The evolving need and challenges to reach LDL-C targets in high-risk patients

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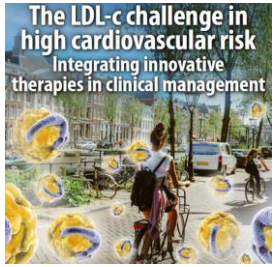
The LDL-c challenge in high cardiovascular risk - Integrating innovative therapies in clinical management



PHYSICIANS' ACADEMY FOR PACE-CME CARDIOVASCULAR EDUCATION

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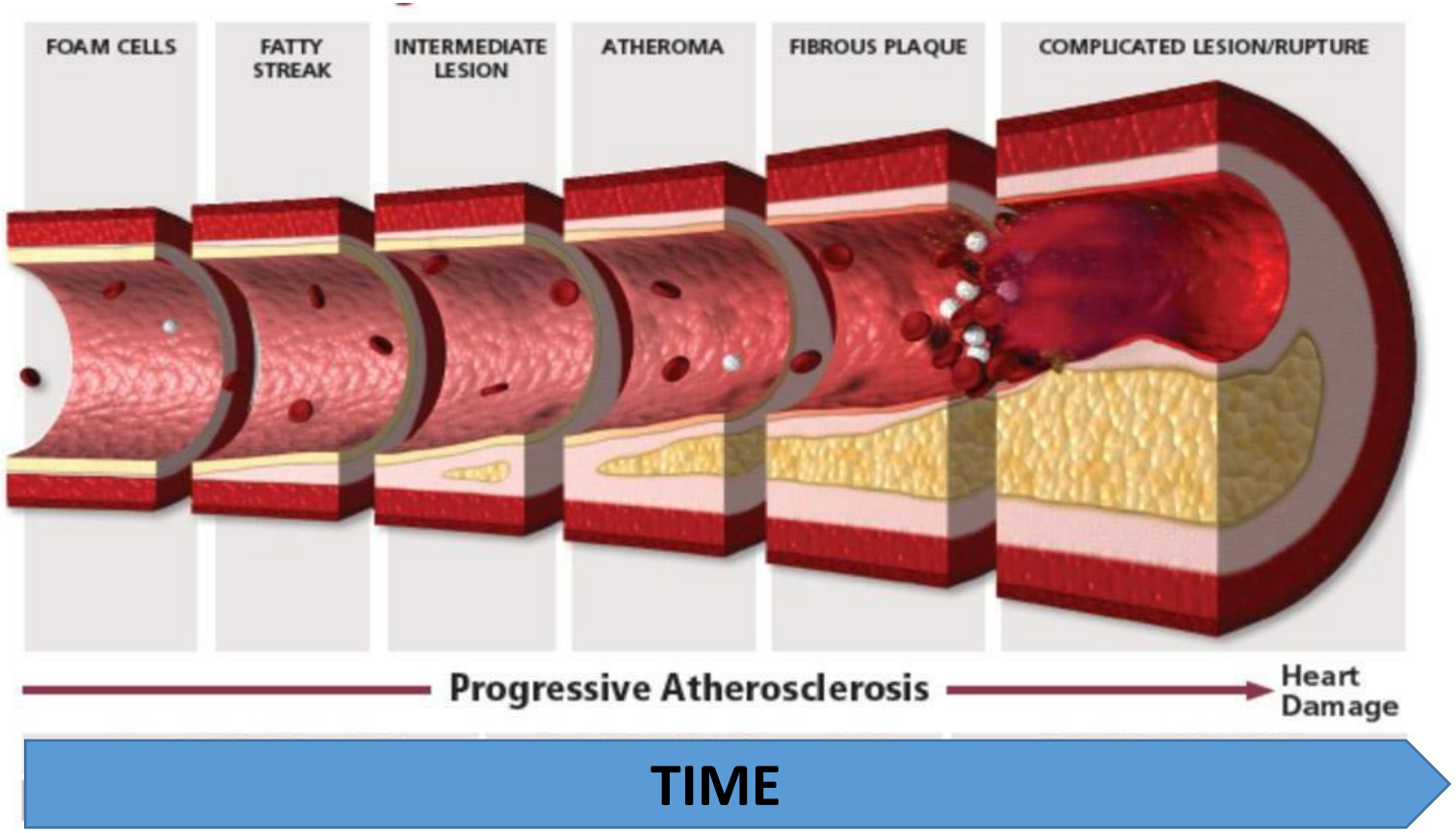
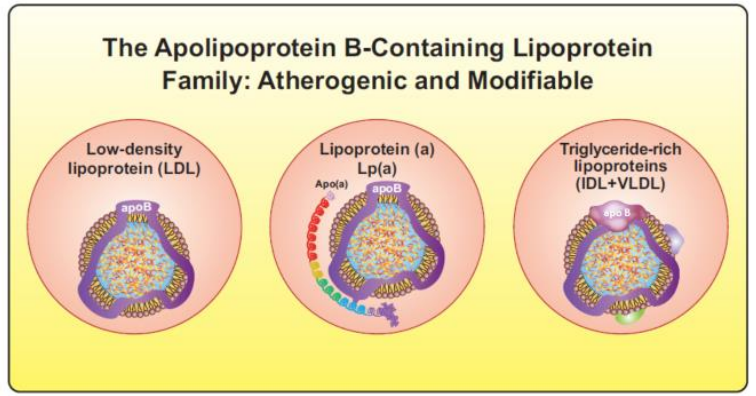
- Options: New Amsterdam Pharma, PEMI31

RELEVANCE OF CHOLESTEROL TO CVD MORTALITY

Worldwide, there are more than 18 million deaths due to CVD each year



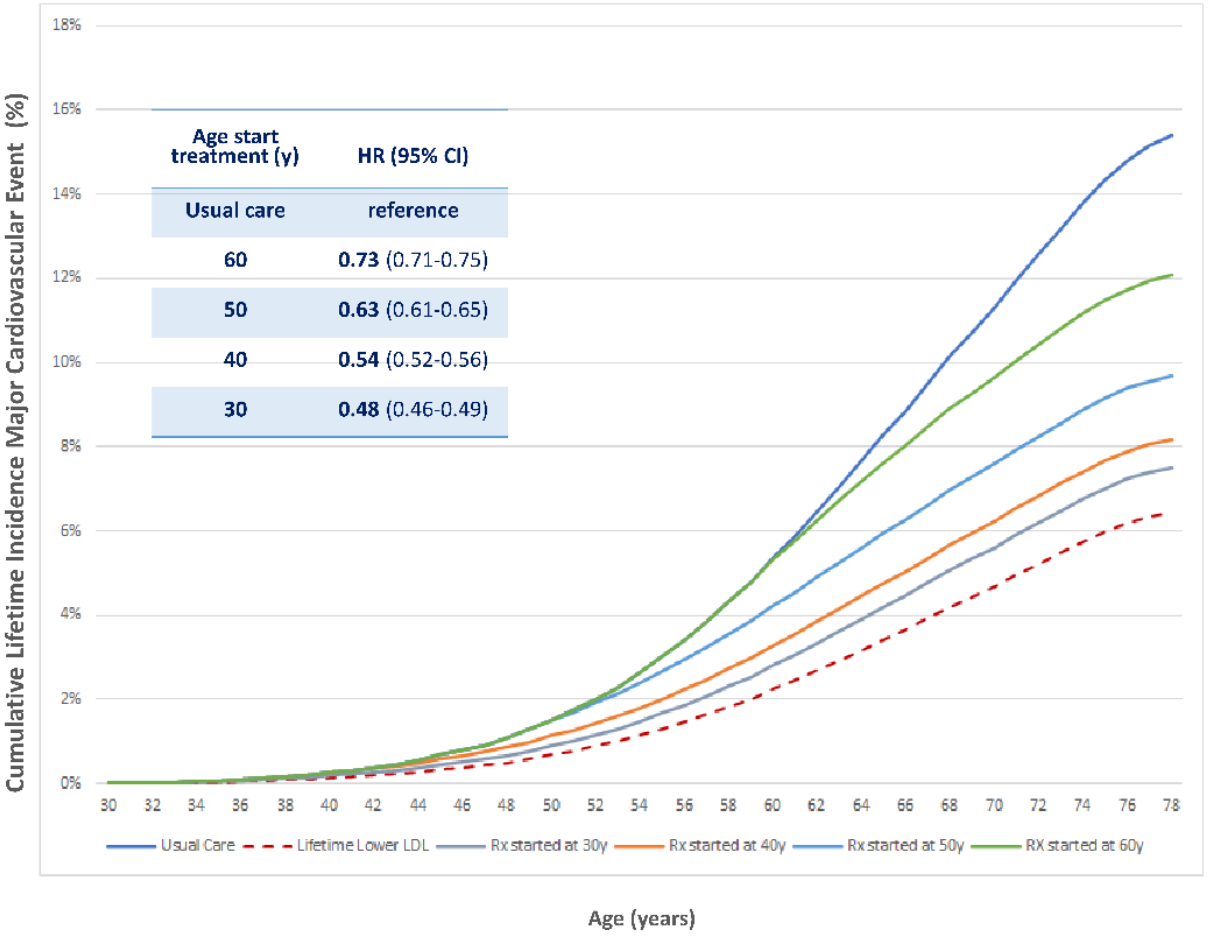


Tokgozoglu L EHJ 2022 doi.org /10.1093/Eurheartj/ehab841

Ray KK et al 2022 WHF Cholesterol Roadmap- Global Heart Journal DOI: https://doi. org/10.5334/gh.1154

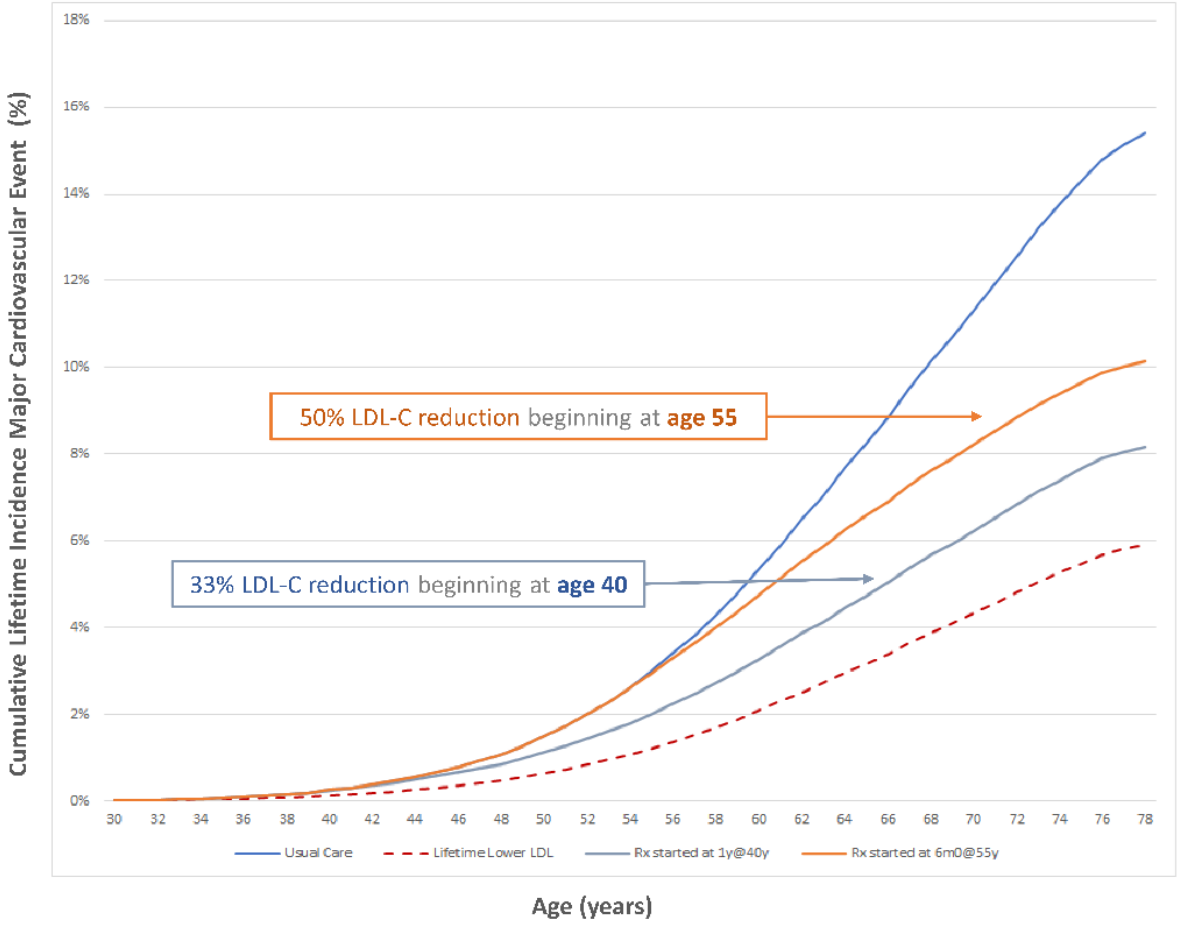
Estimating benefit of initiating LDL-C lowering at different ages and by intensity early vs late in life

A. 50% lower LDL by age at initiation of LDL lowering



Age start treatment (y)	HR (95% CI)
Usual care	reference
60	**0.73** (0.71-0.75)
50	**0.63** (0.61-0.65)
40	**0.54** (0.52-0.56)
30	**0.48** (0.46-0.49)

B. Moderate early LDL Lowering or more intense later LDL lowering

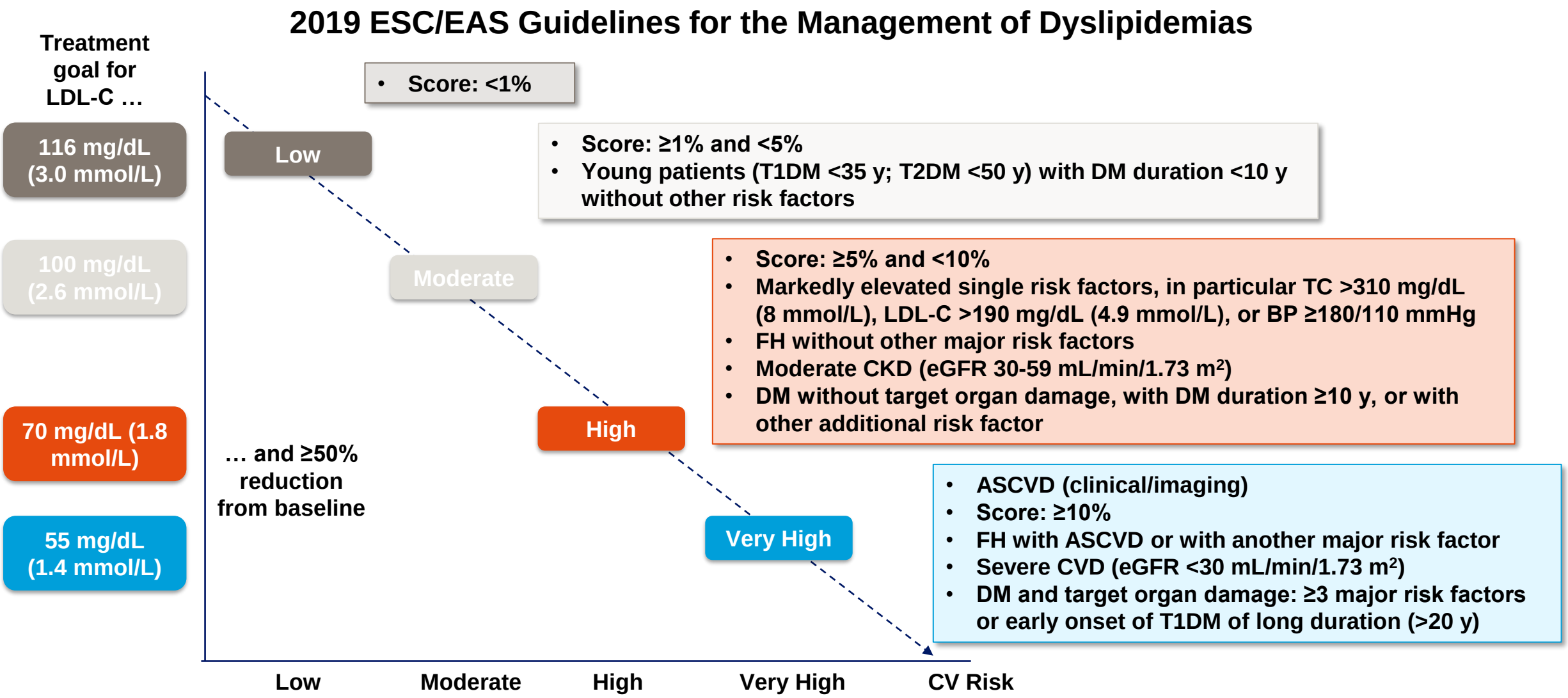


2022 WHF Cholesterol Roadmap- Global Heart DOI: https://doi. org/10.5334/gh.1154

Conceptual framework shift needed

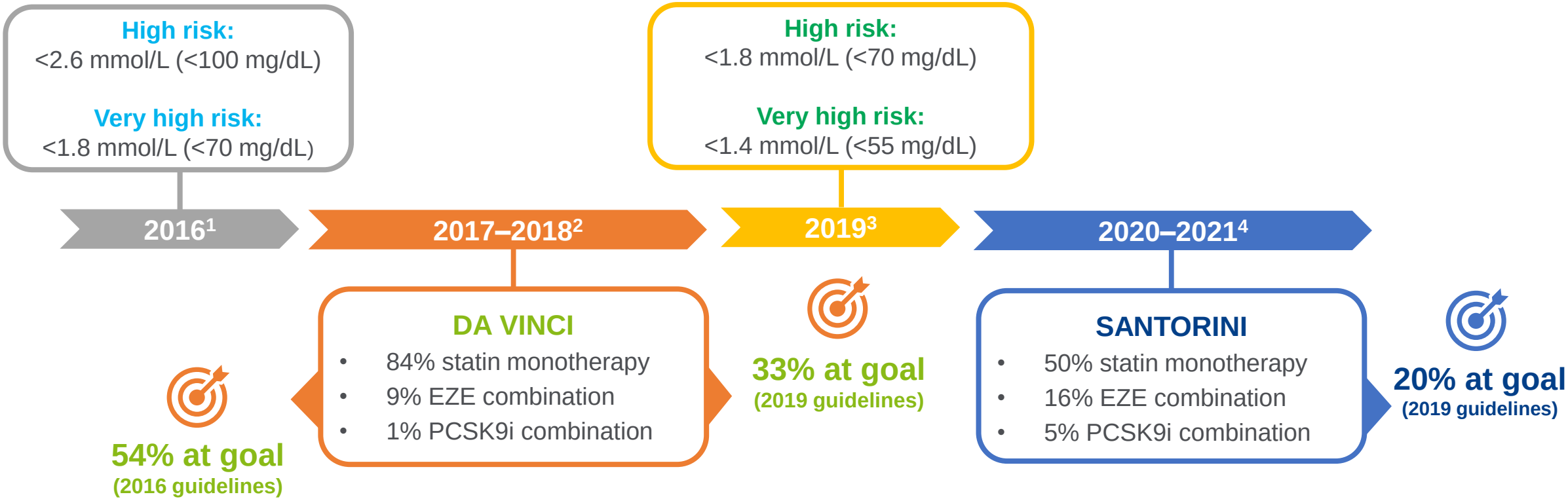
- Start with risk assessment - so you know how aggressively to treat
- Risk isn’t dichotomous or qualitative (high / low etc) but a continuum
- We look at the past eg does clinical ASCVD exist – reflects atherosclerosis burden over time missed year, and then factors that determine future progression – presence or absence of multiple additional risk factors and inherited vulnerability by considering family history

Treatment Goals for LDL-C Across Categories of Total Cardiovascular Disease Risk[1]



1. Mach F et al. *Eur Heart J.* 2020;41:111-188.

2016–2019 ESC/EAS LDL-C Goals and Lipid Management in Clinical Practice



- **ESC/EAS,** European Society of Cardiology/European Atherosclerosis Society;
- **EZE**, ezetimibe; **LDL-C**, low-density lipoprotein cholesterol; **PCSK9i**, proprotein convertase subtilisin/kexin type 9 inhibitor
- 1. Catapano AL, et al. Eur Heart J. 2016;37:2999–3058; 2. Ray KK, et al. Eur J Prev Cardiol. 2021;28:1279–1289; 3. Mach F, et al. Eur Heart J. 2020;41:111–188; 3. 4. Ray KK, et al. Lancet Reg Health Eur. 2023;29:100624

Lipid-lowering Therapy Usage Across Countries

- Results from individual countries largely mirrored the trends observed overall
- Monotherapy was the most commonly used LLT across all patient subgroups regardless of the ASCVD status
- Countries with the highest rates of monotherapy (>70%) were:


United Kingdom
75.6%


Ireland
74.0%


Finland
70.9%

- Countries with the highest rates of combination therapy (>30%) were:


Portugal
45.5%

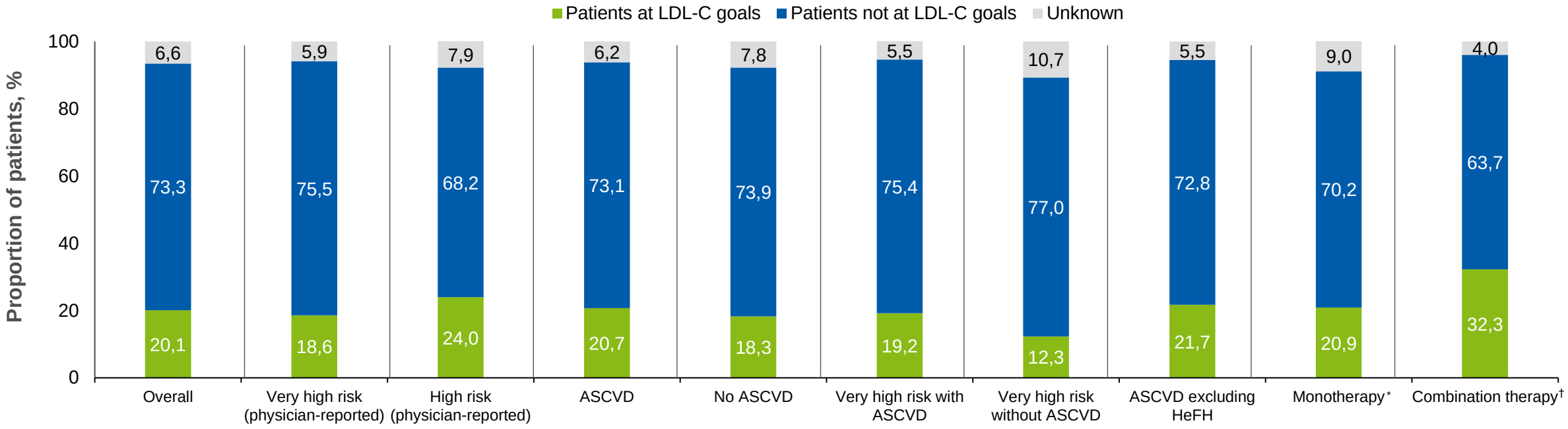

Spain
40.0%


Italy
33.0%

ASCVD, atherosclerotic cardiovascular disease; **LDL-C**, low-density lipoprotein cholesterol; **LLT**, lipid-lowering therapy

Ray KK, et al. Lancet Reg Health Eur. 2023;29:100624

LDL-C Goal Attainment by CV Risk, ASCVD Status and Lipid-lowering Therapy ‡



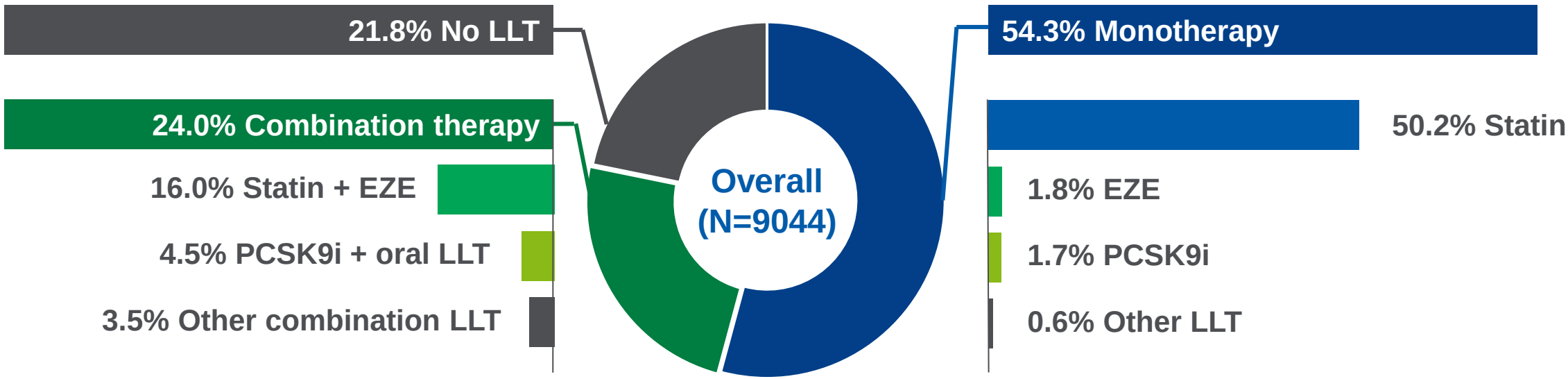
LDL-C (mmol/L), median (IQR):									
2.1 (1.6, 3.0)	2.0 (1.5, 2.8)	2.4 (1.7, 3.4)	2.0 (1.5, 2.9)	2.6 (1.8, 3.5)	2.3 (1.1)‡	2.7 (1.5)‡	2.3 (1.1)‡	2.2 (1.0)†	1.9 (1.0)†

LLT record was missing for patients n=1. Patients receiving monotherapy, n=1023/4902. Patients receiving combination therapy, n=2169. *Monotherapy including: statin alone; ezetimibe alone; PCSK9i alone; bempedoic acid alone; any other oral LLT alone; †Combination therapy including: statin + ezetimibe; PCSK9i combination; bempedoic acid fixed-dose combination; any other oral combination therapy; ‡Data are presented as mean ± SD

ASCVD, atherosclerotic cardiovascular disease; **CV**, cardiovascular; **EZE**, ezetimibe; **FDC**, fixed-dose combination; **HeFH**, familial hypercholesterolaemia **IQR**, interquartile range; **LDL-C**, low-density lipoprotein; **LLT**, lipid-lowering therapy; **PCSK9i**, proprotein convertase subtilisin/kexin type 9 inhibitor; **SD**, standard deviation.

Ray KK, et al. Lancet Reg Health Eur. 2023;29:100624

Lipid-lowering Therapy in the Overall Population



Despite LDL-C levels above the recommended values, the majority of patients received monotherapy and 21.8% of patients had no documented LLT

Missing/not reported risk status, n=6

EZE, ezetimibe; **LDL-C**, low-density lipoprotein cholesterol; **LLT**, lipid-lowering therapy; **PCSK9i**, proprotein convertase subtilisin kexin 9 inhibitor

Ray KK, et al. Lancet Reg Health Eur. 2023;29:100624

Proportion of Patients at LDL-C Goal improved over 1 year with greater use of combination Tx and those not on LLT started

	Overall (N=7210)		High risk (N=2033)		Very high risk (N=5173)	
	Baseline	1-year follow-up	Baseline	1-year follow-up	Baseline	1-year follow-up
LDL-C, mmol/L, mean (SD)	2.42 (1.22)	1.98 (0.95)	2.74 (1.31)	2.29 (1.03)	2.29 (1.15)	1.86 (0.88)
Patients at LDL-C goal, %	21.2	31.2	24.4	34.2	20.0	30.1

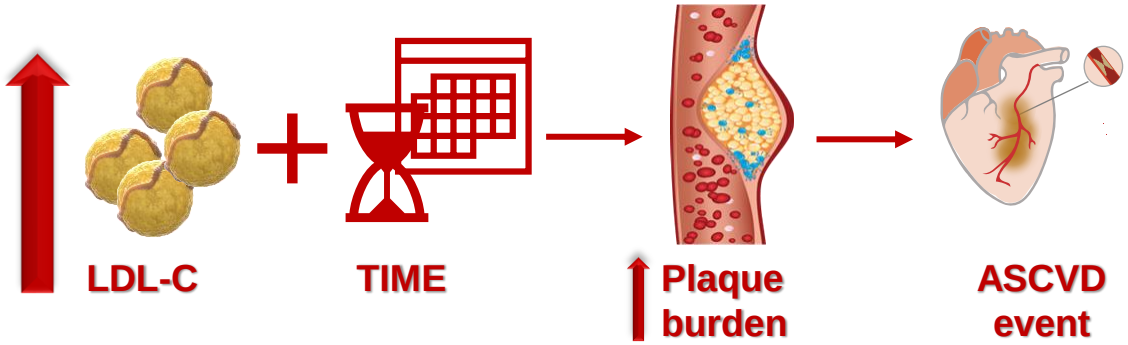
- **Overall, LDL-C was reduced in both risk groups at follow-up versus baseline**
- **Among patients with available LDL-C data, more patients reached their LDL-C goals at follow-up versus baseline**

LDL-C, low-density lipoprotein cholesterol; **SD**, standard deviation

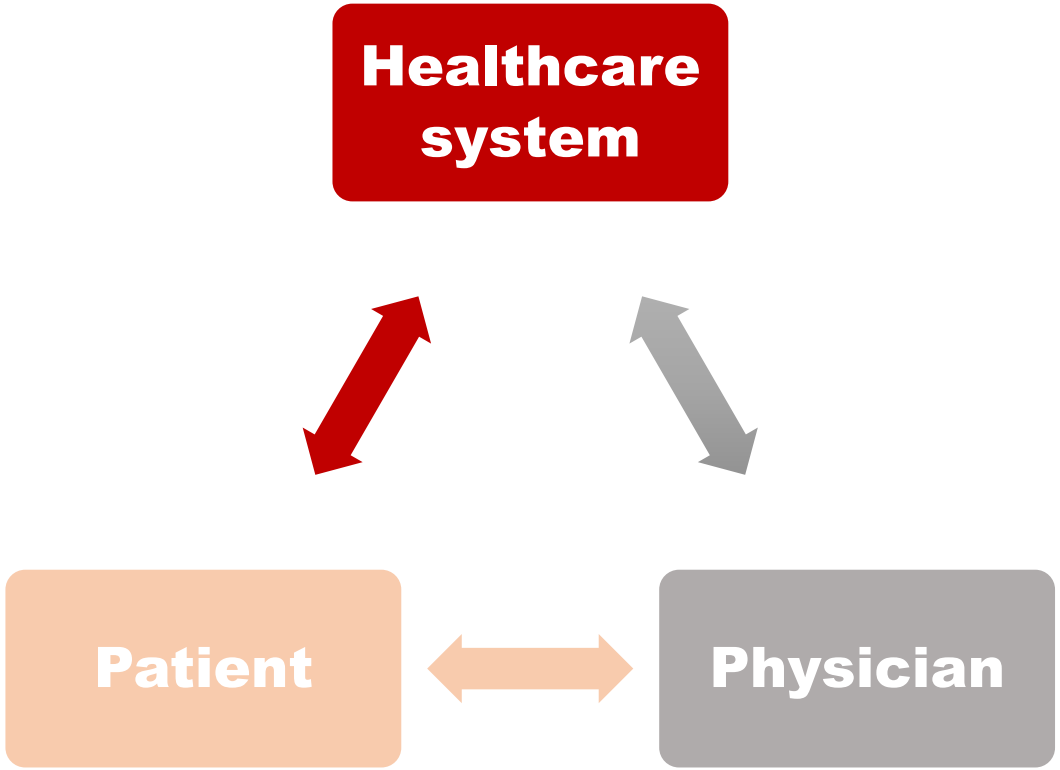
Ray KK, et al. EAS Late Breaking Science

Cholesterol control is fundamental in reducing the risk of ASCVD events[1,2]

Lifetime exposure to elevated LDL-C is a causal and cumulative risk factor for ASCVD[1]



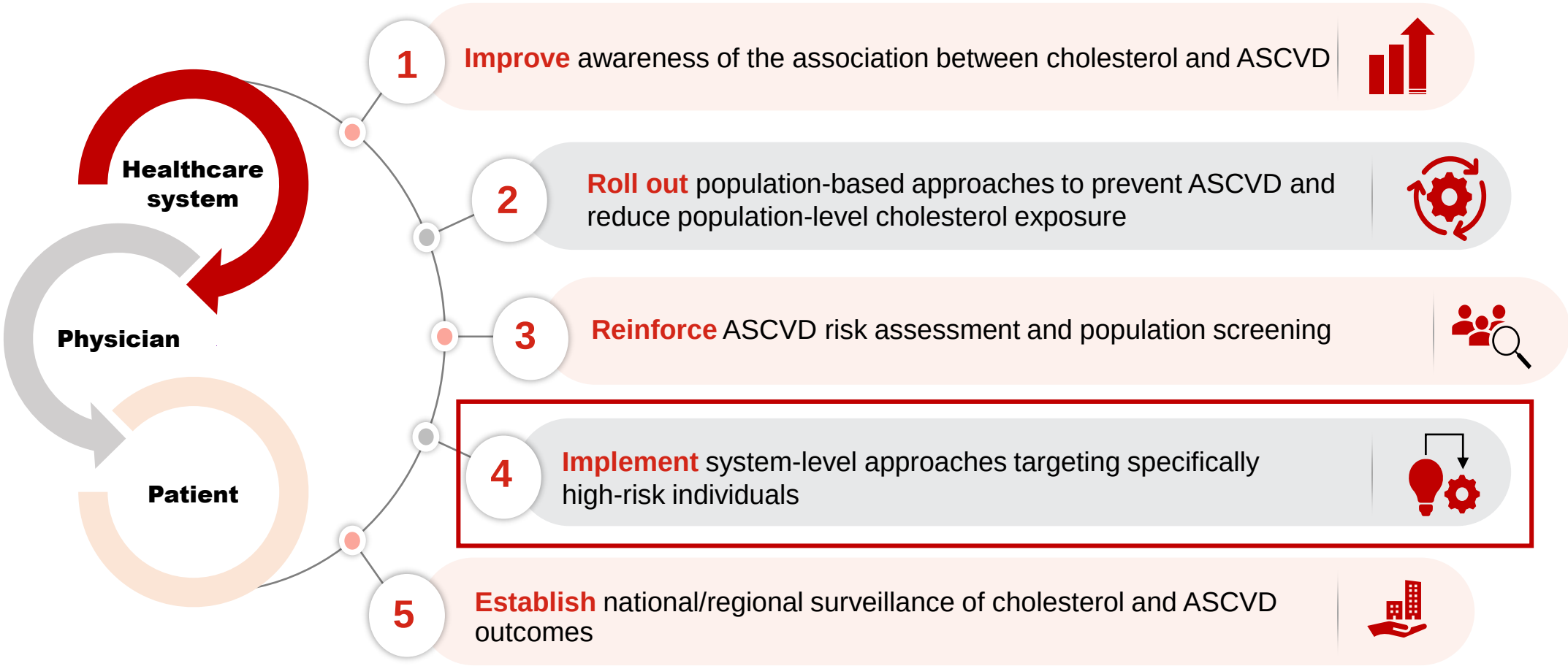
- Sustained **lifetime exposure** to **high cholesterol** leads to an increase in the **plaque burden** and eventually to **ASCVD events**[1]



ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density–lipoprotein cholesterol.

1. Ference BA, et al. *J Am Coll Cardiol*. 2018;72(10):1141-1156; 2. Ray KK, et al. *Global Heart.* 2022;17(1):75.

World Heart Federation Cholesterol Road Map 2022



ASCVD, atherosclerotic cardiovascular disease.

Ray KK et al. *Global Heart.* 2022;17(1):75.

Conclusions

Underestimation of **CV risk** may lead to **undertreatment**

Greater combination therapy use is needed to reach Improve

LDL-C control

- **Doubling** the dose of statin alone lowers LDL-C by **6%**, insufficient to achieve goals

- **ESC/EAS**, European Society of Cardiology/European Atherosclerosis Society; **CV**, cardiovascular; **LDL-C**, low-density lipoprotein cholesterol; **LLT**, lipid-lowering therapy
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