Lp(a) in Special Populations: Aortic Stenosis and Peripheral Arterial Disease

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Lp(a) 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 (AHA) 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 AHA 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:

The Association of Lp(a) and Aortic Stenosis

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Disclosures

Consulting: Novartis, Amgen, Amarin, Esperion,
Amarin, New Amsterdam Pharma, Regeneron

Research Support: NIH, Amgen, Novartis, Janssen,
Eli Lilly, New Amsterdam Pharma, Regeneron

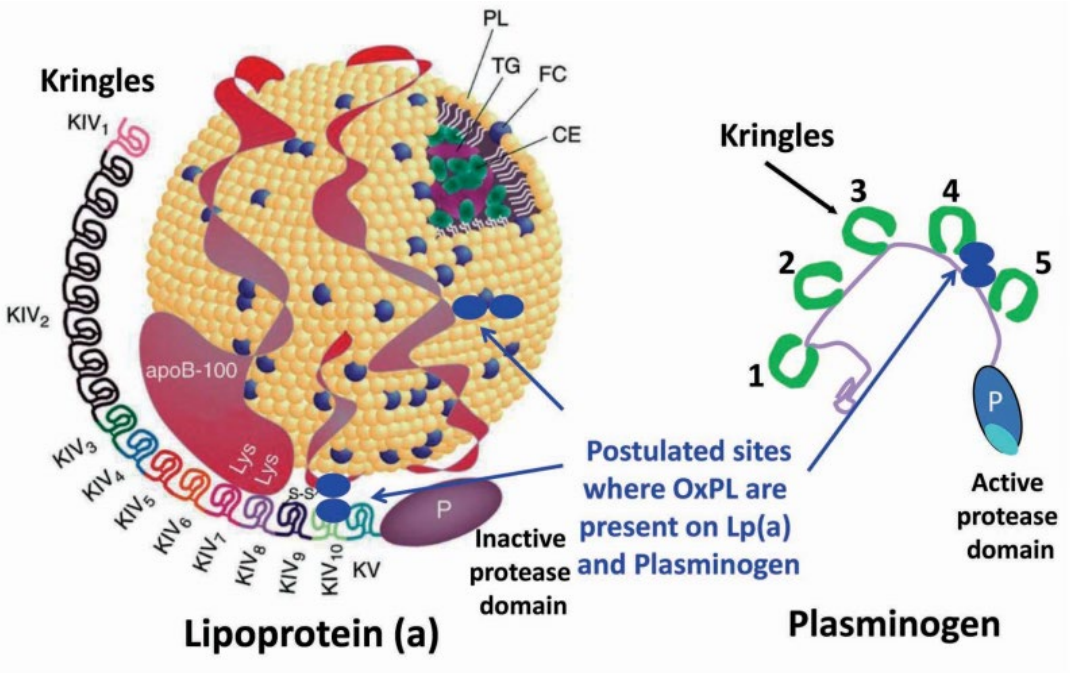
Learning Objectives

- Discuss Lp(a) as a marker of risk
- Describe the pathophysiology of Lp(a) related calcific aortic stenosis
- Describe clinical implications of aortic stenosis and Lp(a)
- Highlight future directions of research

Lipoprotein (a)

Causal and independent association with cardiovascular events

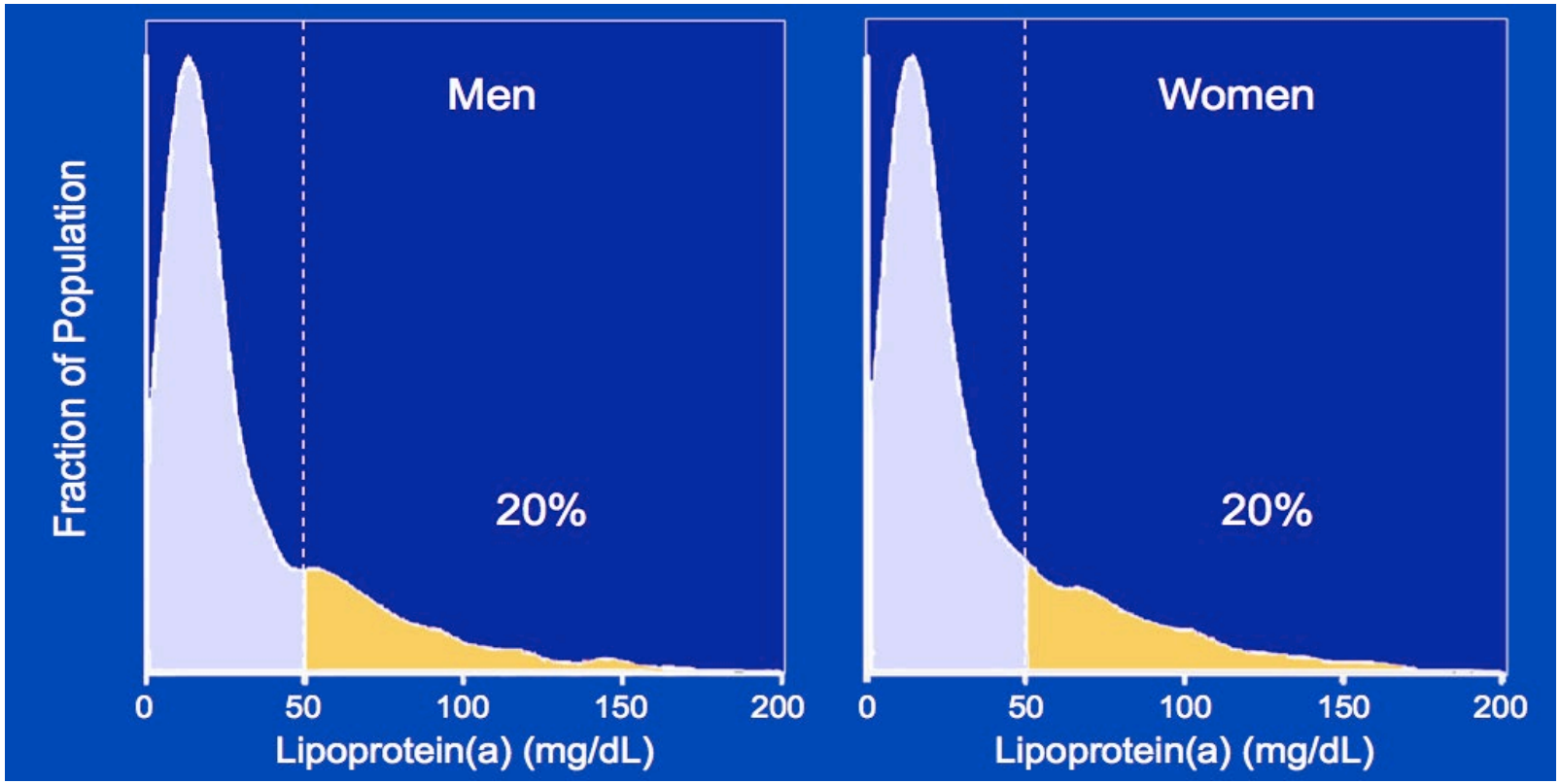
- Genetic origin and expressed from *LPA* locus
- Several isoforms based on number of Kringle Repeats
- Levels don't vary overtime without intervention



- Consists of about 30-45% bound LDL
- Standard lipid assays cannot distinguish free LDL from Lp(a)-LDL
- Pathogenic mechanisms include inflammatory, atherogenic, and thrombotic

Lipoprotein (a): An Update on a Marker of Residual Risk and Associated Clinical Manifestations
Shah, Nishant P. et al.
American Journal of Cardiology, Volume 126, 94 - 102

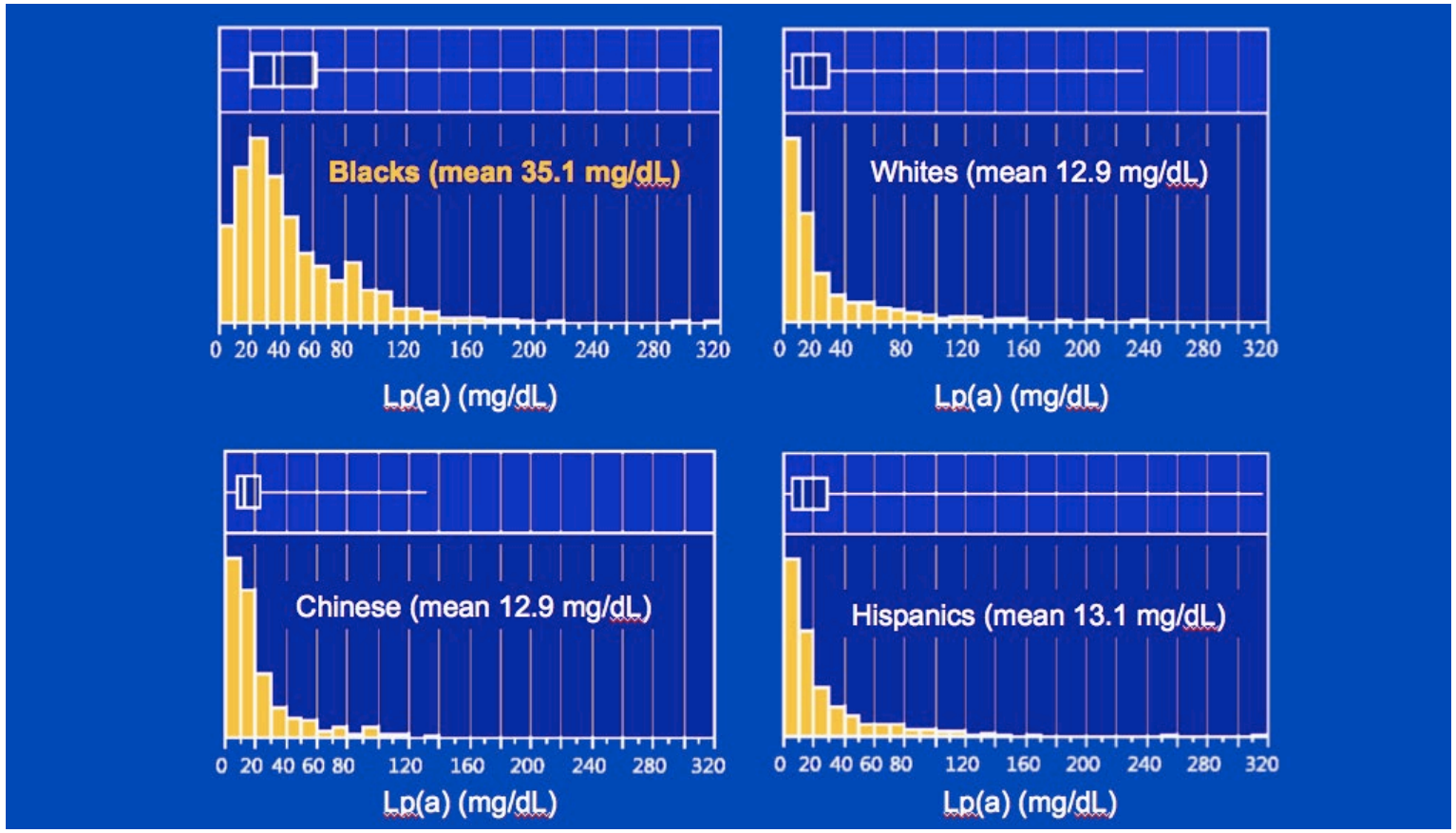
Lp(a) Distribution by Gender



- Elevated in 1/5 patients tested for Lp(a)
- Elevated in 1/3 patients with FH
- Elevated in 1/4 patients with premature ASCVD

Nordestgaard et al. EHJ 2010

Lp(a) Distribution by Race



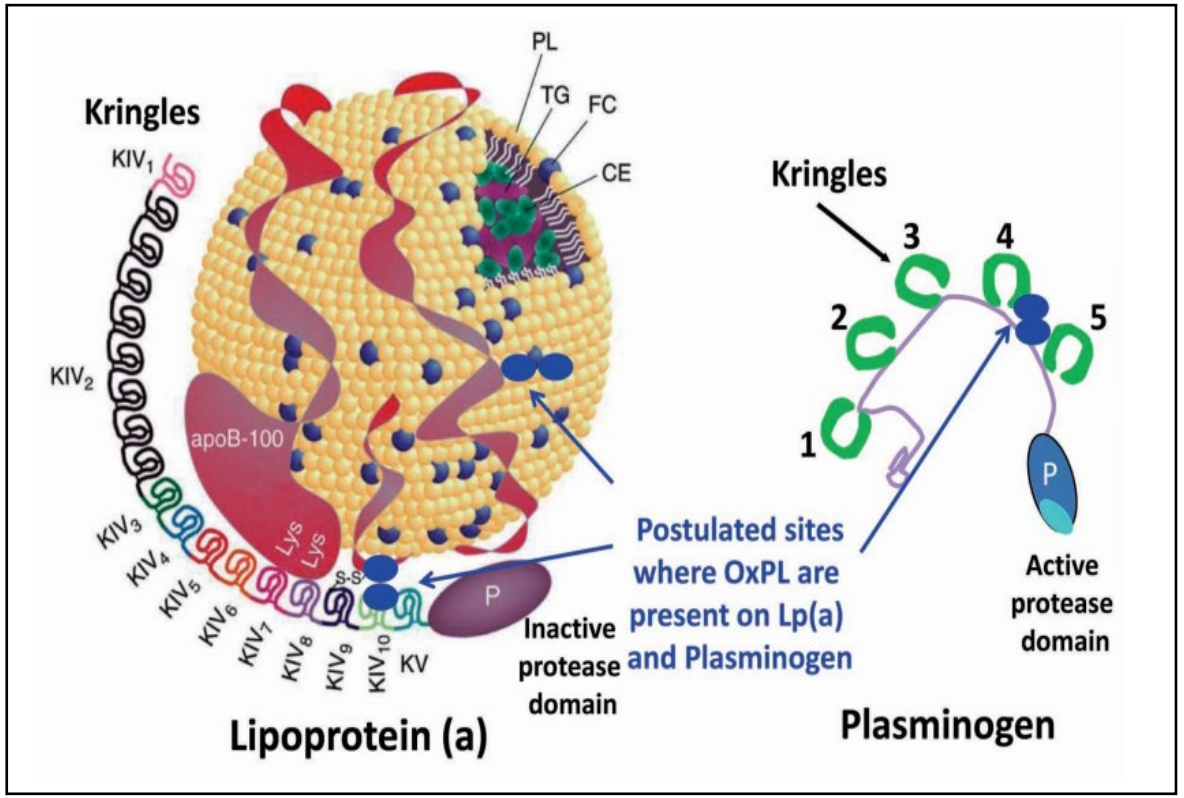
Guan W et al. ATVB 2015

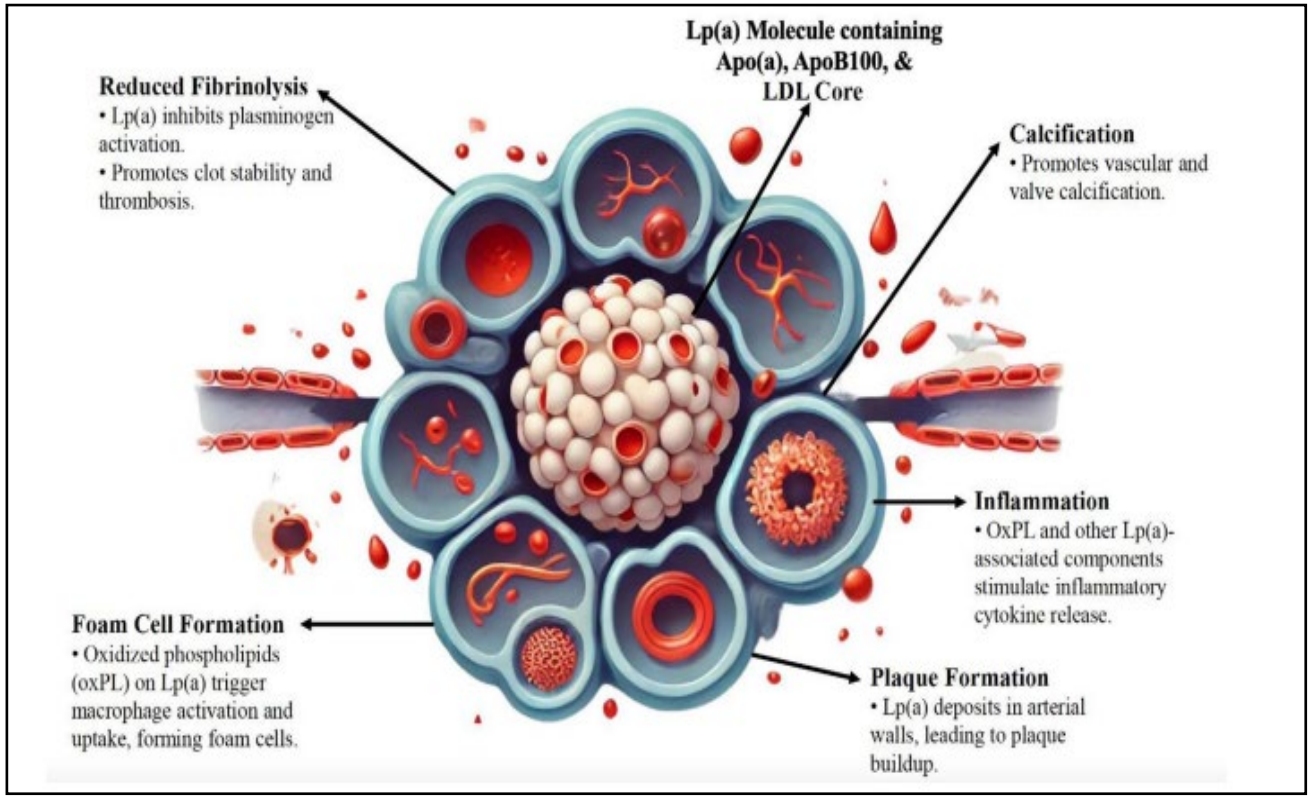
How is Lp(a) related to Aortic Stenosis?

- Calcific aortic valve stenosis is the most prevalent form of valvular disease worldwide, affected nearly 3% of the population over 65 years of age
- There are no current pharmacological treatments indicated to prevent the onset or progression of calcific aortic valve stenosis, and definitive treatment is generally an aortic valve replacement when the stenosis is severe and symptomatic
- Some evidence suggest long term exposure to risk factors such as hypertension or chronic kidney disease can lead to rapid progression of aortic stenosis severity
- Lp(a) has been shown to have an independent and causal association with calcific aortic stenosis beyond traditional risk factors

Rojulpote C,. Role of ^{18}F-NaF-PET in assessing aortic valve calcification with age. Am J Nucl Med Mol Imaging. 2020 Feb 25;10(1):47-56. PMID: 32211218; PMCID: PMC7076301.

Pathophysiology of Lp(a) related Aortic Stenosis





Ashley SC, Kachhy E, Brown KA et al. *Curr Cardiovasc Reports* 2025

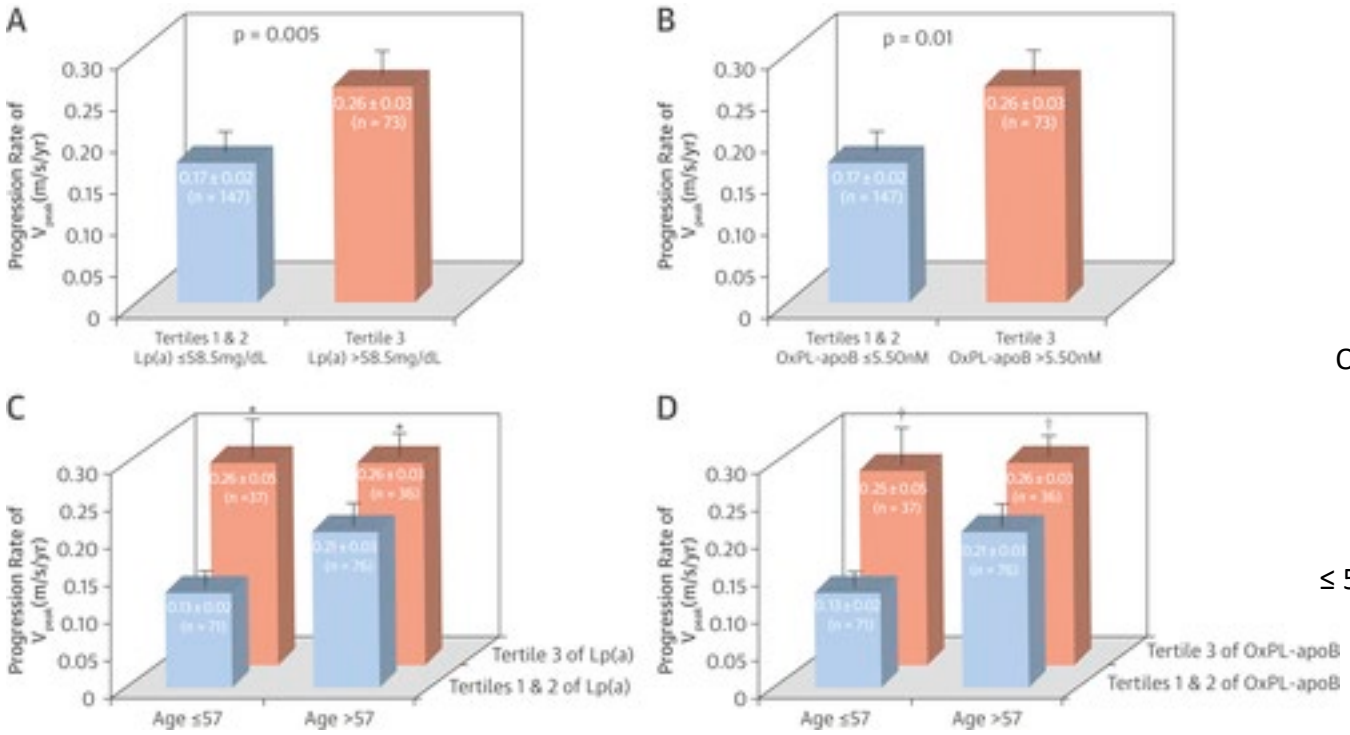
Genetic Origin with Known SNPs Linked to AS

SNP	Gene	Chromosome	Effect and Function	Study Notes	Associated with Coronary Disease
rs10455872	LPA	6	Increased Lp(a) levels, associated with valve calcification	Multiple GWAS; Lp(a) a key risk factor for CAVD	Yes
rs17659543	IL1F9	2	Associated with elevated Lp(a) levels and calcification	Additional variant linked to CAVD progression	Yes
rs13415097	IL1F9	2	Implicated in endothelial integrity and calcification	Suggests role in vascular remodeling	No
rs3798220	LPA	6	Increased Lp(a) levels, promotes calcification	Linked to CAVD and aortic stenosis progression	Yes

CAVS indicates calcific aortic valve stenosis; Lp(a), lipoprotein (a); and GWAS, genome-wide association study

Ashley SC, Kachhy E, Brown KA et al. *Curr Cardiovasc Reports* 2025

Lp(a) and oxidized phospholipid are key mediators



Risk of Being a Rapid Progressor for Patients in Tertile 3

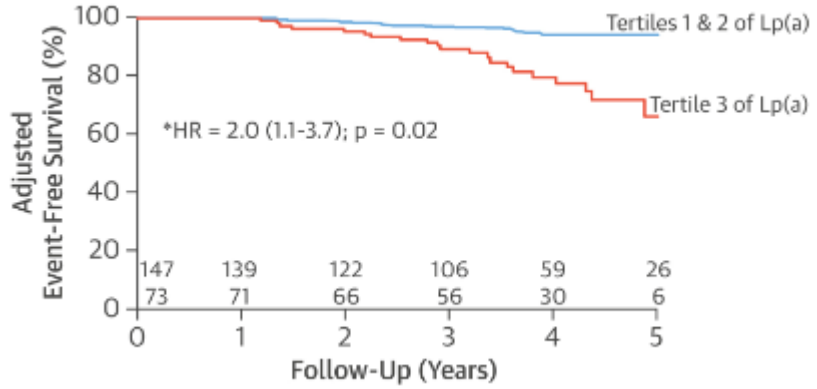
	Univariable Risk		Adjusted Risk	
	OR (95% CI)	p Value	OR (95% CI)	p Value
Overall				
	2.1 (1.2–3.8)	0.009	2.6* (1.4–5.0)	0.003
	2.0 (1.2–4.6)	0.02	2.4* (1.2–4.6)	0.009
≤ 57 years				
	4.0 (1.7–9.5)	0.001	4.9† (1.8–13.7)	0.002
	3.4 (1.4–7.8)	0.005	4.1† (1.4–11.9)	0.01

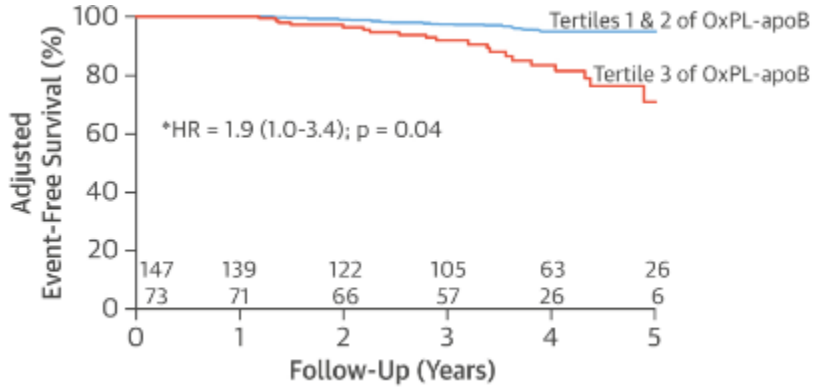
Multivariate model adjusted for age, sex, hypertension, metabolic syndrome, statin use, LDL-C, creatinine, bicuspid aortic valve phenotype, aortic valve calcification score, and baseline peak velocity

Romain Capoulade et al. *JACC* 2015; 66:1236-1246.

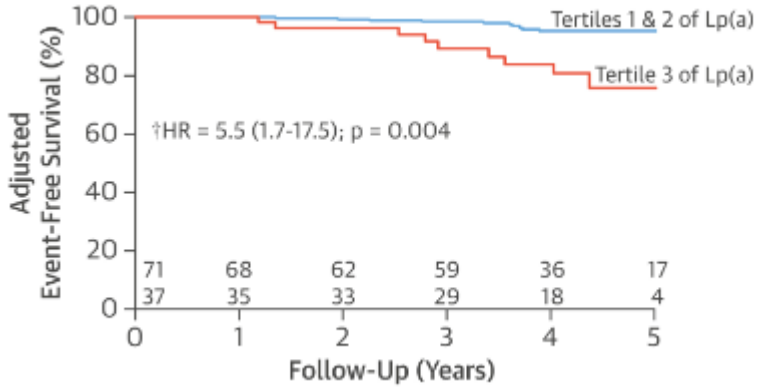
Event Free Survival from Composite of AVR and Cardiac Death

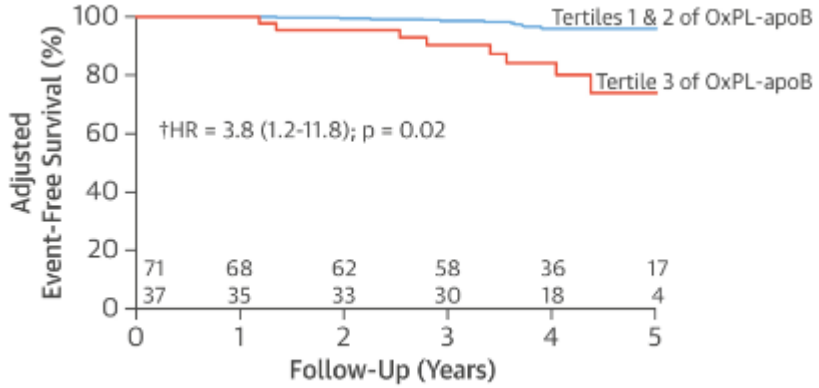
Overall





≤ 57 years of age

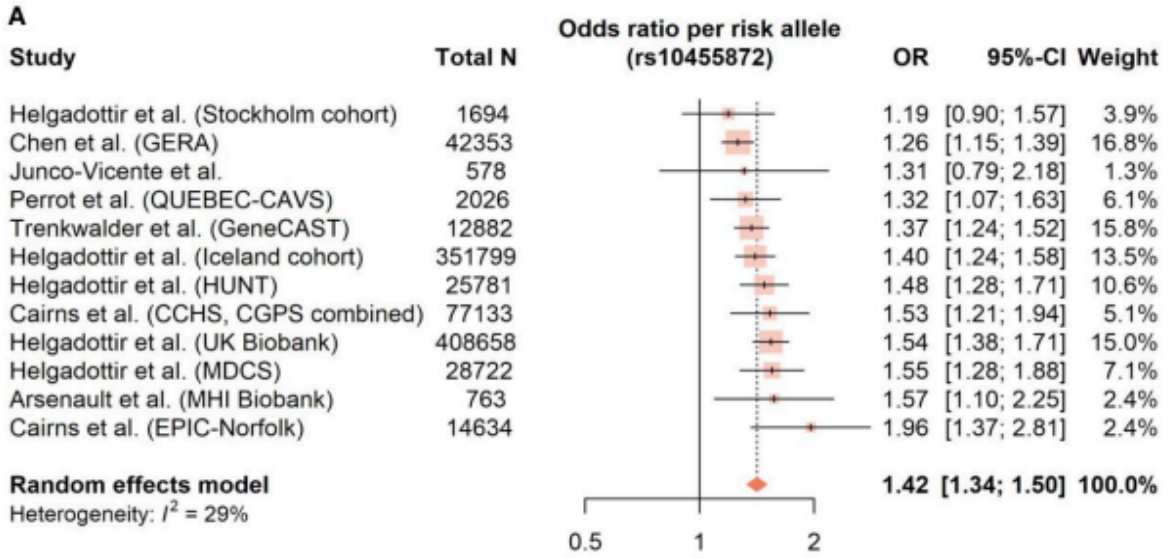




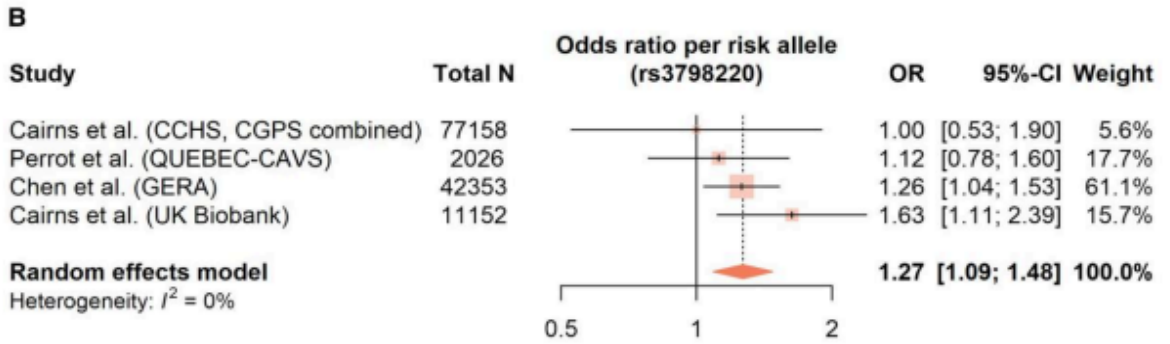
Romain Capoulade et al. *JACC* 2015; 66:1236-1246.

Association with Calcified AS is Consistent Across SNPs

rs10455872



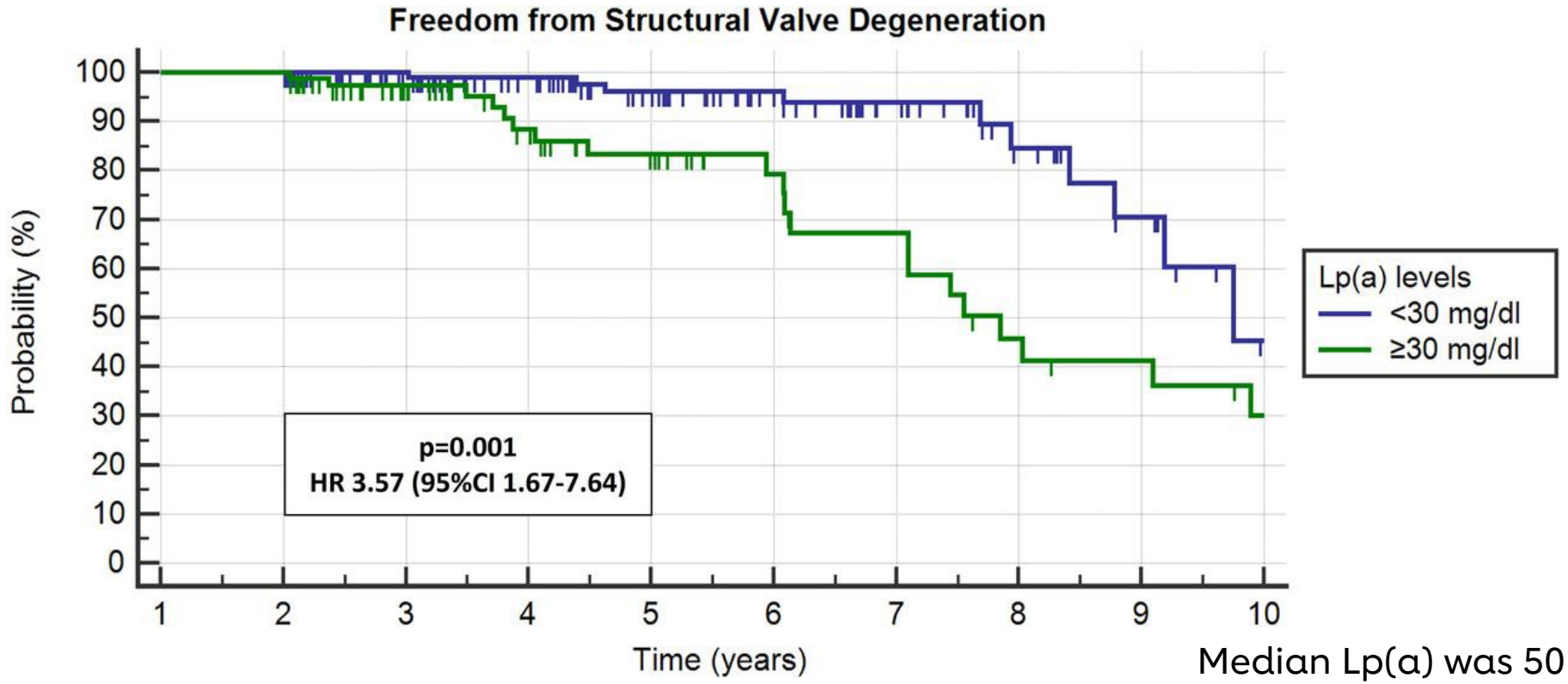
rs3798220



- Those with calcific AS had higher Lp(a) level by 22.63 nmol/L
- Elevated Lp(a) was associated with faster peak velocity rate at 0.09 m/s/year

Pantelidis P, Oikonomou E, Lampsas S et al. *Cardiovasc Research* 2023 119, 1641-1655

Rapid Degeneration in Bioprosthetic Aortic Valves



Median Lp(a) was 50.0 (IQR 72.0) mg/dL in those with degenerative valves vs 15.6 (IQR 48.6) mg/dL in non-degenerative valves

Juan M Farina et al. Heart 2024;110:299-305

Screening Recommendations for ASCVD Risk

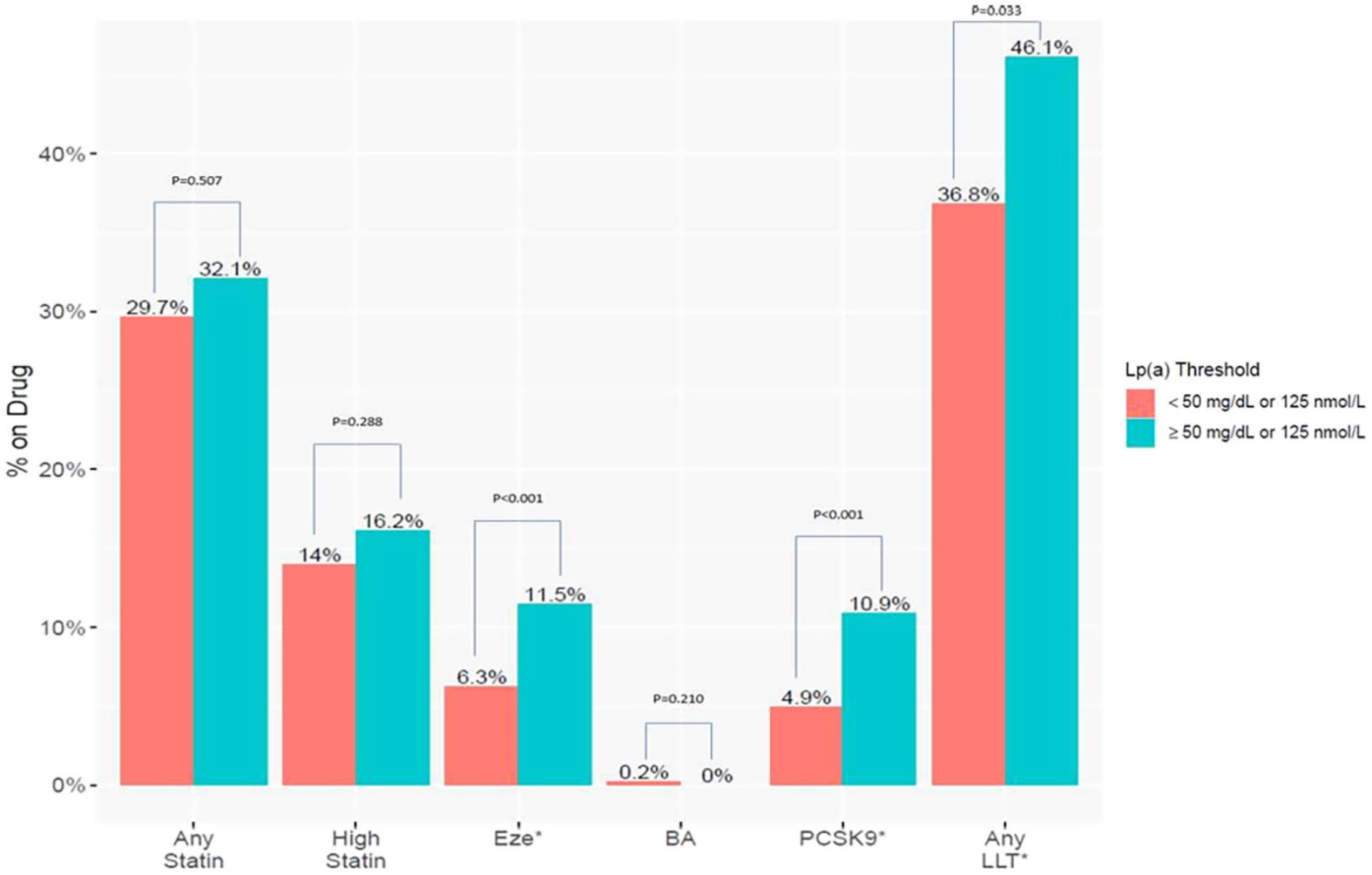
Society	Clinical Lp(a) Recommendations
2018 ACC/AHA Cholesterol Guidelines	Screen Lp(a) in at risk patients. Reasonable to initiate treatment if Lp(a) ≥ 50mg/dL
2019 European Society of Cardiology Cholesterol Guidelines	One time screening of Lp(a) to identify those at extreme elevations (>180mg/dL) or less extreme elevation who are at higher overall risk

Grundy SM, et al. 2018 AHA/ACC Cholesterol Guideline. *Circulation*. 2019;139:e1082-1143.
Mach F, et al. 2019 ESC/EAS Dyslipidaemia Guidelines. *Eur Heart J*. 2020;41:111-188.

What's really happening?

Among 595,684 patients across 5 large health systems:

- Lp(a) testing rates were low at 0.4%
- Females, older individuals, and members of the Black race were less likely to be tested
- Those with an Lp(a) test, regardless of value, were likely to be initiated on lipid lowering therapy
- Those with elevated levels were more likely to initiate non-statin therapies



Shah NP, Mulder H.et al. JAHA 2024

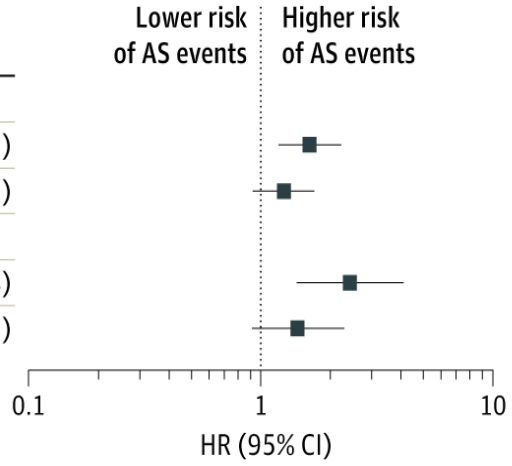
Impact of various therapeutics on Lp(a) levels

Drug	Effect on Lipoprotein(a)
Statins	• ~13% decrease (CARDS) • ~15% decrease • No significant effect
Ezetimibe	• No effect
Niacin	• ~22.9% dose-independent decrease
PCSK9 inhibitors	• ~26.9% decrease (FOURIER) • ~25.6% decrease (alirocumab) • Confirmed in meta-analyses
Inclisiran	• ~18.6% decrease (ORION-11)
Mipomersen	• ~26.4% decrease
CETP inhibitors	• Up to ~40% decrease (evacetrapib) • ~14% decrease (anacetrapib) • ~33.8% and ~55.6% decrease (obicetrapib)
ASO and siRNA	• ~80% and ~72% decrease (pelacarsen) • ~70.5% to ~100.5% decrease (olpasiran) • Up to ~98% decrease (SL430)

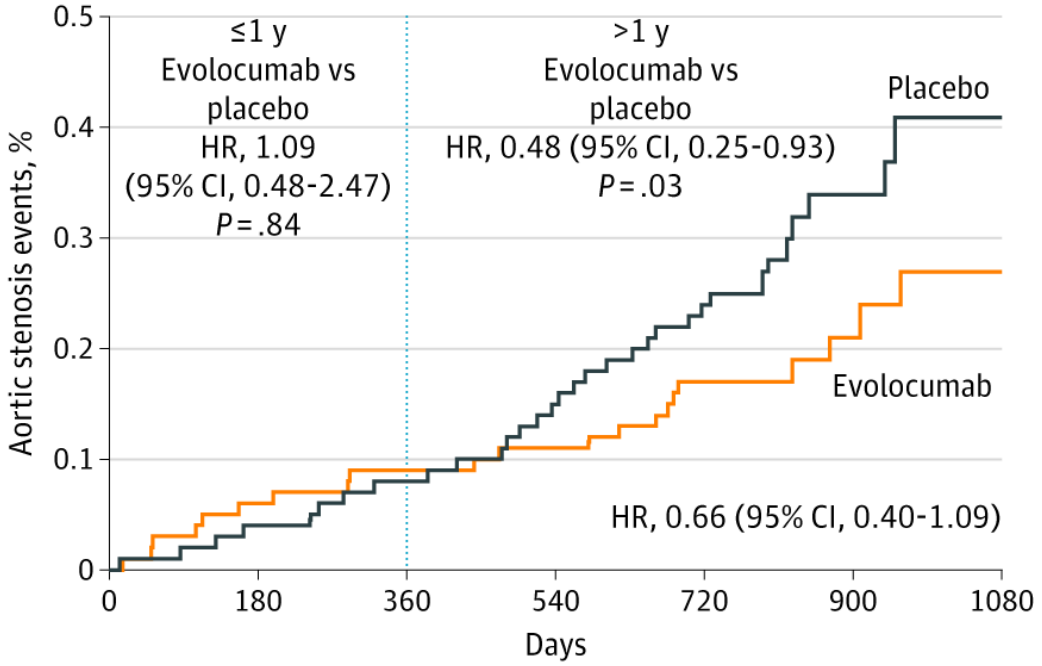
Lipoprotein (a): An Update on a Marker of Residual Risk and Associated Clinical Manifestations
Shah, Nishant P. et al.
American Journal of Cardiology, Volume 126, 94 - 102

Exploratory Analysis from FOURIER on AS Events

Outcomes	HR (95% CI)	P value
AS Events		
Lp(a)	1.55 (1.17-2.05)	.002
LDL-C (corrected)	1.23 (0.93-1.61)	.14
AVR		
Lp(a)	2.22 (1.38-3.58)	.001
LDL-C (corrected)	1.39 (0.92-2.11)	.12



Multivariable model adjusted for age, sex, diabetes, hypertension, smoking, and eGFR



No. at risk				
PBO	13 780	13 515	8616	1019
EVO	13 784	13 540	8651	982

Bergmark BA, O'Donoghue ML, Murphy SA et al. *JAMA Cardiology* 2020 5;(6): 709-713

Other Lp(a) targeting agents

Zerlasiran (SLN360)

- siRNA based therapy
- Reduction in Lp(a) up to -96%

Nissen S, Wolski K.et al. JAMA 2022

Lebodisran

- siRNA based therapy
- Reduction in Lp(a) up to -97% and sustained reduction at one year

Nissen S, Linnebjerg H.et al. JAMA 2023

Muvalaplin
(oral agent)

- Oral therapy to disrupts creation of Lp(a)
- Reduction in Lp(a) up to -86%

Nicholls SJ, Ni W.et al. JAMA 2024

Calcified AS Specific Trials Underway

- Phase II, randomized clinical trial on the effect of PCSK9 inhibitors on calcific aortic valve disease (NCT04968509)

- Phase II, randomized clinical trial on the effect of Pelacarsen on calcific aortic valve disease (NCT0564381)

Clinical Implications

Test for Lp(a) to stratify ASCVD risk, but also in patients who have been identified to have some degree of AS especially if young

In patients with elevated Lp(a) levels:

1) Lower LDL as low as possible, (consider an LDL-C < 70mg/dL) to modify ASCVD risk
2) Consider Aspirin therapy if bleeding risk is low for further ASCVD risk modification
3) Modify remaining modifiable risk factors: HTN, obesity, DM, lifestyle
4) Cascade screening of all first degree relatives
5) For patients identified with AS, routine imaging surveillance and monitoring for symptoms
6) Consider opportunity for clinical trials

Conclusion

- Test for Lp(a) as management strategies exist today
- Lp(a) has been linked to progression of calcified aortic stenosis and observed to have an association with degeneration of bioprosthetic valves
- Pathophysiologic mechanisms involve inflammatory pathways as a mediator for valve calcification
- Clinical trials exploring the therapeutic impact on calcific AS with therapies that modify Lp(a) are underway
- There is a need for more research to better understand Lp(a)'s effect beyond vascular disease

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University of Colorado
Anschutz Medical Campus

Lp(a) and Peripheral Artery Disease

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Disclosures

- **VOYAGER PAD funded through grants from Bayer and Janssen to CPC Clinical Research**

- **Dr. Bonaca is the Executive Director of CPC, a non-profit academic research organization affiliated with the University of Colorado, that receives or has received research grant/consulting funding between August 2021 and present from: Abbott Laboratories, Agios Pharmaceuticals, Inc., Alexion Pharma, Alnylam Pharmaceuticals, Inc., Amgen Inc., Angionetics, Inc., Anthos Therapeutics, ARCA Biopharma, Inc., Array BioPharma, Inc., AstraZeneca and Affiliates, Atentiv LLC, Audentes Therapeutics, Inc., Bayer and Affiliates, Beth Israel Deaconess Medical Center, Better Therapeutics, Inc., Boston Clinical Research Institute, Bristol-Meyers Squibb Company, Cambrian Biopharma, Inc., Cardiol Therapeutics Inc., CellResearch Corp., Cleerly Inc., Cook Regentec LLC, CSL Behring LLC, Eidos Therapeutics, Inc., EP Trading Co. Ltd., EPG Communication Holdings Ltd., Epizon Pharma, Inc., Esperion Therapeutics, Inc., Everly Well, Inc., Exicon Consulting Pvt. Ltd., Faraday Pharmaceuticals, Inc., Foresee Pharmaceuticals Co. Ltd., Fortress Biotech, Inc., HDL Therapeutics Inc., HeartFlow Inc., Hummingbird Bioscience, Insmed Inc., Ionis Pharmaceuticals, IQVIA Inc., Janssen and Affiliates, Kowa Research Institute, Inc., Kyushu University, Lexicon Pharmaceuticals, Inc., Medimmune Ltd., Medpace, Merck & Affiliates, Nectero Medical Inc., Novartis Pharmaceuticals Corp., Novo Nordisk, Inc., Osiris Therapeutics Inc., Pfizer Inc., PhaseBio Pharmaceuticals, Inc., PPD Development, LP, Prairie Education and Research Cooperative, Prothena Biosciences Limited, Regeneron Pharmaceuticals, Inc., Regio Biosciences, Inc., Saint Luke's Hospital of Kansas City, Sanifit Therapeutics S.A., Sanofi-Aventis Groupe, Silence Therapeutics PLC, Smith & Nephew plc, Stanford Center for Clinical Research, Stealth BioTherapeutics Inc., State of Colorado CCPD Grant, The Brigham & Women's Hospital, Inc., The Feinstein Institutes for Medical Research, Thrombosis Research Institute, University of Colorado, University of Pittsburgh, VarmX, Virta Health Corporation, Worldwide Clinical Trials Inc., WraSer, LLC, and Yale Cardiovascular Research Group.**
- **Dr. Bonaca receives support from the AHA SFRN under award numbers 18SFRN3390085 (BWH-DH SFRN Center) and 18SFRN33960262 (BWH-DH Clinical Project).**

Clinical Case – Patient S.N.

50 YO Man in good health

Developed acute onset of right leg pain and presented to the ED. Noted to have no pulses. CTA showed acute thrombotic occlusion of the right common femoral artery with SFA, profunda and popliteal disease. Treated with thrombolysis and limb was salvaged

- LDL 148, HDL 42, TG 139, Cr 0.84
- BP 118/60, eGFR 80
- A1C 4.8%
- Non-smoker
- BMI 25.2
- Athletic
- No family history

Treated with aspirin, clopidogrel, high-intensity statin
Thrombophilia workup negative

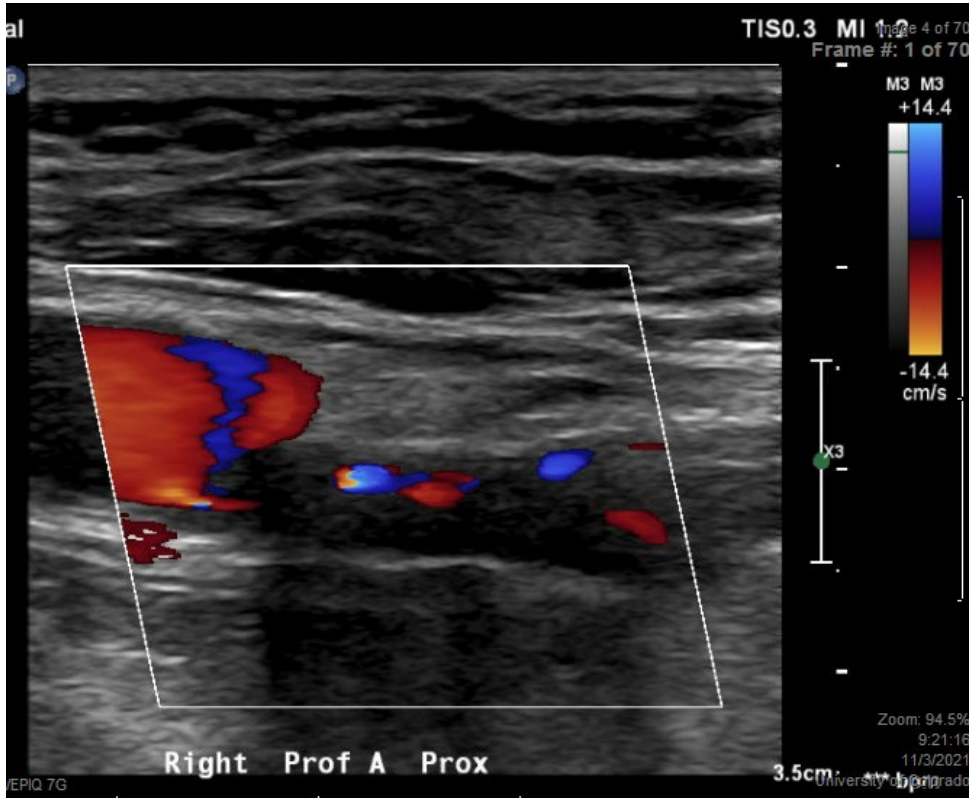
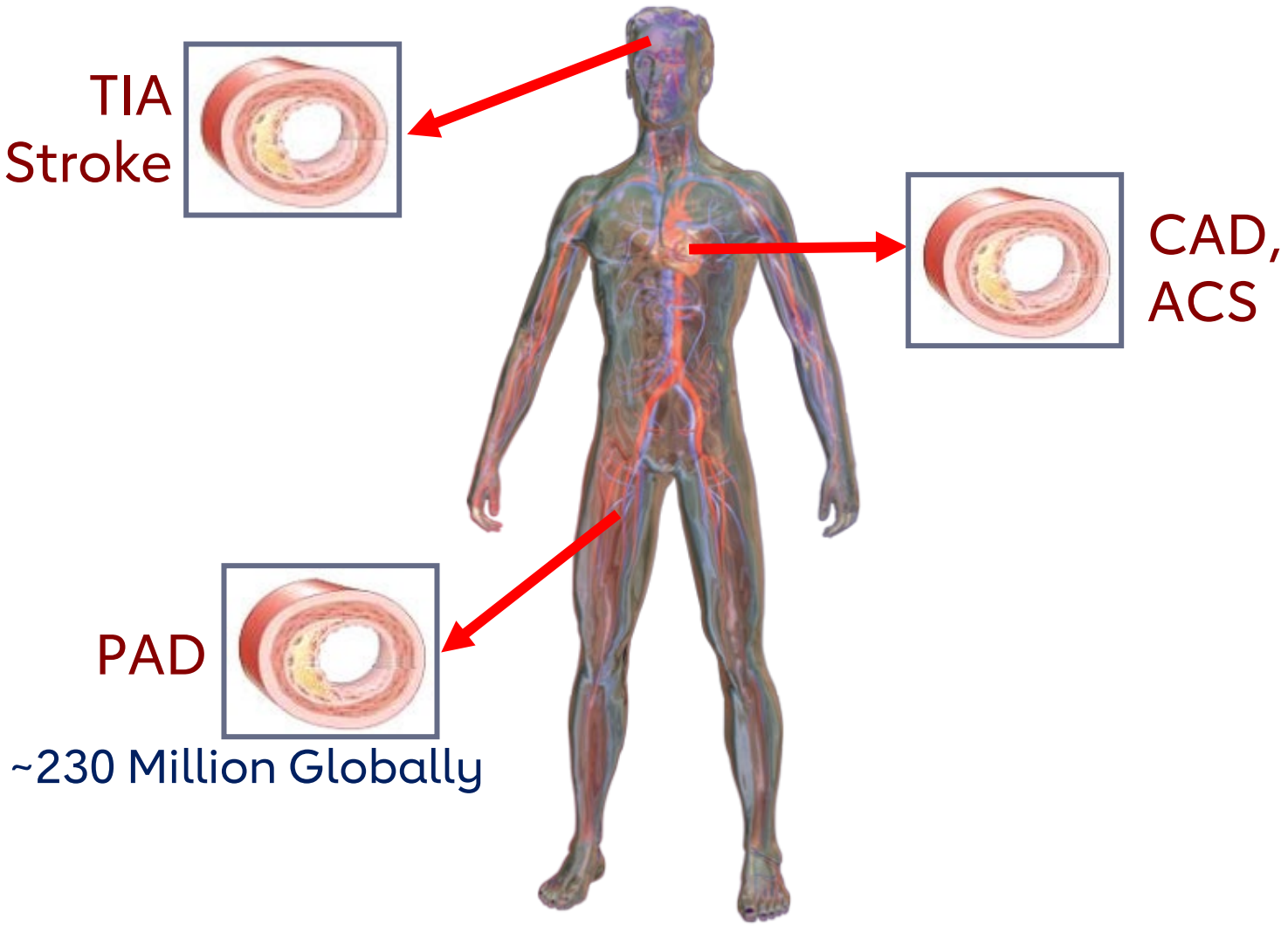


Image provided by presenter

Atherosclerosis is a Systemic Disease



Tsao CW, Aday AW, et al. Heart disease and stroke statistics update: A report from the American Heart Association. *Circulation* (2023) 147(8)e93-e621.
https://doi.org/10.1161/CIR.0000000000001123

A Prevalent and Morbid Form of Atherosclerosis

Current estimate:
230 million globally &
~8.5 million in the US

Selvin E and Erlinger TP. Prevalence of and risk for peripheral artery disease in the United States. *Circulation* (2004) 110, 738-43. DOI: 10.1161/01.CIR.0000137913.26087.F0

Criqui MH, Fronek A, et al, The prevalence of peripheral arterial disease in a defined population. *Circulation* (1985) 71(3), 510-515. https://doi.org/10.1161/01.CIR.71.3.510

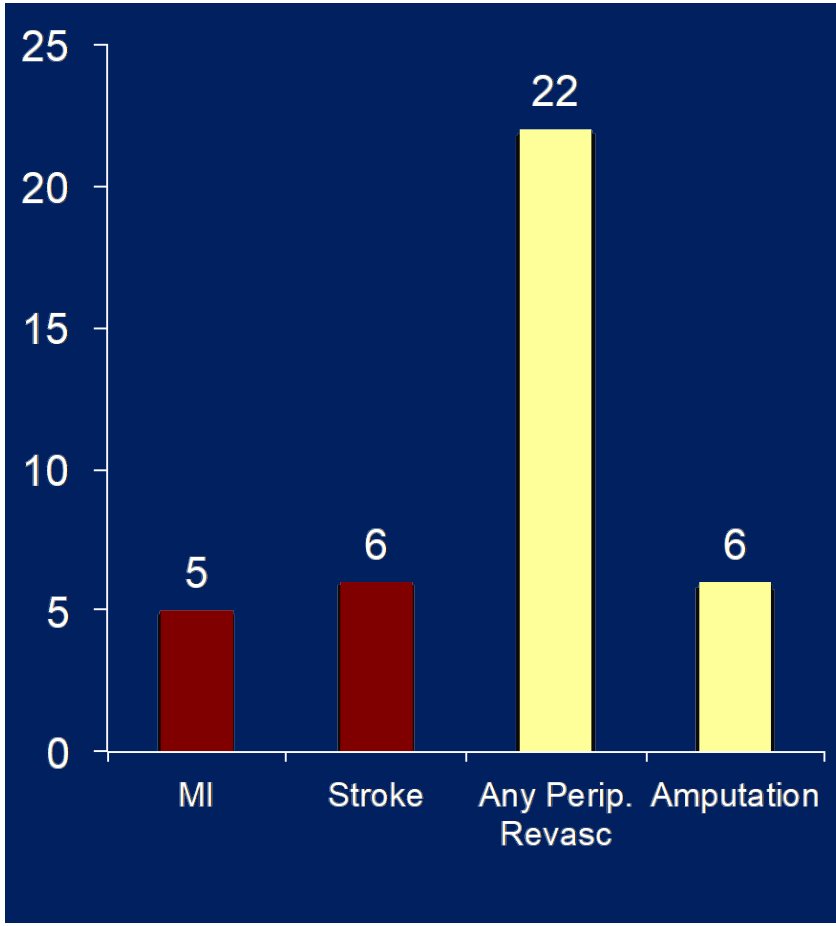
Meijer WT, Arnos AW, et al. Peripheral Artery Disease in the Elderly: The Rotterdam Study. *ATVB* (1998), 18(2), 185-92. https://doi.org/10.1161/01.ATV.18.2.185

Diehm C, Schuster A, et al. High prevalence of peripheral artery disease and co-morbidity in 6880 primary care patients: cross-sectional study. *Atherosclerosis* (2004) 172(1), 195-205.

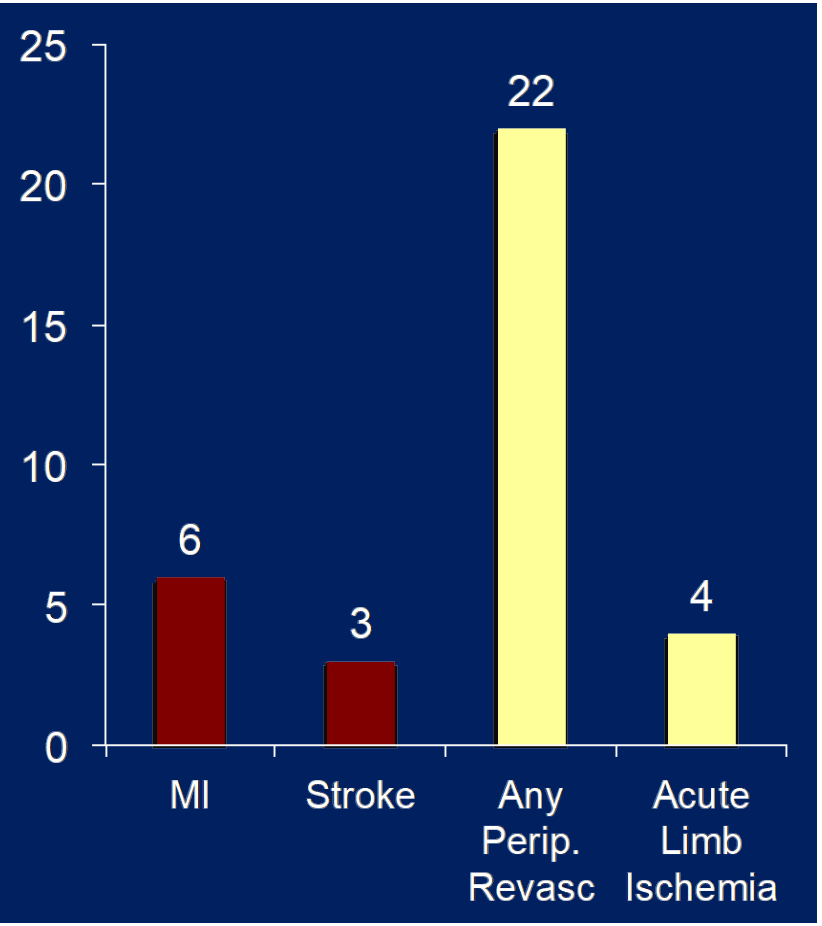
Hirsch AT, Criqui MH, et al. Peripheral Arterial Disease Detection, Awareness, and Treatment in Primary Care. *JAMA* (2001), 286(11), 1317-1324. doi:10.1001/jama.286.11.1317

Adverse Limb Events are Frequent in Patients with PAD

Events in PAD Patients at 4 Years
REACH Registry

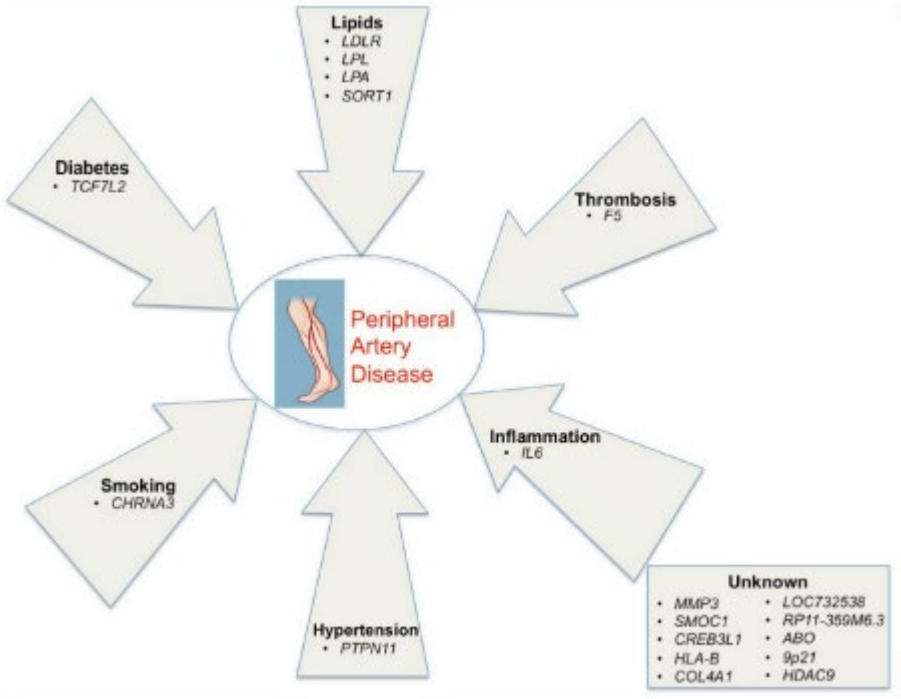


Events in PAD Patients at 3 Years
TRA2P-TIMI 50



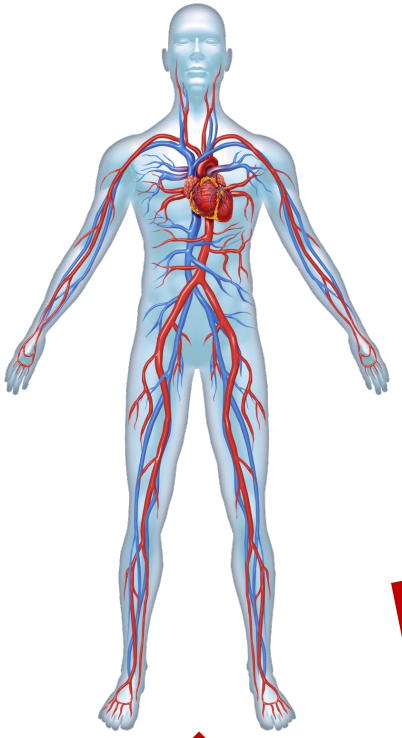
Kumbhani DJ, Steg GPh, et al. Statin therapy and long-term adverse limb outcomes in patients with peripheral artery disease: insights from the REACH registry. *Eur Heart J* (2014) 35, pp.2864-2872. https://doi.org/10.1161/ATVBAHA.112.255521
Bonaca MP, Scirica BM, et al. Vorapaxar in patients with peripheral artery disease - results from TRAP2P-TIMI50. *Circulation* (2013), 127(14), 1522-1529. https://doi.org/10.1161/CIRCULATIONAHA.112.000679

Risk in PAD Driven by Multiple Axes



Lifestyle (exercise, diet)

Lipid Risk
LDL-C
Lp(a)
Remnant Chol



Thrombosis Risk

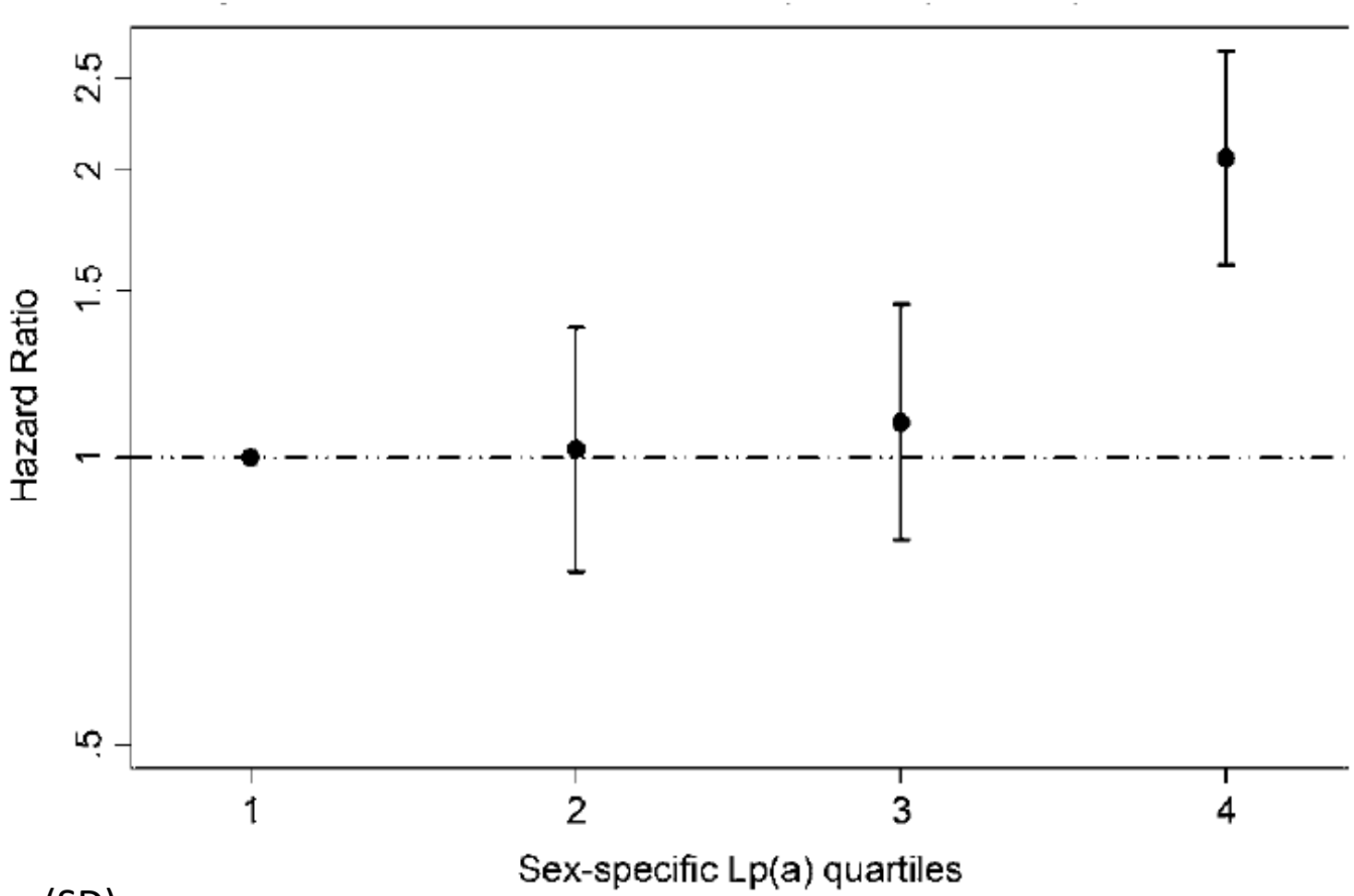
Diabetes Risk (micro and macrovascular)

Smoking Risk

Inflammatory Risk

Presenter Provided Images

Incident peripheral artery disease vs Lp(a) in EPIC NORFOLK



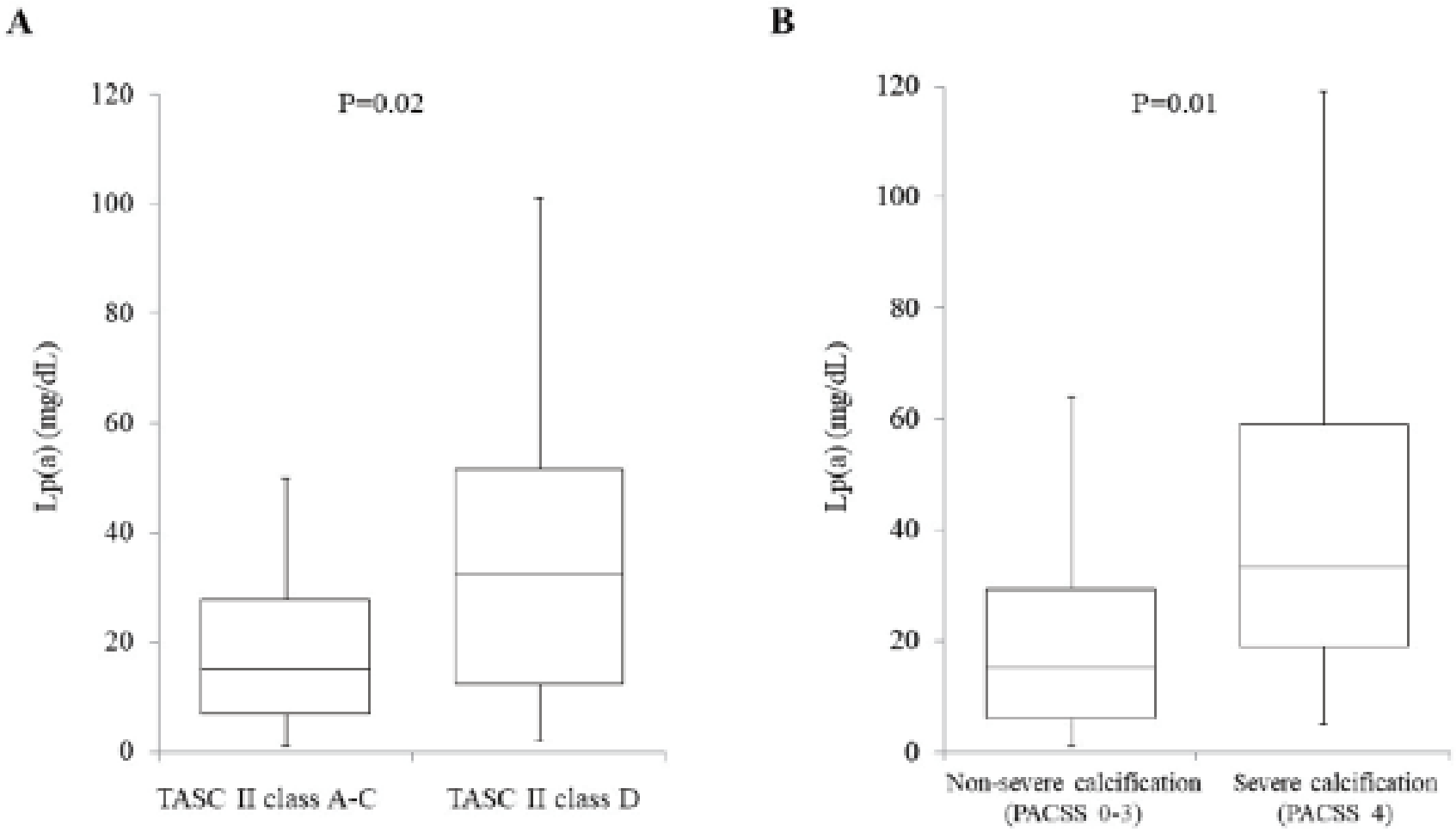
Risk gradient independent of LDL-C

Mean (SD) Lp(a) mg/dL	4.1±1.1	8.5±1.5	17.3±4.3	**54.7±25**

An Affiliate of:

Gurdesani D et al., *ATVB* 2012; 32:3058-3065

Modestly elevated Lp(a) Associated with More Severe PAD



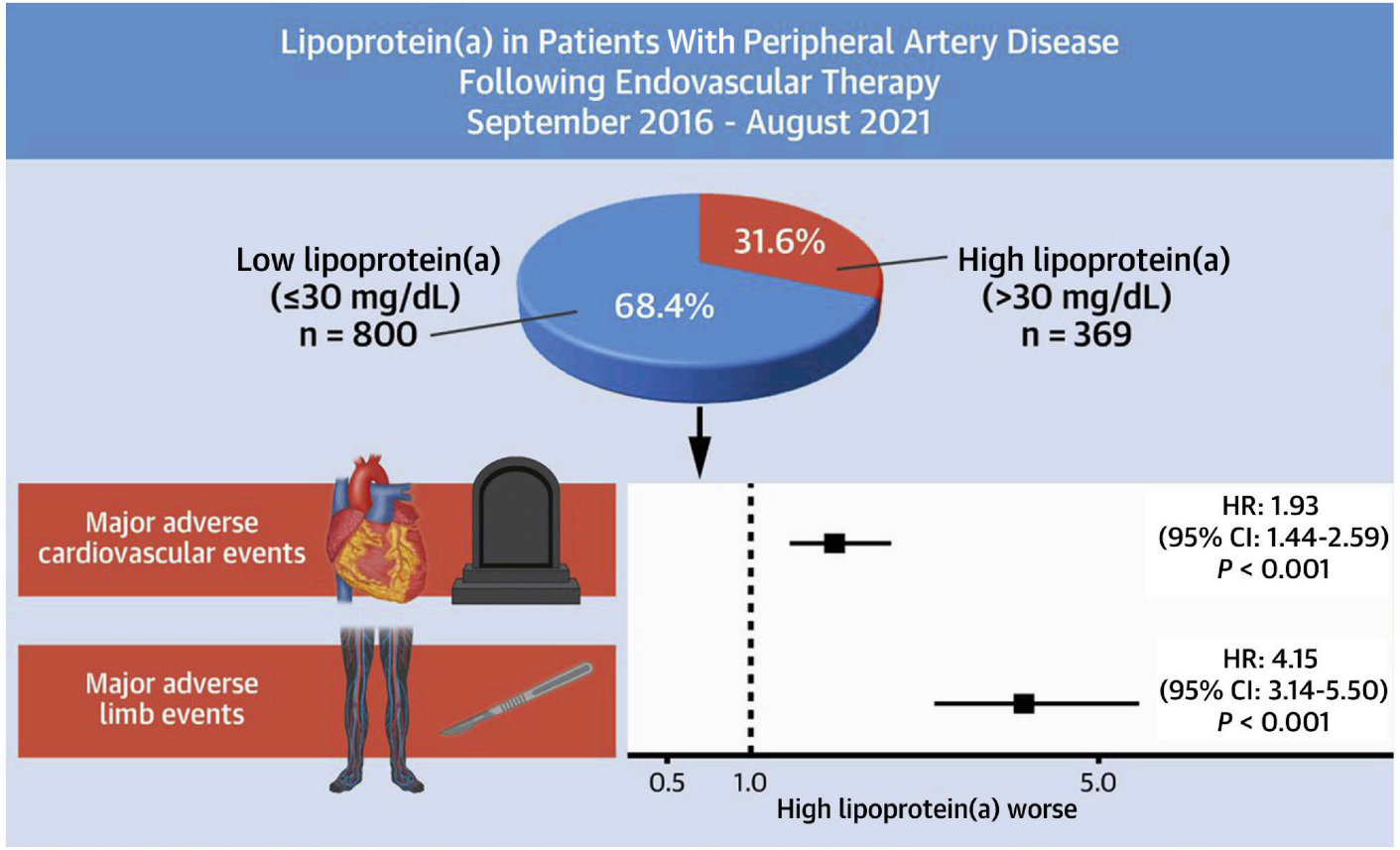
An Affiliate of:

CPC Clinical Research

Yanaka K, et al J Atheroscler Thromb. 2021 May 1;28(5):555-561

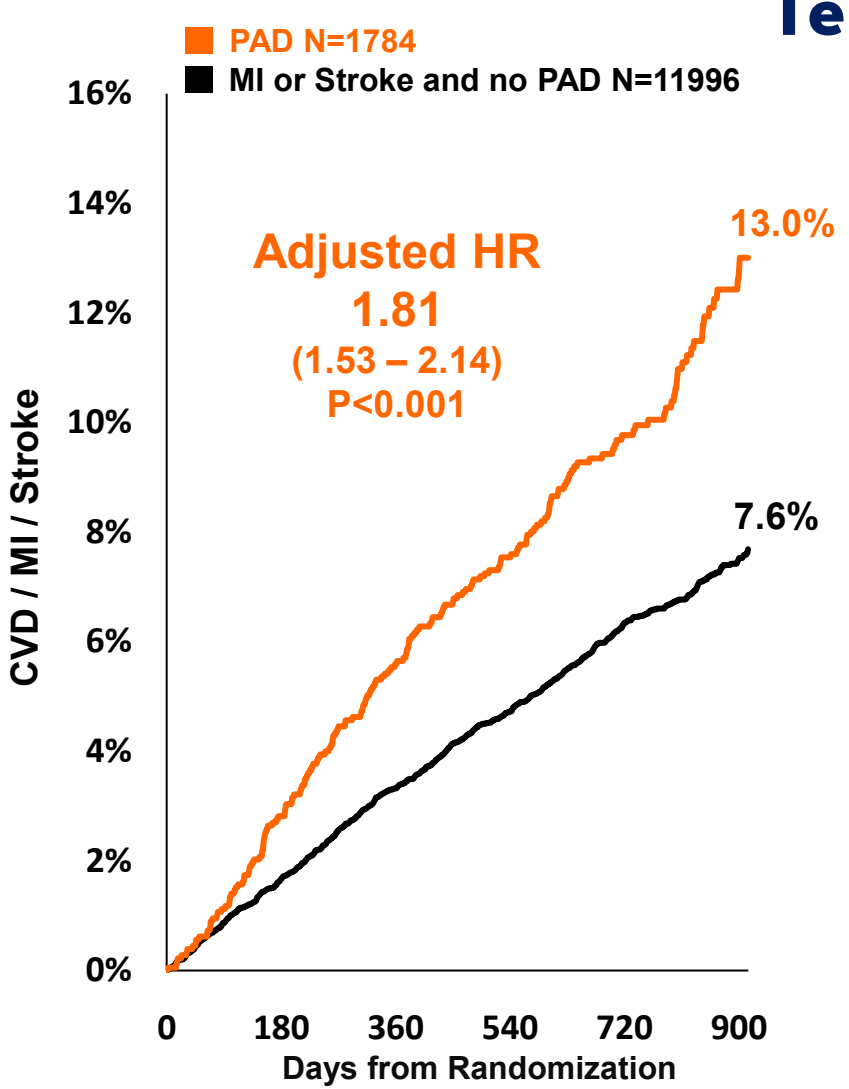
Lp(a) and MALE after Lower Extremity Revascularization

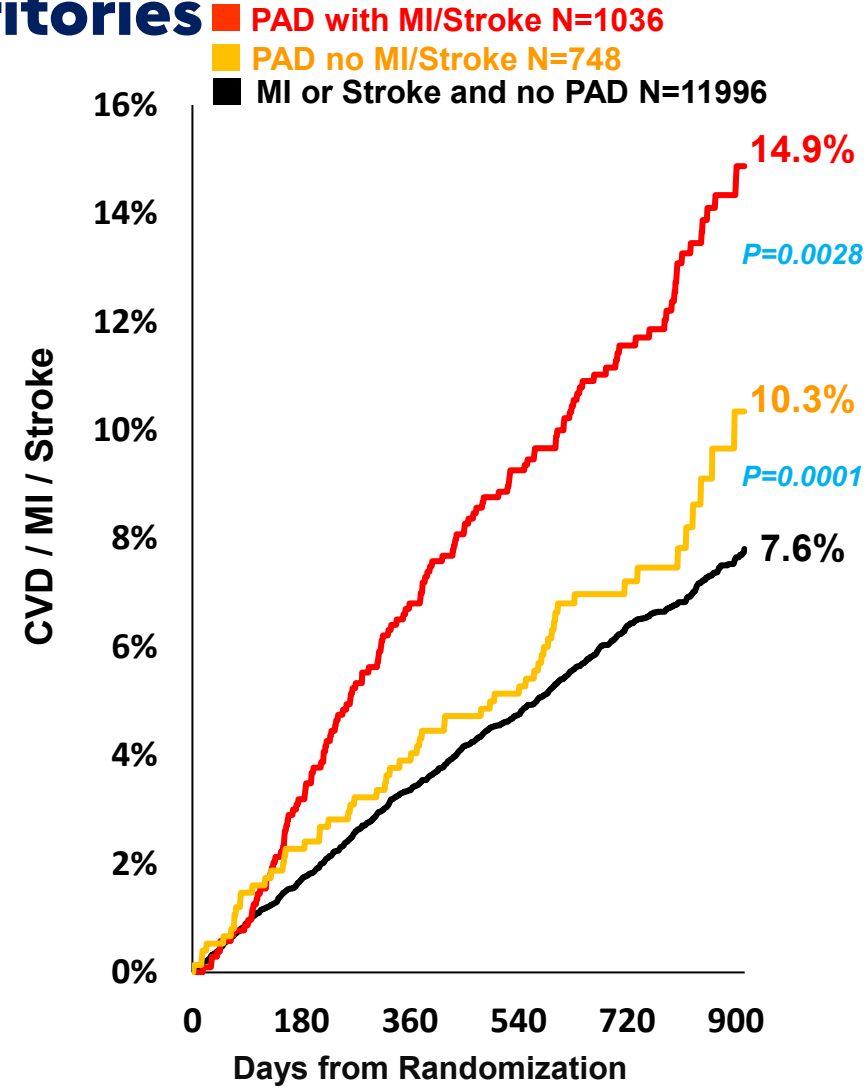
CENTRAL ILLUSTRATION: The Relationship Between Baseline Lipoprotein(a) and Future Cardiovascular and Limb Events in Patients With Peripheral Artery Disease Following Endovascular Therapy



Tomoi Y, et al. J Am Coll Cardiol Intv. 2022;15(14):1466-1476.

Malignant Atherosclerosis Patients with PAD Have the Highest Risk of MACE, Particularly if Combined with Other Symptomatic Territories





adjusted age, sex, race, BMI, diabetes, hypertension, smoking, eGFR, CHF, prior MI, CABG/PCI, and history of stroke or TIA.

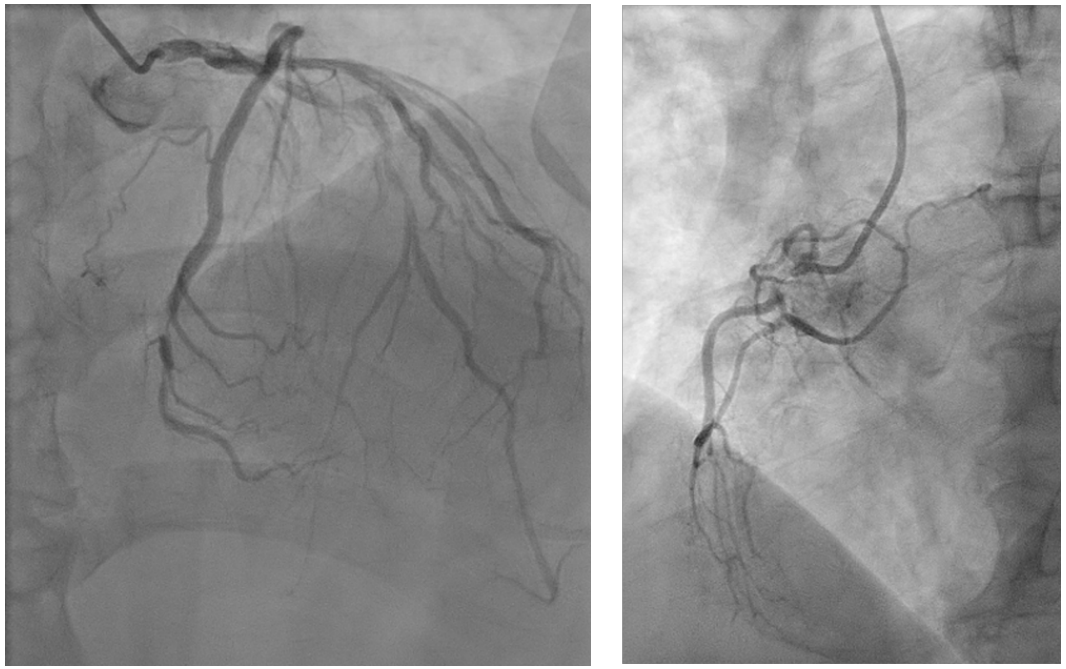
Bonaca MP, Nault P, et al. Low density lipoprotein cholesterol lowering with evolocumab and outcomes in patients with peripheral artery disease. *Circulation* (2018) 137, 338-350. https://doi.org/10.1161/CIRCULATIONAHA.117.032235

Clinical Case cont'd

Two years later:
Develops chest pain and pressure after a long day mountain biking. Pain progresses and he goes to the ED where he is diagnosed with a non-ST elevation MI.

Med Flight to referral center in Denver:
Diagnosed with multivessel CAD treated with CABG

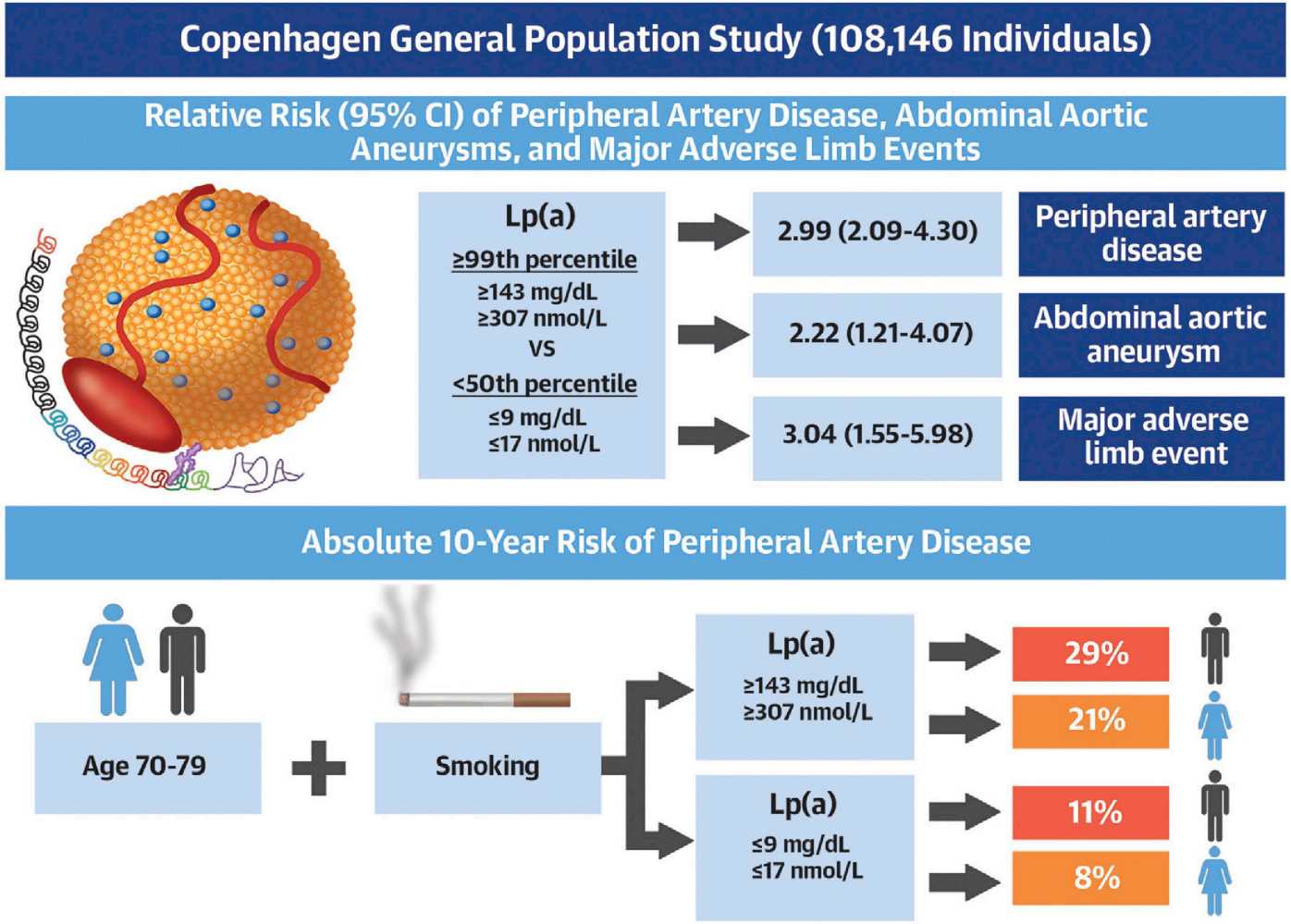
- LDL 63 mg/dL and adherent
- A1C 4.8%, Non-smoker
- BMI 25.0
- Athletic, intensive dietary changes x 2 years



Presenter Provided Images

Follows up in vascular clinic and asks:
"I have PAD and CAD but no risk factors. I try to do everything right. What is causing this?"

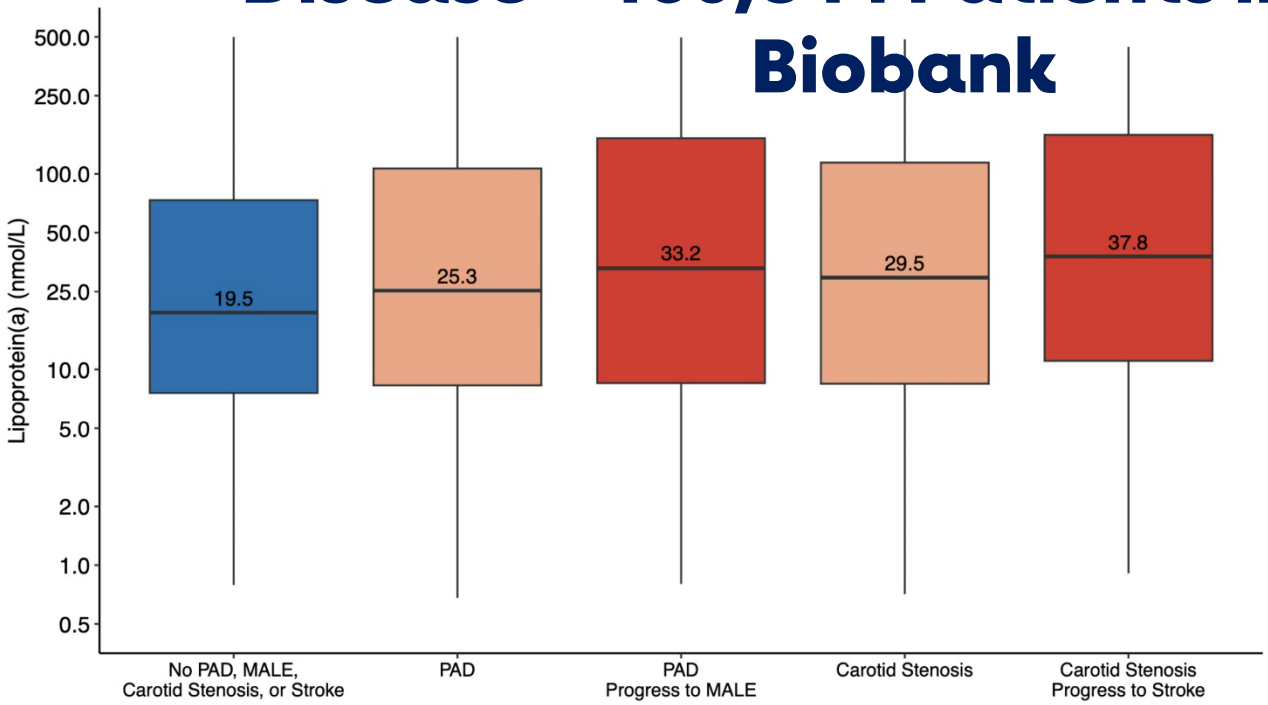
CENTRAL ILLUSTRATION: Lipoprotein(a) and Risks of Peripheral Artery Disease, Abdominal Aortic Aneurysm, and Major Adverse Limb Events

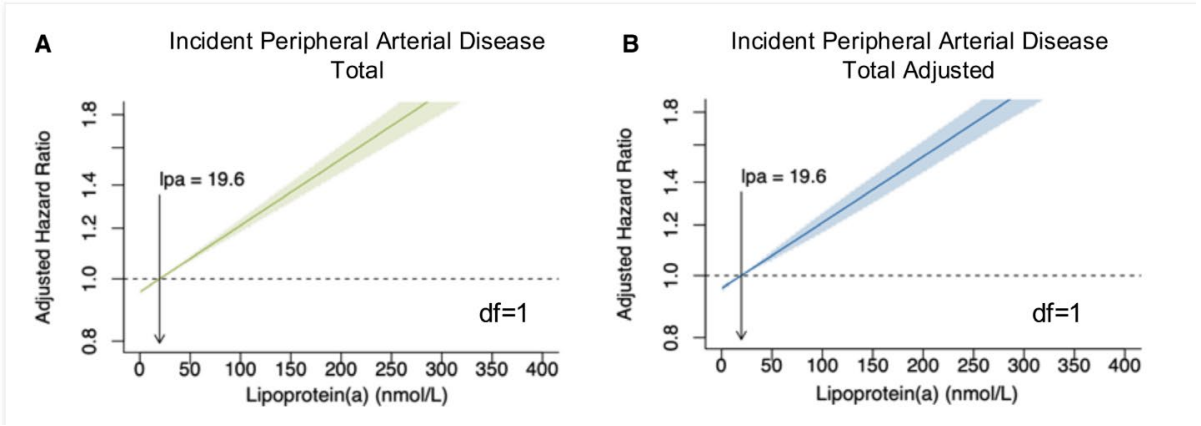


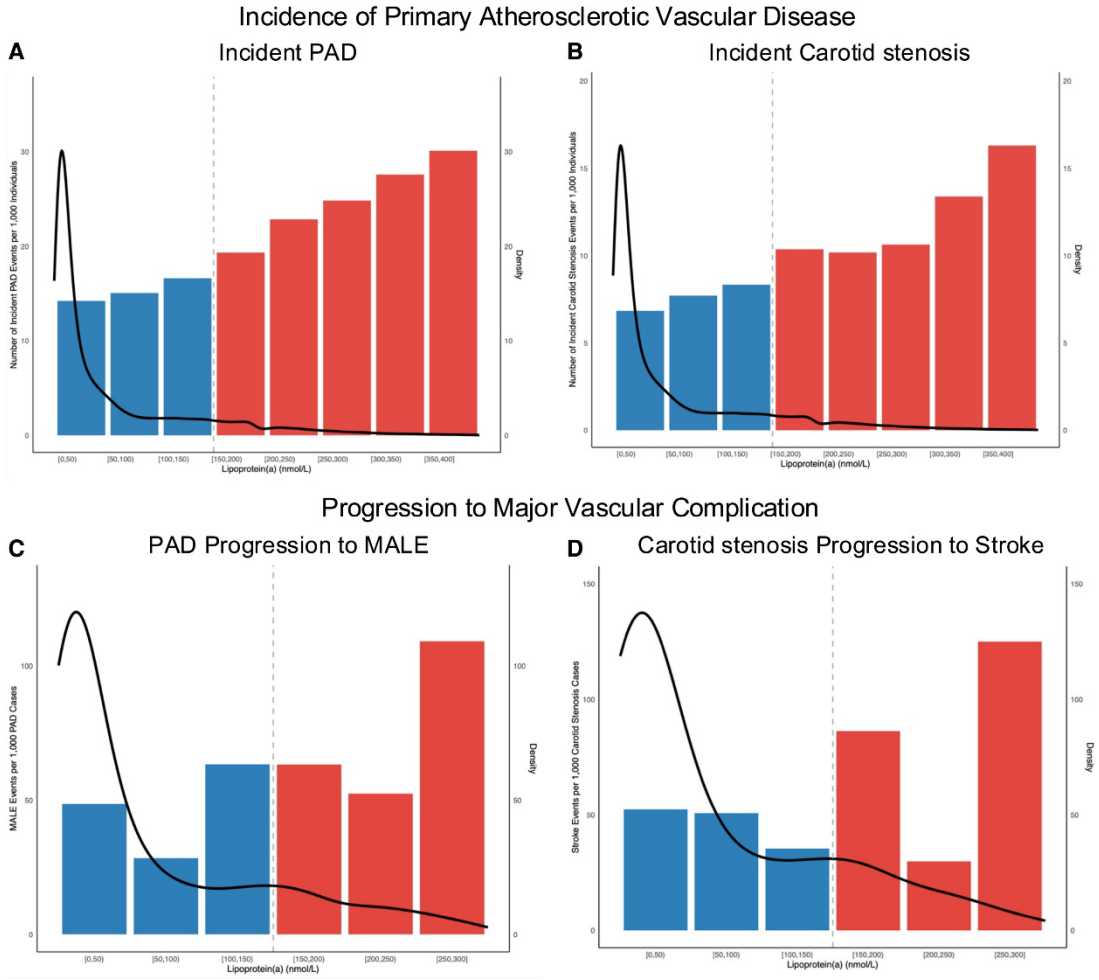
Thomas PE, et al. J Am Coll Cardiol. 2023;82(24):2265-2276.

Thomas, P, Vedel-Krogh, S, Nielsen, S. et al. Lipoprotein(a) and Risks of Peripheral Artery Disease, Abdominal Aortic Aneurysm, and Major Adverse Limb Events. *JACC*. 2023 Dec, 82 (24) 2265–2276.
https://doi.org/10.1016/j.jacc.2023.10.009

Lp(a) and Non-Coronary Vascular Disease – 460,544 Patients in the UK Biobank





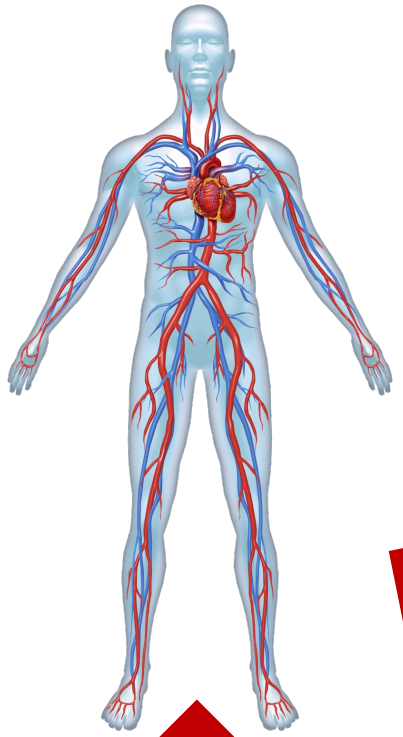


Bellomo et al. Circulation 2025

Risk in PAD Driven by Multiple Axes – What about Patient S.N.?

Lifestyle (exercise, diet)

Active, healthy diet, normal BMI



Lipid Risk (LDL & Lpa?)

LDL ~60 mg/dL

Lp(a) 129 mg/dL

Thrombosis Risk

No thrombophilia

Diabetes Risk (micro and macrovascular)

Does not have diabetes

Smoking Risk

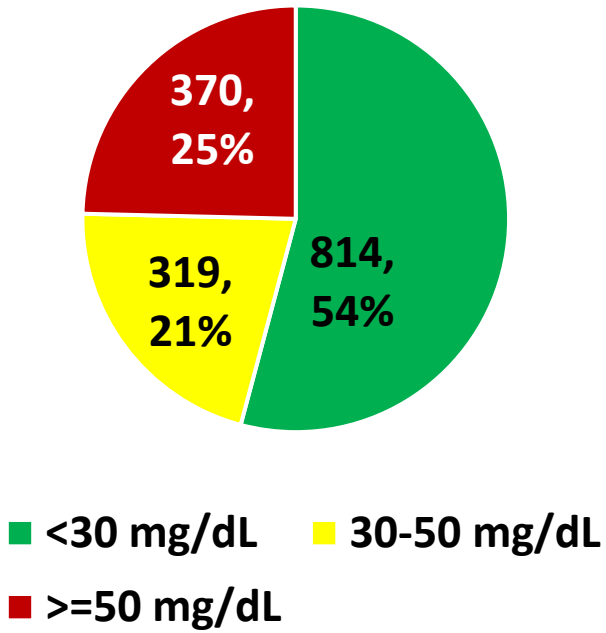
Never smoker

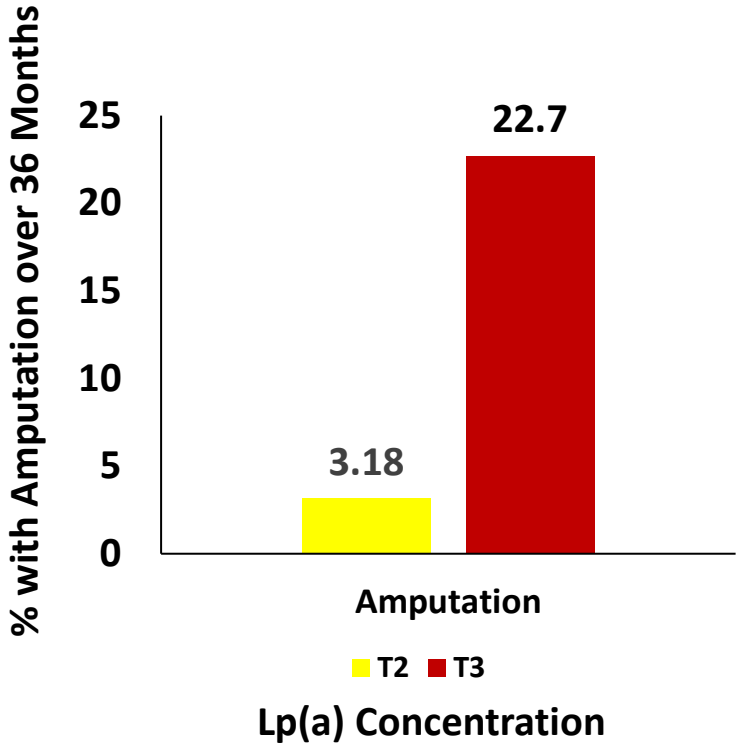
Inflammatory Risk

1.221

Association between Lp(a) and amputation

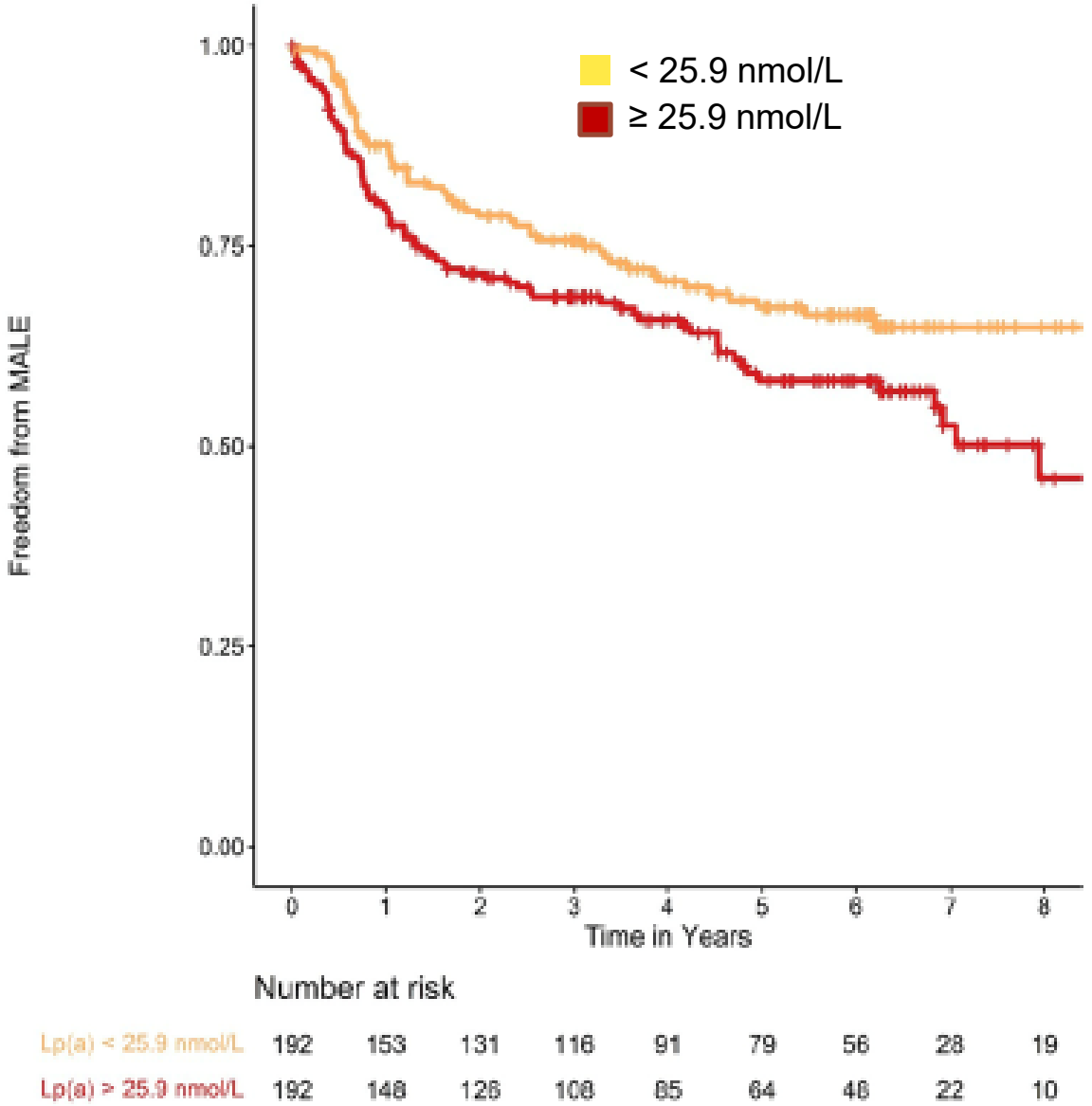
1503 patients with symptomatic PAD followed for 36 months
122 MI, 114 stroke, 58 amputations





Munoz-Torrero et al. Atherosclerosis 2018;276:10-14

Modest Lp(a) elevation associated with greater risk of limb revascularization



An Affiliate of:

Verwer MC, et al. Atherosclerosis. 2021 Nov 24:S0021-9150(21)01447-7

Lp (a) and lower limb peripheral revascularization

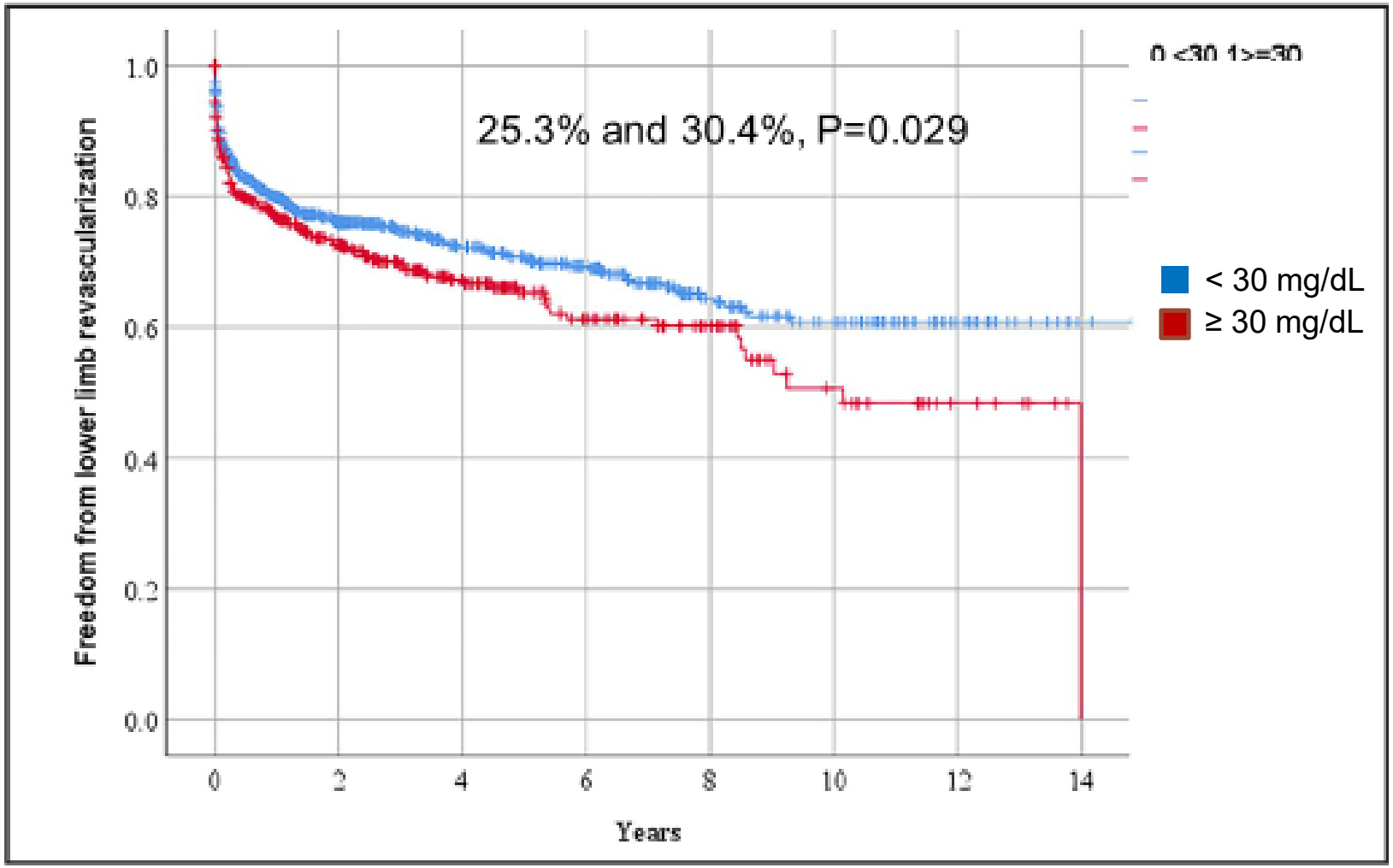


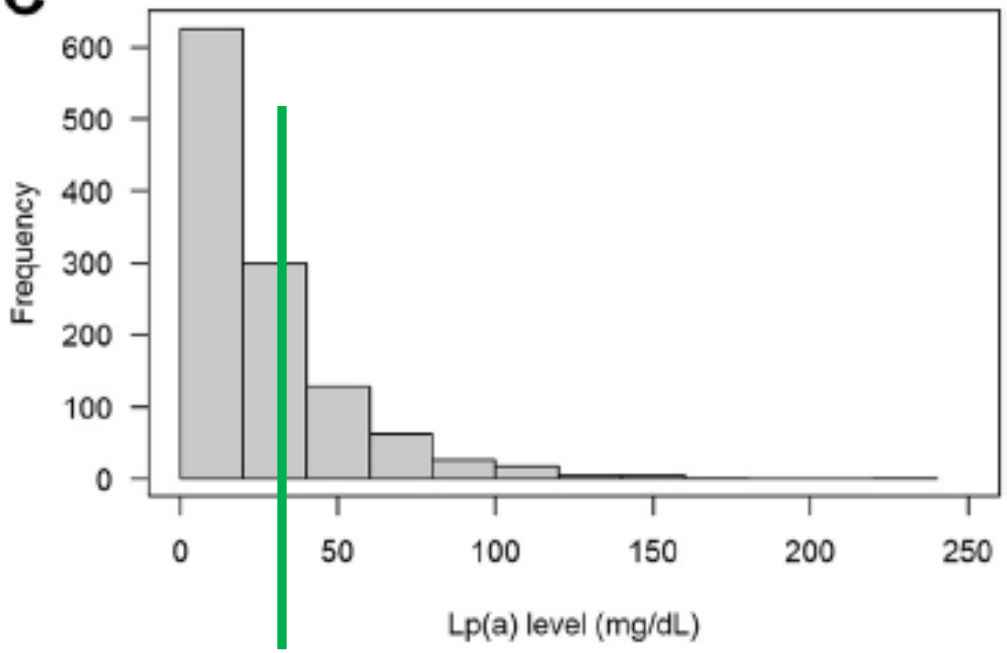
Figure 2. **Freedom from requirement for lower limb peripheral revascularization in people referred for management of peripheral artery disease in relationship to serum lipoprotein (a) ≥30 mg/dL.**

An Affiliate of:

Golledge J, et al. J Am Heart Assoc. 2020 Mar 17;9(6):e015355.

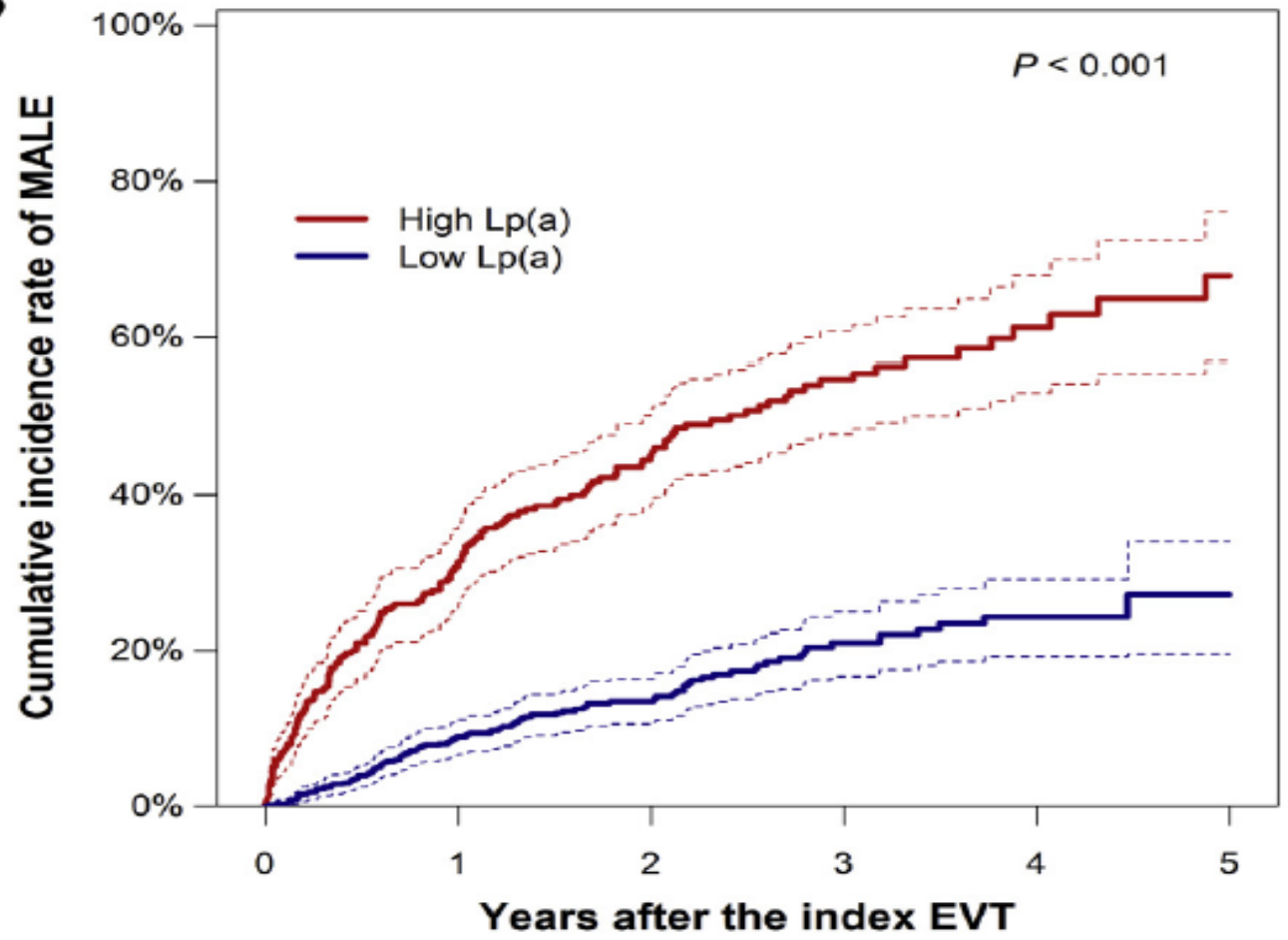
Lp(a) and MALE after Lower **Extremity** Revascularization

C



30 mg/dL

B



Number at risk / Number of events						
High Lp(a)	369 / 1	183 / 102	113 / 134	57 / 151	27 / 157	9 / 160
Low Lp(a)	800 / 0	481 / 58	289 / 78	157 / 97	60 / 102	7 / 103
Estimate ± SE						
High Lp(a)	0.3±0.3%	31.5±2.6%	45.0±3.0%	54.7±3.3%	61.2±3.8%	67.9±4.8%
Low Lp(a)	0.0±0.0%	9.0±1.1%	13.5±1.5%	20.9±2.1%	24.4±2.5%	27.2±3.7%

Tomoi et al. JACC Cardiovasular Interventions 2022

Lp(a) and MALE after Lower Extremity Revascularization

Author & Year	Cutpoint	Outcome
Yanaka et al 2021	Cutpoint ~30 mg/dL	Lesion Severity
Verwer et al 2021	25.9 nmol/L	MALE Peripheral revascularization
Goledge et al 2020	30 mg/dL	Peripheral revascularization
Tomoi et al 2022	30 mg/dL	MALE Peripheral revascularization

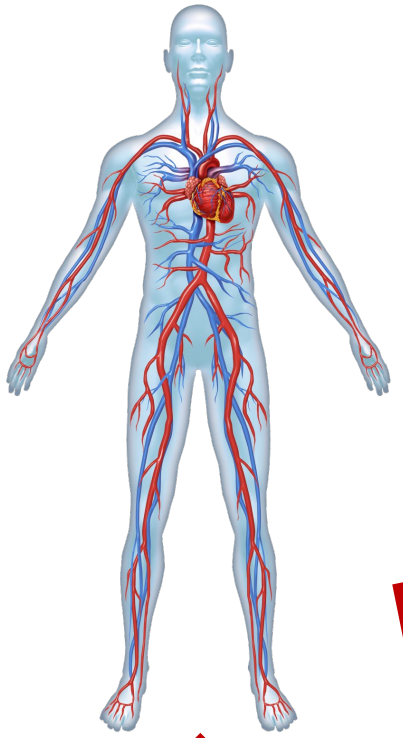
Lower concentrations of Lp(a) associated with risk in patients who already have PAD and after intervention

How to Manage ?

- *Push to lower LDL target (<55 and ideally 30 or lower)*
- *Favor PCSK9i if possible (FOURIER and ODYSSEY results)*
- *Consider apheresis?*

Active, healthy diet, normal BMI

Lifestyle (exercise, diet)



Lipid Risk (LDL & Lpa?)

LDL ~60 mg/dL
Lp(a) ?

Thrombosis Risk

No thrombophilia

Diabetes Risk (micro and macrovascular)

Does not have diabetes

Inflammatory Risk

hsCRP low

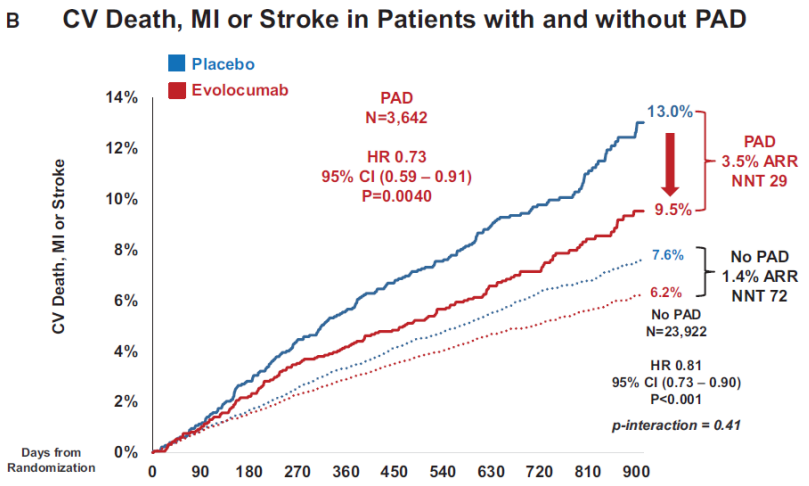
Smoking Risk

Never smoker

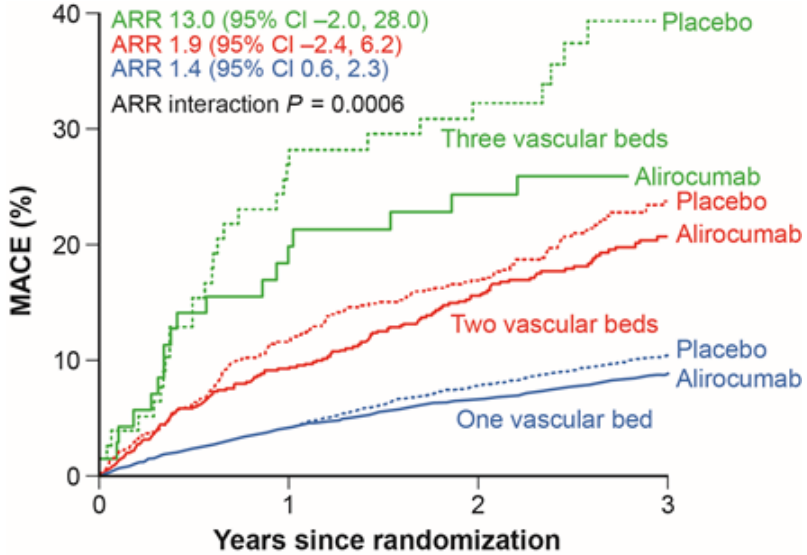
An Affiliate of:

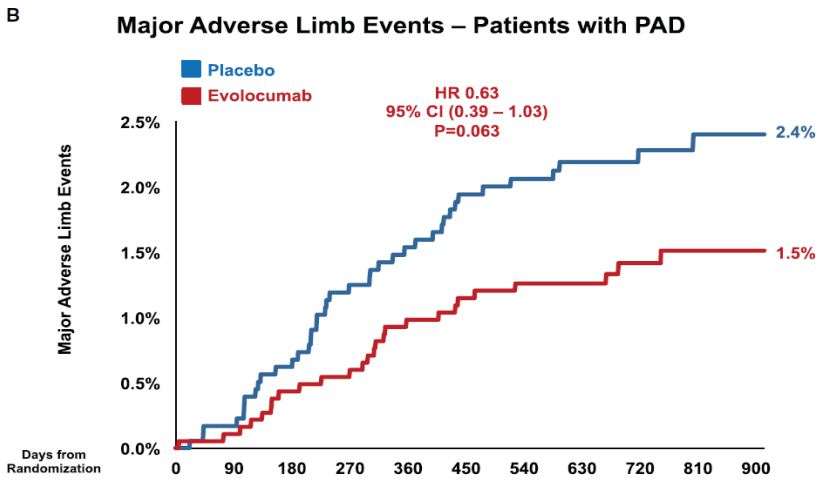
CPC Clinical Research

PCSK9i Reduce MACE & MALE in Patients with PAD

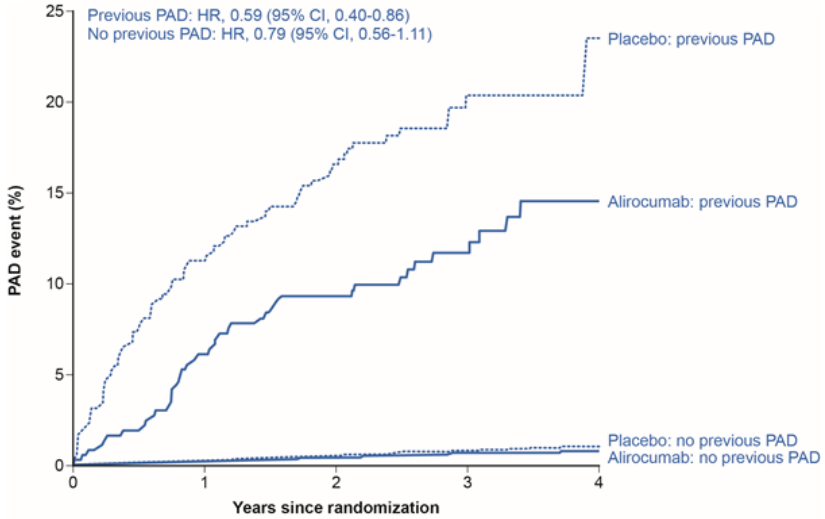


MACE





MALE



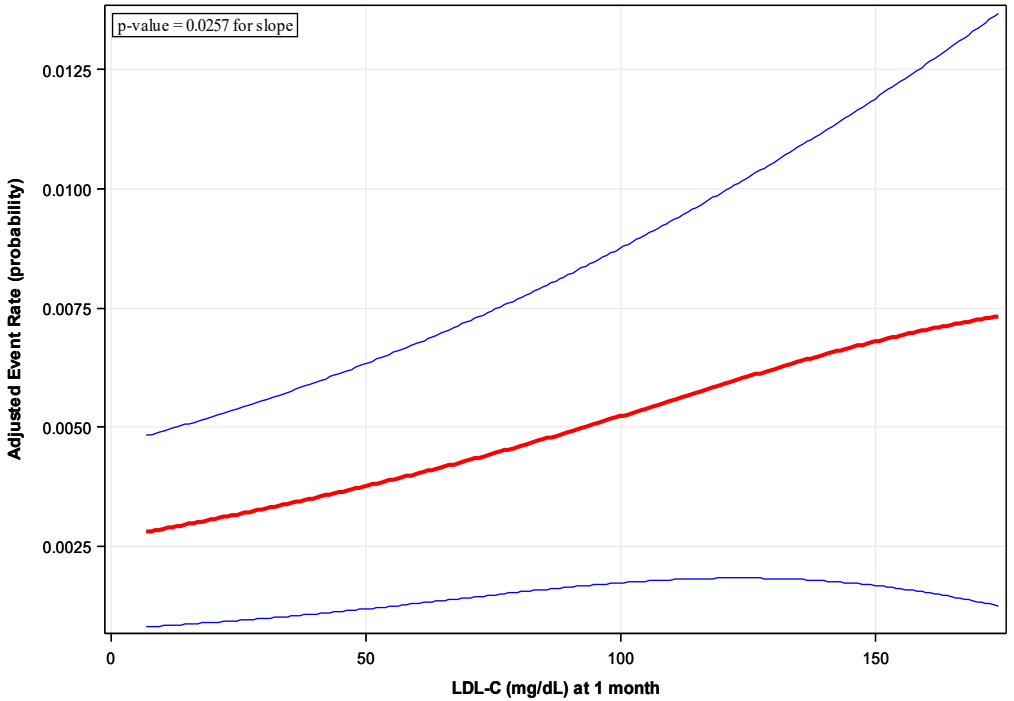
An Affiliate of:

Modified from Bonaca MP, Nault P, et al. Low density lipoprotein cholesterol lowering with evolocumab and outcomes in patients with peripheral artery disease. *Circulation* (2018) 137, 338-350.

Schwartz GG, Steg PG, et al. Peripheral artery disease and venous thromboembolic events after acute coronary syndrome. *Circulation* (2020) 141(20), 1608-17. https://doi.org/10.1161/CIRCULATIONAHA.120.046524

Jukema JW, Zihilstra LE, et al. Effect of alirocumab on stroke in ODYSSEY OUTCOMES *Circulation* (2019) 140 (25) 2054-62. https://doi.org/10.1161/CIRCULATIONAHA.119.043826

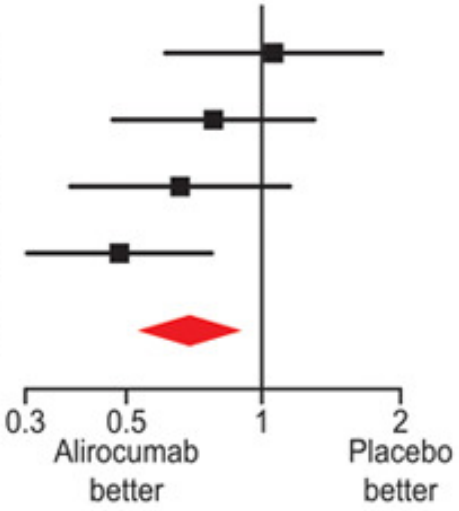
Benefit of PCSK9i for MALE associated with LDL-C and Lp(a)



PAD events: lipoprotein(a)

Subgroup	PAD incidence Alirocumab n/N (%)	PAD incidence Placebo n/N (%)	Relative risk reduction HR (95% CI)
Quartile 1	26/2327 (1.1)	25/2403 (1.0)	1.05 (0.61-1.83)
Quartile 2	28/2438 (1.1)	33/2293 (1.4)	0.78 (0.47-1.29)
Quartile 3	21/2356 (0.9)	33/2373 (1.4)	0.66 (0.38-1.14)
Quartile 4	26/2341 (1.1)	54/2393 (2.3)	0.48 (0.30-0.77)
Overall	**101/9462 (1.1)**	**145/9462 (1.5)**	**0.69 (0.54-0.89)**

P_{trend} = .03



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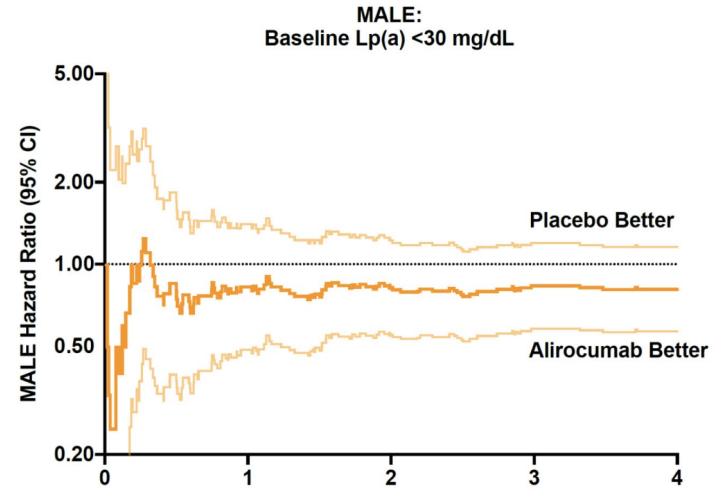
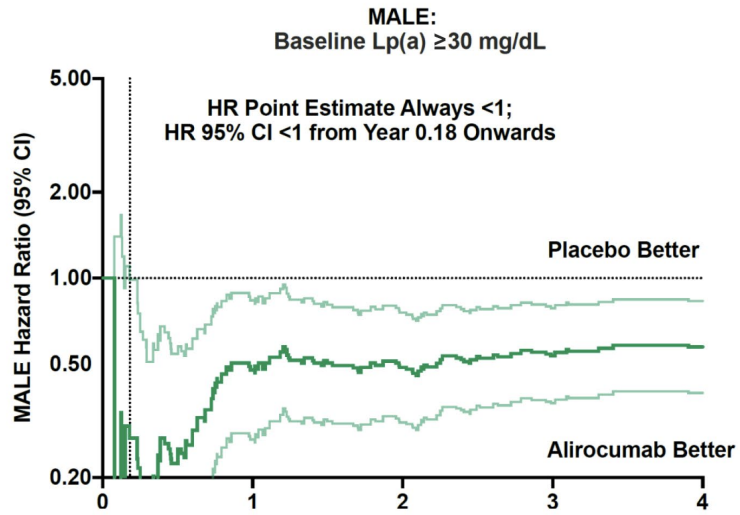
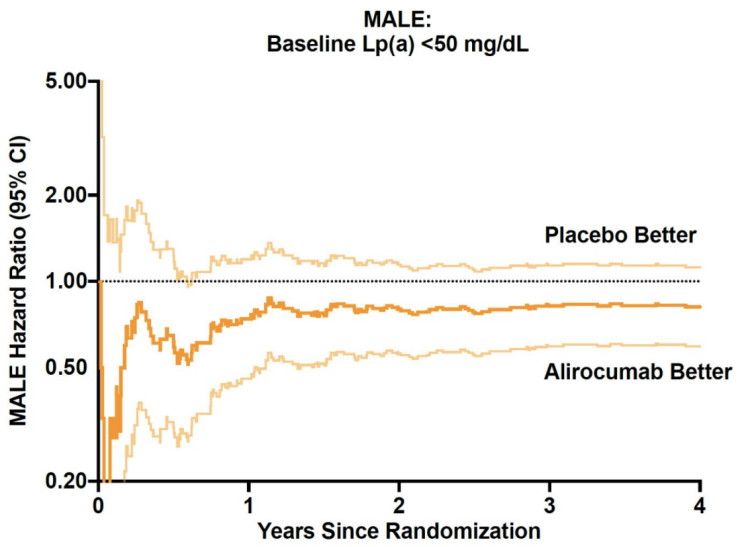
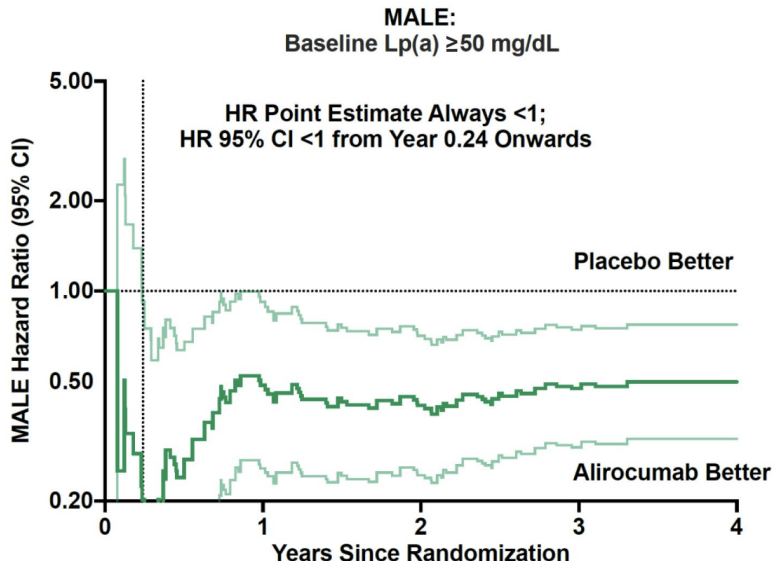
Schwartz GG, Steg PG, et al. Peripheral artery disease and venous thromboembolic events after acute coronary syndrome. *Circulation* (2020) 141(20), 1608-17

Benefit of Alirocumab for MALE by Baseline Lp(a)









An Affiliate of:

Ray, K, Szarek, M, Bhatt, D. et al. Lipoprotein(a) identifies patients with acute coronary syndromes who derive cardiovascular benefit from alirocumab, particularly for limb events. JACC. null2025, 0 (0) .
https://doi.org/10.1016/j.jacc.2025.08.043.

- *Re-enforce healthy lifestyle*

Active, healthy diet, normal BMI

Lifestyle (exercise, diet)

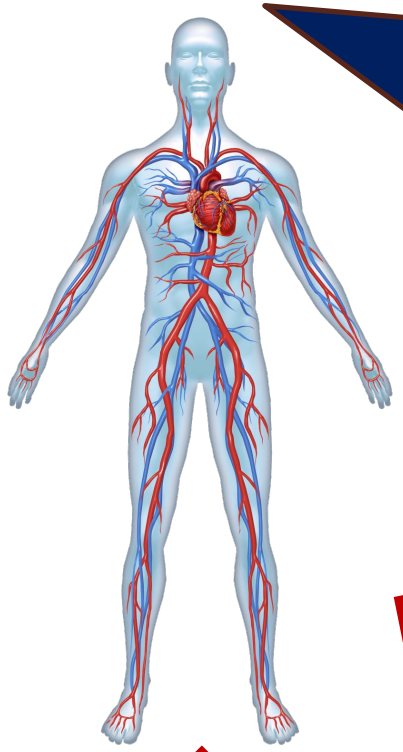
- *Further support for healthy lifestyle*
- *Family screening*
- *Interested in research studies and new therapies*

- *Push to lower LDL target (<55 and ideally 30 or lower)*
- *Favor PCSK9i if possible (FOURIER and ODYSSEY results)*
- *Consider apheresis*

Lipid Risk (LDL & Lpa?)

LDL ~60 mg/dL

Lp(a) ?



Thrombosis Risk

No thrombophilia

- *On aspirin monotherapy*
- *Added rivaroxaban 2.5 mg twice daily (indicated for PAD) due to higher risk profile*

- *Re-enforce preventive testing and healthy lifestyle*

Diabetes Risk (micro and macrovascular)

Does not have diabetes

Inflammatory Risk

hsCRP low

Smoking Risk

Never smoker

- *Further support tobacco abstinence*

An Affiliate of:

CPC Clinical Research

When to Check Lp(a)?

1. **All patients once in a lifetime (evolving practice) → many are doing now!**

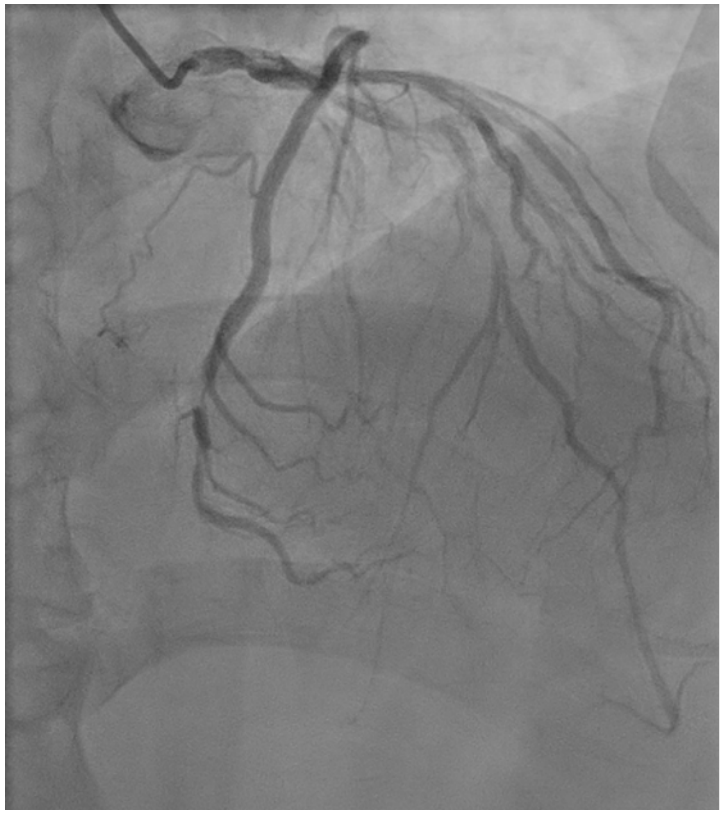
2. **Previously – a selective approach:**

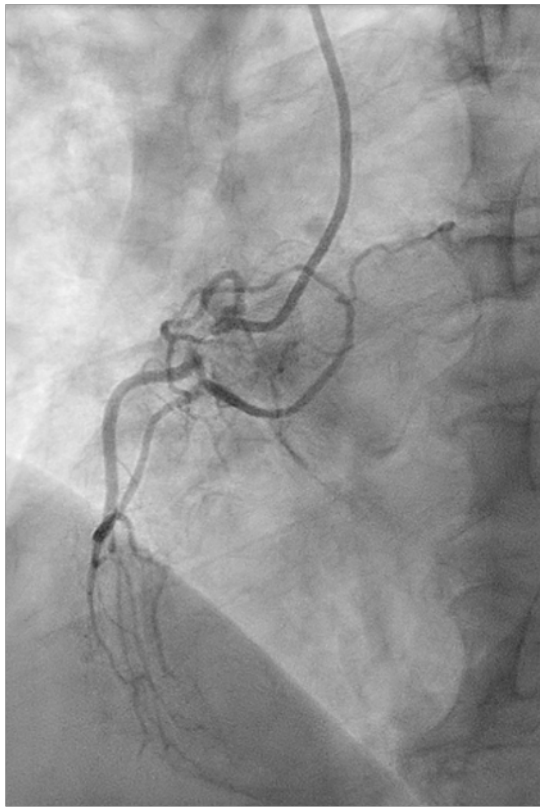
    - **Early onset disease (PAD, AS, aneurysm)**
    - **Malignant phenotype (polyvascular disease, adverse limb outcomes, recurrent thrombotic events)**
    - **Recurrent events / poor outcomes after revascularization**
    - **Disease in absence of other clear risk factors (e.g. age, diabetes, smoking)**
    - **Disease progression despite control of conventional risk factors**

Clinical Case

After measuring Lp(a)

- **Identified a clear uncontrolled risk factor**
- **Discussed importance of family screening**
- **Added PCSK9i now with LDL-C of 10 mg/dL**
- **Discussion of plasmapheresis**
- **On waiting list for opportunity to enroll in a clinical trial or for when specific therapies available if shown efficacious**





Presenter Provided Images

Questions and Discussion

Lp(a) Resources