3925-3946.

Key Points EAS 2022 Consensus Statement: Lp(a) in ASCVD and Aortic Valve Stenosis

1. ↑ Lp(a) is RF even at very low levels LDL-C
2. Lp(a) ASCVD risk per-particle may exceed LDL: arterial inflammation, high Lp(a) accelerated progression of CAC and necrotic core
3. Children: Lp(a) >30 mg/dL (>75 nmol/L) ↑ risk (recurrent) arterial ischemic stroke
4. Lp(a) conversion factor of 2.5: [Lp(a) 2.5 nmol/L = 1 mg/dL]

Kronenberg F, et al. Eur Heart J. 2022 Oct 14;43(39):3925-3946.

American Heart Association.

Journal of Clinical Lipidology (2024) 000, 1–12

Journal of Clinical Lipidology

Koschinsky ML, et al. J Clin Lipidol. 2024 Mar 29:S1933-2874(24)00033-3.

A focused update to the 2019 NLA scientific statement on use of lipoprotein(a) in clinical practice

Marlys L. Koschinsky, PhD, Archna Bajaj, MD, MSCE, Michael B. Boffa, PhD, Dave L. Dixon, PharmD, Keith C. Ferdinand, MD, Samuel S. Gidding, MD, Edward A. Gill, MD, Terry A. Jacobson, MD, Erin D. Michos, MD, MHS, Maya S. Safarova, MD, PhD, Daniel E. Soffer, MD, Pam R. Taub, MD, Michael J. Wilkinson, MD, Don P. Wilson, MD, Christie M. Ballantyne, MD*

Summary: 2024 NLA Lp(a) Scientific Statement

- Now sufficient evidence to support recommendation to measure Lp(a) at least once in every adult for risk stratification.
- Lp(a) levels < 75 nmol/L (30 mg/dL) considered low risk
- Lp(a) levels ≥125 nmol/L (50 mg/dL) considered high risk, and
- Lp(a) 75 -125 nmol/L (30–50 mg/dL) intermediate risk.
- Cascade screening first-degree relatives of patients with elevated Lp(a) can identify additional individuals at risk who require intervention.
- Patients with elevated Lp(a) should receive early, more-intensive risk factor management

Koschinsky ML, et al. J Clin Lipidol. 2024 Mar 29:S1933-2874(24)00033-3.

Summary: 2024 NLA Lp(a) Scientific Statement

- Previously proposed correction for Lp(a)-C to adjust the LDL-C calculation may lead to the undertreatment of high-risk pts and should not be used
- Although statins may increase Lp(a) levels, concerns about Lp(a) elevation should not be reason to discourage/discontinue statins
- High-risk pts w/ elevated Lp(a) who need additional LDL-C lowering after max tolerated statin therapy, a PCSK9 inhibitor may address residual risk
- Lipoprotein apheresis approved by FDA for use in pts with clinically diagnosed FHH and either documented CAD or PAD who have Lp(a) level ≥ 60 mg/dL and LDL-C ≥ 100 mg/dL despite max tolerated lipid-lowering therapy

Koschinsky ML, et al. J Clin Lipidol. 2024 Mar 29:S1933-2874(24)00033-3.

American Heart Association.

Lp(a) and ASCVD Risk Reduction:

What We Know Now and What Will the Future Hold?

Effects of Currently Available FDA-Approved Lipid-Lowering Therapies on Lp(a)

	Mechanism of Action	Effect on Lp(a)	Clinical Benefit
Statins	HMG-CoA Ri—prevents endogenous cholesterol production and facilitates LDL-R clearance of LDL particles	Increases Lp(a) by 8% to 24%	None by Lp(a) lowering, but significant through LDL-C lowering
Niacin	Down-regulates transcriptional activity of LPA promoter gene	Decreases Lp(a) up to 30%	No clinical benefit despite effects LDL, Lp(a), and HDL
PCSK9i	Increases Lp(a) and LDL-C clearance	Decreases Lp(a) by 14% to 35%	RTCs secondary analyses, significant benefit CV risk reduction with elevated Lp(a)
Lp(a) apheresis	Extracorporeal binding of Lp(a) and LDL filtration system	Decreases Lp(a) by 64%	Observational data significant reduction MACE. RCT underway

Malick et al JACC VOL. 81, NO. 16, 2023 Lp(a)-Lowering Therapeutic Trial Design APRIL 25, 2023:1633 – 1645

Two classes nucleic acid therapeutics — antisense oligonucleotides (ASO) and short interfering RNAs (siRNAs) degrading messenger RNA code for synthesis of apolipoprotein(a) required Lp(a) formation and minimizes circulation

- Four nucleic acid therapeutics — administered sq —now in clinical testing:
- *Pelacarsen*. ASO per month, phase 3 Lp(a) HORIZON outcomes trial (NCT04023552). Results -2025.
- *Olpasiran*. siRNA, q 12 weeks, phase 3 OCEAN(a) outcomes trial (NCT05581303). Results -2027.
- *Zerlasiran*. siRNA (dose frequency?) phase 2.
- *Lepodisiran*. siRNA, q once or twice a year, phase 2 trial (NCT05565742).

https://consultqd.clevelandclinic.org/lipoproteina-progress-on-one-of-the-last-untreatable-frontiers-of-cardiovascular-risk. Accessed May 14, 2024.

American Heart Association.

Patient information and education

American Heart Association

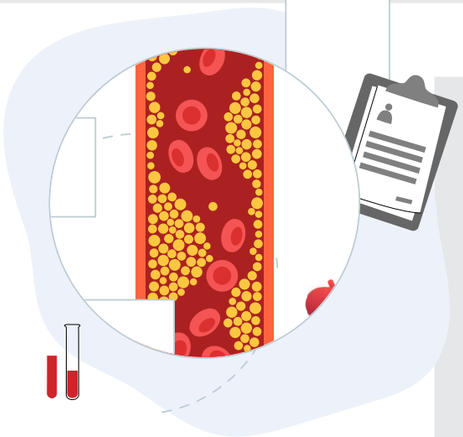
Understanding the Lp(a) Test

1

What should prompt a talk with my health care professional about a screening?

- Family or personal history of heart disease or premature cardiovascular disease
- Known family history of high Lp(a)
- Diagnosis of familial hypercholesterolemia (FH) - inherited condition that causes the body to poorly recycle LDL or bad cholesterol, which increases the risk of cardiovascular disease

- The standard cholesterol test, also known as a lipid panel, does not include Lp(a).
- Talk to your health care professional about adding a simple blood test for Lp(a) to your lipid panel during your doctor's visit or at a diagnostic lab center.



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		and heart disease?

Take Home Messages

- LDL-C is primary target to reduce ASCVD outcomes, but residual CV risk remains
- Lp(a) is an independent, common, inherited causal risk factor for ASCVD
- Higher Lp(a) South Asian and African ancestry
- Universal Lp(a) screening can help predict ASCVD risk and guide intensity of current treatment

Take Home Messages

- Since Lp(a) discovery, no specific therapies approved
- siRNA and antisense oligonucleotides appear to effectively ↓ Lp(a) to non-atherogenic levels
- Will lowering Lp(a) → clinical benefit?

Thank You.

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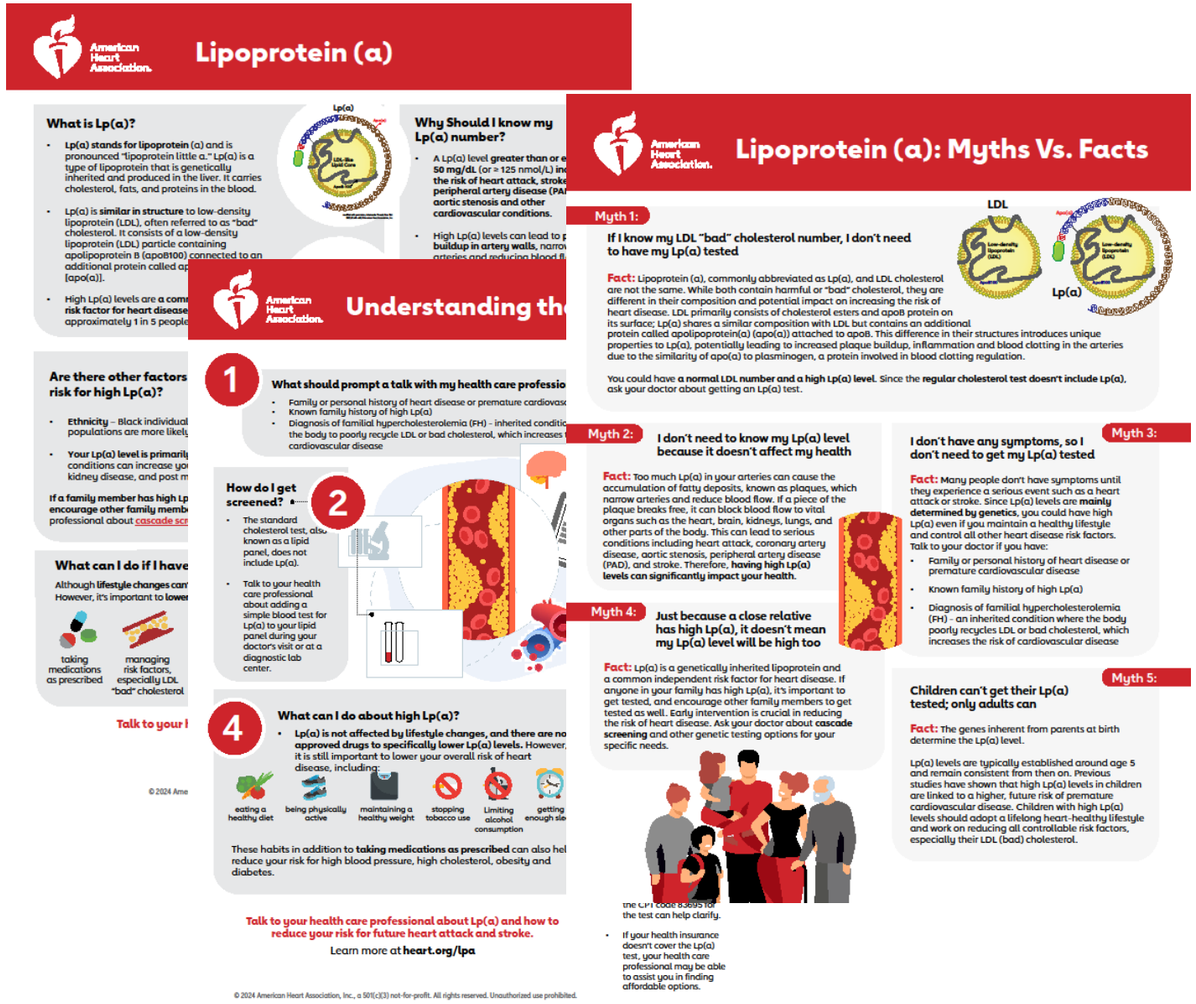
Questions and Discussion

Lp(a) Resources



Lipoprotein (a)

What is Lp(a)?

- **Lp(a) stands for lipoprotein** (a) and is pronounced "lipoprotein little a." Lp(a) is a type of lipoprotein that is genetically inherited and produced in the liver. It carries cholesterol, fats, and proteins in the blood.
- Lp(a) is **similar in structure** to low-density lipoprotein (LDL), often referred to as "bad" cholesterol. It consists of a low-density lipoprotein (LDL) particle containing apolipoprotein B (apoB100) connected to an additional protein called ap [apo(a)].
- High Lp(a) levels are a **com risk factor for heart disease** approximately 1 in 5 people

Why Should I know my Lp(a) number?

- A Lp(a) level **greater than or e 50 mg/dL** (or > 125 nmol/L) in **the risk of heart attack, stroke peripheral artery disease (PA aortic stenosis and other cardiovascular conditions.**
- High Lp(a) levels can lead to **buildup in artery walls**, narro arteries and reducing blood fl

Are there other factors risk for high Lp(a)?

- **Ethnicity** – Black individual populations are more likel
- **Your Lp(a) level is primaril** conditions can increase yo kidney disease, and post m

If a family member has high Lp encourage other family memb professional about cascade scr

What can I do if I have

Although **lifestyle changes can** However, it's important to **lowe**

taking medications as prescribed

managing risk factors, especially LDL "bad" cholesterol

Talk to your

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Understanding th

1 What should prompt a talk with my health care professio

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2 How do I get screened?

- The standard cholesterol test, also known as a lipid panel, does not include Lp(a).
- Talk to your health care professional about adding a simple blood test for Lp(a) to your lipid panel during your doctor's visit or at a diagnostic lab center.

4 What can I do about high Lp(a)?

- **Lp(a) is not affected by lifestyle changes, and there are no approved drugs to specifically lower Lp(a) levels.** However, it is still important to lower your overall risk of heart disease, including:

eating a healthy diet | being physically active | maintaining a healthy weight | stopping tobacco use | Limiting alcohol consumption | getting enough sle

These habits in addition to **taking medications as prescribed** can also hel reduce your risk for high blood pressure, high cholesterol, obesity and diabetes.

Talk to your health care professional about Lp(a) and how to reduce your risk for future heart attack and stroke.

Learn more at **heart.org/lpa**

Lipoprotein (a): Myths Vs. Facts

Myth 1:

If I know my LDL "bad" cholesterol number, I don't need to have my Lp(a) tested

LDL

Lp(a)

Fact: Lipoprotein (a), commonly abbreviated as Lp(a), and LDL cholesterol are not the same. While both contain harmful or "bad" cholesterol, they are different in their composition and potential impact on increasing the risk of heart disease. LDL primarily consists of cholesterol esters and apoB protein on its surface; Lp(a) shares a similar composition with LDL but contains an additional protein called apolipoprotein(a) (apo(a)) attached to apoB. This difference in their structures introduces unique properties to Lp(a), potentially leading to increased plaque buildup, inflammation and blood clotting in the arteries due to the similarity of apo(a) to plasminogen, a protein involved in blood clotting regulation.

You could have **a normal LDL number and a high Lp(a) level.** Since the **regular cholesterol test doesn't include Lp(a),** ask your doctor about getting an Lp(a) test.

Myth 2:

I don't need to know my Lp(a) level because it doesn't affect my health

Fact: Too much Lp(a) in your arteries can cause the accumulation of fatty deposits, known as plaques, which narrow arteries and reduce blood flow. If a piece of the plaque breaks free, it can block blood flow to vital organs such as the heart, brain, kidneys, lungs, and other parts of the body. This can lead to serious conditions including heart attack, coronary artery disease, aortic stenosis, peripheral artery disease (PAD), and stroke. Therefore, **having high Lp(a) levels can significantly impact your health.**

Myth 3:

I don't have any symptoms, so I don't need to get my Lp(a) tested

Fact: Many people don't have symptoms until they experience a serious event such as a heart attack or stroke. Since Lp(a) levels are **mainly determined by genetics**, you could have high Lp(a) even if you maintain a healthy lifestyle and control all other heart disease risk factors. Talk to your doctor if you have:

- Family or personal history of heart disease or premature cardiovascular disease
- Known family history of high Lp(a)
- Diagnosis of familial hypercholesterolemia (FH) – an inherited condition where the body poorly recycles LDL or bad cholesterol, which increases the risk of cardiovascular disease

Myth 4:

Just because a close relative has high Lp(a), it doesn't mean my Lp(a) level will be high too

Fact: Lp(a) is a genetically inherited lipoprotein and a common independent risk factor for heart disease. If anyone in your family has high Lp(a), it's important to get tested, and encourage other family members to get tested as well. Early intervention is crucial in reducing the risk of heart disease. Ask your doctor about **cascade screening** and other genetic testing options for your specific needs.

Myth 5:

Children can't get their Lp(a) tested; only adults can

Fact: The genes inherent from parents at birth determine the Lp(a) level.

Lp(a) levels are typically established around age 5 and remain consistent from then on. Previous studies have shown that high Lp(a) levels in children are linked to a higher, future risk of premature cardiovascular disease. Children with high Lp(a) levels should adopt a lifelong heart-healthy lifestyle and work on reducing all controllable risk factors, especially their LDL (bad) cholesterol.

the CPT code 83695 for the test can help clarify.

- If your health insurance doesn't cover the Lp(a) test, your health care professional may be able to assist you in finding affordable options.

www.heart.org/lpa

1

LP(a) measurement obtained:
- (●) This hospitalization
- ( ) Prior to this hospitalization
- ( ) Planned after discharge
- ( ) No measurement documented

LP(a) Value: [ ]

LP(a) Unit: ( ) nmol/L ( ) mg/dl

LP(a) Not Documented: [ ]

2

Referred for Lipid Management (●) Yes ( ) No ( ) NC

3

LP(a) treatment plan:
- [ ] None
- [ ] Lipoprotein apheresis
- [ ] Patient education on LP(a)
- [ ] Referred to lipid management
- [ ] Risk factor management
- [ ] Other

American Heart Association® Get With The Guidelines® Stroke

American Heart Association® Get With The Guidelines® Coronary Artery Disease