VŠEOBECNÁ FAKULTNÍ NEMOCNICE V PRAZE

1. LÉKAŘSKÁ FAKULTA Univerzita Karlova

Screening Lp(a): a co dále...

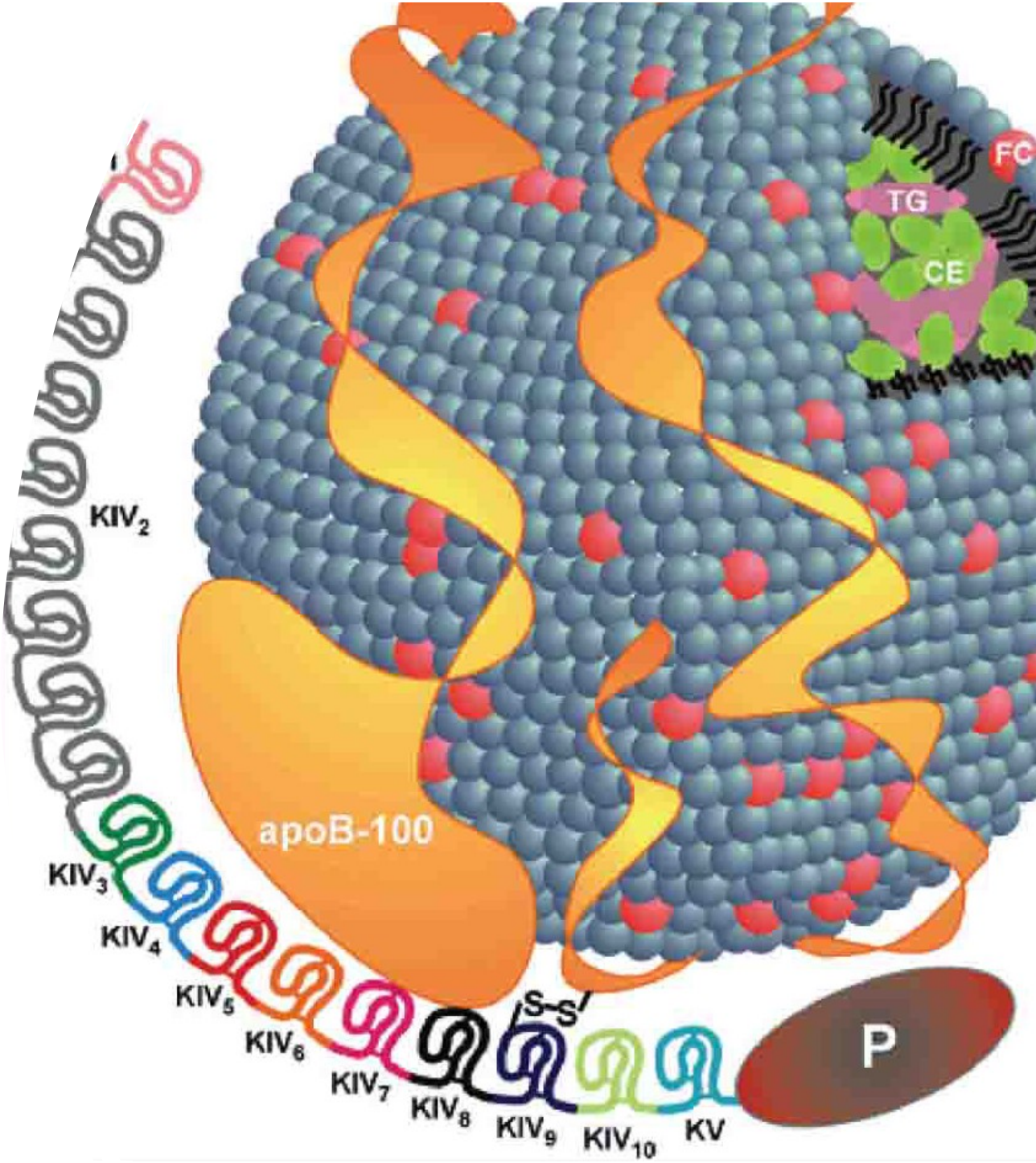
Michal Vrablík

Centrum preventivní kardiologie

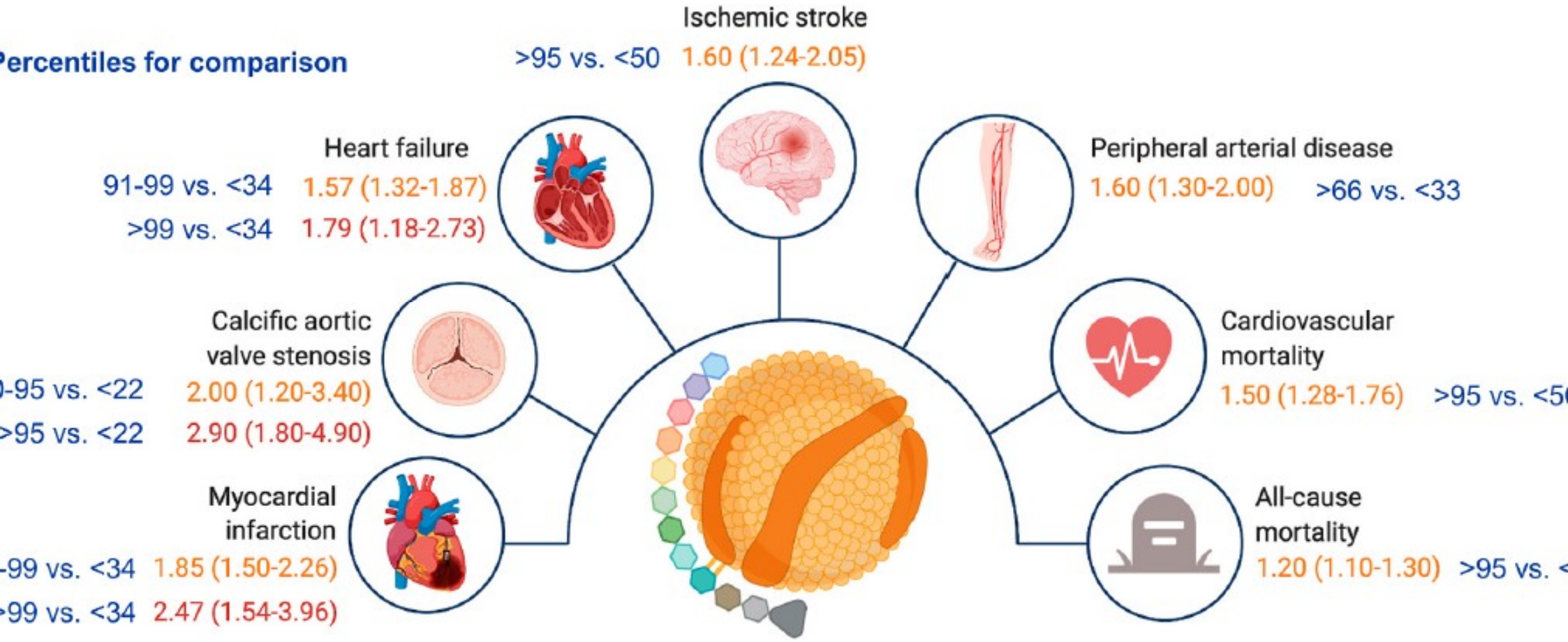
3. Interní klinika 1. LF UK a VFN, Praha

Lipoprotein (a)

- LDL částice s disulfidicky vázaným peptidovým řetězcem (a)
- Většina osob vytváří 2 různé apo(a) odlišné délky řetězců apo(a)
- Gen pro apo(a)- *LPA* – mutace genu pro plazminogen
- KrignleIV 1-10, KIV2 repetitivní 3-40krát



Lp(a) nezvyšuje riziko všech AS příhod stejně



Kronenbertg F et al. Atherosclerosis 374 (2023) 1

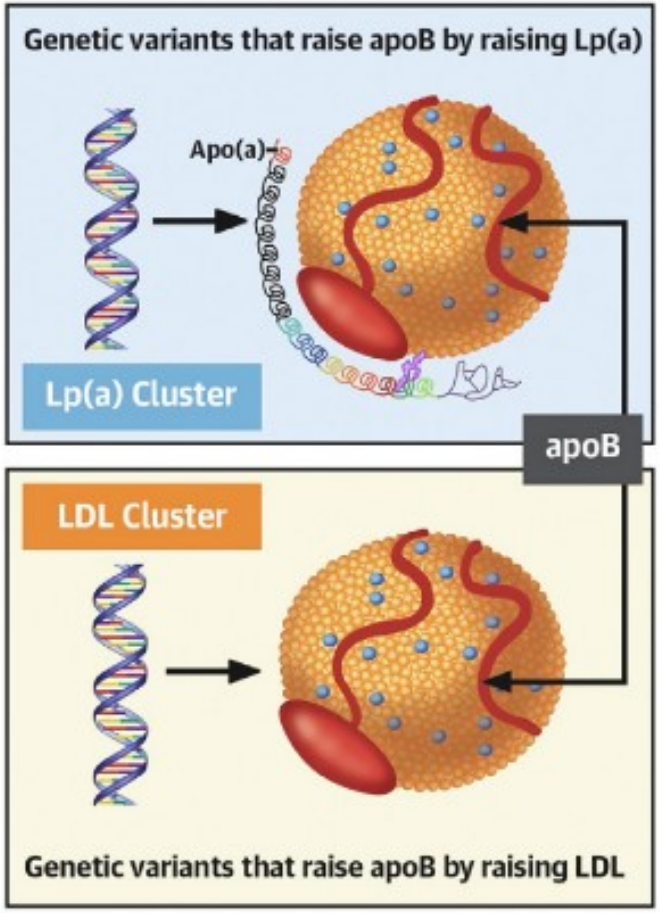
Částice Lp(a) je 6krát více aterogenní než částice LDL

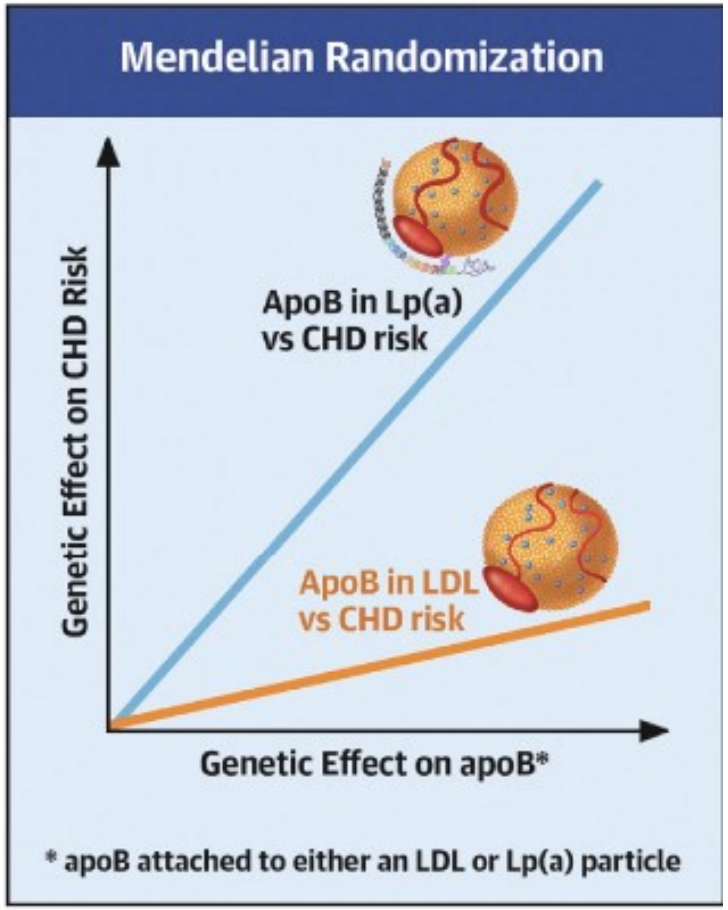
Key Question

How atherogenic is 1 particle of Lp(a) compared to 1 particle of LDL?

Key Methodology

Both Lp(a) and LDL contain 1 apoB per-particle. Here, we identified genetic variants (SNPs) that affected plasma levels of either LDL particles or Lp(a) particles. For these 2 genetic SNP "clusters," we related the change in apoB to the respective change in CHD risk. This way, we directly compared the atherogenicity of LDL and Lp(a), particle for particle.

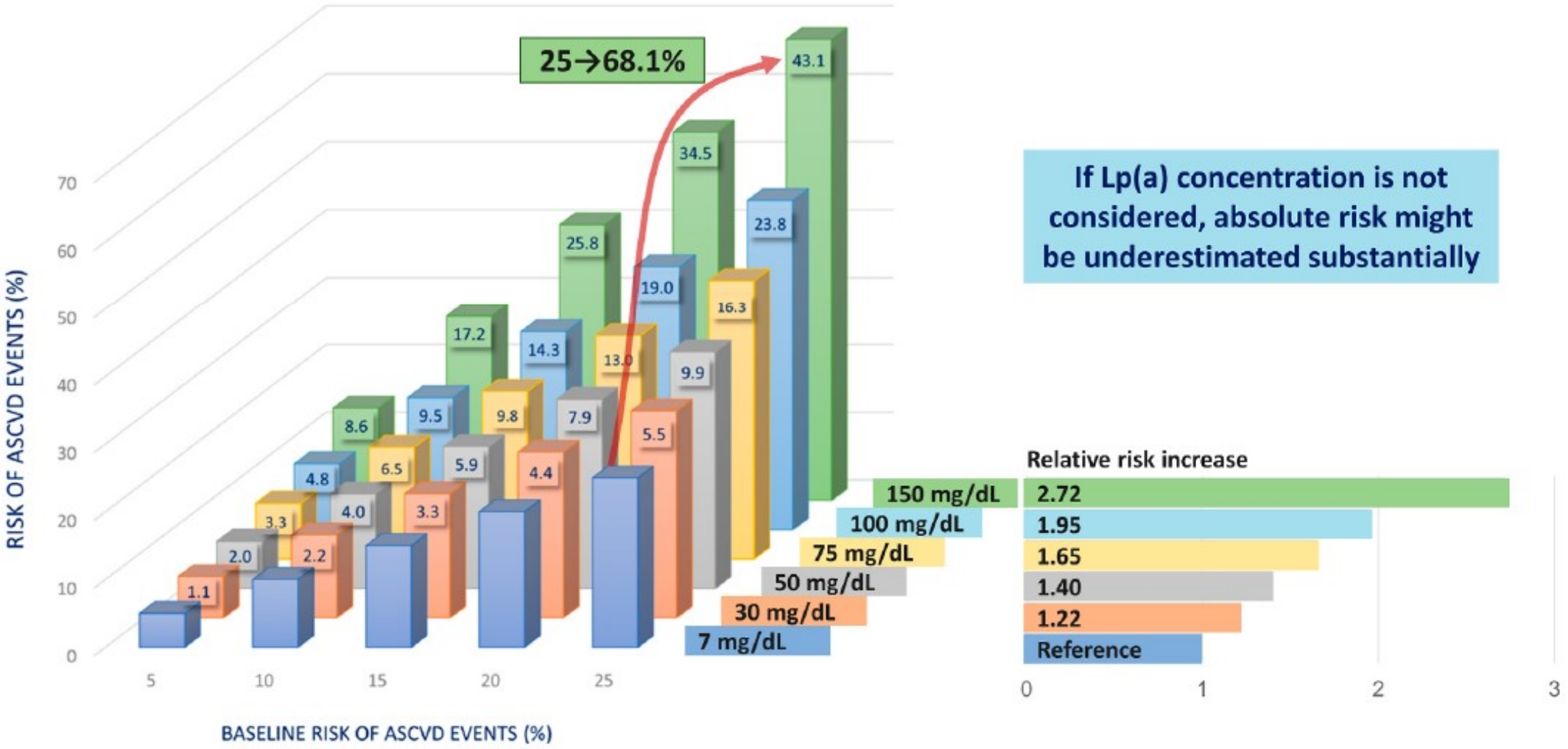




Take-Home Message: In most people, LDL particles are much more abundant than Lp(a) and carry the greatest proportion of overall CVD risk; however, on a per-particle basis, Lp(a) is about 6 times more atherogenic than LDL.

Björnson, E, Adiels, M, Taskinen, M. et al. Lipoprotein(a) Is Markedly More Atherogenic LDL: An Apolipoprotein B-Based Genetic Analysis. *JACC*. 2024 Jan, 83 (3) 385–395.

Riziko spojené s hladinami Lp(a) stoupá spojitě



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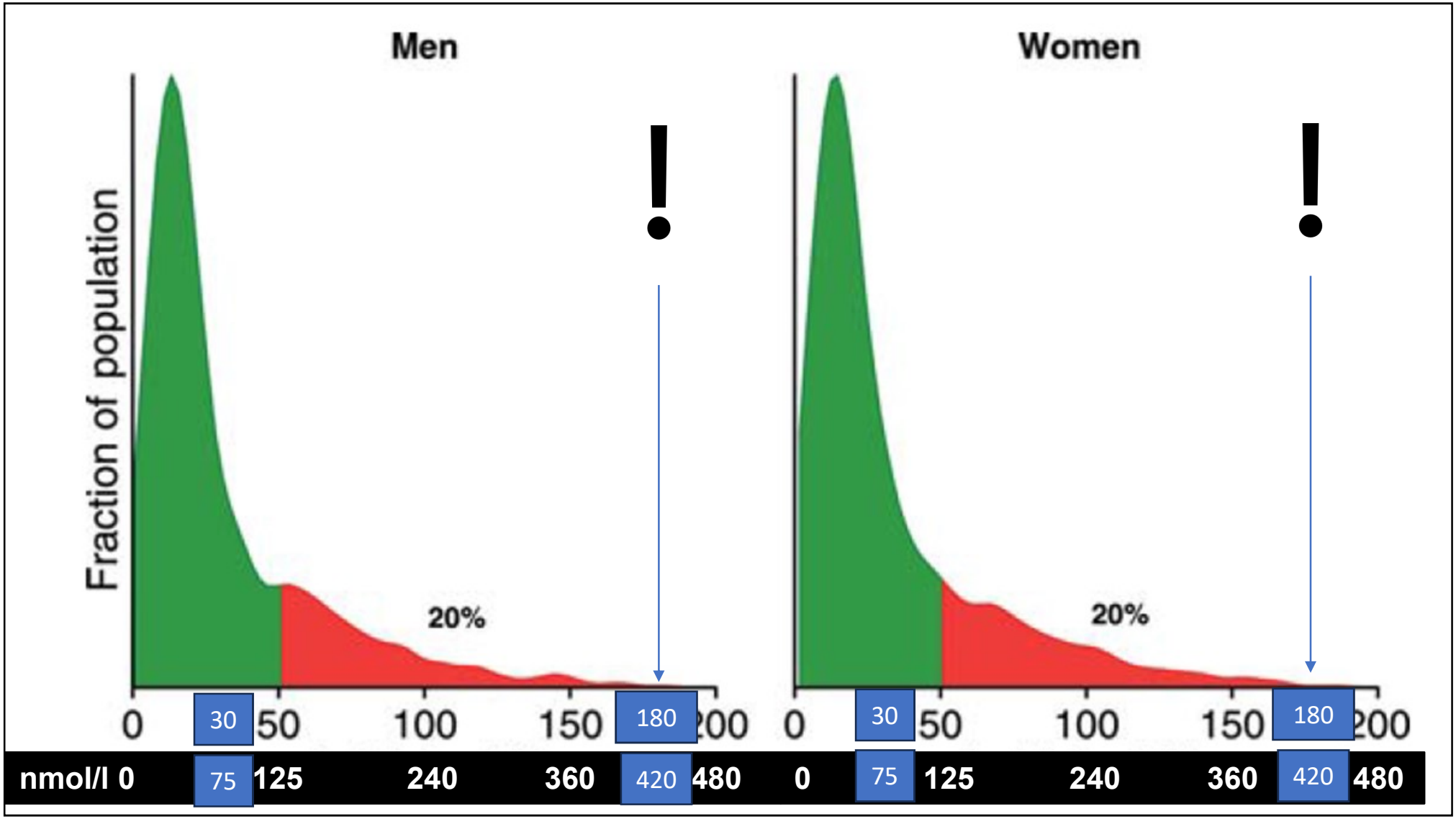
Jak často je koncentrace Lp(a) vysoká ?

Hladina geneticky determinována z 90 %

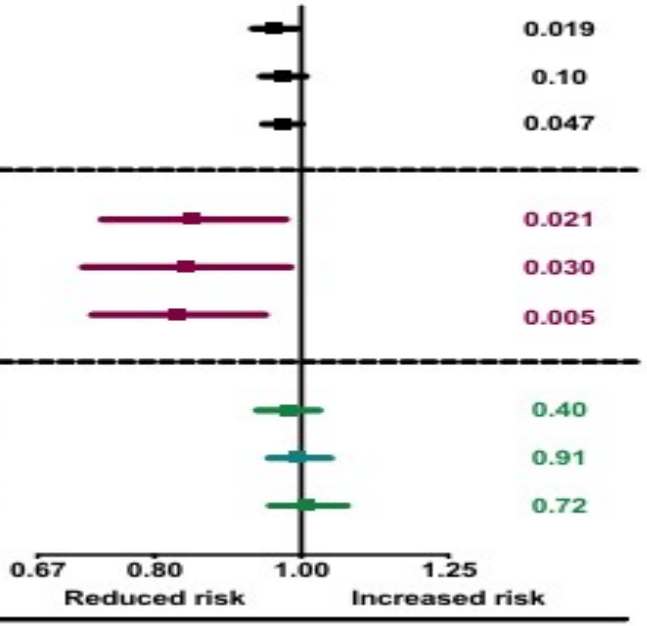


Nordestgaard BG et al. Eur Heart J 2010 ;3

Na metodě stanovení hladiny Lp(a) nezáleží ?

	Baseline	Change baseline to Month 4	Percent change baseline to Month 4
IA-mass, mg/dL			
All patients ($n = 5500$)	20.9 (6.8, 58.5)	−5.1 (−13.4, 0)	−23.8 (−46.5, 0)
Patients ≥50 mg/dL ($n = 1636$)	81.5 (63.6, 111.0)	−17.6 (−30.9, −7.2)	−21.7 (−33.5, −9.4)
Patients <50 mg/dL ($n = 3864$)	11.2 (4.7, 24.0)	−3.2 (−8.0, 0)	−25.6 (−54.6, 0)
IA-molar, nmol/L			
All patients ($n = 5500$)	43.5 (13.2, 149.7)	−11.9 (−31.7, −2.1)	−26.9 (−49.1, −5.0)
Patients ≥125 nmol/L ($n = 1654$)	206.3 (163.1, 276.1)	−44.7 (−72.8, −18.7)	−21.4 (−31.9, −9.4)
Patients <125 nmol/L ($n = 3846$)	20.4 (9.0, 49.3)	−7.3 (−17.7, 0)	−33.2 (−56.8, 0)
MS-molar, nmol/L			
All patients ($n = 5500$)	40.9 (14.3, 138.8)	−10.4 (−28.1, −2.7)	−27.5 (−46.6, −9.6)
Patients ≥125 nmol/L ($n = 1536$)	200.5 (157.0, 270.2)	−40.9 (−67.6, −16.4)	−20.4 (−30.7, −8.6)
Patients <125 nmol/L ($n = 3964$)	22.3 (10.2, 50.0)	−7.1 (−16.0, −2.0)	−33.2 (−52.7, −10.1)

	Lp(a) Measure	Month 4 Median Lp(a) Reduction	Month 4 Median LDL-C Reduction	HR (95% CI) for Median Lp(a) Reduction	p-value
All Patients	IA-mass	5.1 mg/dL	55.0 mg/dL	0.960 (0.929, 0.993)	0.019
	IA-molar	11.9 nmol/L	55.0 mg/dL	0.973 (0.941, 1.006)	0.10
	MS-molar	10.4 nmol/L	55.0 mg/dL	0.972 (0.944, 1.000)	0.047
Patients With Elevated Baseline Lp(a)	IA-mass >=50 mg/dL	17.6 mg/dL	55.0 mg/dL	0.849 (0.739, 0.976)	0.021
	IA-molar >=125 nmol/L	44.7 nmol/L	54.4 mg/dL	0.840 (0.718, 0.983)	0.030
	MS-molar >=125 nmol/L	40.9 nmol/L	54.4 mg/dL	0.830 (0.728, 0.946)	0.005
Patients Without Elevated Baseline Lp(a)	IA-mass <50 mg/dL	3.2 mg/dL	55.0 mg/dL	0.980 (0.935, 1.027)	0.40
	IA-molar <125 nmol/L	7.3 nmol/L	55.2 nmol/L	0.997 (0.952, 1.045)	0.91
	MS-molar <125 nmol/L	7.1 nmol/L	55.2 nmol/L	1.010 (0.954, 1.071)	0.72



Michael Szarek, Esther Reijnders, Ph Gabriel Steg, et al. Comparison of change in lipoprotein(a) mass and molar concentrations by alirocumab and risk of subsequent cardiovascular events in ODYSSEY OUTCOMES, *European Journal of Preventive Cardiology*, Volume 31, Issue 10, August 2024, Pages e75–e78, https://doi.org/10.1093/eurjpc/zwae110

Metody – Studie INTERASPIRE

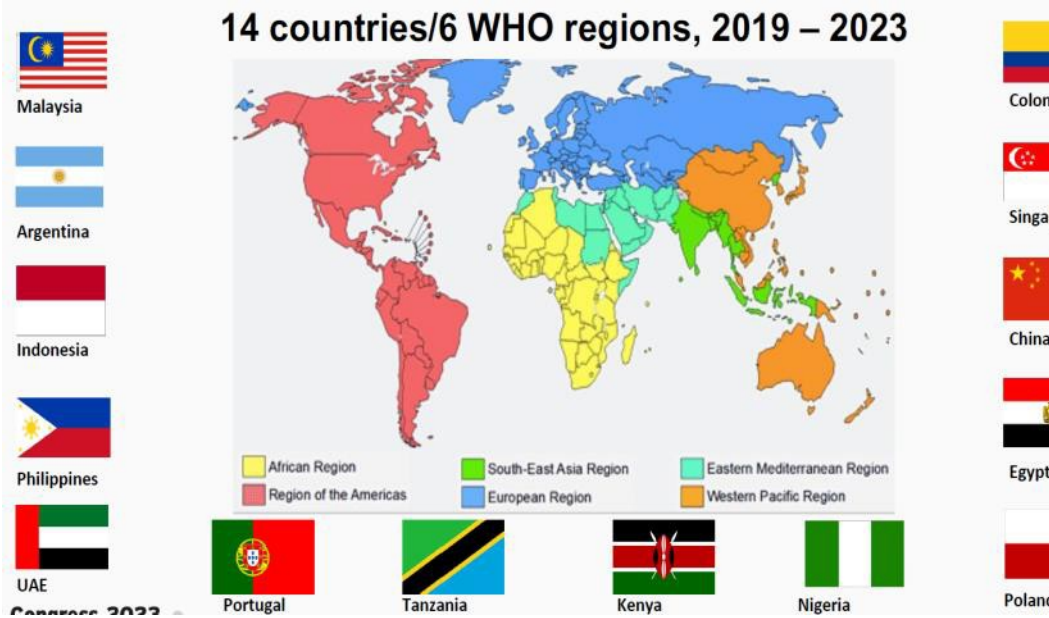
INTERASPIRE : Mezinárodní průzkum zahrnující pacienty s nedávno diagnostikovanou ICHS.

Analyzováno 13 zemí: mimo Egypt (žádná Lp(a) data).

Standardizované Testování: Rozhovor s pacientem a analýza v centrální laboratoři.

Prevalence: 115, 150 , 175 , 200 nmol/l (ASKVO riziko, kritéria klinických studií).

Management rizikových faktorů: Fokus na pacienty s Lp(a) ≥115 nmol/l.

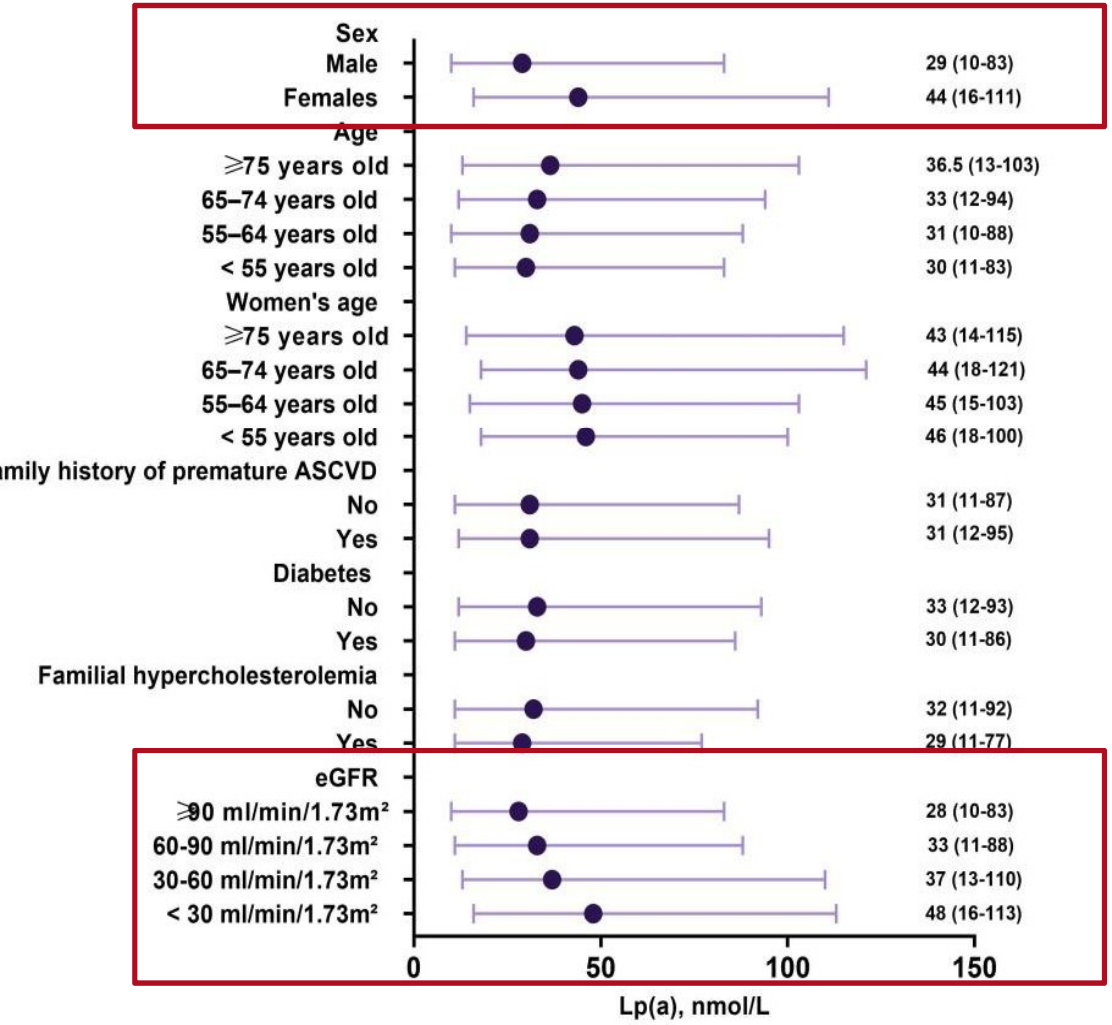


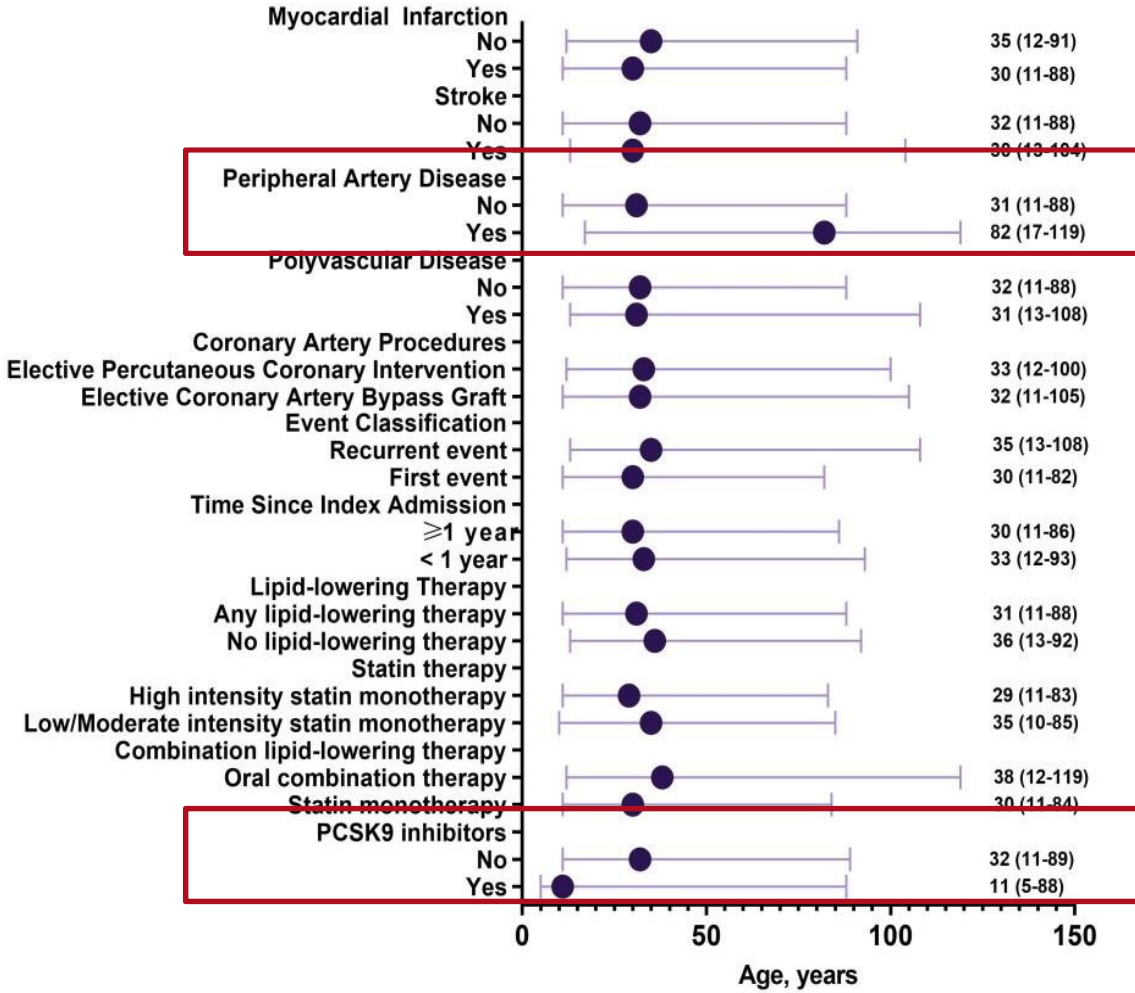
SKVO, aterosklerotické kardiovaskulární onemocnění; , ischemická choroba srdeční; Lp(a), lipoprotein(a) ; WHO, Světová zdravotnická organizace.

y. K et al, 2024: A global perspective of Lp(a) levels in patients with coronary heart disease - Implications for risk factor control & future trials from the INTERASPIRE Study, ESC Congress 2024

sledky (IV)

a) je vyšší u žen, u pacientů s renálním onemocněním a u nemocných s DK, Lp(a) je nižší u pacietnů léčených PCSK9i

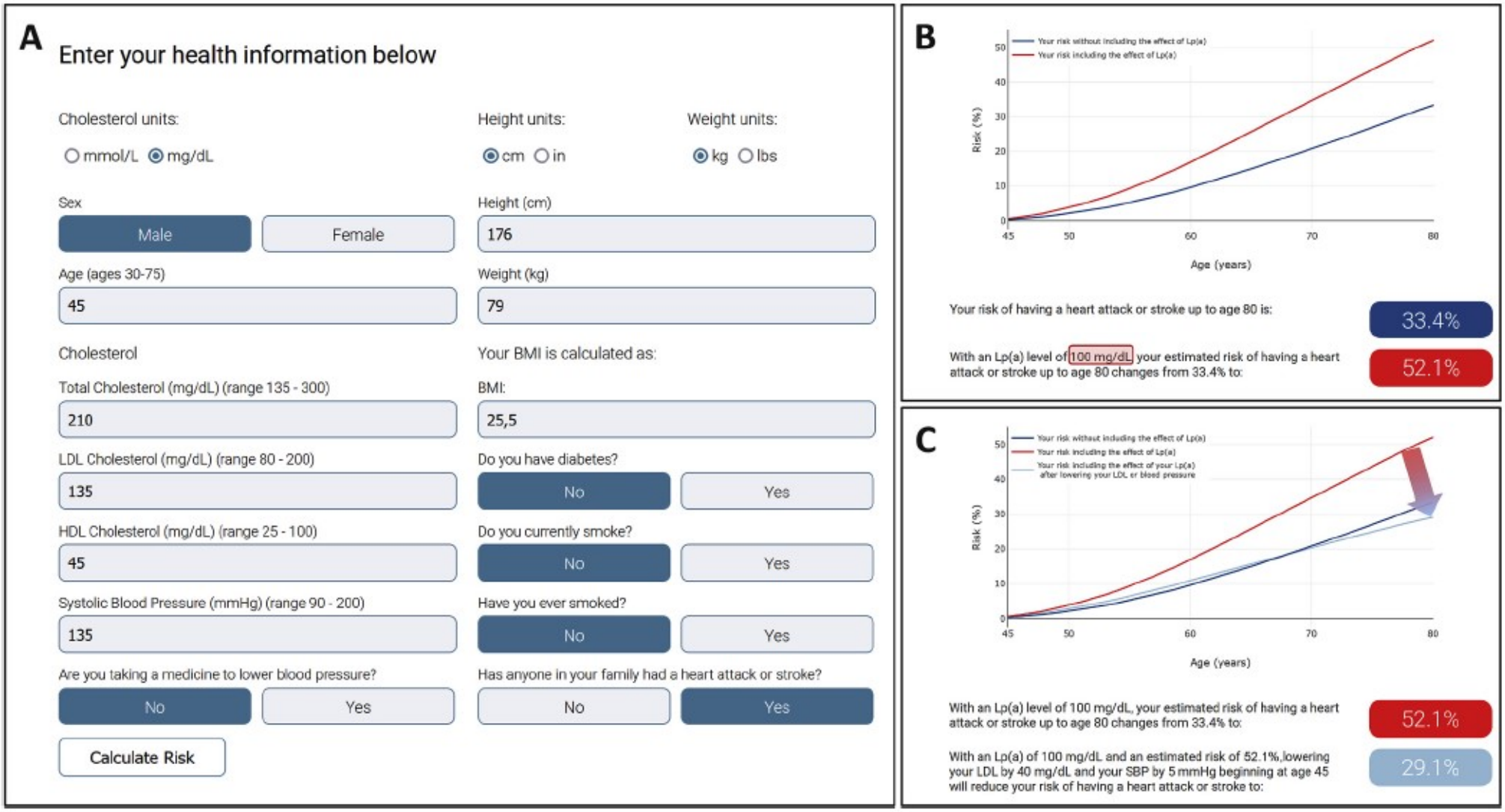




Lp(a), lipoprotein(a); PAD, onemocnění periferních tepen; PCSK9i, inhibitor proprotein konvertázy subtilisin/kexin typu 9.

y. K et al, 2024: A global perspective of Lp(a) levels in patients with coronary heart disease - Implications for risk factor control & future trials from the INTERASPIRE Study, ESC Congress 2024

Algoritmus zohledňující hladiny Lp(a) při hodnocení rizika ASKVO

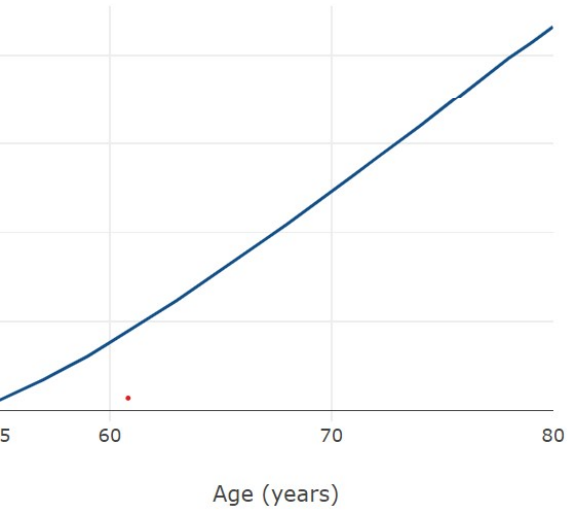


Kronenbertg F et al. Atherosclerosis 374 (2023) 1

Muž, 55 let, LDL-C 4,5, HT, pozitivní RA ASKVO

Bez Lp(a)

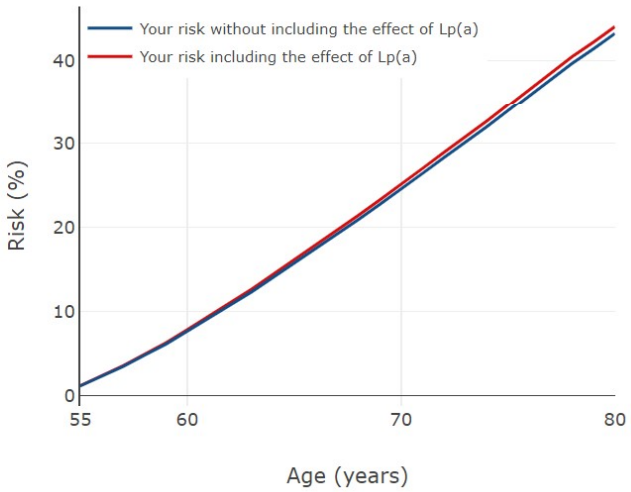
Your risk of having a heart attack or stroke



f having a heart attack or stroke up to **43.2%**

Lp(a) 25 nmol/l

Your risk of having a heart attack or stroke

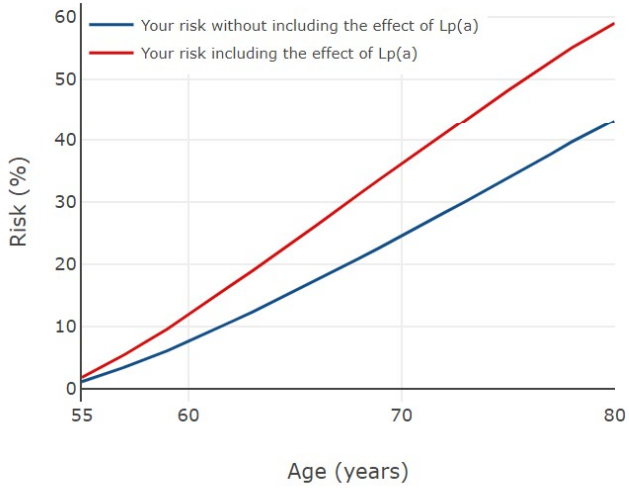


Your risk of having a heart attack or stroke up to age 80 is: **43.2%**

With an Lp(a) level of 25 nmol/L, your estimated risk of having a heart attack or stroke up to age 80 changes from 43.2% to: **44.0%**

Lp(a) 170 nmol/l

Your risk of having a heart attack or stroke



Your risk of having a heart attack or stroke up to age 80 is: **43**

With an Lp(a) level of 170 nmol/L, your estimated risk of having a heart attack or stroke up to age 80 changes from 43.2% to: **59**

www.lpaclinicalguidance.com

ámka: Snížení LDL snižuje absolutní kardiovaskulární riziko, ale nesnižuje hladinu Lp(a). Vzhledem k tomu reziduální riziko ze zvýšené hladiny Lp(a) přetrvává. asné době se vyvíjejí účinné léčebné přípravky snižující hladinu Lp(a) a jejich dostupnost se očekává v blízké budoucnosti. Tyto nové terapie nabízí naději na př ení kardiovaskulárního rizika u osob s vysokou hladinou Lp(a).

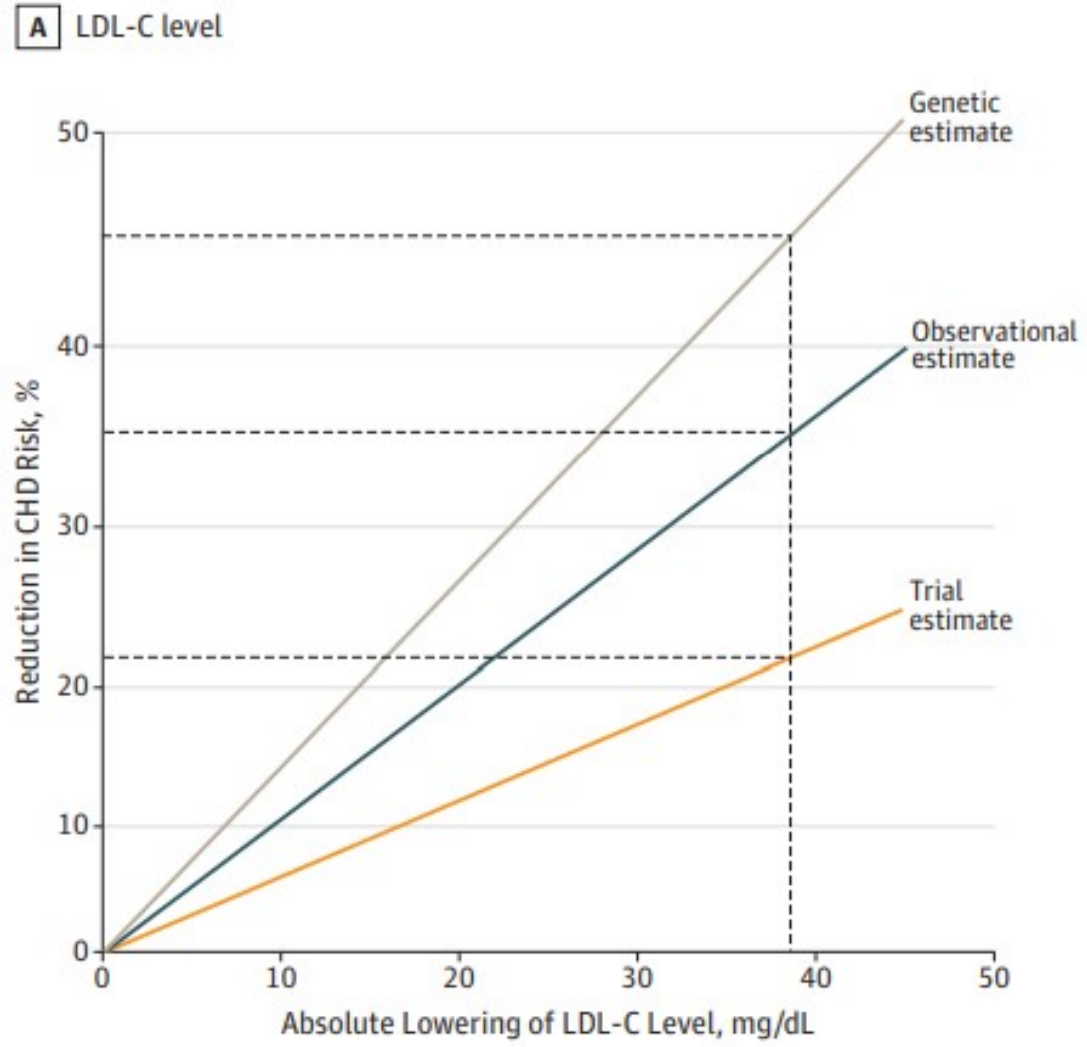
Doporučená intenzifikace snižování LDL-C na základě hladiny Lp(a)

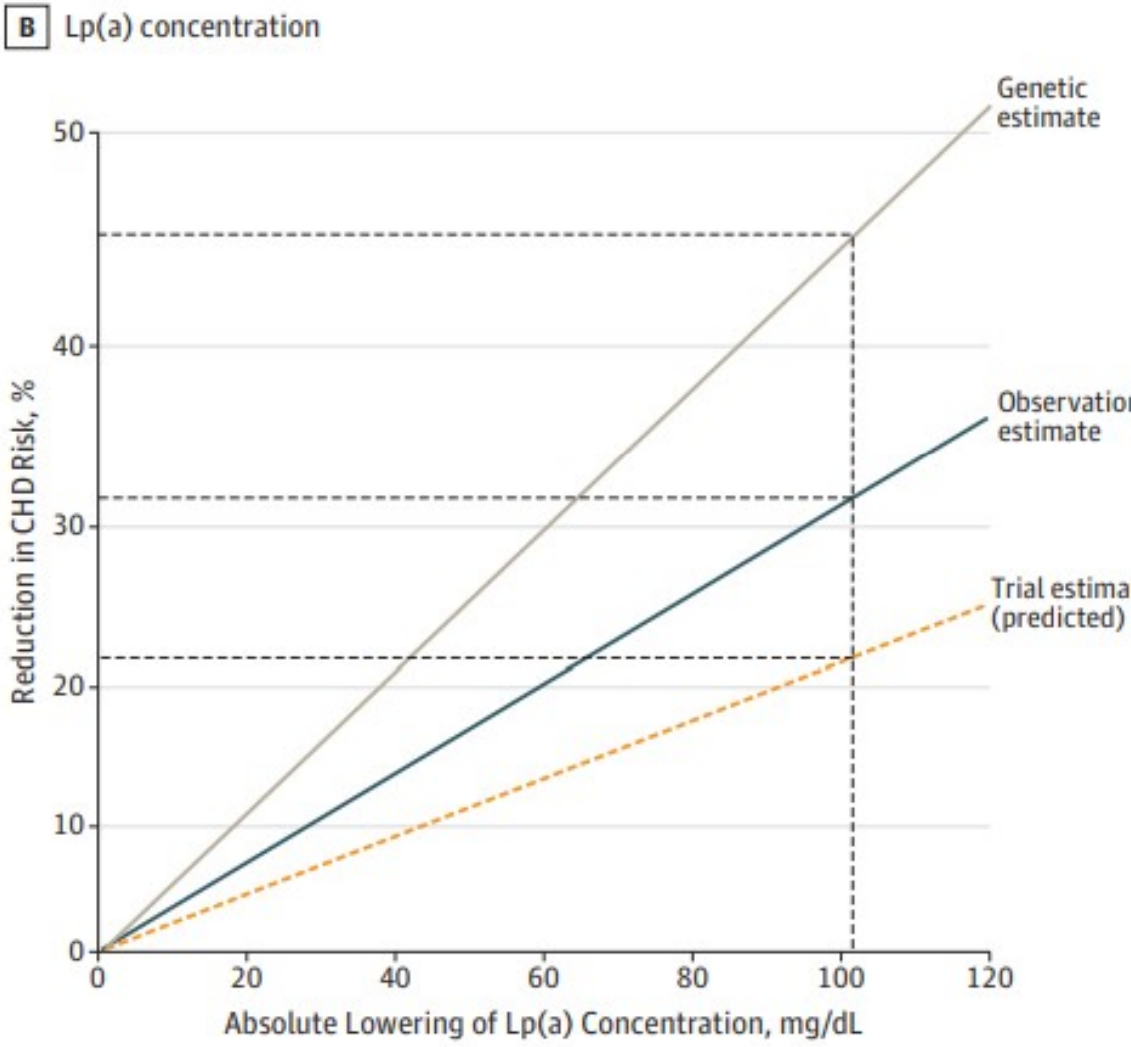
B Intensification of LDL-C reduction needed to reduce the global cardiovascular risk to a similar extent as the risk attributable to elevated Lp(a) depending on age at which LDL-C reduction is initiated

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.

Kronenberg F et al. European Heart Journal (2022) **43**, 3925–3

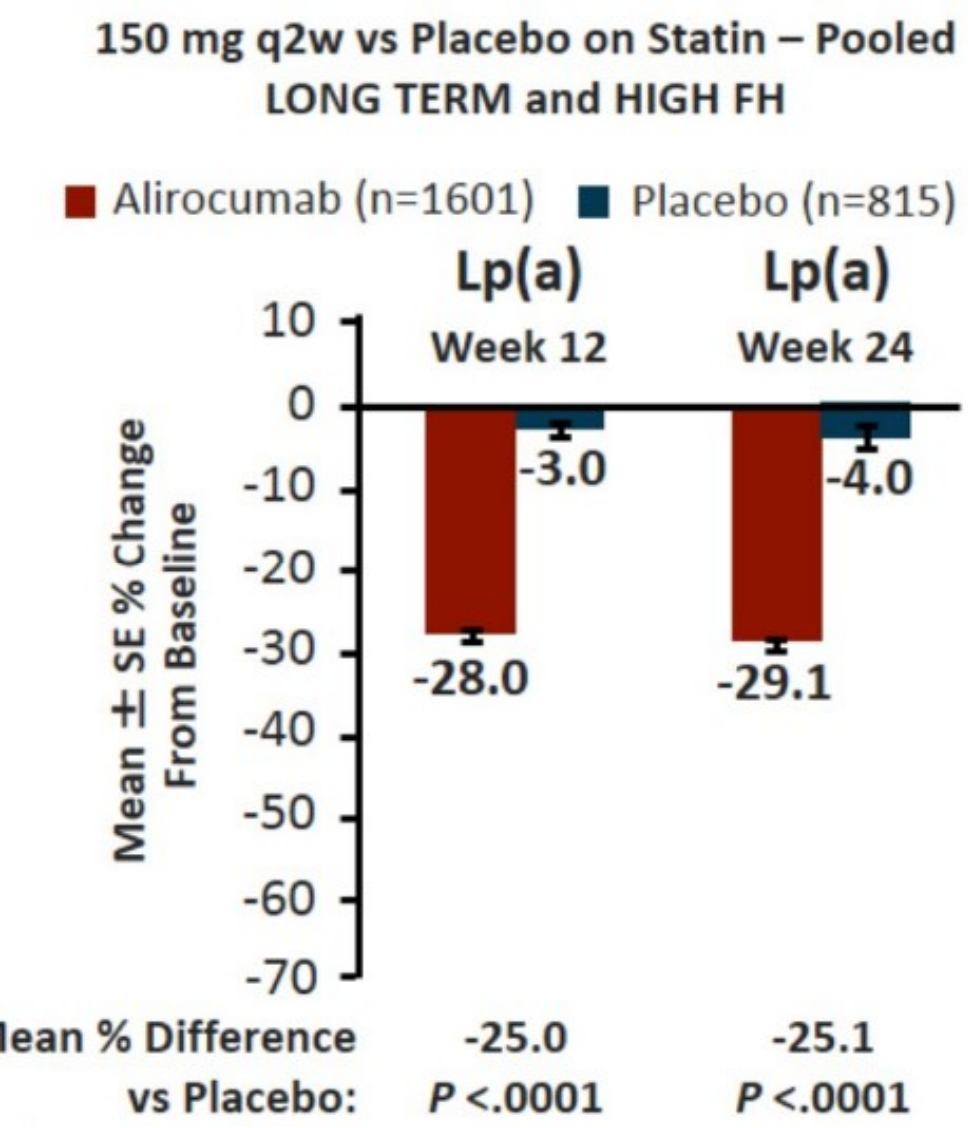
Jak moc je nutné Lp(a) redukovat k dosažení klinicky významného snížení rizika ASKVO ?

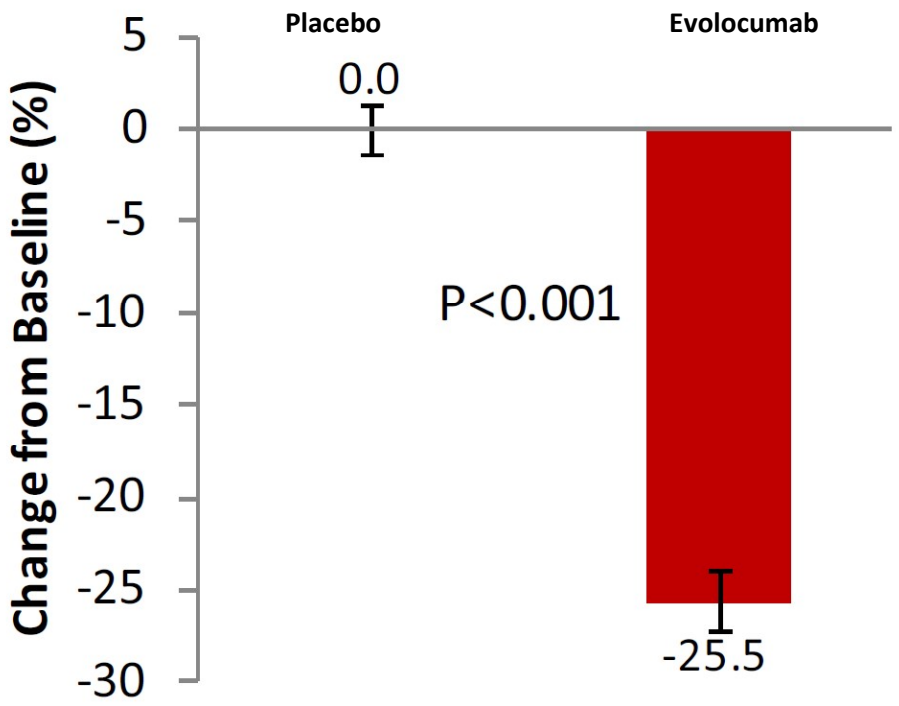




Burgess S et al. JAMA Cardiol. 2018;3(7):6

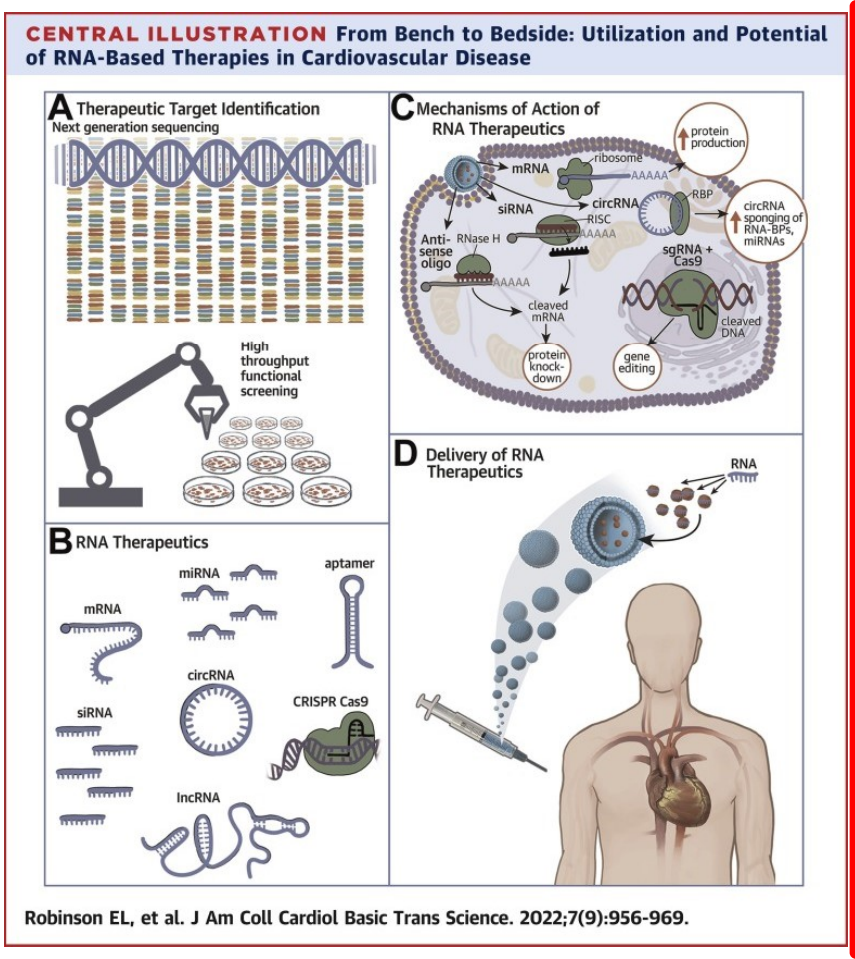
Lp(a) a PCSK9 inhibice

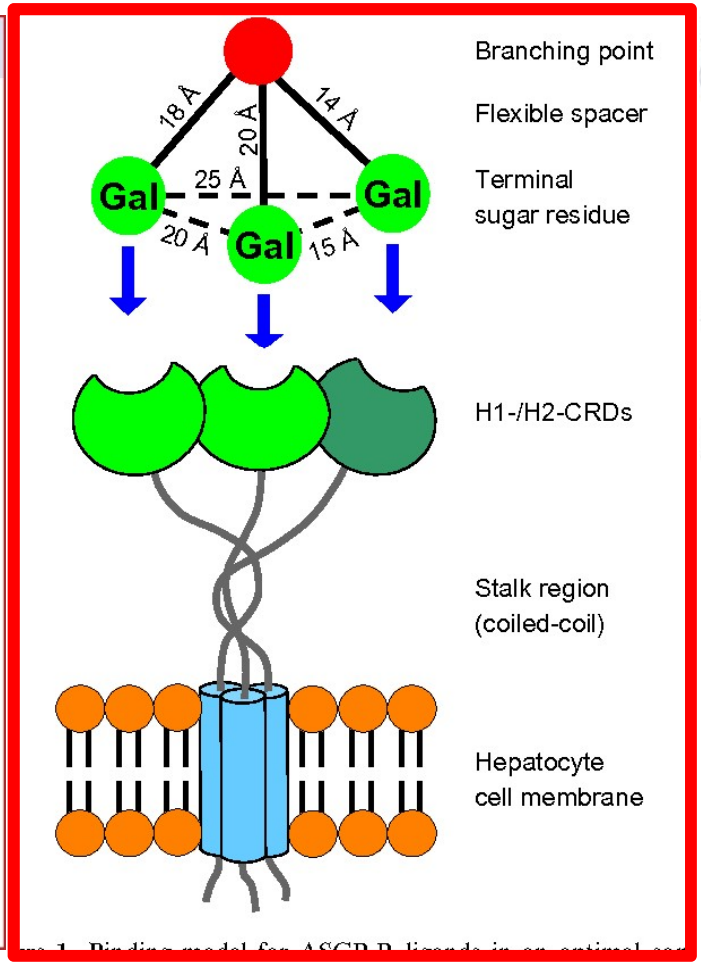


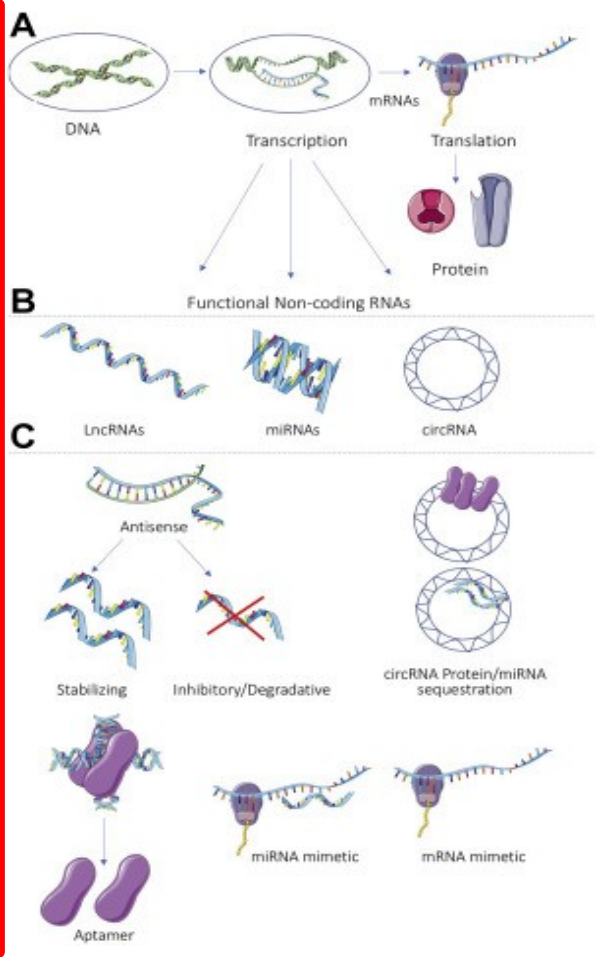


Gaudet ESC 2015
Sabatine, NEJM 2015 - 4465 pts

RNA terapeutika: současnost a budoucnost léčby DLP



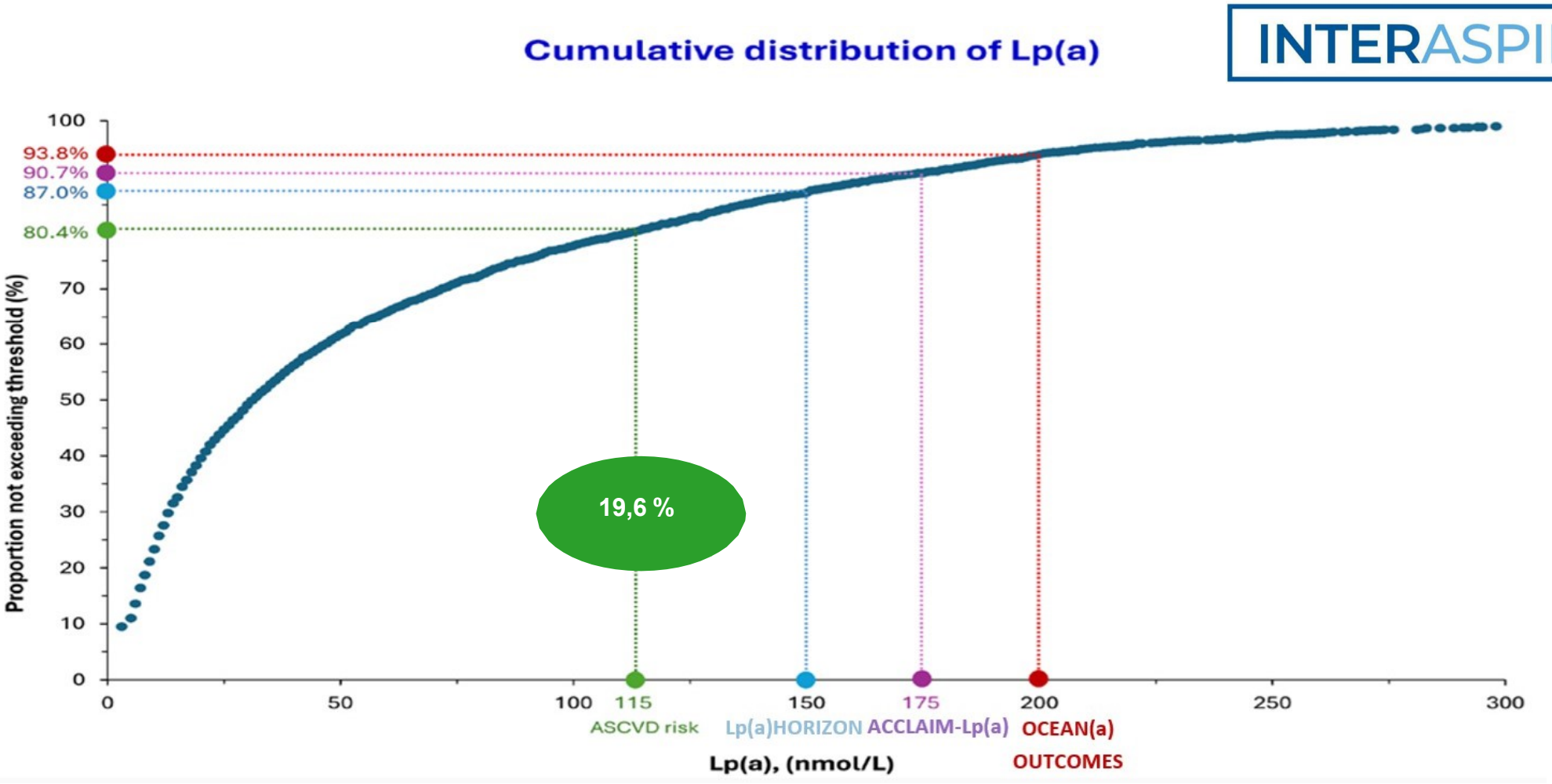




ací pacienti jsou ve studiích s Lp(a) snižujícími terapiem

ední věk: 60,2 ± 10,2 let | 21,1 % ženy

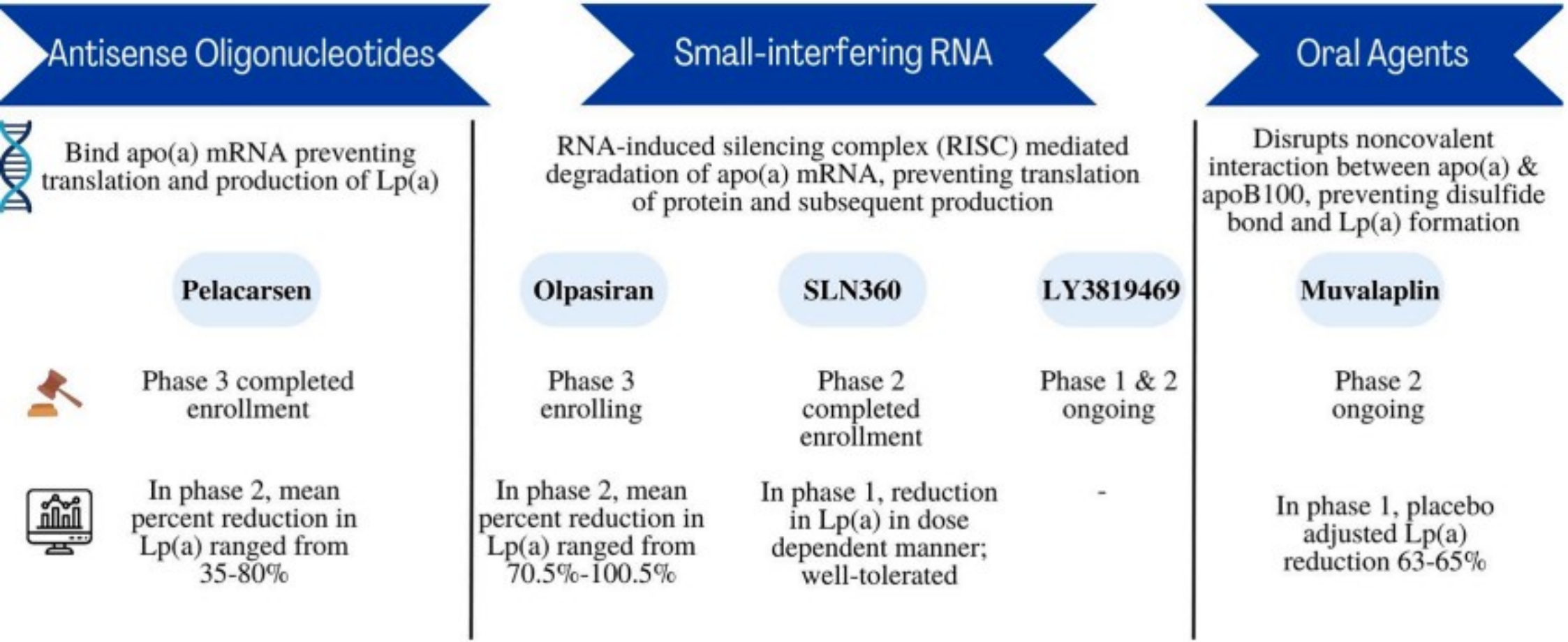
(a): medián **32 nmol/l (IQR:11-89)**



ICHS - ischemická choroba srdeční; IQR - mezikvartilní poměr; Lp(a) - lipoprotein(a).

y. K et al, 2024: A global perspective of Lp(a) levels in patients with coronary heart disease - Implications for risk factor control & future trials from the INTERASPIRE Study, ESC Congress 2024
don

Lp(a) snižující terapie ve 3. fázích studií



et al., 2024: Lipoprotein(a): Emerging insights and therapeutics, American Journal of Preventive Cardiology, https://doi.org/10.1016/j.ajpc.2024.100641.

Kdo řekl screening Lp(a) ?

Národní KV plán ČR: schválen vládou ČR 11. prosince 2024

Designovaný EU komisař pro zdravotnictví, Olivér Varhélyi, slíbil EU KV plán

Council of the European Union

Brussels, 21 October 2024
(OR. en)

14565/24

LIMITE

SAN 594

WORKING DOCUMENT

From:	Presidency
To:	Delegations
Subject:	Draft Council Conclusions on the improvement of cardiovascular health in the European Union

Delegations will find in Annex a revised Presidency compromise proposal for Council Conclusions

Jak to tedy prakticky udělat ?

U dětí

1. Stanovit koncentraci Lp(a) v rámci screeningu FH u dětí z postižených rodin

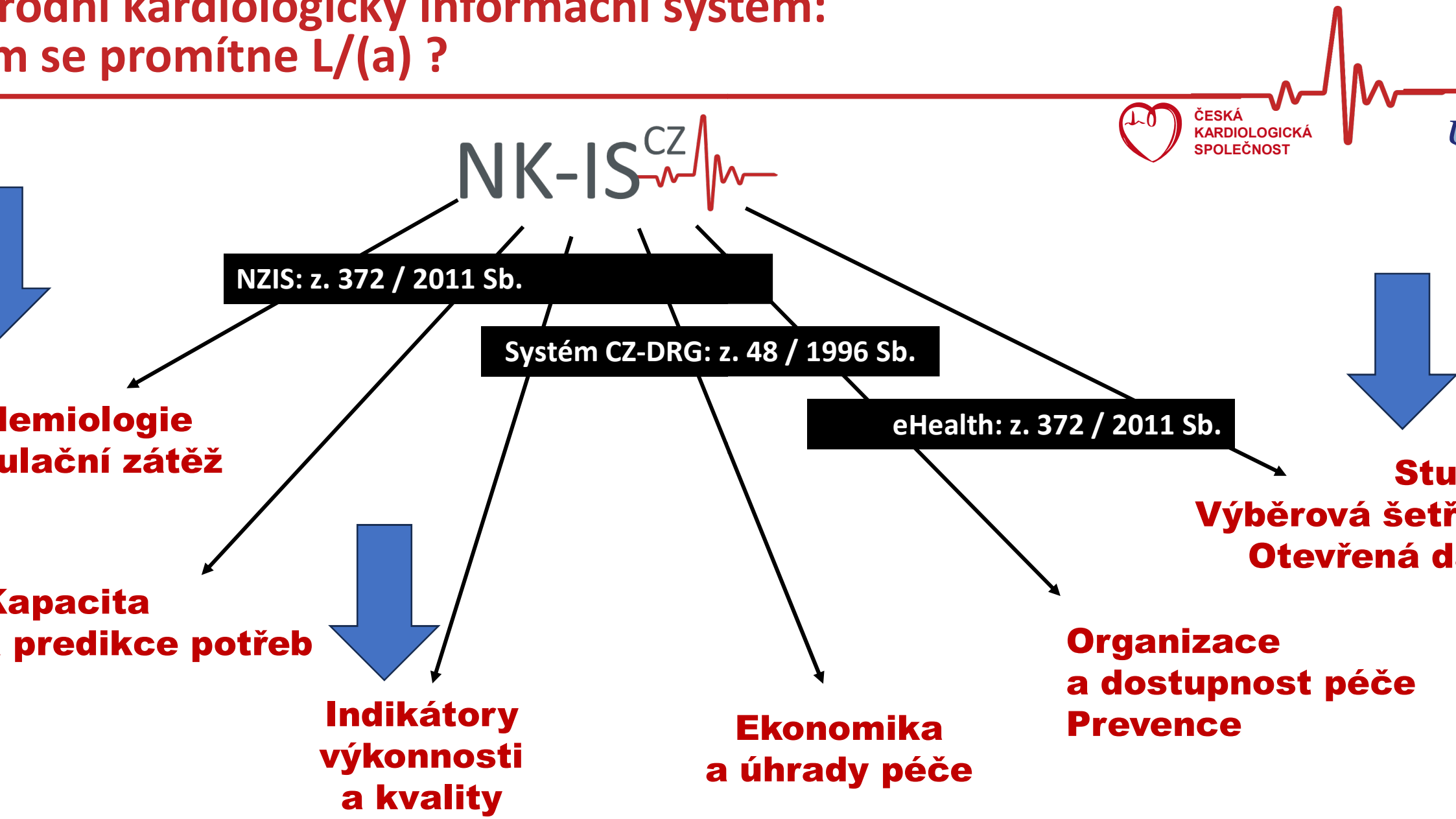
2. Stanovit koncentraci Lp(a) u dětí v rodinách s vysokou koncentrací Lp(a) u rodičů

U dospělých

1. V rámci vstupní preventivní prohlídky VPL
2. Ve věku:
   - 30
   - 40
   - 50 let, pakliže není hladina Lp(a) již známa
3. Ve věku 60 let, resp. ve věku menopauzy u žen

Zanesení diagnózy do dokumentace: MKN-10 kód E78. 41

rodní kardiologický informační systém:
m se promítne L/(a) ?



ČESKÁ KARDIOLOGICKÁ SPOLEČNOST

EAS konsenzus k Lp(a) v souhrnu

ESC European Society of Cardiology

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

ipoprotein(a) in atherosclerotic
ardiovascular disease and aortic
European Atherosclerosis Soci
onsensus statement

an Kronenberg [1], Samia Mora [2], Erik S.G. Stroes
oit J. Arsenault [5], Lars Berglund[6], Marc R. Dweck [7],
es Lambert [9], François Mach[10], Catherine J. McNeal
rick M. Moriarty[12], Pradeep Natarajan [13], Børge G.
G. Parhofer [16], Salim S. Virani [17], Arnold von Ec
d F. Watts[19], Jane K. Stock[20], Kausik K. Ray[21], Lale
Alberico L. Catapano [23,24]

of Genetic Epidemiology, Medical University of Innsbruck, Innsbruck, Austria; [2]Center for Lipid Metabolomics, Division
Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, USA; [3]Department of Vascular Medic
iversity of Amsterdam, Amsterdam, the Netherlands; [4]Centre for Naturally Randomized Trials, University of Cambrid
aire de Cardiologie et de Pneumologie de Québec, and Department of Medicine, Faculty of Medicine, Université Lava
School of Medicine, University of California-Davis, Davis, Sacramento, CA, USA; [7]British Heart Foundation Centre f
of Edinburgh, Chancellors Building, Little France Crescent, Edinburgh EH16 4SB, UK; [8]Roberts Research Institute, S
ondon, Ontario, Canada; [9]Inserm, UMR 1188 Diabète Athérothrombose Thérapies Réunion Océan Indien (DéTR
e; [10]Department of Cardiology, Geneva University Hospital, Geneva, Switzerland; [11]Division of Cardiology, Dep
1st St., USA; [12]University of Kansas Medical Center, Kansas City, KS, USA; [13]Cardiovascular Research Center, Ma
m in Medical and Population Genetics and Cardiovascular Disease Initiative, Broad Institute of Harvard and
openhagen General Population Study, Herlev and Gentofte Hospital, Copenhagen University Hospital,
edical Sciences, University of Copenhagen, Copenhagen, Denmark; [16]Medizinische Klinik und Poliklinik
rdiovascular Research, Baylor College of Medicine & Michael E. DeBakey Veterans Affairs Medical Cente
h, University of Zurich, Zurich, Switzerland; [19]Medical School, University of Western Australia, and De
ustralia; [20]European Atherosclerosis Society, Mässans Gata 10, SE-412 51 Gothenburg, Sweden; [21]Imp
y Care and Public Health, School of Public Health, Imperial College London, London, UK; [22]Department of
epartment of Pharmacological and Biomolecular Sciences, University of Milano, Milano, Italy; and [24]IRCCS

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udio abstract of this contribution.

+43 512 9003 70560, Fax: +43 512 9003 73560; Email: florian.kronenberg@i-med.ac.at

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