Lp(a) in Women's Heart Health: The Missing Piece in Residual Cardiovascular Risk

Dr. Stephanie Saucier MD, FACC
Co-Director, Women's Heart Wellness Program for Hartford Healthcare's Heart and Vascular Institute
Medical Director of Hartford Region Cardiac Rehabilitation Program

Dr. Hilary Wagner DO, MS
Noninvasive Cardiologist

American Heart Association.

Disclaimer Slide

The recommendations and opinions presented by our guest speakers may not represent the official position of the American Heart Association. The materials are for educational purposes only, and do not constitute an endorsement or instruction by the Heart Association. The American Heart Association does not endorse any product or device.

Housekeeping

Audio:
All attendees are muted.

Video:
Only Panelists will be on camera.

CC Closed Captions:
are available and can be engaged by clicking on the CC icon at the bottom of your screen.

Recording:
This session is being recorded and will be shared afterward.

Q&A:
Use the Q&A panel for questions anytime.

Technical Help:
If you experience issues, try leaving and rejoining the webinar or checking your internet connection.

Stay until the end for **live Q&A**.

"Resources" icon located at the bottom of your screen (looks like three pieces of paper). Choose "Documents" and click on the arrow to download the resource.

Connect with us
www.heart.org/lpadiscovery

Lp(a) CHC Discovery Project

Lp(a), also known as lipoprotein(a), is an independent, inherited and causal risk factor for cardiovascular disease, the leading cause of death and disability worldwide. High Lp(a) levels affect approximately 1 in 5 people worldwide.

The American Heart Association launched a 3-year national initiative, the Lp(a) Discovery Project, to increase Lp(a) testing by improving processes across care settings through national education. As an enhancement to this work, the Association launched the Lp(a) CHC Discovery Project which seeks to identify various approaches and barriers to testing for Lp(a) within community health centers.

Scan to discover more:

Disclosure

Stephanie Saucier

MD, FACC

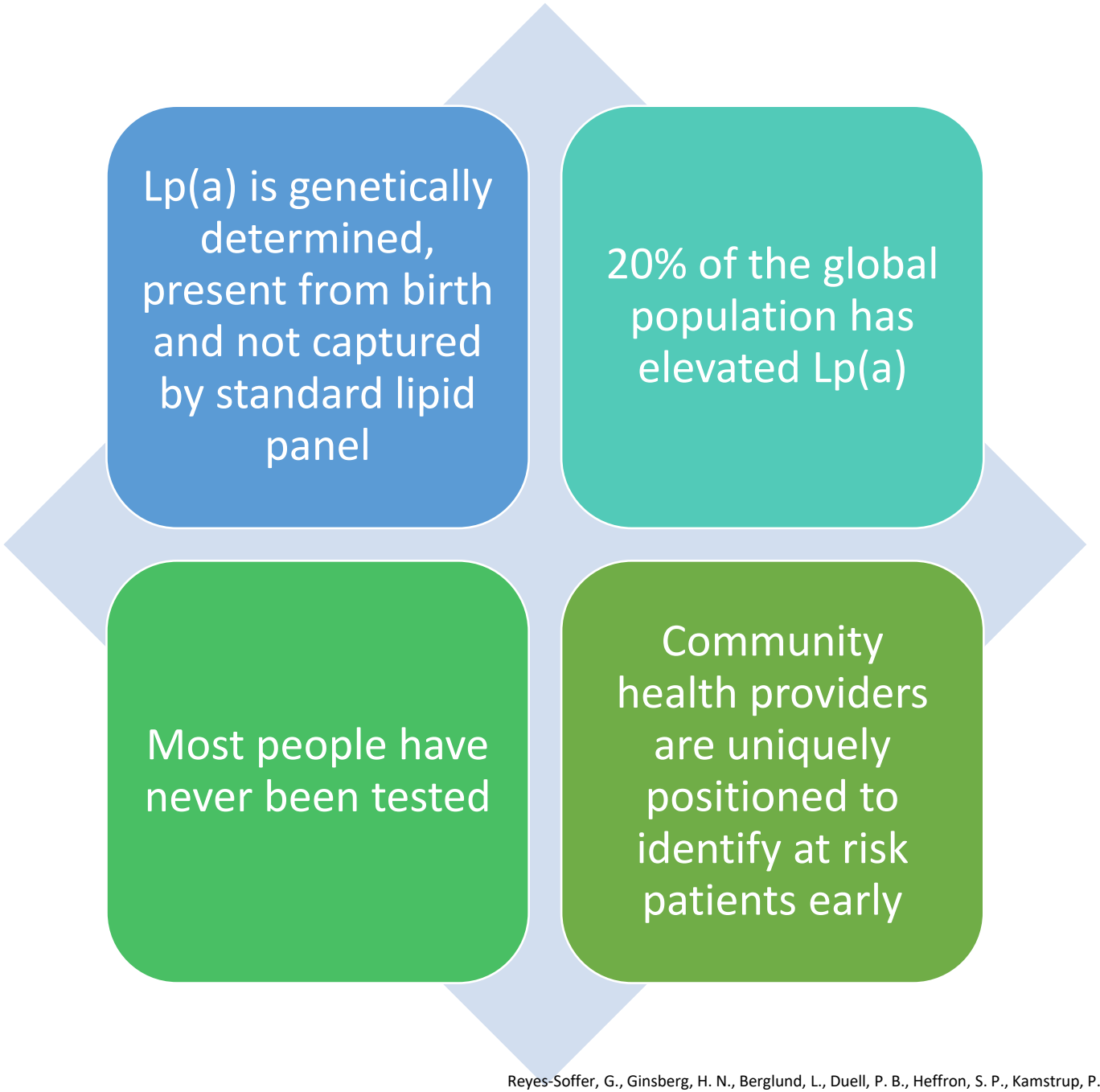
FINANCIAL DISCLOSURE:

- Amgen- Speakers Bureau
- Novartis- Non-branded Content
- Arrowhead- Speakers Bureau
- Cardamyst- Speakers Bureau

Outline

- Why Lp(a) matters
- What is it and why it’s different
- Lp(a) in women – sex-specific data
- Who to test, what to do and your role
- Case based learning
- Q&A

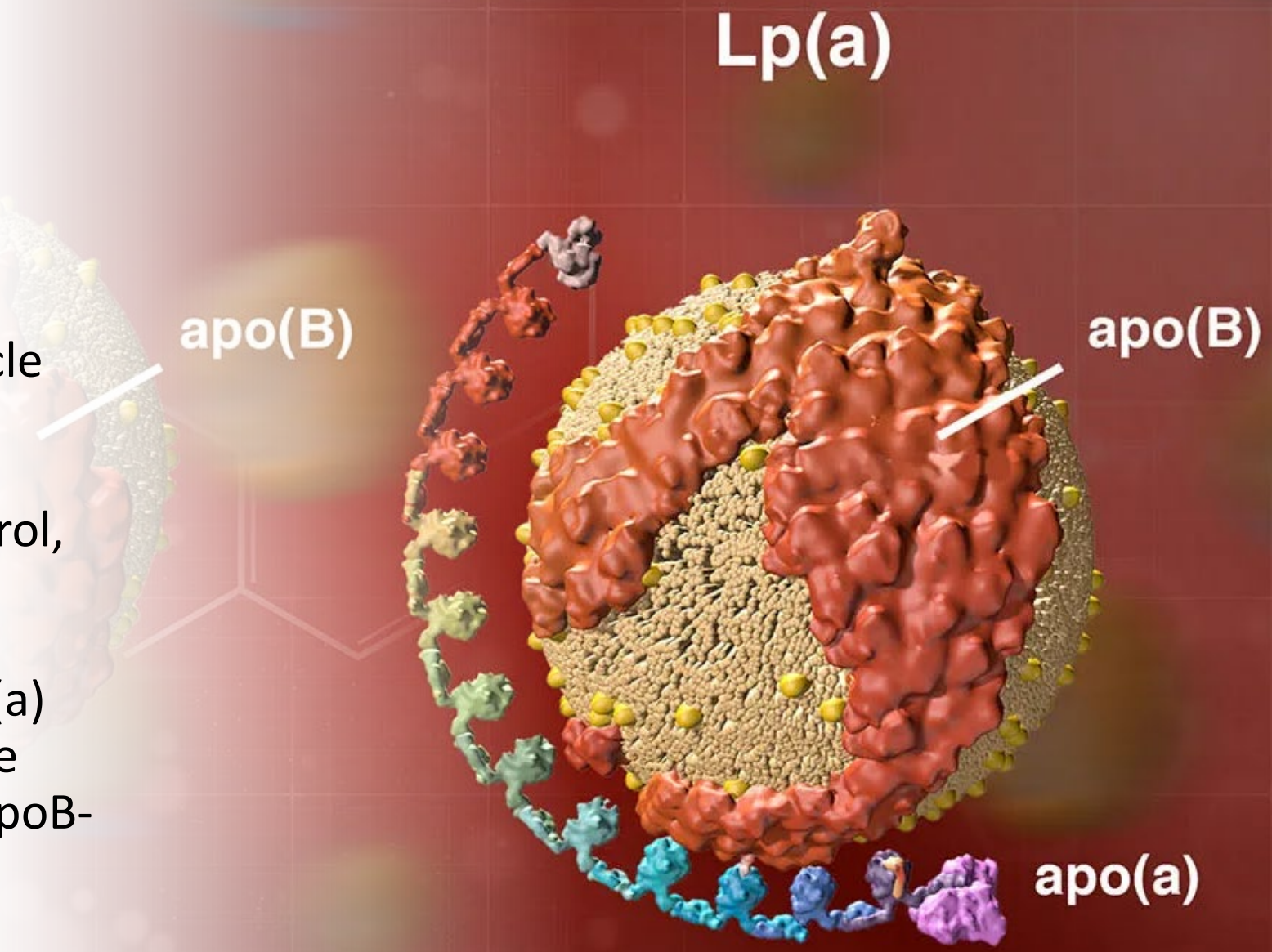
Why Lp(a) Matters



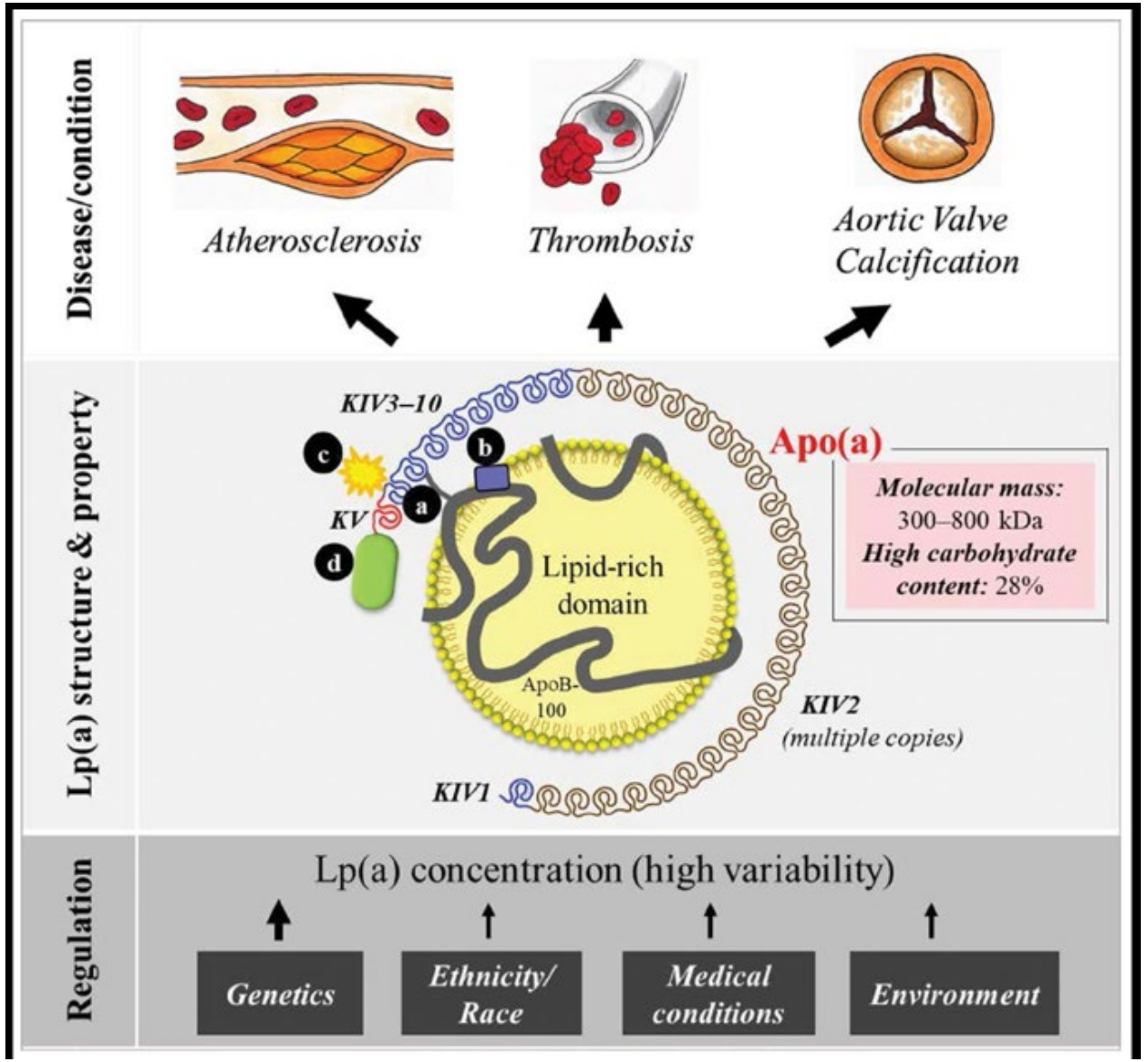
Reyes-Soffer, G., Ginsberg, H. N., Berglund, L., Duell, P. B., Heffron, S. P., Kamstrup, P. R., Lloyd-Jones, D. M., Marcovina, S. M., Yeang, C., & Koschinsky, M. L. (2022).

Lp(a) Basics

- Contains LDL like particle that is composed of apolipoprotein B-100, phospholipid, cholesterol, cholesterol esters and triglycerides. There is a unique apolipoprotein(a) that is linked by a single disulfide bond to the apoB-100.



Illustrative schematic of LDL and Lp(a) structure (apo[a] bound to apoB-containing particle), adapted from published literature.



Reyes-Soffer G, Ginsberg HN, Ramakrishnan R. The metabolism of lipoprotein (a): an ever-evolving story. *J Lipid Res*. 2017;58:1756–1764. doi: 10.1194/jlr.R077693

Lipoprotein (a)

Independent and causal risk factor for atherosclerotic cardiovascular disease

In the absence of an acute illness the level of Lp(a) is stable throughout an individual's lifetime and unaffected by lifestyle

More than 90% of the Lp(a) concentration is explained by an autosomal dominant pattern of inheritance and is fully expressed by 1-2 years of age

Lp(a) reaches adult levels by 5 years of age

[1] Reyes-Soffer G et al. *Arterioscler Thromb Vasc Biol.* 2023 [2] Nordestgaard BG et al. *Lancet.* 2024 [3] Alebna PL, Mehta A. ACC. 2023 [4] Al-Dalakta A et al. *Cleve Clin J Med.* 2025
[5] Alebna PL et al. ACC. 2023

How does Lp(a) Cause Disease

- Promotes atherosclerosis and thrombosis
- The similarity of apo(a) to the proenzyme plasminogen – increases the protentional of Lp(a) to compete with plasminogen for fibrin binding and decrease fibrinolysis
- Lp(a) can increase plasminogen activator inhibitor-1 secretion from vascular endothelial cells, block tissue factor pathway inhibitor and promote platelet aggregation all which contribute to increased clot formation
- Lp(a) is the preferential carrier of oxidized phospholipids in the plasma that mediate a variety of proinflammatory responses in vascular cells

Tsimikas, S. (2013). *Lipoprotein(a) in cardiovascular diseases*. **BioMed Research International**, 2013, Article 650989.

High > 125 nmol/L

- 40% increased ASCVD risk

Very high > 250 nmol/L

- 2x increased ASCVD risk

Measurement Pearl

- Units matter (nmol/L vs. mg/dL) they are not directly interconvertible
- Isoform-insensitive assays are preferred

Blumenthal RS, Morris PB, Gaudino M, et al.
2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines.
J Am Coll Cardiol. Published online March 13, 2026.
doi:10.1016/j.jacc.2025.11.016

LA allele size has an inverse correlation between apo(a) isoform size and Lp(a) levels

Median Lp(a) levels are higher among African and South Asian ancestry groups

Carriers of rs10455872 or rs3798220 have fewer kringle repeats, higher Lp(a) concentrations and higher risk

Reyes-Soffer G, Ginsberg HN, Berglund L et al. Lipoprotein(a): A Genetically Determined, Causal, and Prevalent Risk Factor for Atherosclerotic Cardiovascular Disease: A Scientific Statement From the American Heart Association. Arterioscler Thromb Vasc Biol 2022; 42:e48-e60.

Association of LPA Variants With Risk of Coronary Disease and the Implications for Lipoprotein(a)- Lowering Therapies

Mendelian randomization analysis involving more than 80,000 patients and 150,000 controls

CAD risk was proportionally associated with the absolute change in plasma lipoprotein(a) mass concentration

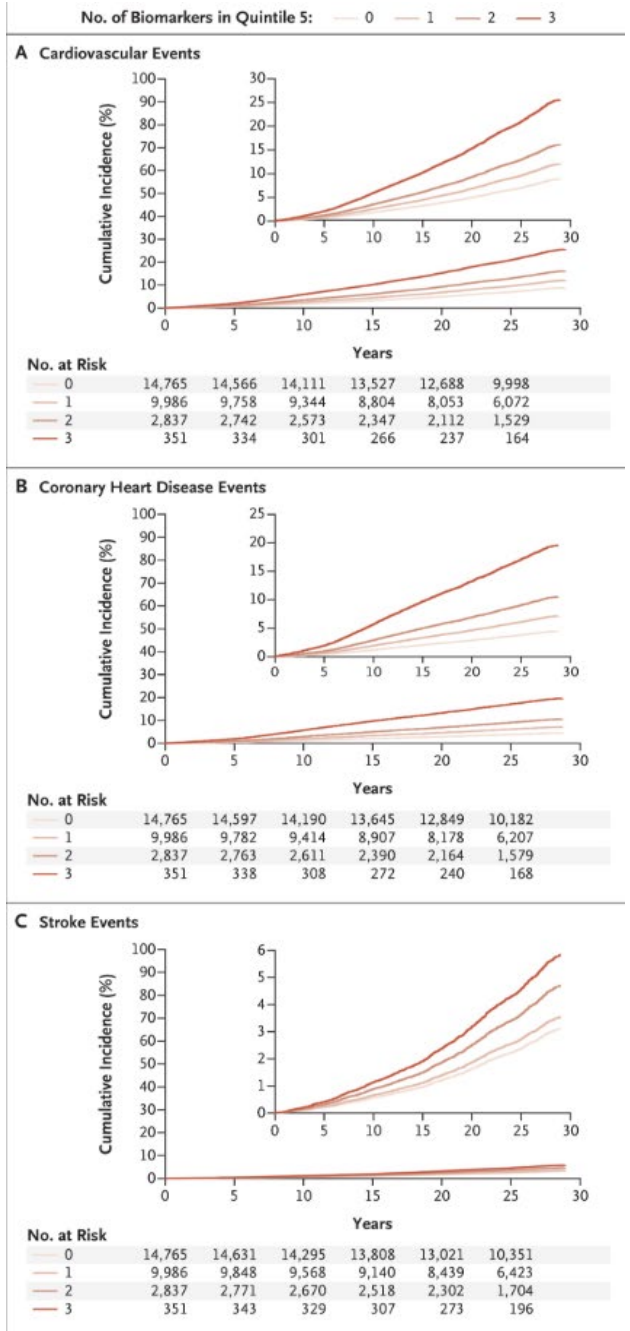
A 101.5 mg/dL change in Lp(a) was associated with the same coronary heart disease risk as a 38.67mg/dL change in LDL cholesterol level

Lp(a) concentration must be lowered by approximately 100mg/dL to achieve the same reduction in coronary heart disease risk as can be achieved by lowering LDL cholesterol level by 38.67mg/dL

Burgess S., Ference B.A., Staley J.R., et. al.: Association of LPA variants with risk of coronary disease and the implications for lipoprotein(a)-lowering therapies: a Mendelian randomization analysis. JAMA Cardiol 2018; 3: pp. 619-627.

Lp(a) in Women – Sex Specific Data

- Women have higher Lp(a) levels than men
- The Women's Health Study (n= 28,000, 30 year follow up)
  - Lp(a) as an independent predictor of MACE
  - Additive risk when combined with elevated hsCRP and LDL-C



Inflammation, Cholesterol, Lipoprotein(a), and 30-Year Cardiovascular Outcomes in Women. N Engl J Med. December 4, 2024.

Lp(a) increases up to 27% after menopause

Lp(a) can double during pregnancy

HRT reduces Lp(a) 17-23%

Black women have the highest median Lp(a) levels

Simony SB, Mortensen MB, Langsted A, Afzal S, Kamstrup PR, Nordestgaard BG. Sex differences of lipoprotein(a) levels and associated risk of morbidity and mortality by age: The Copenhagen General Population Study. Atherosclerosis. 2022 Aug;355:76-82. doi: 10.1016/j.atherosclerosis.2022.06.1023. Epub 2022 Jun 27. PMID: 35803767

Who to Test…What to Do… and Your Role

2026 Lipid Guideline recommend measuring testing Lp(a) once in a lifetime for all adults, ideally with the first lipid panel

Prioritize testing in family history of premature ASCVD, postmenopausal women, high prevalence racial/ethnic groups

What to do…

Aggressive LDL-C lowering

- LDL goal < 70

Lp(a) should be used as a risk enhancer and should tip the scale toward statin initiation

Remind patients that Lp(a) is predominantly genetic and is not their fault

Historical Treatments Evaluated

- **Mipomersen**
- Antisense oligonucleotide against ApoB-100
- Reduced Lp(a) by 20-30% however had significant hepatotoxicity

- **Lomitapide**
- Microsomal triglyceride transfer protein inhibitory
- Inhibits VLDL thus lowering secretion of apob-100 containing lipoproteins
- 15-20% reduction
- Hepatotoxic effects

Does Drug Therapy Affect Risk in ASCVD patients with ↑Lp(a)?

	Impact on Lp(a)	Effect on ASCVD Outcomes
Statins	Minimal or mild ↑	Rosuvastatin 20 mg daily reduced ASCVD risk equally in all ethnicities, whether Lp(a) above or below median[1]
Ezetimibe	Minimal ↓ as monotherapy[2]	Unknown
PCSK9 inhibitors	Evolocumab ↓ by median 27%	Reduces RR of CHD death, MI or urgent revascularization 23% if Lp(a) >37 nmol/L (NNT_{3y} 40) vs. those with Lp(a) ≤37 (NNT_{3y} 105)[4]
	Alircomab ↓ by median 29%[3]	Proportion of MACE reduction attributable to changes in Lp(a) greatest in those with Lp(a) >59.6 mg/dL[5]

1. Khera AV et al. Circulation. 2014 Feb 11;129(6):635-42. 2. Awad K et al. Drugs 2018;78:453-62.
3. Gaudet D et al. Am J Cardiol 2017;119: 40-64. 4. O'Donoghue M et al. Circulation. 2019;139:1483–1492
5. Presented by V. Bittner ACC19

Antisense Oligonucleotide against LPA and short interfering RNA therapies

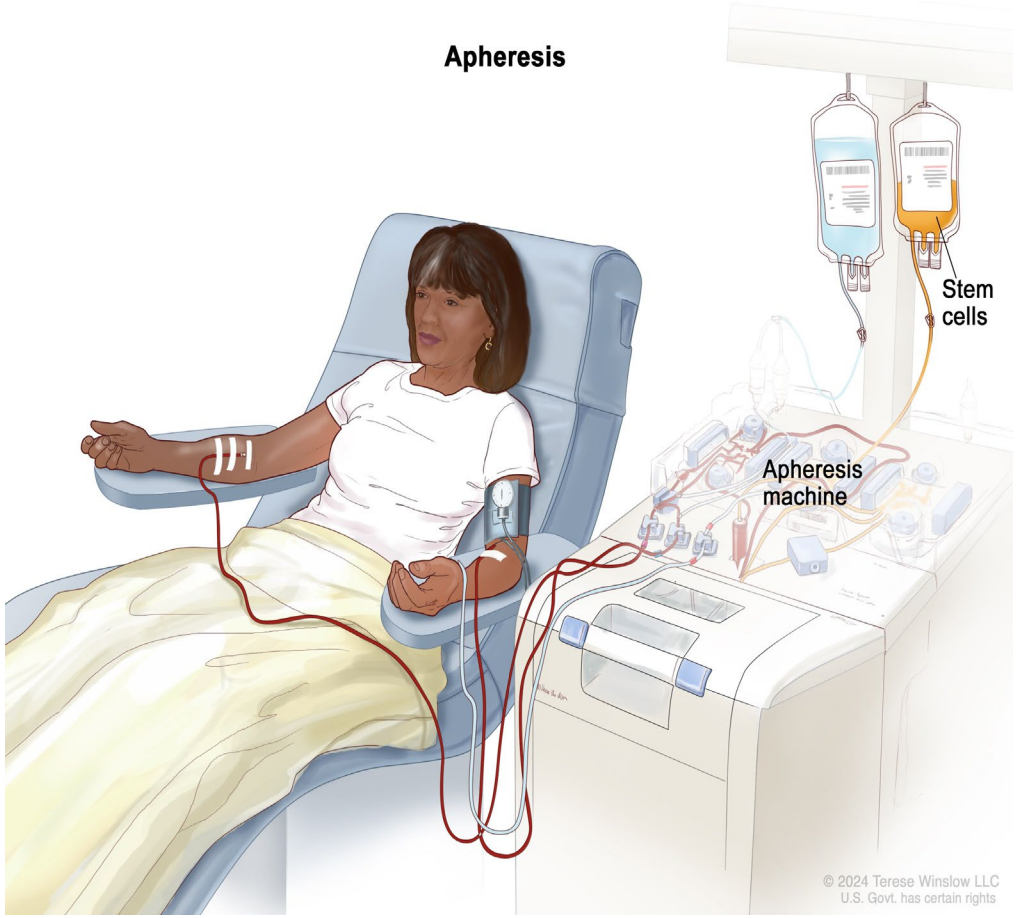
- Target hepatic apo(a) production
- Demonstrating significant reductions in Lp(a)

Molecule	Type	Company	Route/Dosing	Max Lp(a) Reduction	Expected Results
Pelacarsen	ASO	Novartis	SQ Monthly	80%	2026
Olpasiran	siRNA	Amgen	SQ 12 weeks	98%	2026
Lepodisiran	siRNA	Eli Lilly	SQ 6 Month	98%	2029
Zerlasiran	siRNA	AstraZeneca	SQ 16-24 weeks	98%	TBD
Muvalaplin	Small molecule inhibitor	Eli Lilly	Oral Daily	86%	TBD

Data derived from published clinical trials and pipeline analyses of lipoprotein(a)-lowering therapies, including pelacarsen, olpasiran, lepodisiran, zerlasiran, and muvalaplin.

Lipid Apheresis for Lp(a)

- Most effective treatment available only current FDA approved treatment
- Lowers Lp(a) by 60-80%
- Associated with significant MACE reduction in individuals with progressive ASCVD
- Pro(a)LiFe study
- Less accessible and more intrusive
- FDA approved use of apheresis in individuals with ASCVD who have LDL > 100mg/dL and Lp(a) > 60 mg/dL



[1]Koschinsky 2024 [2]AHA Statement 2024 [3]Nugent 2020 [4]Klingel 2025

Terese Winslow LLC. (2024). Apheresis [Illustration]. National Cancer Institute

Lipoprotein Apheresis for Lipoprotein(a) – Associated Cardiovascular Disease: Prospective 5 years of Follow-Up and Apolipoprotein(a) Characterization

- Prospective observational multicenter study included 170 patients with Lp(a) and progressive cardiovascular disease
- Lipid apheresis has a lasting effect on prevention of cardiovascular events in patients with Lp(a)
- Regular ongoing apheresis was associated with stabilization of progressive CVD
- Annual incidence rates for MACE and ACVE were 855 and 81% lower during chronic apheresis in comparison to the progressive phase of prior to starting apheresis
- Lp(a) concentration seemed to comprehensively reflect Lp(a) associated cardiovascular risk

Roeseler E., Julius U., Heigl F., et. al.: Lipoprotein apheresis for lipoprotein(a)-associated cardiovascular disease: prospective 5 years of follow-up and apolipoprotein(a) characterization. Arterioscler Thromb Vasc Biol 2016; 36: pp. 2019-2027.

Antithrombotic Treatment

Low dose ASA is effective in lowering risk among patients with ASCVD as well as primary prevention

Possible link to aspirin lowering Lp(a) through reduction of apo(a) production in hepatocyte cultures

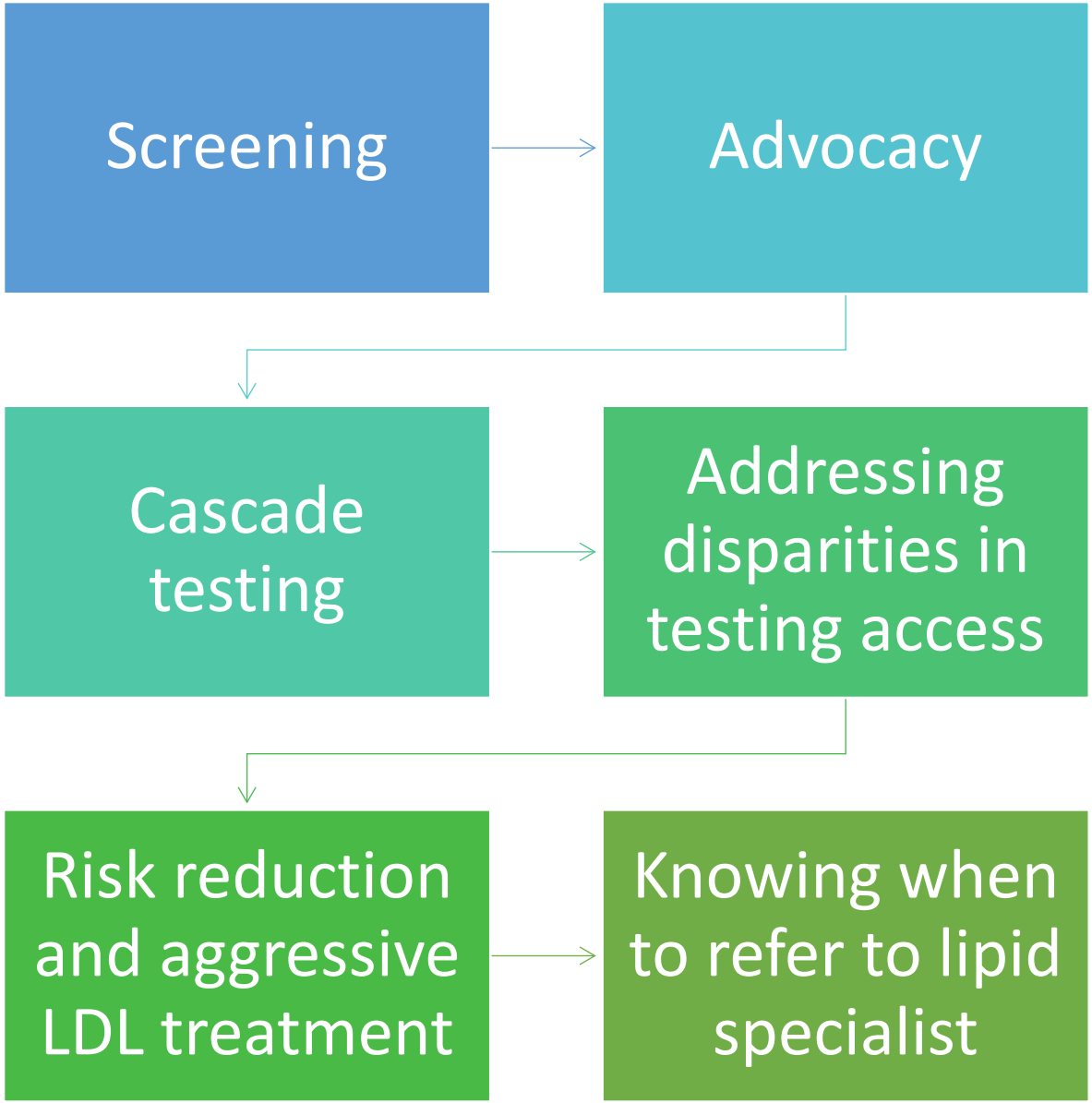
ASPREE trial – sub study showed patients with LPA polymorphism had 46% RRR for combined endpoint of MACE

Patients with elevated Lp(a) benefit more from low-dose aspirin therapy than the general population for primary prevention of ASCVD

Additional randomized control studies are needed

Sukkari MH, Al-Bast B, Al Tamimi R, Giesing W, Siddique M. Is there a benefit of aspirin therapy for primary prevention to reduce the risk of atherosclerotic cardiovascular disease in patients with elevated Lipoprotein (a)-A review of the evidence. Am J Prev Cardiol. 2023 Sep 1;15:100579. doi: 10.1016/j.ajpc.2023.100579. PMID: 37736358; PMCID: PMC10509658.

Your Role


Screening
Advocacy
Cascade testing
Addressing disparities in testing access
Risk reduction and aggressive LDL treatment
Knowing when to refer to lipid specialist

Case Based Learning

Dr. Hilary Wagner DO

Disclosure

Hilary Wagner

MD

FINANCIAL DISCLOSURE:

- None

UNLABELED/UNAPPROVED USES DISCLOSURE:

- None

Case #1

38 y.o Black woman, BMI 26, non-smoker, no personal CVD history. Mother MI at 52

Lipid panel LDL 118 mg/dL, HDL-58, TG 95

10-year ASCVD risk 2.8%

Should Lp(a) be checked?

Lp(a) 180 nmol/L

How does this change management?

Should her siblings and children be tested?

Case #2

56 y.o F who is 4 years postmenopausal, on atorvastatin 20mg

LDL-C 72 mg/dL

Lp(a) checked 10 years ago was 95 nmol/L

Patient asks, “my cholesterol is green – do I still need to worry?”

Should Lp(a) be rechecked?

- Lp(a) now 145 nmol/L

She then asks… should I go on HRT to lower my Lp(a)?

Should LDL-C target be more aggressive?

Case #3

63 y.o F, MI at age 54, new angina requiring PCI

On maximally tolerated statin and zetia

LDL-C 55 mg/dL

Lp(a) 310 nmol/L

Her LDL is at goal why is she having recurrent events?

What else can be done?

Take Home Points

Lp(a) is genetically determined, causal, independent risk factor for ASCVD

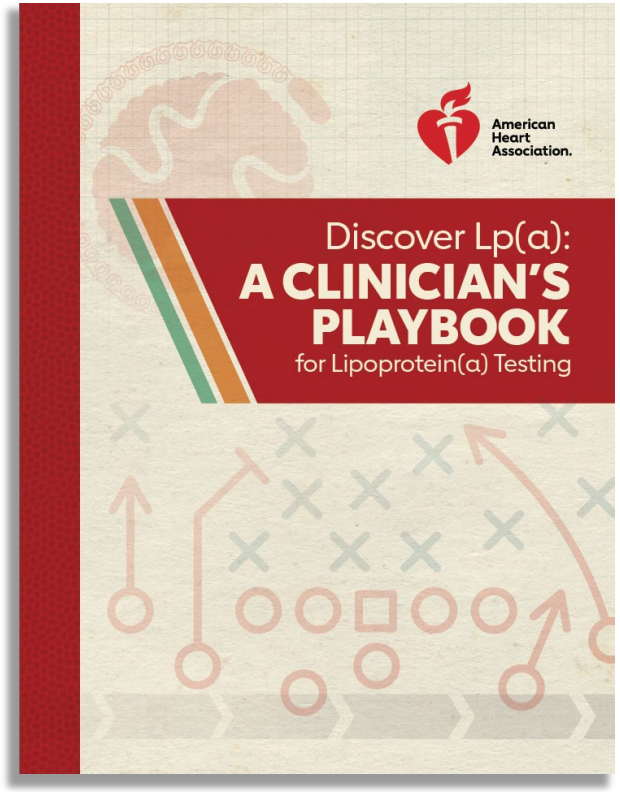
Test every adult at least once

Women have higher Lp(a) than men, and levels rise after menopause, consider repeat testing after 50

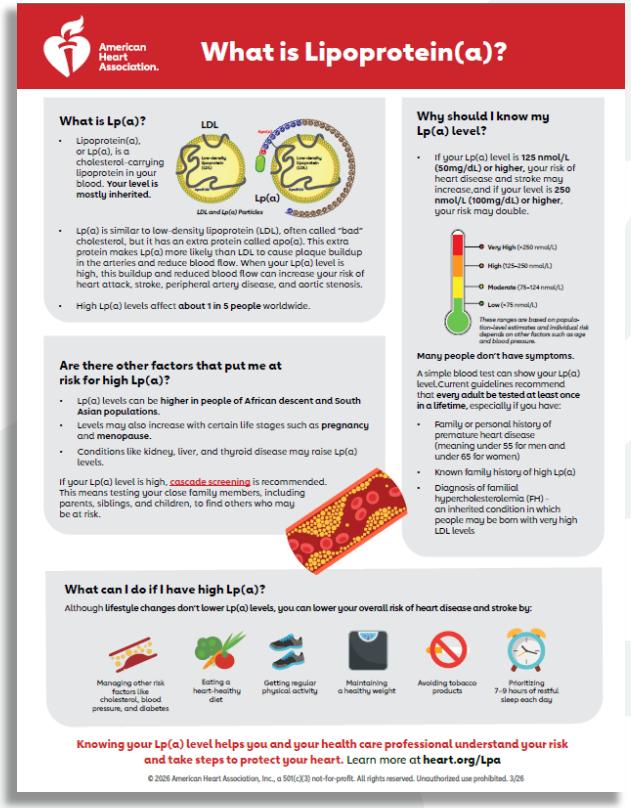
No approved pharmacologic approed Lp(a) specific therapy – current strategy is aggressive LDL lowering and risk factor modification

Questions and Discussion

Lp(a) Discovery Resources



Discover more professional education resources on our website:
www.heart.org/lpadiscovery



Discover more patient education resources on our website:
www.heart.org/lpa