Za vším hledejme nejen ženu, ale i Lp(a)….

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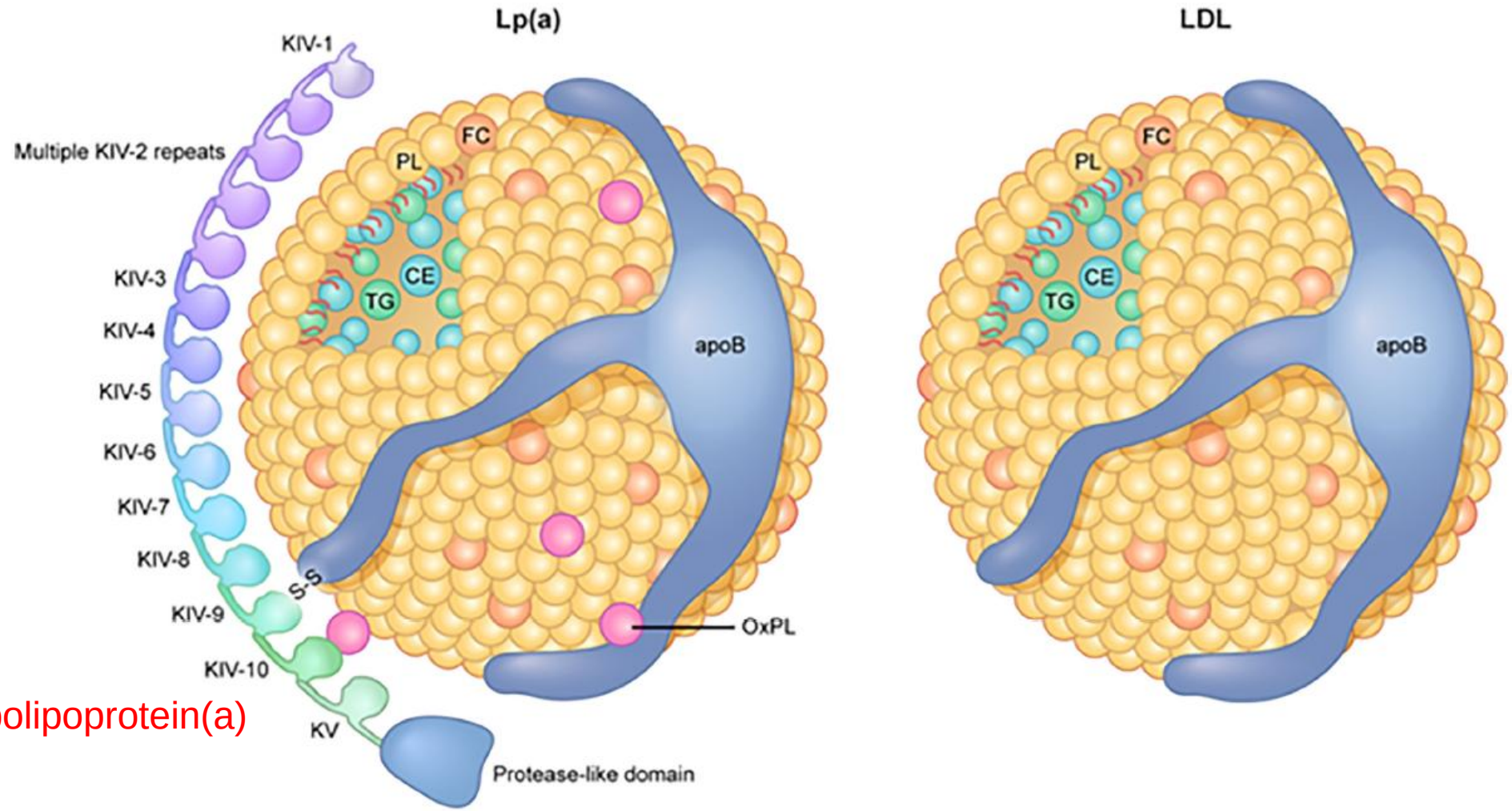
Praha

XXXIII. VÝROČNÍ SJEZD ČESKÉ KARDIOLOGICKÉ SPOLEČNOSTI

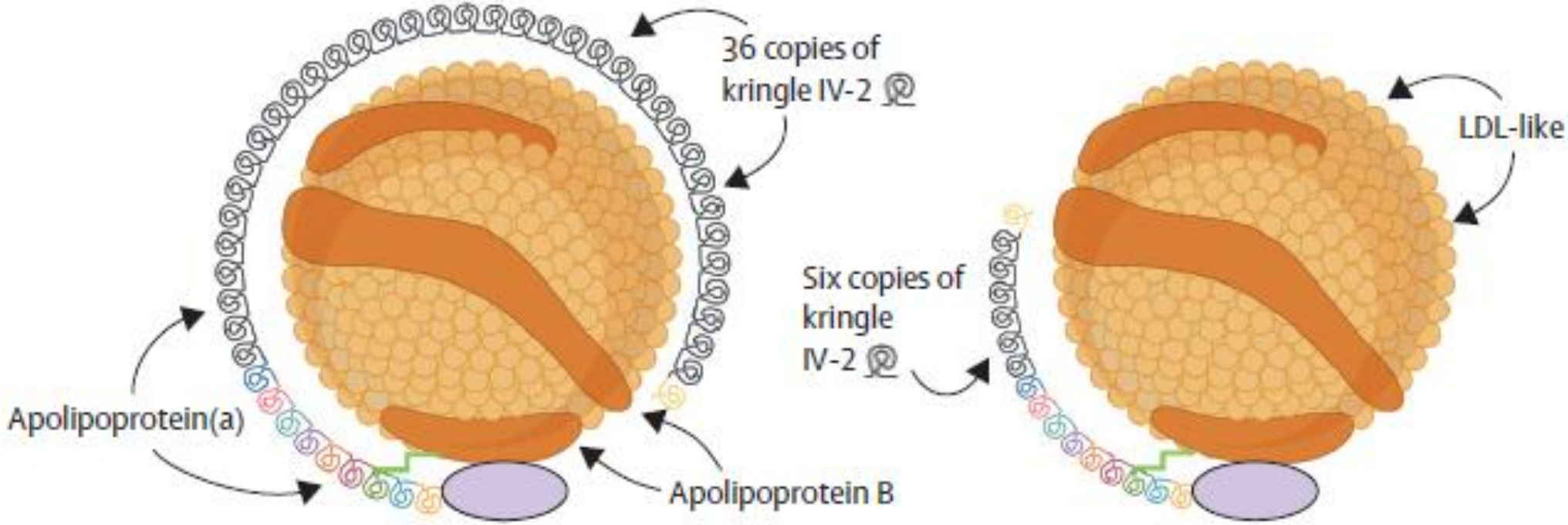
Struktura Lp(a) a LDL



Apolipoprotein(a)

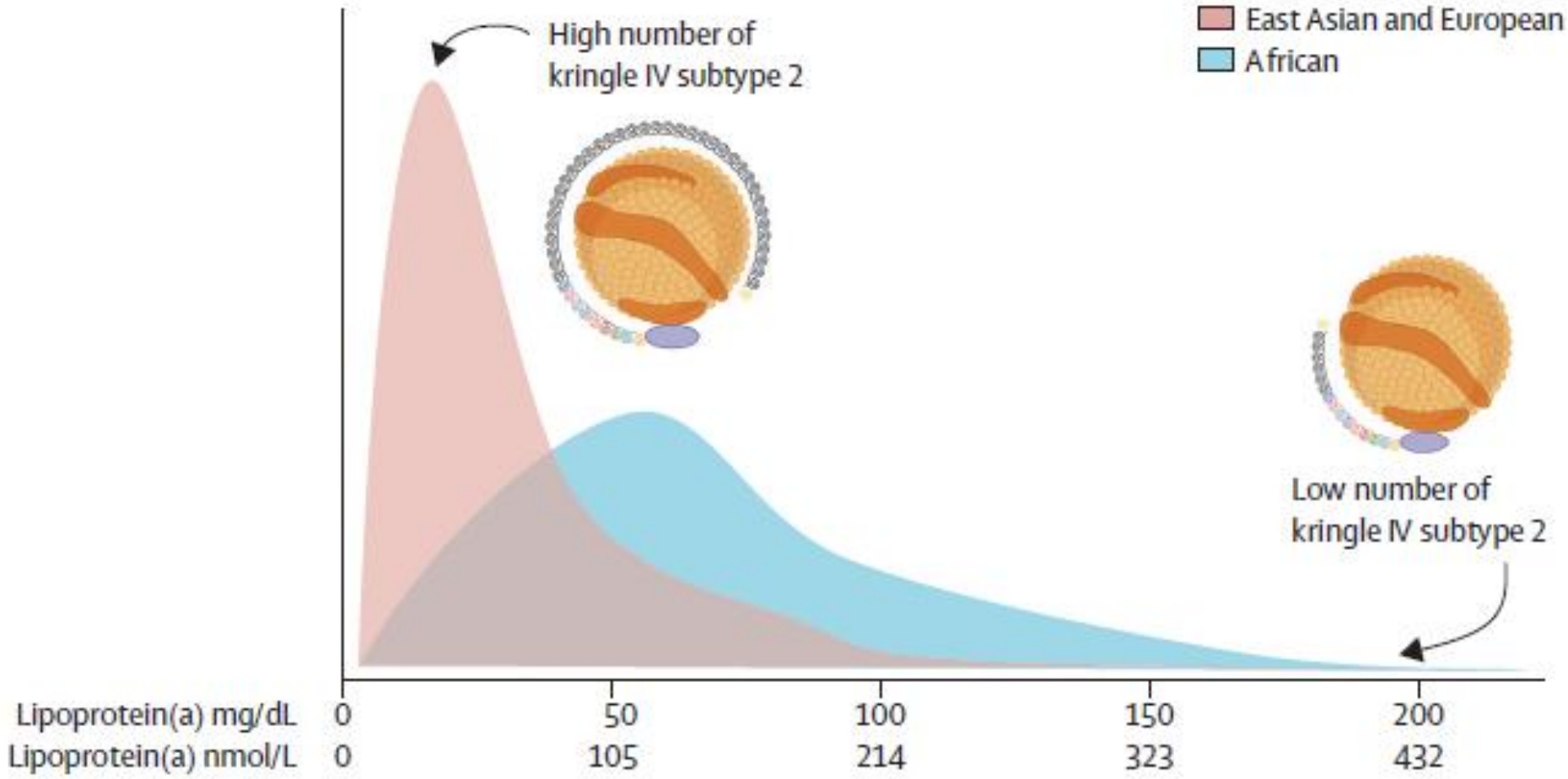
J Am Heart Assoc 2024; 13:e033654

Struktura Lp(a)



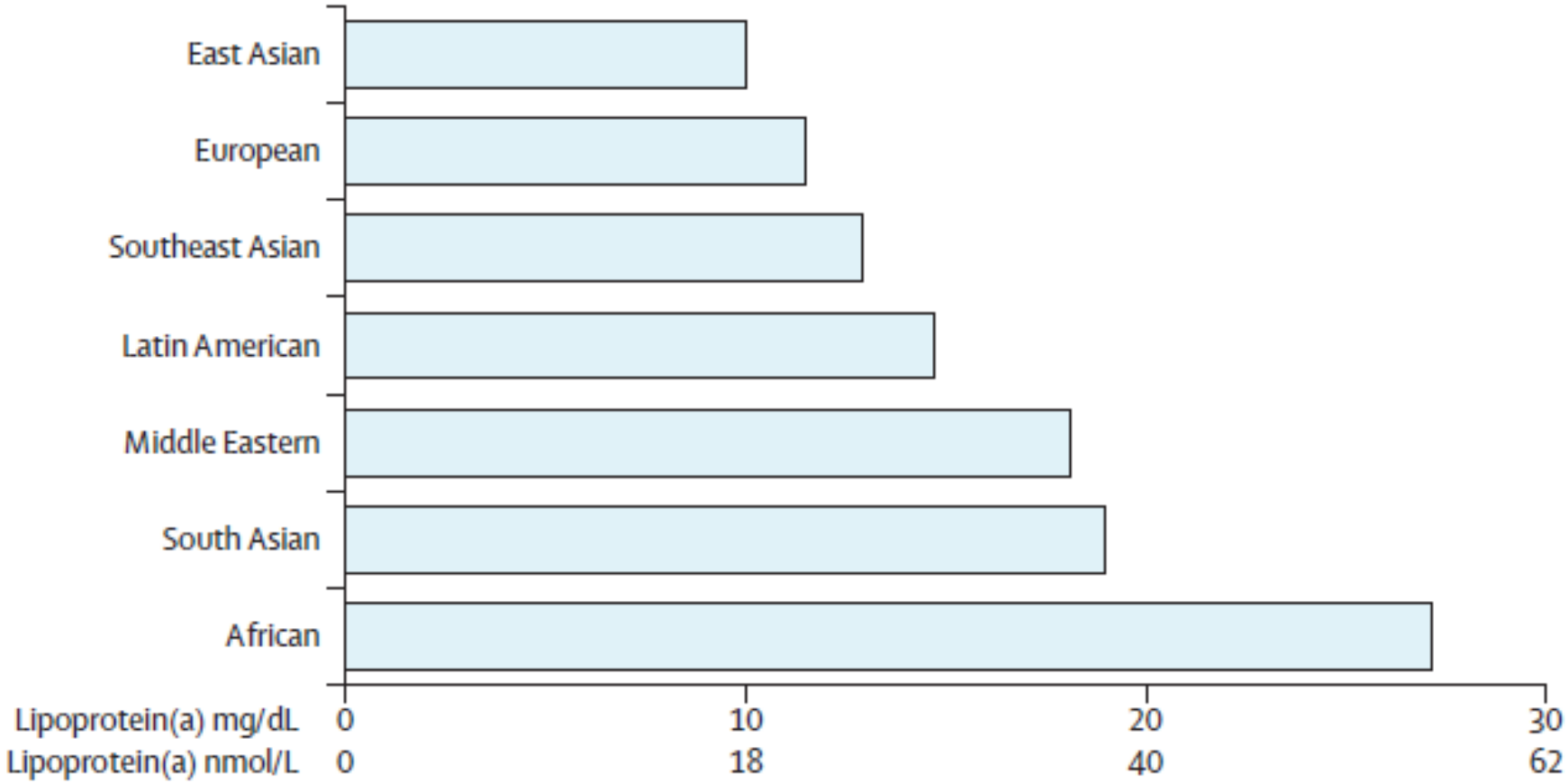
Lancet 2024; 404:1255-64

Lp(a) - struktura a plazmatické koncentrace



Lancet 2024;404:1255-64

Lipoprotein(a) u různých etnik (medián)



Lancet 2024;464: 1255-64

Lipoprotein(a) – historické poznámky

Kare Ingmar Berg (1932 – 2009)

- 1963 objeven Kare Bergem
- 1987 objeven gen LPA (Richard Lawn, Angelo Scanu et al.)

- 2009 Lp(a) potvrzen jako kauzální RF pro ICHS
  Kamstrup PR et al., JAMA 2009;301:2331-39
  Clarke R et al., N Engl J Med 2009;361:2518-28

- 2013 Lp(a) identifikován jako kauzální RF pro kalcifikaci a stenózu Ao chlopně
  Thanassoulis G et al., N Engl J Med 2013;368: 503-12
  Kamstrup PR et al., JACC 2014;63: 470-2

- 2010 EAS Consensus Panel: screening Lp(a) u osob ve středním a vysokém riziku AS KVO

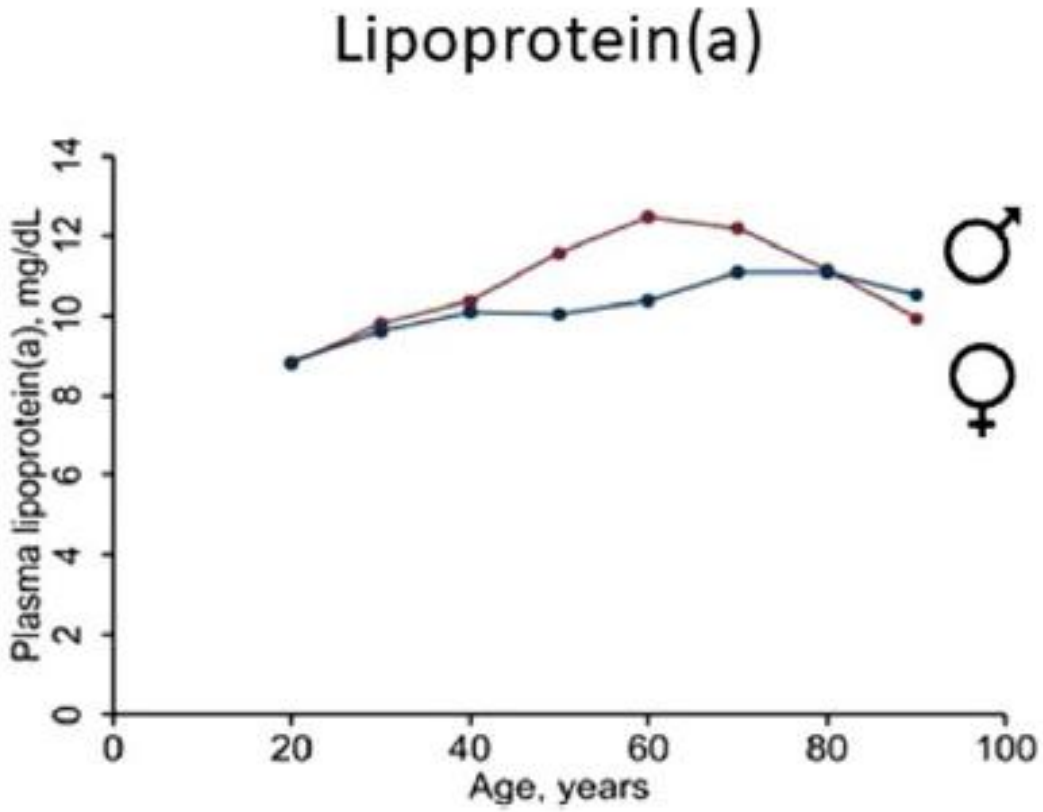
- 2019 ESC/EAS Guidelines for the management of dyslipidemias:
  screening Lp(a) 1x v průběhu života u všech osob

Doporučení pro interpretaci výsledků měření Lp(a)

	koncentrace [nmol/l]	koncentrace [mg/dl]
nízká hodnota	< 75	< 30
šedá zóna	75–125	30–50
zvýšená hodnota	> 125	> 50
velmi vysoká hodnota*	> 430	> 180

AtheroRev 2023; 8.172-176

Copenhagen General Population Study

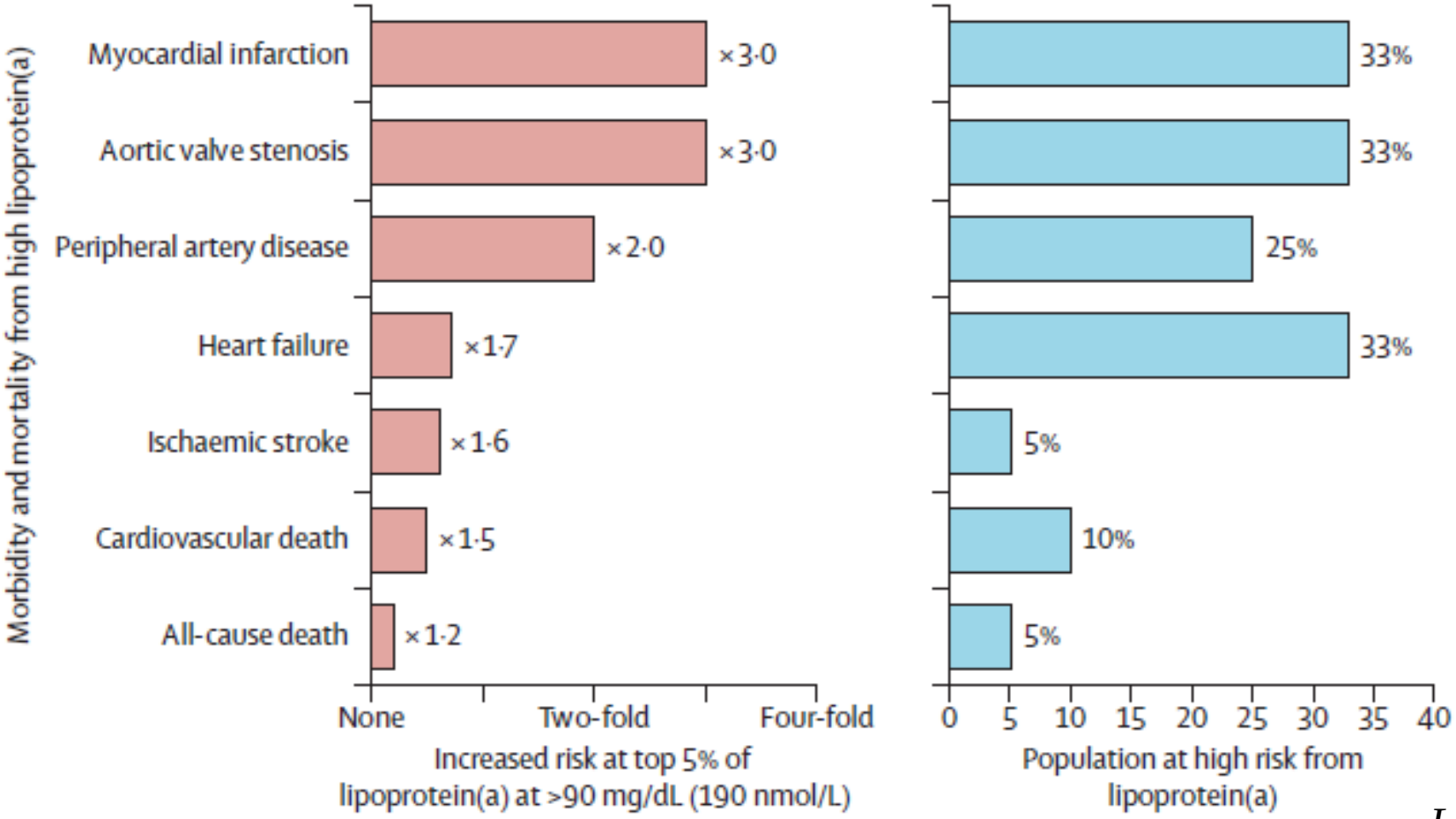


Muži 48 314
Ženy 59 278

Eur Heart J 2023 Aug 23;
Epub ahead of print

KV morbidita a mortalita ve vztahu k nejvyšším hodnotám Lp(a) v plazmě

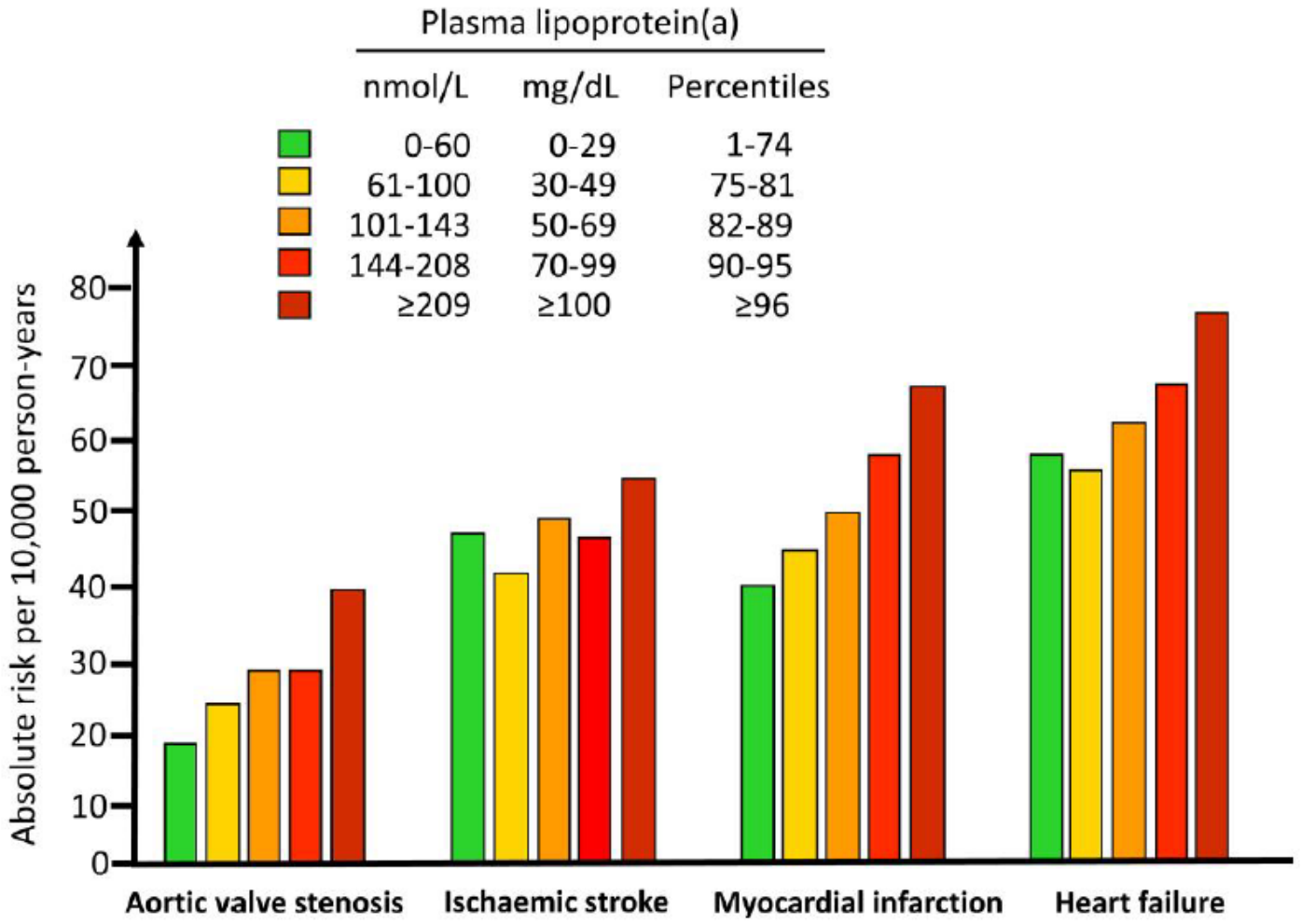
Copenhagen City Heart Study; Copenhagen General Population Study



Lancet 2024;404: 1255-64

Risk of clinical outcomes with Lp(a) concentration

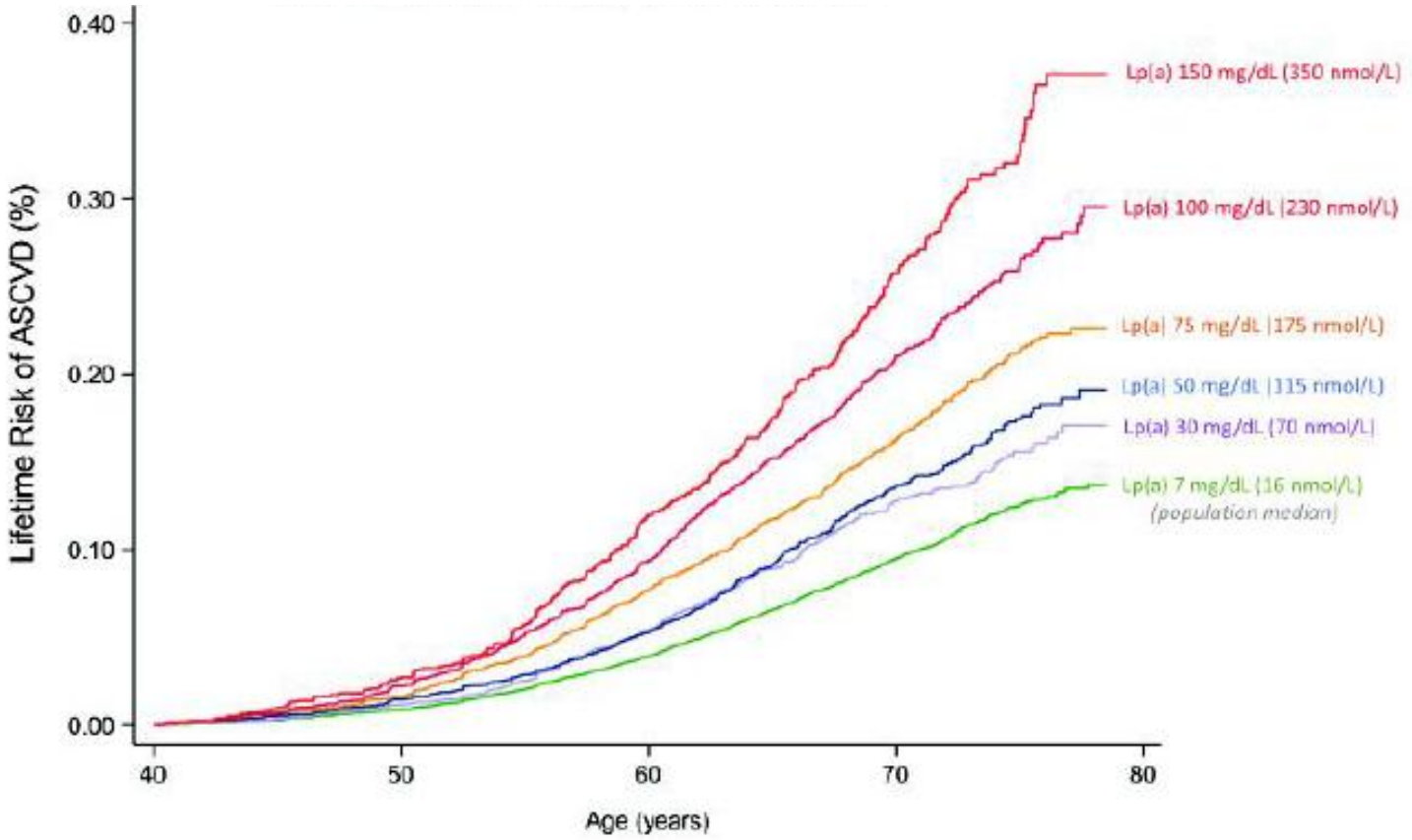
Copenhagen General Population Study



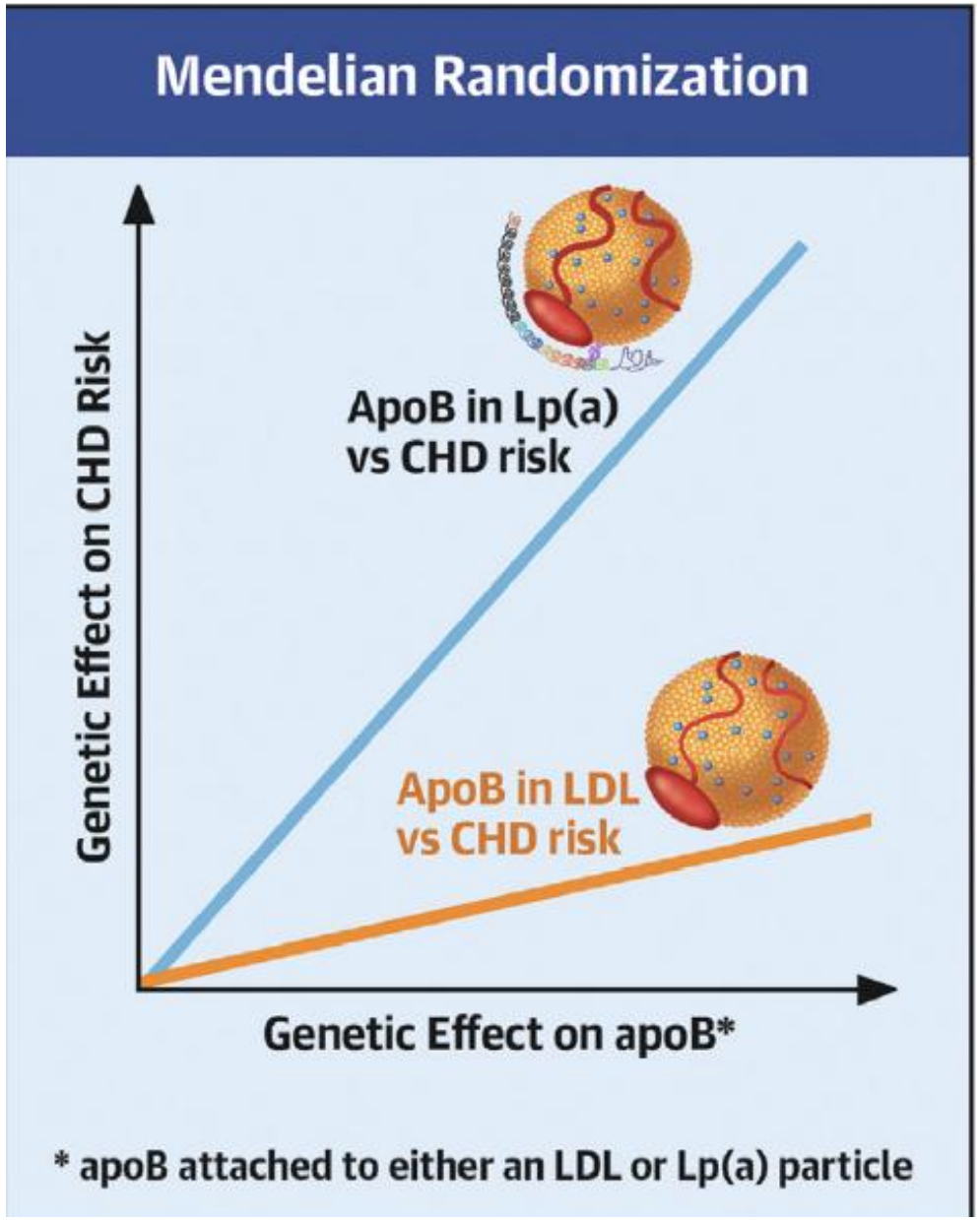
Eur Heart J 2022; 43:3925-3946

Lifetime risk for major CV events with increasing higher Lp(a)

UK Biobank



Eur Heart J 2022;43:3925-3946



UK Biobank Study

JACC 2024;83:385-395

Lipoprotein (a) testing patterns among subjects with a measured lipid panel: The Mayo Clinic experience

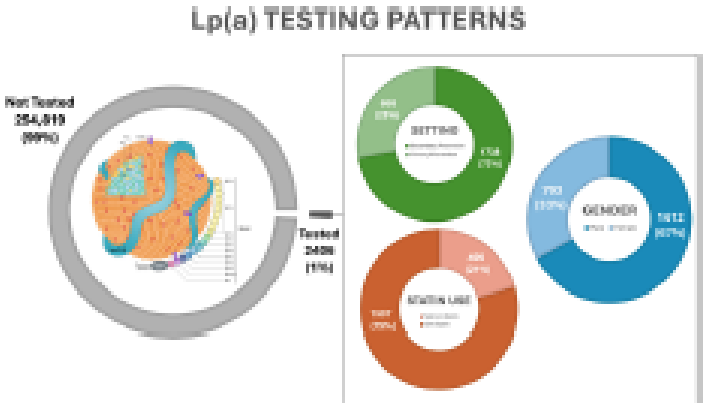
Matteo Manzato [a], Jeffery W. Meeusen [b], Leslie J. Donato [b], Allan S. Jaffe [a,b], Vlad C. Vasile [a,b,*]

[a] Department of Cardiovascular Diseases, Mayo Clinic College of Medicine, Rochester, Minnesota 55905, USA
[b] Department of Laboratory Medicine and Pathology, Mayo Clinic College of Medicine, Rochester, Minnesota 55905, USA

HIGHLIGHTS

- Lipoprotein (a) is undertested, even at tertiary referral centers.
- Females are less frequently tested than males, despite similar LDL-c values.
- Lp(a) testing mainly occurs in a secondary, rather than a primary, prevention setting.

GRAPHICAL ABSTRACT



May 1, 2022 – April 30, 2023

Am J Prev Cardiol 2024;20:100886

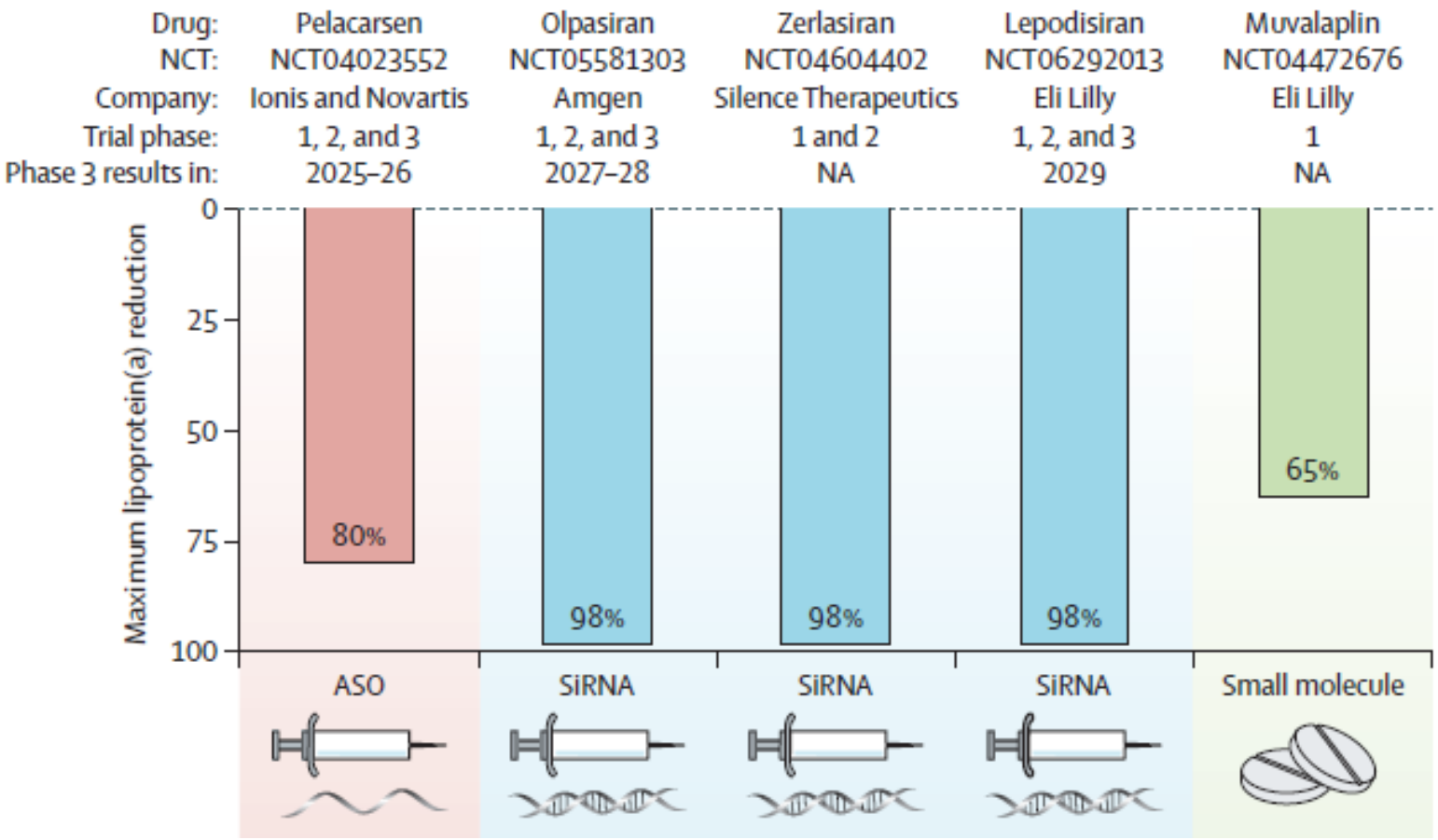
Současné možnosti ovlivnění Lp(a)

Agresivní ovlivňování všech známých RF KVO

- Dosažení cílových hodnot LDL-chol.
- Úprava životosprávy: neovlivňuje Lp(a)

- Statiny, ezetimib, k. bempedoová neovlivňují Lp(a)
- PCSK9i: pokles Lp(a) o 25 %
- Aferéza: pokles Lp(a) o 35 %
- Niacin: pokles Lp(a) o 35 %

Snížení Lp(a)



Lancet 2024; 404:1255-64

Large trials assessing the effect of Lp(a) reduction on CV outcomes

Drug (Mechanism)	Trial, Status, ClinicalTrials.gov number	No. of Patients	Baseline Lipoprotein(a) Level	Main Inclusion Criteria	Primary End Point	Start Date, Estimated Completion Date
Pelacarsen (ASO)	Lipoprotein(a)-HORIZON, phase 3, NCT04023552	8323 (enrolled)	≥70 mg/dl or approx. ≥175 nmol/liter	MI, ischemic stroke, or revascularized PAD	MACE†	2019, early 2026
Olpasiran (siRNA)	OCEAN(a), phase 3, NCT05581303	7297 (enrolled)	≥200 nmol/liter	MI or coronary revascularization with percutaneous coronary intervention and at least 1 additional risk factor	MACE†	2022, late 2026
Lepodisiran (siRNA)	ACCLAIM-lipoprotein(a), phase 3, NCT06292013	12,500 (planned)	≥175 nmol/liter	ASCVD or age >55 yr with high risk of first ASCVD event	MACE†	2024, 2029

* ASCVD denotes atherosclerotic cardiovascular disease, ASO antisense oligonucleotide, MI myocardial infarction, PAD peripheral artery disease, and siRNA small interfering RNA.

† MACE (major adverse cardiovascular event) is a composite of death from a cardiovascular cause, nonfatal myocardial infarction, nonfatal stroke, or urgent coronary revascularization. The primary end point of the olpasiran trial did not include nonfatal stroke.

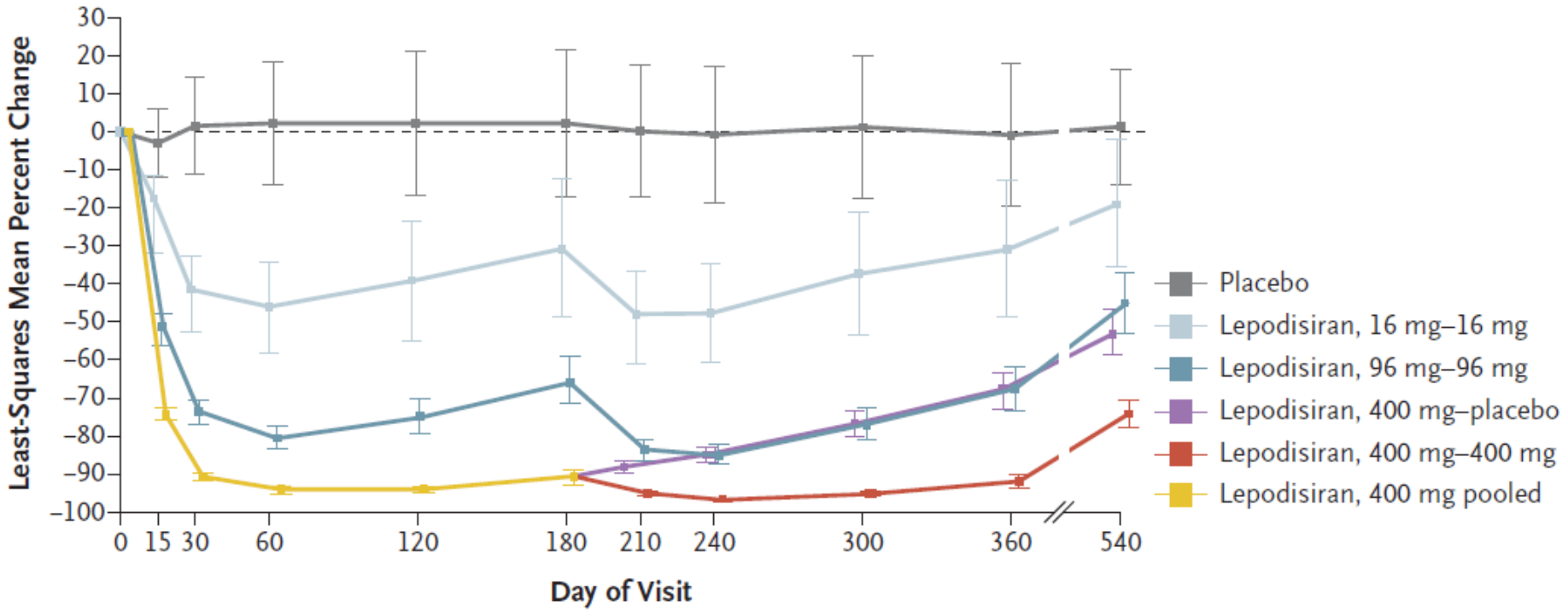
N Engl J Med 2025;392:1740-1742

The NEW ENGLAND JOURNAL of MEDICINE

Lepodisiran — A Long-Duration siRNA Targeting Lipoprotein(a)

A Research Summary based on Nissen SE et al. | 10.1056/NEJMoa2415818 | Published on March 30, 2025

A Change in Lipoprotein(a) Concentration



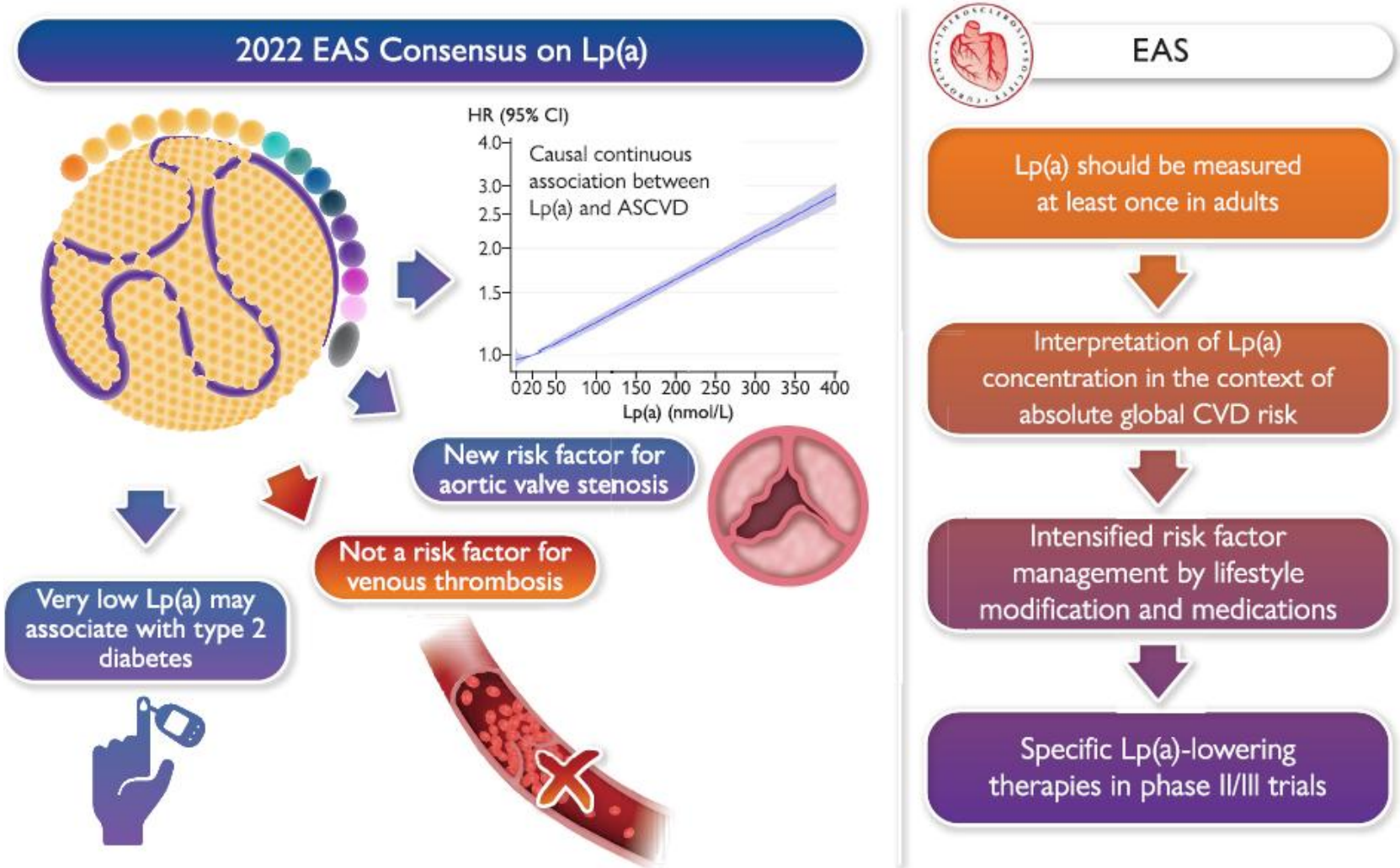
No. of Participants										
Placebo	69	69	68	68	67	66	64	64	64	64	60
Lepodisiran, 16 mg–16 mg	36	36	36	35	36	35	33	33	33	33	32
Lepodisiran, 96 mg–96 mg	74	73	73	73	72	72	67	67	69	68	65
Lepodisiran, 400 mg–placebo	72	71	71	69	70	69	65	66	64	64	62
Lepodisiran, 400 mg–400 mg	69	69	67	68	68	63	61	63	63	63	61

NEJM 2025;392:1673-83

Závěry

- Cca 20 % populace v Evropě má vyšší Lp(a), které jsou spojeny s vyšším rizikem AS KVO a aortální stenózy.

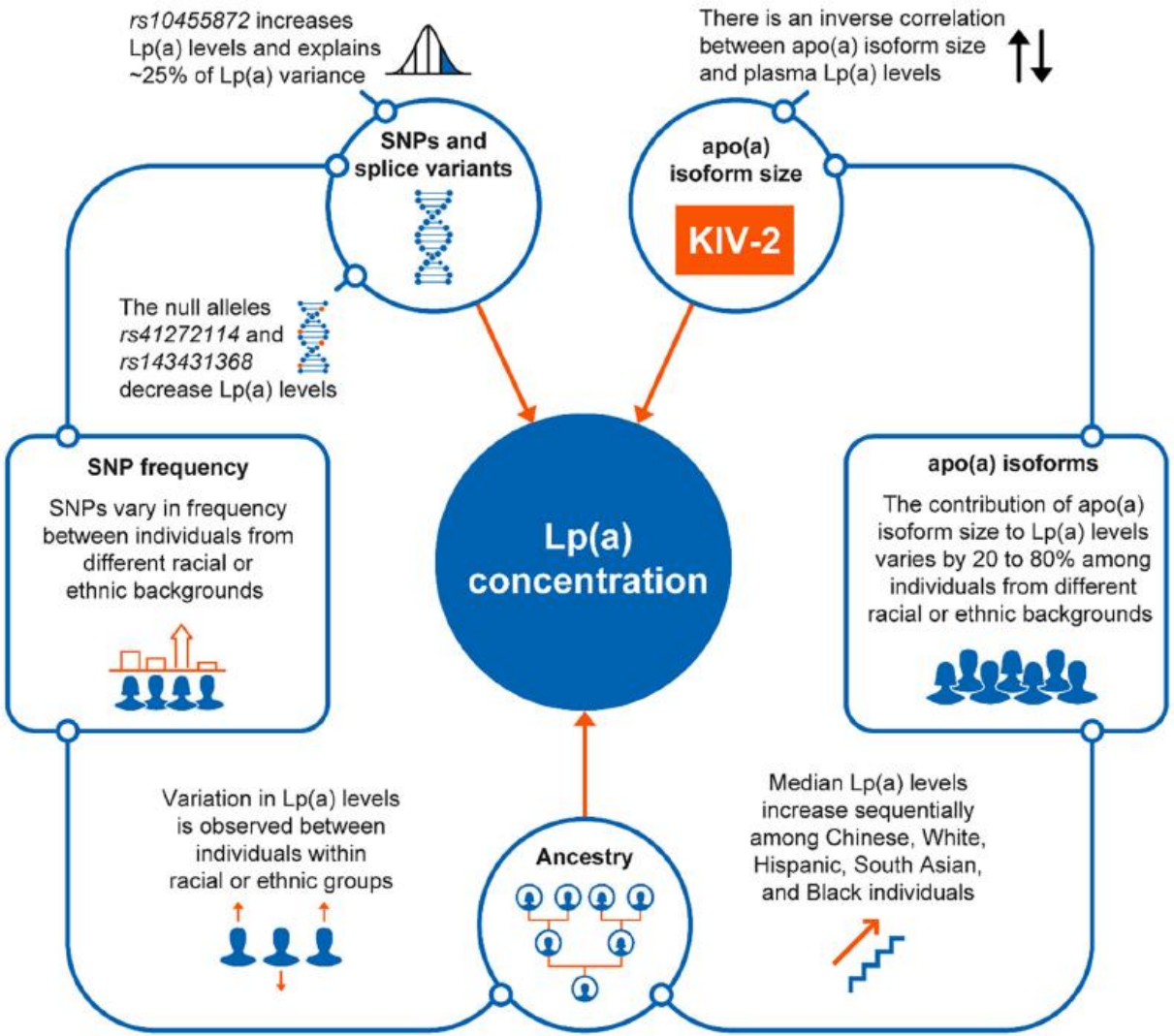
- Lp(a) má být stanoven u všech osob 1x během života (vyjma žen v postmenopauze) s cílem identifikovat osoby s vysokým rizikem AS KVO, u kterých by měly být agresivně ovlivňovány všechny známé RF KVO.
- Probíhají velké klinické studie fáze III
  - pelacarsen (antisense oligonukleotid)
  - olpasiran, lepodisiran (SiRNA)



Eur Heart J 2022;43:3925-46

ČAKO
Česká Aliance pro
Kardiovaskulární Onemocnění

24. BŘEZEN JE DEN POVĚDOMÍ O LP(A)



Eur Heart J 2023 Aug 23;
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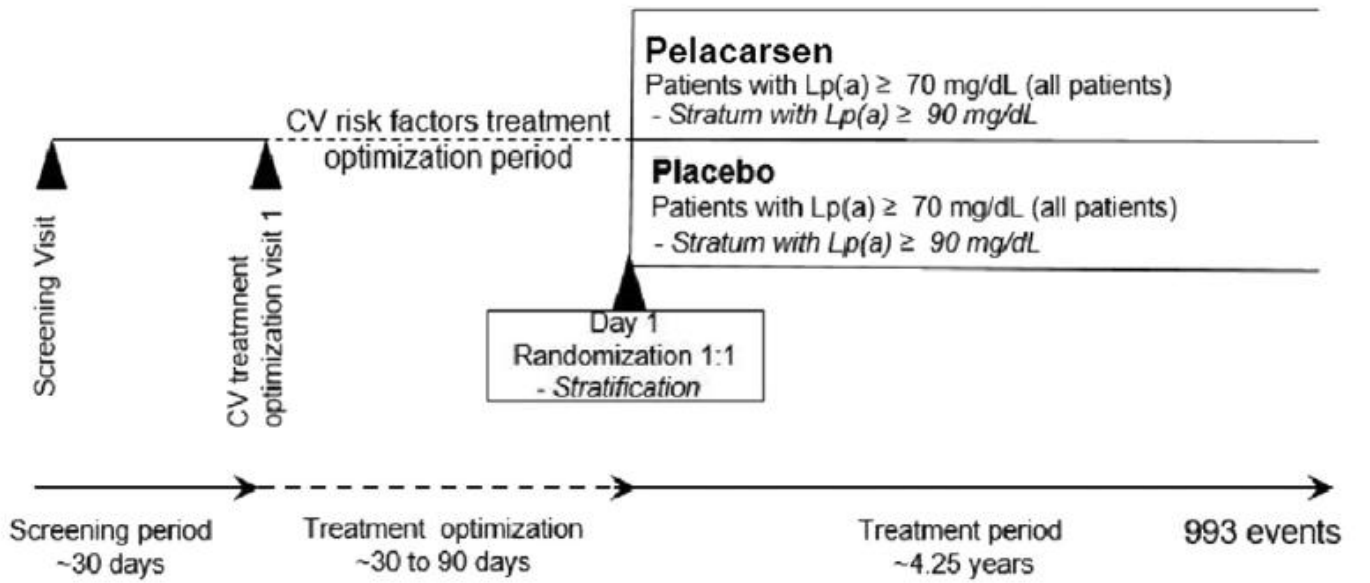

Solid line indicates mandatory study periods
Dashed line indicates the option of a patient to go through a CV treatment optimization period, if needed

Eur Heart J 2023 Aug 23;
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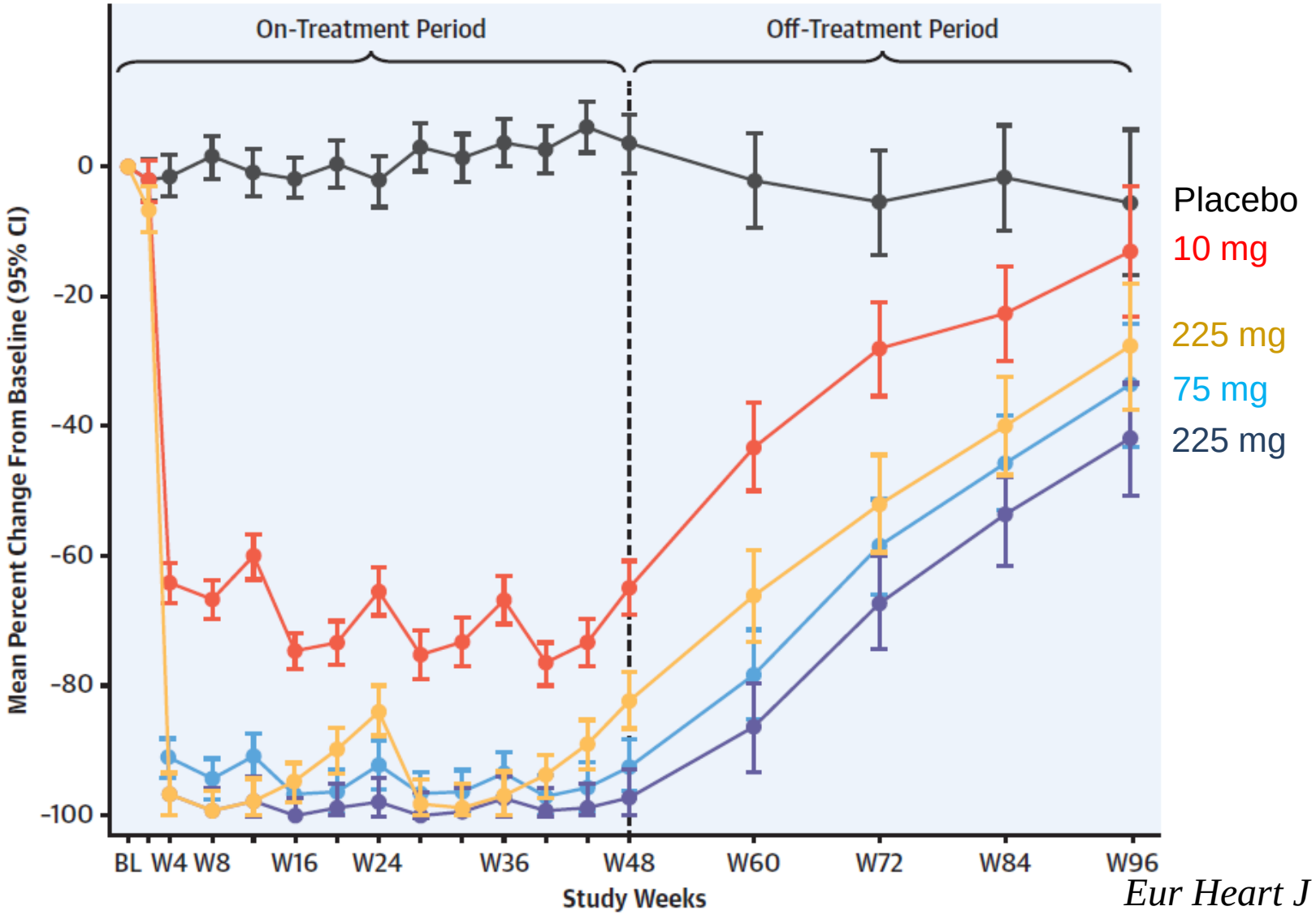

Eur Heart J 2023 Aug 23;
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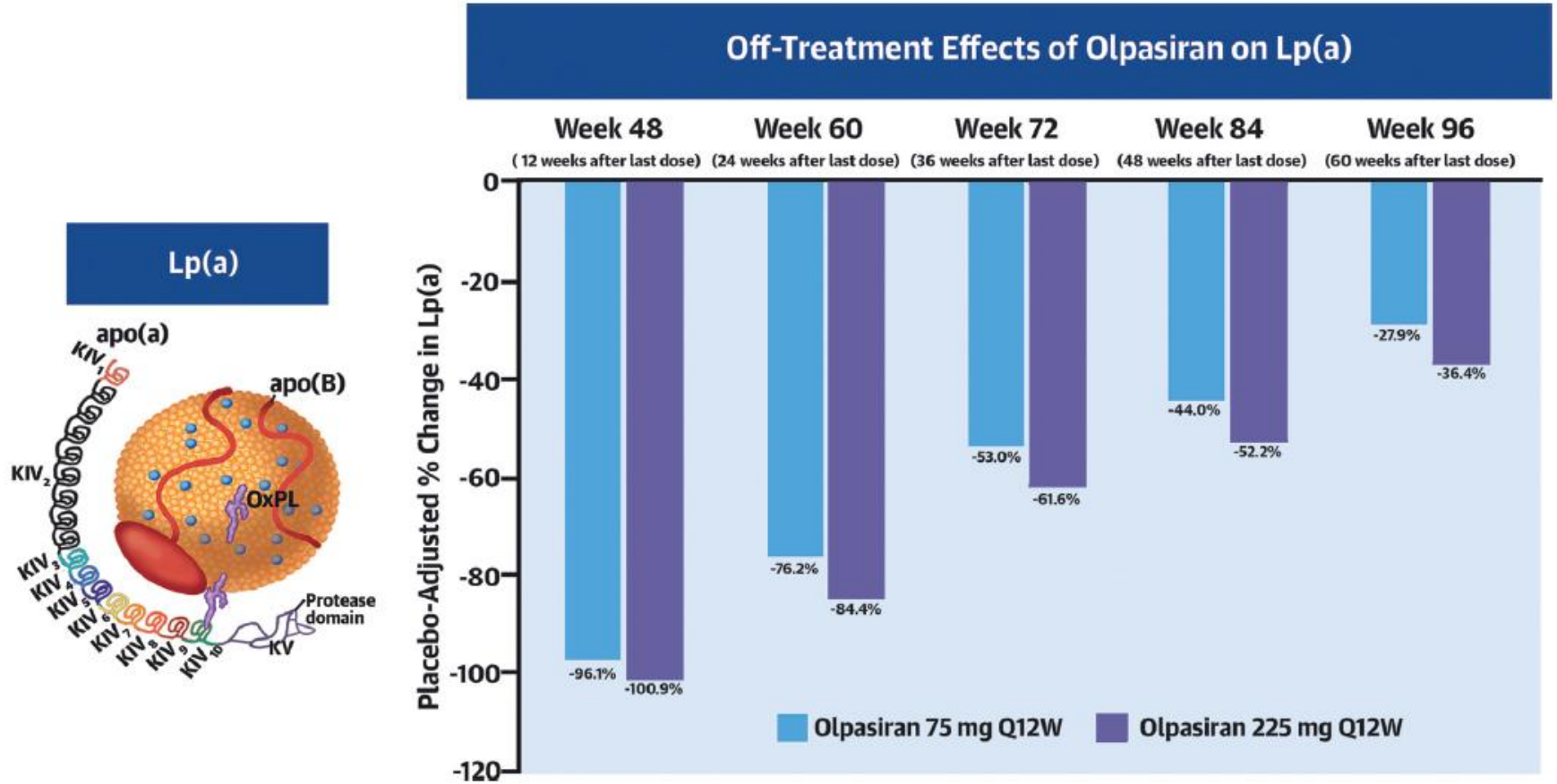
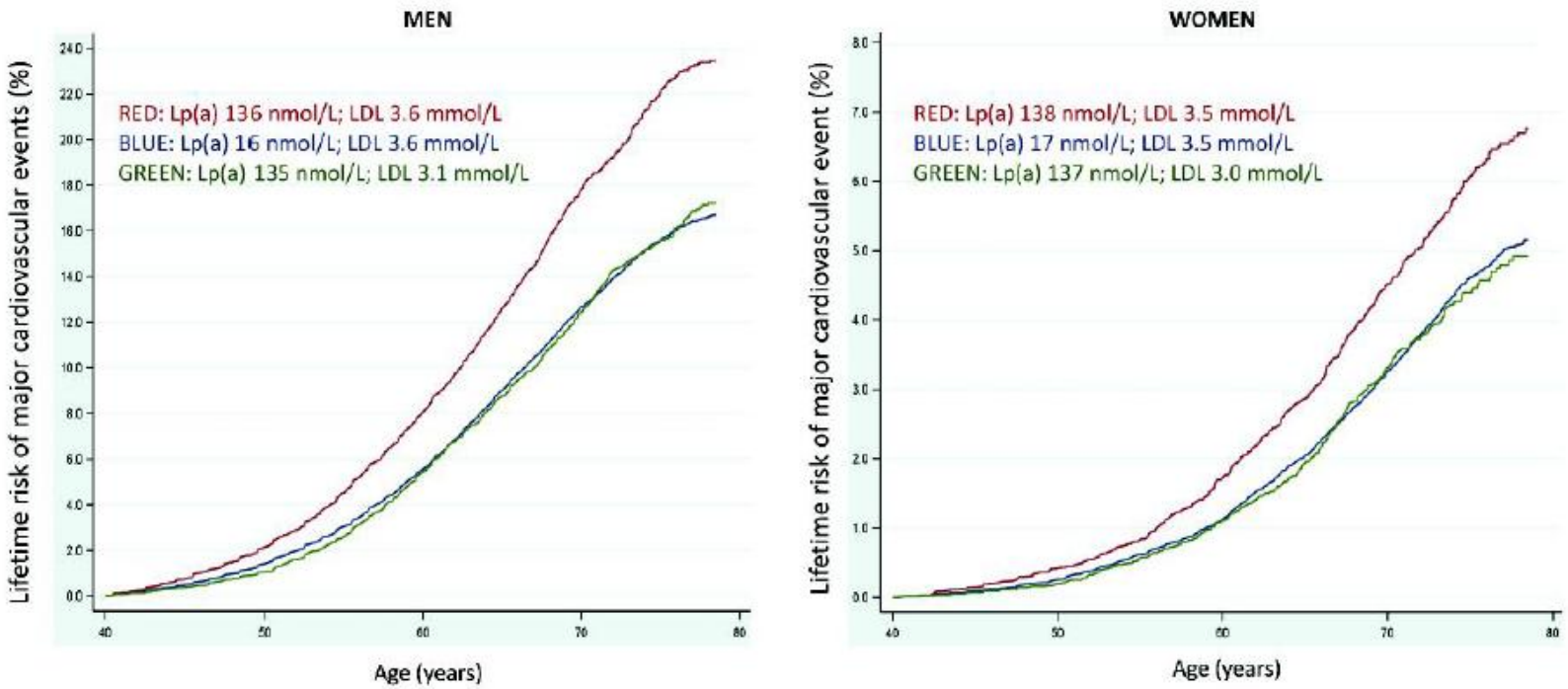


O'Donoghue ML, et al. J Am Coll Cardiol. 2024;84(9):790-797.

Eur Heart J 2023 Aug 23;
Epub ahead of print

Lifetime risk of major cardiovascular events with higher lifetime exposure to Lp(a) and lower lifetime exposure to LDL-C



Eur Heart J 2023 Aug 23;
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Intensification of LDL-C reduction needed to reduce the global cardiovascular risk to a similar extent as the risk attributable to elevated Lp(a) depending on age at which LDL-C reduction is initiated

Lp(a) nmol/L	Δ Lp(a) compared to median	Lp(a) percentile	HR for MCVE due to increased Lp(a)	Intensification of LDL-C reduction (nmol/L) needed to mitigate the increased risk caused by Lp(a)			
				Begin age 30y	Begin age 40y	Begin age 50y	Begin age 60 y
320	300	99	2.56	1.2 mmol/L	1.4 mmol/L	1.7 mmol/L	2.3 mmol/L
270	250	97.5	2.19	1.0 mmol/L	1.2 mmol/L	1.5 mmol/L	1.9 mmol/L
220	200	93.5	1.87	0.8 mmol/L	0.9 mmol/L	1.2 mmol/L	1.5 mmol/L
170	150	90	1.60	0.6 mmol/L	0.7 mmol/L	0.9 mmol/L	1.1 mmol/L
120	100	82.5	1.37	0.4 mmol/L	0.5 mmol/L	0.6 mmol/L	0.8 mmol/L
70	50	75	1.17	0.2 mmol/L	0.2 mmol/L	0.3 mmol/L	0.4 mmol/L
20	ref.	50	ref.	ref.	ref.	ref.	ref.

Eur Heart J 2023 Aug 23;
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