



SISA LOMBARDIA 24 ottobre 2019

Qual'è il prezzo da pagare se non portiamo a target il colesterolo LDL dei nostri pazienti?



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Faculty Disclosure

<input type="checkbox"/>	No, nothing to disclose
<input checked="" type="checkbox"/>	Yes, please specify:

<i>Company Name</i>	<i>Honoraria/ Expenses</i>	<i>Consulting/ Advisory Board</i>	<i>Funded Research</i>	<i>Royalties/ Patent</i>	<i>Stock Options</i>	<i>Ownership/ Equity Position</i>	<i>Employee</i>	<i>Other (please specify)</i>
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Eli Lilly	X							
MSD	X							
Abbott - Mylan	X							
Servier	X							
SANOFI	X							
Chiesi	X							

What is the price to pay if we are not at goal?

- **LDL-C management in Europe: are we at or near the goals ? EUROASPIRE IV-V and EURIKA**
- **Burden of expected CVD events when our patients are not at goal (residual LDL-C risk)**
- **Cost associated with the burden of CVD events**
- **Take home message**



2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk



2019 ESC/EAS GUIDELINES: CV RISK CATEGORIES

VERY HIGH RISK	HIGH RISK	MODERATE RISK	LOW RISK
<p>People with any of the following:</p> <ul style="list-style-type: none"> • Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularisation (PCI, CABG, and other arterial revascularisation procedures), stroke and TIA, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound • Diabetes Mellitus with target organ damage,* or at least three major risk factors, or early onset of T1DM of long duration (>20 years) • Severe CKD (eGFR <30 mL/min/1.73 m²) • A calculated SCORE ≥10% for 10-year risk of fatal CVD • FH with ASCVD or with another major risk factor 	<p>People with:</p> <ul style="list-style-type: none"> • Markedly elevated single risk factors, in particular TC >8 mmol/L (>310 mg/dL), LDL-C >4.9 mmol/L (>190 mg/dL), or BP ≥180/110 mmHg • Patients with FH without other major risk factors • Patients with DM without target organ damage, with DM duration ≥10 years or another additional risk factor • Moderate CKD (eGFR 30—59 L/min/1.73 m²) • A calculated SCORE ≥ 5% and <10% for 10-year risk of fatal CVD 	<ul style="list-style-type: none"> • Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years, without other risk factors • Calculated SCORE ≥1 % and <5% for 10-year risk of fatal CVD 	<ul style="list-style-type: none"> • Calculated SCORE <1% for 10-year risk of fatal CVD

*Defined as microalbuminuria, retinopathy, or neuropathy.

ASCVD = atherosclerotic cardiovascular disease; ACS = acute coronary syndrome; BP = blood pressure; CABG = coronary artery bypass graft surgery; CKD = chronic kidney disease; CT = computed tomography; CVD = cardiovascular disease; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate; FH = familial hypercholesterolaemia; LDL-C = low-density lipoprotein cholesterol; MI = myocardial infarction; PCI = percutaneous coronary intervention; SCORE = Systematic Coronary Risk Estimation; T1DM = type 1 DM; T2DM = type 2 DM; TC = total cholesterol; TIA = transient ischaemic attack.

Adapted from: Mach F, et al. Eur Heart J 2019. doi:10.1093/eurheartj/ehz455. Epub ahead of print.



RECOMMENDED TREATMENT GOALS FOR LDL-C LOWERING THERAPY: 2016 VS 2019

Risk category	LDL goals (starting with untreated LDL-C)	
	2016	2019
Very-high risk	<1.8 mmol/L (70 mg/dL) or >50% ↓ if LDL-C 1.8–3.5 mmol/L (70–135 mg/dL)	<1.4 mmol/L (<55 mg/dL) and >50% ↓
High-risk	<2.6 mmol/L (100 mg/dL) or >50% ↓ if LDL-C 2.6–5.2 mmol/L (100–200 mg/dL)	<1.8 mmol/L (<70 mg/dL) and >50% ↓
Moderate-risk	<3.0 mmol/L (115 mg/dL)	<2.6 mmol/L (<100 mg/dL)
Low-risk	<3.0 mmol/L (115 mg/dL)	<3.0 mmol/L (<115 mg/dL)

For patients with ASCVD experiencing a **second vascular event within 2 years** while taking maximumly tolerated statin-based therapy, an **LDL-C goal of <1.0 mmol/L (<40 mg/dL) is recommended**

LDL-C = low-density lipoprotein cholesterol.

Adapted from: Catapano AL, et al. Eur Heart J 2016;37:2999-3058. Mach F, et al. Eur Heart J 2019. doi:10.1093/eurheartj/ehz455. Epub ahead of print.

Low Rates of Both Lipid-Lowering Therapy Use and Achievement of LDL-C Targets in Individuals at High-Risk for Cardiovascular Disease across Europe

12 European countries*; **Primary CVD prevention patients** (n = 7641).
10-year risk of CVD-related mortality was calculated using the SCORE algorithm

Use of lipid-lowering therapy.

	High-risk(SCORE \geq 5%, or receiving LLT) (n = 5019)	Very-high-risk(SCORE \geq 10%, or diabetes mellitus) (n = 2970)
Any LLT	3278 (65.3)	1469 (49.5) \approx50%!!!
Statins alone	2862 (87.3)	1299 (88.4)
Statins with additional non-statin LLT ^a	178 (5.4)	86 (5.9)
Non-statin LLT ^a	238 (7.3)	84 (5.7)

^aNon-statin LLT: ezetimibe, fibrates, nicotinic acid, anion exchange resins.

LLT, lipid-lowering therapy; SCORE, Systematic Coronary Risk Evaluation.

doi:10.1371/journal.pone.0115270.t002

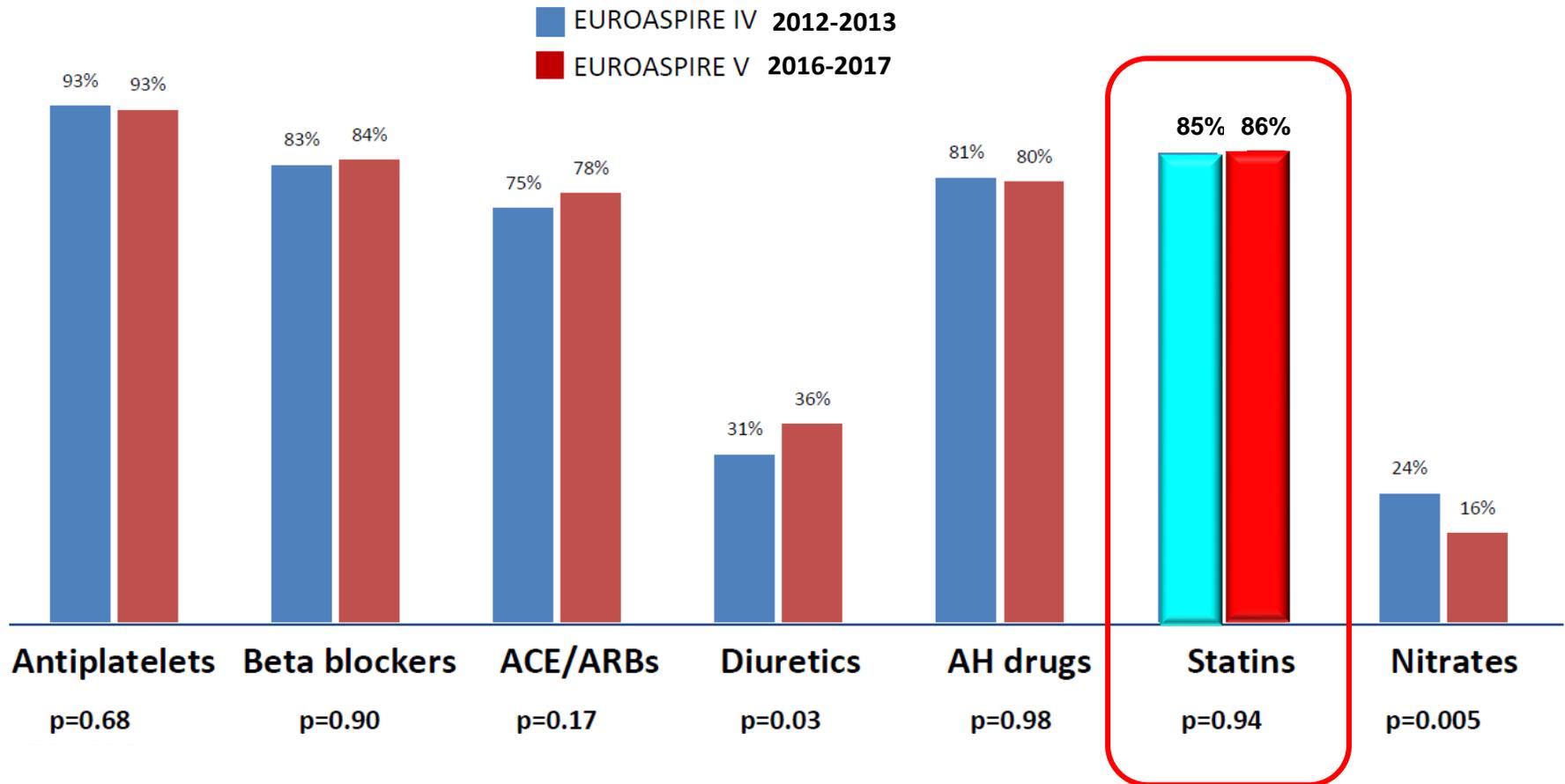
Very high CV risk: 8.4% on high-intensity statin (atorvastatin \geq 40 mg/d, rosuvastatin \geq 20 mg/d)

*Austria, Belgium, France, Germany, Greece, Norway, Russia, Spain, Sweden, Switzerland, Turkey, and the UK

EUROASPIRE SURVEYS IV-V

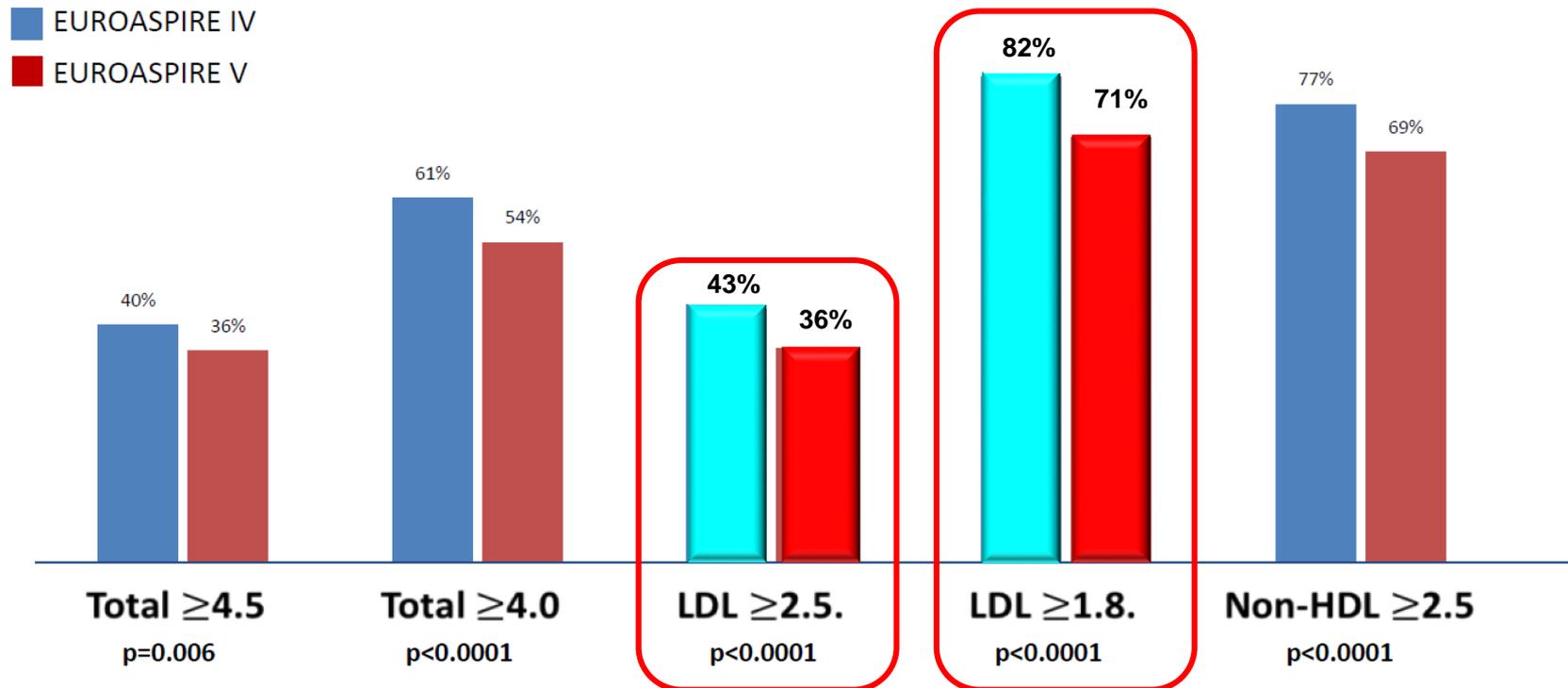
- Up to 27 Countries, 130 Centers, 7825 patients with CHD, 7998 Interviewees
- Consecutive patients, men and women <80 yrs., hospitalized at least 6 months and at most 3 years prior the interview:
 - Elective or emergency **CABG**
 - Elective or emergency **PCI**
 - Acute Myocardial Infarction (**STEMI, NSTEMI**)
- **Proportion of coronary patients** achieving the European lifestyle, risk factor and **therapeutic targets** for cardiovascular for cardiovascular disease Prevention as defined by the **European Societies Guidelines** on CVD prevention

EUROASPIRE SURVEYS IV-V



EUROASPIRE SURVEYS IV-V

EUROASPIRE IV and V Cholesterol mmol/L; Total, LDL and HDL

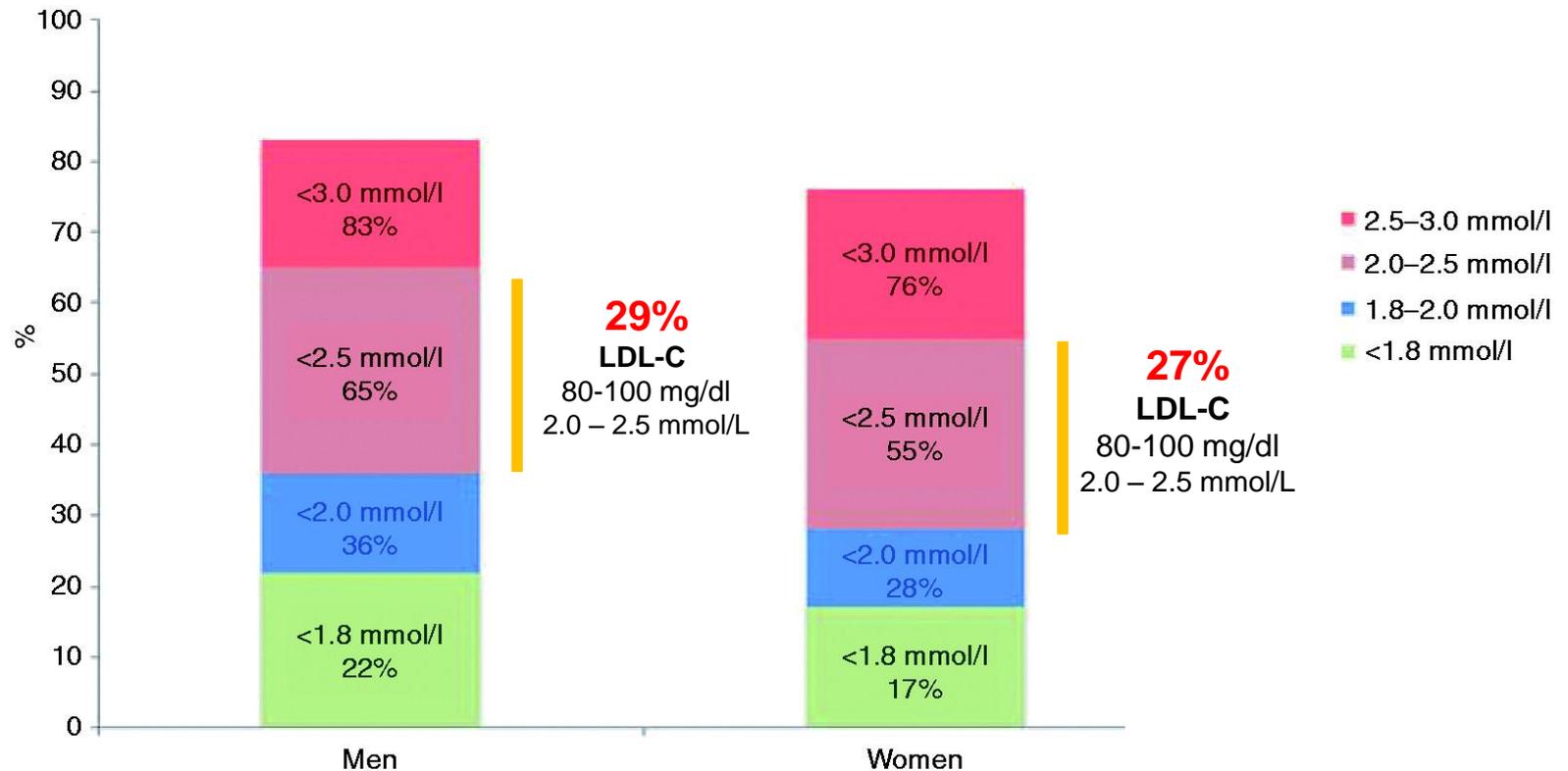


2.5 mmol/L= 100 mg/dl; 1.8 mmol/L= 70 mg/dl

What is the price to pay if we are not at goal?

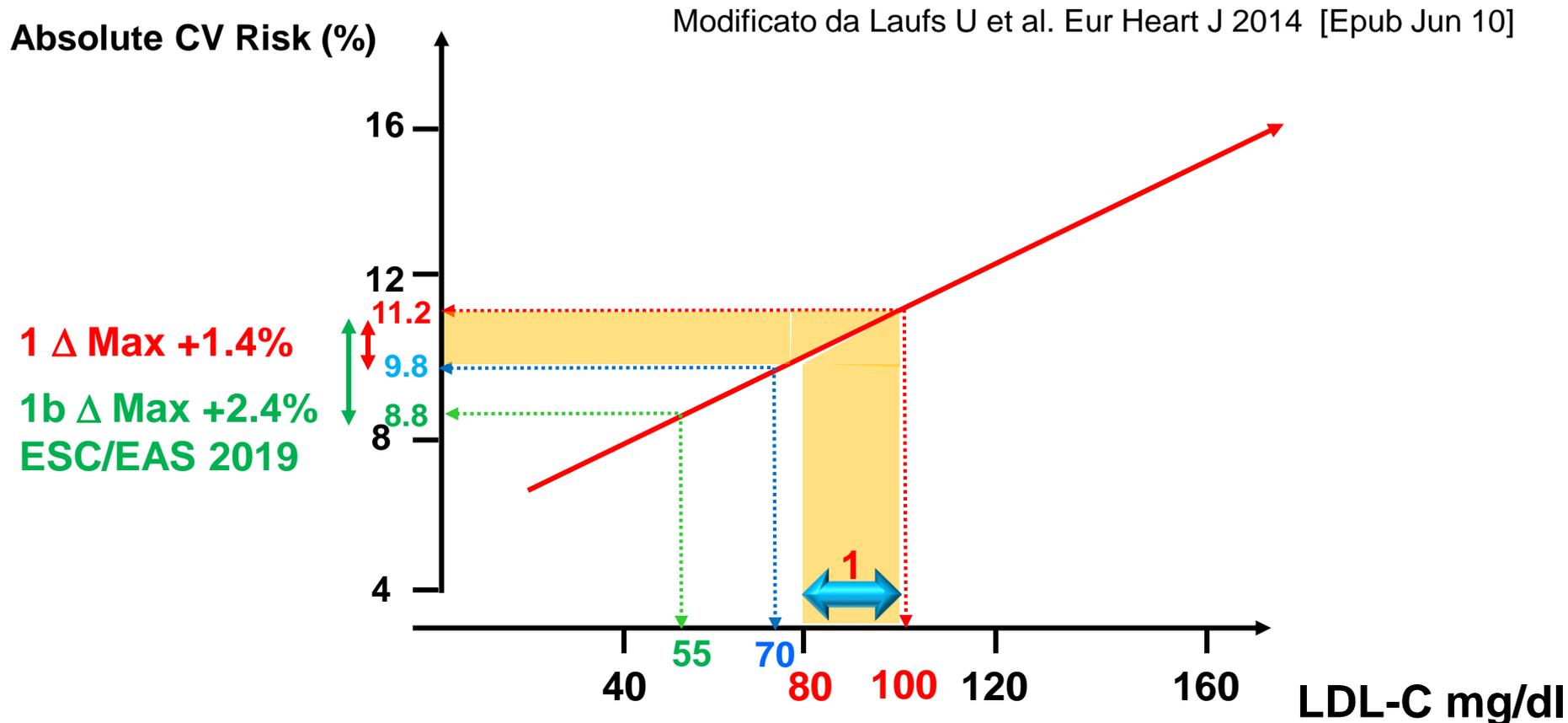
- **LDL-C management in Europe: are we at or near the goals ? EUROASPIRE IV-V and EURIKA**
- **Burden of expected CV events when our patients are not at goal (residual LDL-C risk)**

EUROASPIRE IV



Proportions (%) at LDL-cholesterol goal in patients on lipid lowering medication by sex *at interview*.

Diminishing risk reduction for the same relative LDL-C lowering with lower baseline LDL-C

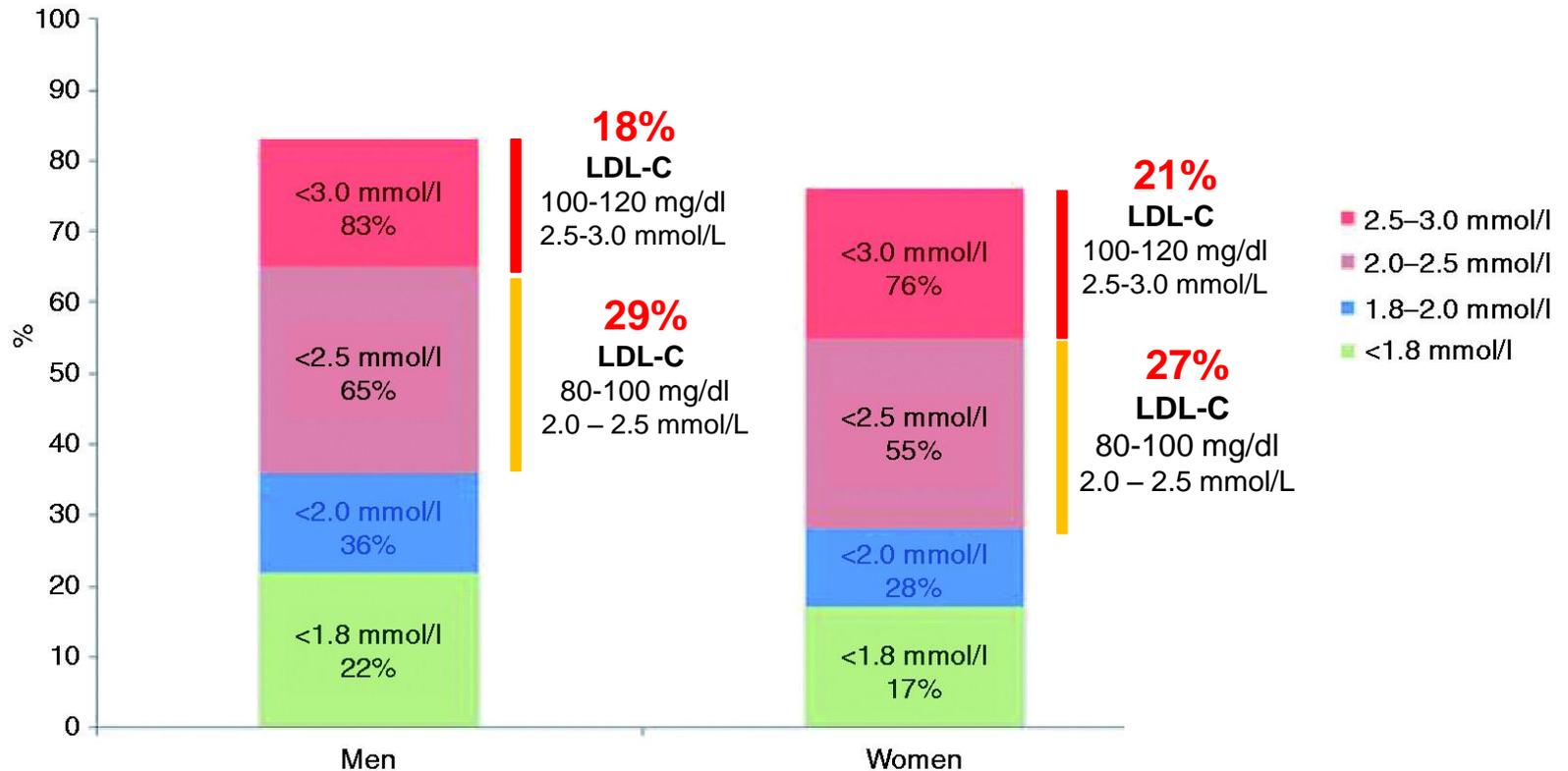


1) LDL-C= 80-100 mg/dl 2.0-2.5 mmol/L (\approx 30-35% of EUROASPIRE IV-V Population)

In this scenario we may expect **up to 3 extra CV events/100 pts over 10 yrs (ESC/EAS 2016)**
up to 4.8 extra CV events/100 pts over 10 yrs (ESC/EAS 2019)

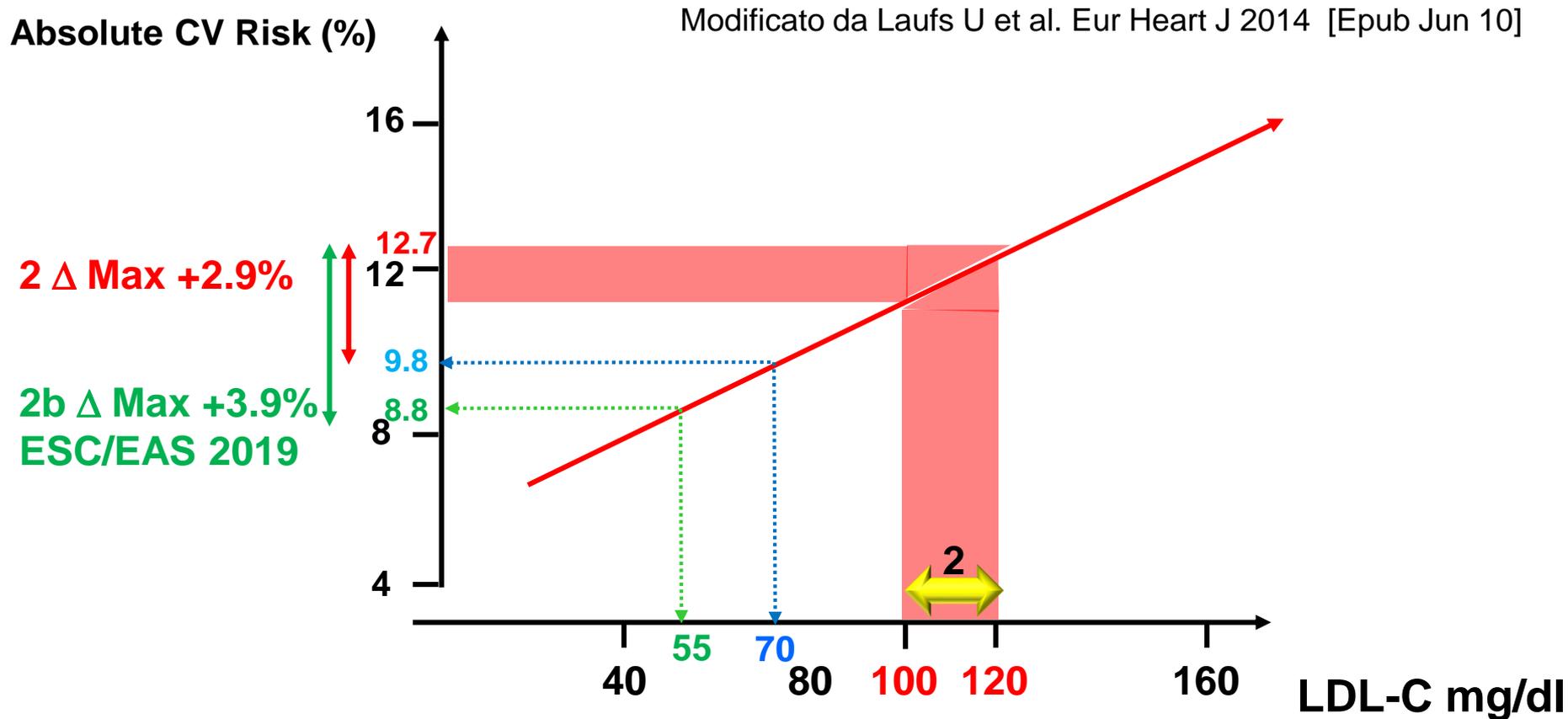
EUROASPIRE IV

EUROSPIRE V: LDL-C >2.6 mmol/L MEN 31%, WOMEN 42



Proportions (%) at LDL-cholesterol goal in patients on lipid lowering medication by sex *at interview*.

Diminishing risk reduction for the same relative LDL-C lowering with lower baseline LDL-C



2) LDL-C= 100-120 mg/dl 2.5-3.0 mmol/L (≈20% of EUROASPIRE IV Population)

In this scenario we may expect **up to 6 extra CV events/100 pts over 10 yrs (ESC/EAS 2016)**
up to 8 extra CV events/100 pts over 10 yrs (ESC/EAS 2019)

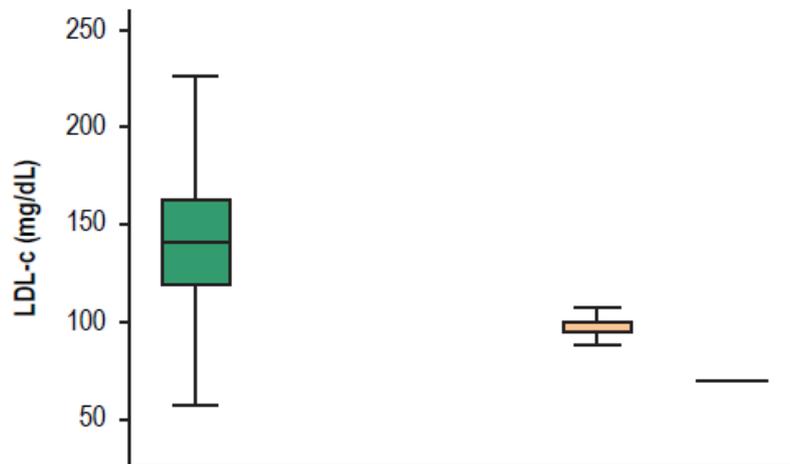
The Expected Cardiovascular Benefit of Plasma Cholesterol Lowering with or Without LDL-C Targets in Healthy Individuals at Higher Cardiovascular Risk

Fernando Henpin Yue Cesena,¹ Antonio Gabriele Laurinavicius,¹ Viviane A. Valente,¹ Raquel D. Conceição,¹ Raul D. Santos,^{1,2} Marcio S. Bittencourt,^{1,3}

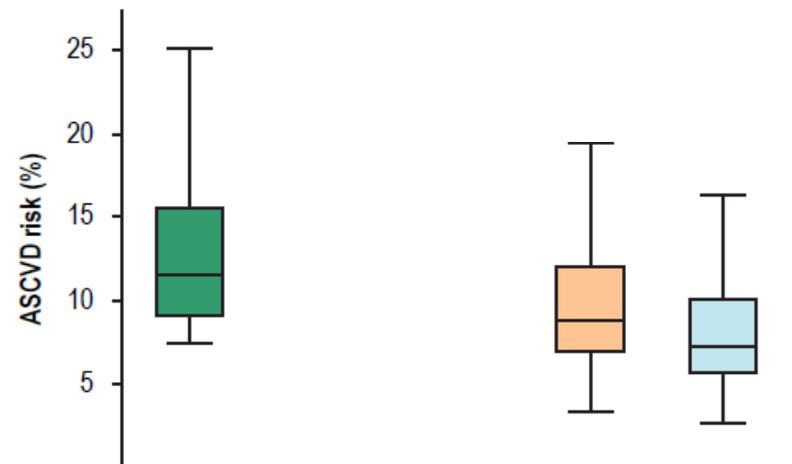
Hospital Israelita Albert Einstein;¹ Instituto do Coração (InCor) - Faculdade de Medicina da Universidade de São Paulo;² Hospital Universitário da Universidade de São Paulo;³ São Paulo, SP – Brazil

1897 subjects with a calculated 10-year risk for atherosclerotic cardiovascular disease (ASCVD) $\geq 7.5\%$
LDL-C 141 ± 33 mg/dl, ASCVD risk $13.7 \pm 6.1\%$, 57 ± 7 yrs age

(A) Distribution of LDL-C



(B) 10-year risk for atherosclerotic cardiovascular disease at baseline (ACC/AHA 2013)



Baseline

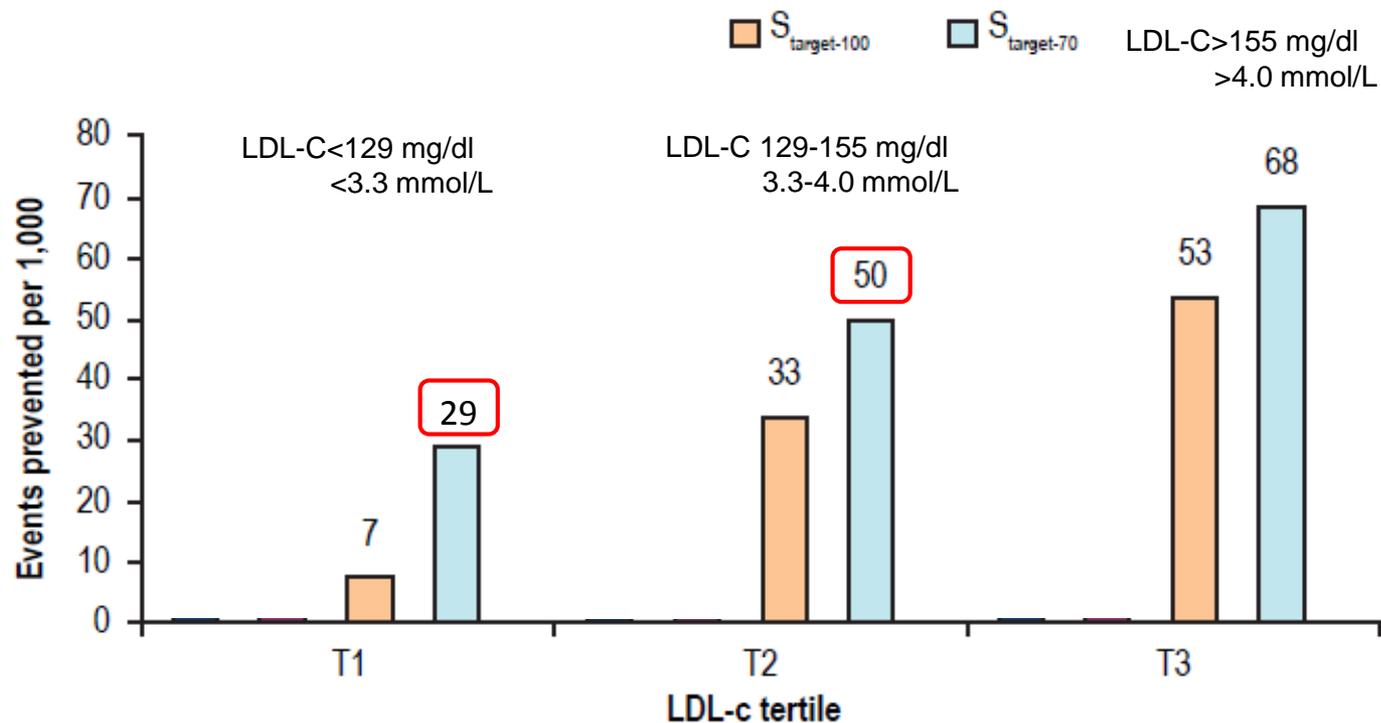
S_{target-100}

S_{target-70}

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Estimated number of events prevented in 10 years per 1,000 individuals assigned to the simulated strategy, according to baseline LDL-C (based on CTTC Meta-Analysis)

ASCVD Risk Categories and LDL-C Treatment Goals

Risk category	Risk factors/10-year risk	Treatment goals		
		LDL-C (mg/dL)	Non-HDL-C (mg/dL)	Apo B (mg/dL)
Extreme risk	<ul style="list-style-type: none"> – Progressive ASCVD including unstable angina in individuals after achieving an LDL-C <70 mg/dL – Established clinical cardiovascular disease in individuals with DM, stage 3 or 4 CKD, or HeFH – History of premature ASCVD (<55 male, <65 female) 	<55	<80	<70
Very high risk	<ul style="list-style-type: none"> – Established or recent hospitalization for ACS, coronary, carotid or peripheral vascular disease, 10-year risk >20% – DM <u>or</u> stage 3 or 4 CKD with 1 or more risk factor(s) – HeFH 	<70	<100	<80
High risk	<ul style="list-style-type: none"> – ≥2 risk factors and 10-year risk 10%-20% – DM or stage 3 or 4 CKD with no other risk factors 	<100	<130	<90
Moderate risk	≤2 risk factors and 10-year risk <10%	<100	<130	<90
Low risk	0 risk factors	<130	<160	NR

Abbreviations: ACS, acute coronary syndrome; apo, apolipoprotein; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; DM, diabetes mellitus; HeFH, heterozygous familial hypercholesterolemia; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NR, not recommended.

Barter PJ, et al. *J Intern Med.* 2006;259:247-258; Boekholdt SM, et al. *J Am Coll Cardiol.* 2014;64(5):485-494; Brunzell JD, et al. *Diabetes Care.* 2008;31:811-822; Cannon CP, et al. *N Engl J Med.* 2015;372(25):2387-2397; Grundy SM, et al. *Circulation.* 2004;110:227-239; Heart Protection Study Collaborative Group. *Lancet.* 2002;360:7-22; Jellinger P, Handelsman Y, Rosenblit P, et al. *Endocr Practice.* 2017;23(4):479-497; Lloyd-Jones DM, et al. *Am J Cardiol.* 2004;94:20-24; McClelland RL, et al. *J Am Coll Cardiol.* 2015;66(15):1643-1653; NHLBI. NIH Publication No. 02-5215. 2002; Ridker PM, *J Am Coll Cardiol.* 2005;45:1644-1648; Ridker PM, et al. *JAMA.* 2007;297(6):611-619; Sever PS, et al. *Lancet.* 2003;361:1149-1158; Shepherd J, et al. *Lancet.* 2002;360:1623-1630; Smith SC Jr, et al. *Circulation.* 2006;113:2363-2372; Stevens RJ, et al. *Clin Sci.* 2001;101(6):671-679; Stone NJ. *Am J Med.* 1996;101:4A40S-48S; Weiner DE, et al. *J Am Soc Nephrol.* 2004;15(5):1307-1315.





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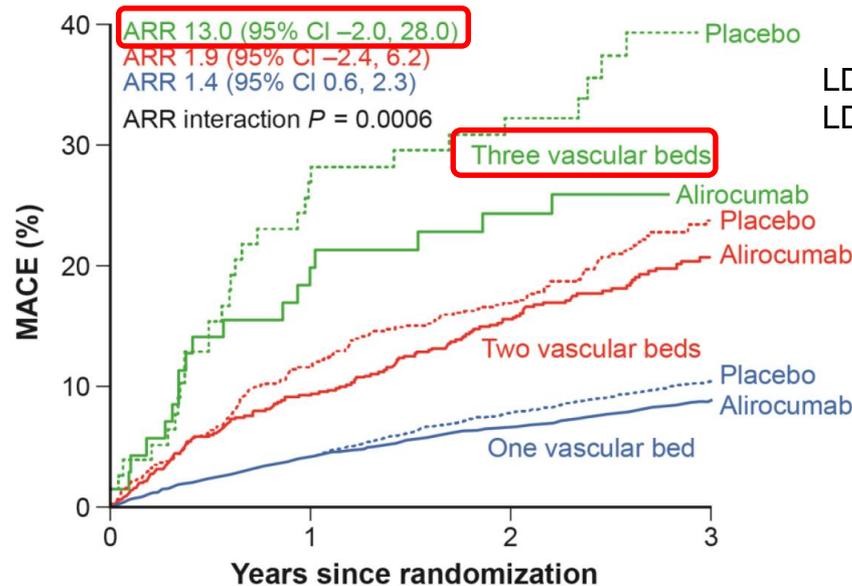
LDL-C = low-density lipoprotein cholesterol.

Adapted from: Catapano AL, et al. Eur Heart J 2016;37:2999-3058. Mach F, et al. Eur Heart J 2019. doi:10.1093/eurheartj/ehz455. Epub ahead of print.

ODYSSEY OUTCOMES: Post ACS patients with Polyvascular Disease Derive Large Absolute Benefit From Alirocumab

MACE: one, two or three vascular beds

MACE: coronary heart disease death, nonfatal MI, fatal/nonfatal ischemic stroke, or unstable angina requiring hospitalization



LDL-C placebo 100 mg/dl (2.5 mmol/L)
LDL-C Alirocumab 53 mg/dl (1.4 mmol/L)

Absolute Risk Reduction (ARR) with Alirocumab:

1. 1.4% (1 vascular bed)
2. 1.9% (2 vascular beds)

3. 13.0% (3 vascular beds)

p = 0,0006.

Scenario 3 (Three Vascular Beds Involved) in patients with an LDL-C of 100 mg/dl (2.5) vs 53 mg/dl (1.4) we may expect **up to 20 extra CV events/100 pts over 5 yrs!!!**

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THE ECONOMIC COST OF CARDIOVASCULAR DISEASE FROM 2014-2020 IN SIX EUROPEAN ECONOMIES

Quantifying the economic cost of CVD

Total economic cost of cardiovascular disease

Direct cost

Cost-of-illness
approach

Indirect cost

Value of output approach

Health care costs

This includes primary, acute, hospital in- and outpatient care and medication costs

Productivity lost from mortality

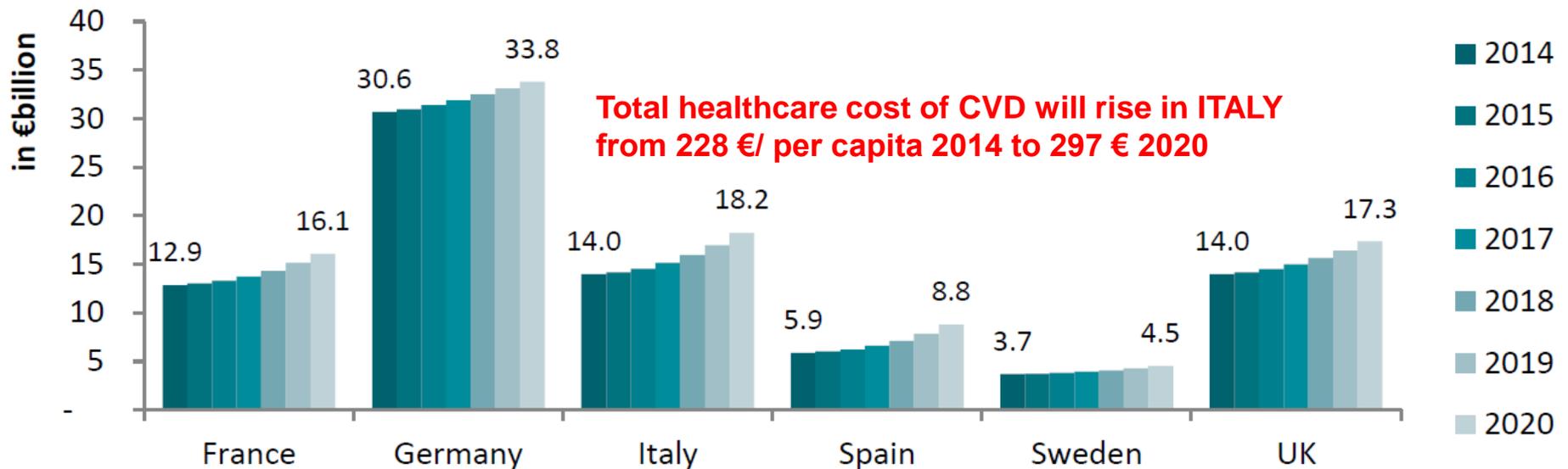
Mortality costs represent the value of foregone earnings from premature deaths caused by CVD

Productivity lost from morbidity

Morbidity costs represent the value of foregone earnings from lost productivity including (i) workloss of currently employed individuals and (ii) sickness

The economic cost of cardiovascular disease from 2014-2020 in six European economies

Total healthcare cost of CVD, forecasts 2014-2020, in € billion



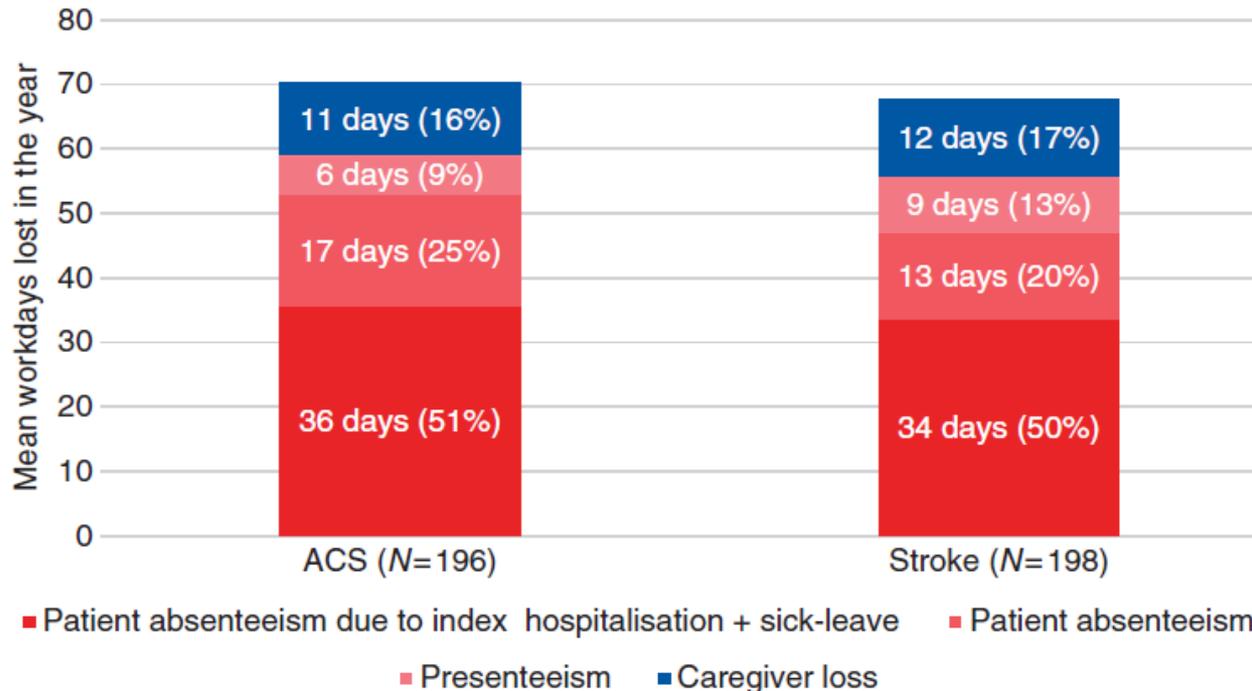
By the end of the decade, the six countries combined will face CVD related healthcare costs of **€98.7 billion** from **€ 81** in 2014

Patient and caregiver productivity loss and indirect costs associated with cardiovascular events in Europe

Kornelia Kotseva¹, Laetitia Gerlier², Eduard Sidelnikov³,
Lucie Kutikova³, Mark Lamotte², Pierre Amarenco⁴
and Lieven Annemans⁵

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Mean patient and caregiver annual workdays lost in ACS and stroke.



**Indirect cost
€13,953 per
ACS case**

**Indirect cost
€13,773 per
stroke case**

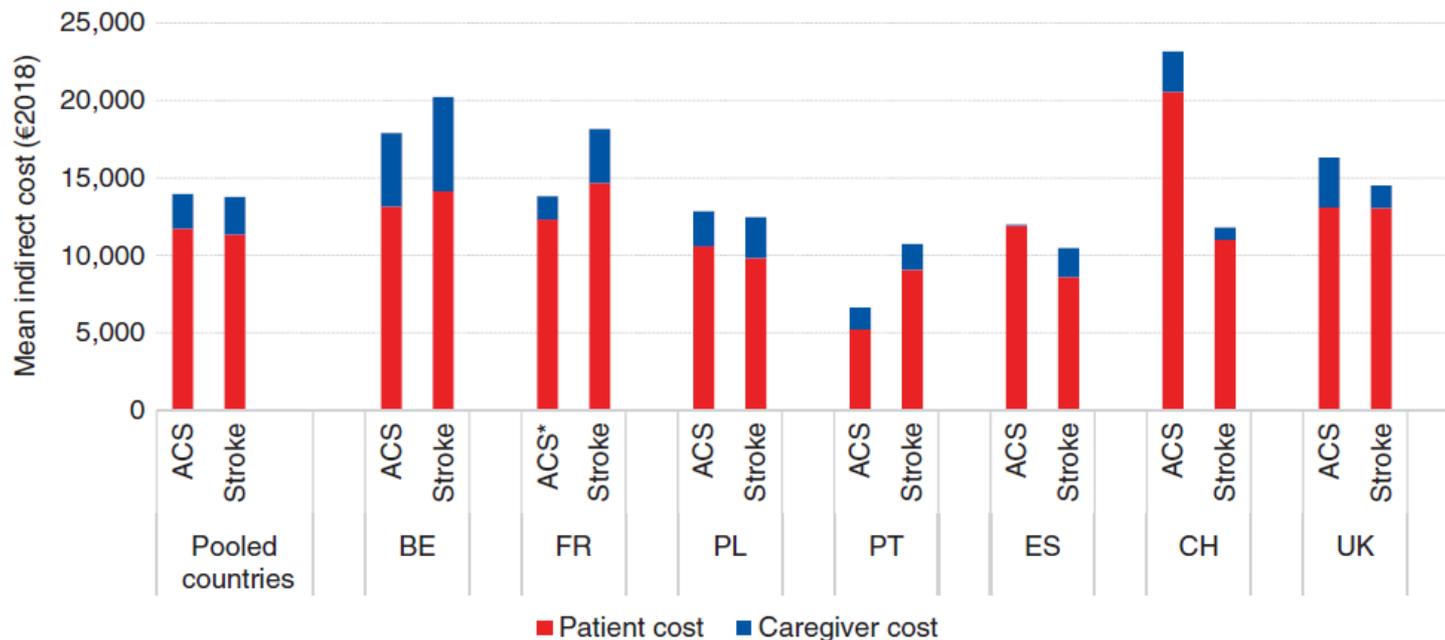
The European Cardiovascular Disease Statistics 2017 report that indirect costs account for 47% of total cardiovascular economic burden.

Patient and caregiver productivity loss and indirect costs associated with cardiovascular events in Europe

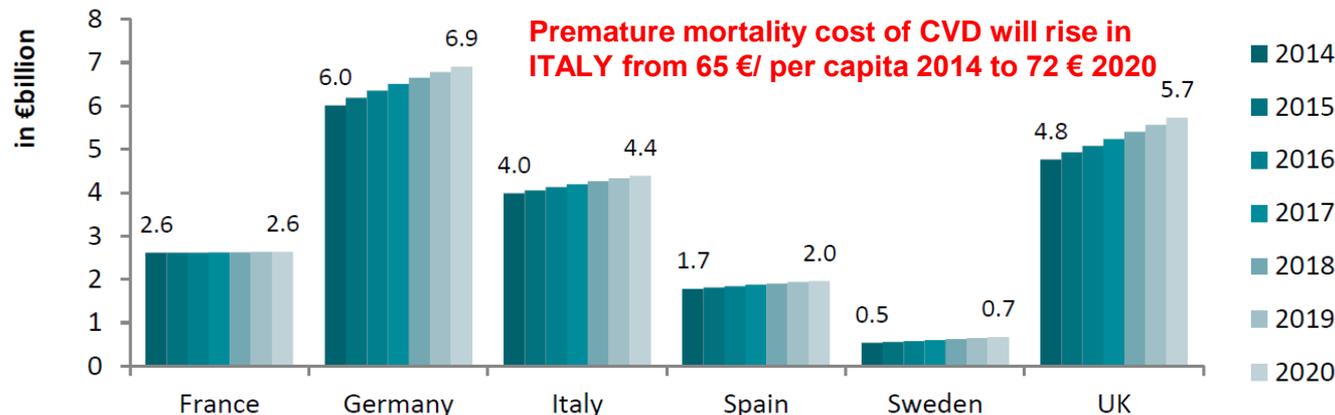
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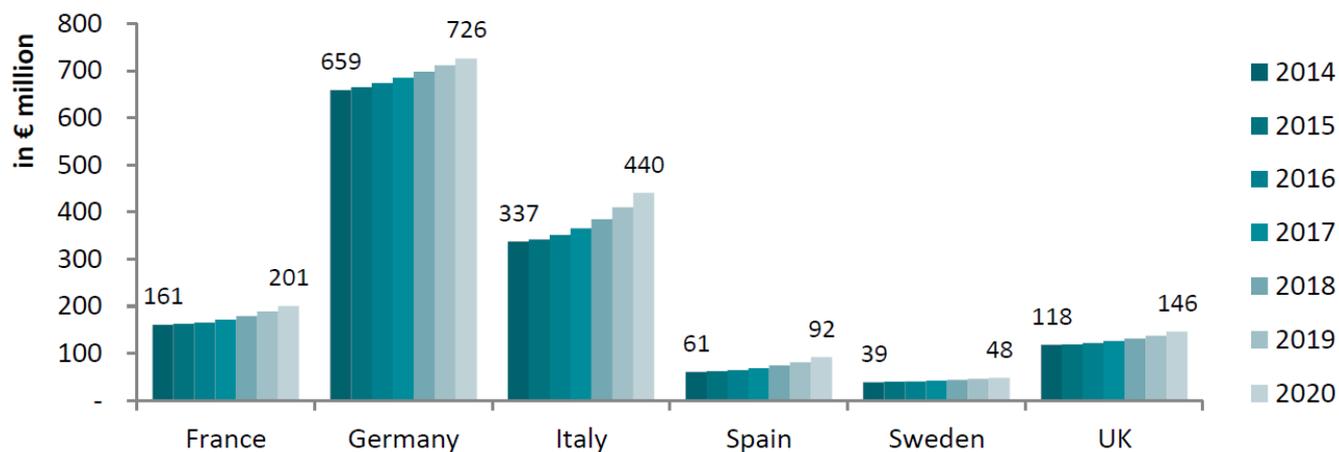
Mean patient and caregiver annual indirect costs in ACS and stroke



The economic cost of cardiovascular disease from 2014-2020 in six European economies



Mortality costs attributable to CVD, forecasts 2014-2020, in €billion



Morbidity costs attributable to CVD, forecasts 2014-2020, in €million

SUMMARY

- LDL-C treatment in PATIENTS AT VERY HIGH CV RISK (LDL-C<1.8 mmol/L):
 - Primary prevention (EURIKA): up to 50% not on any lipid lowering therapy and 1 in 10 achieving the appropriate LDL-C goals
 - Secondary prevention (EUROASPIRE V): 86% on statin therapy but only 29% (1 out of 3) achieving LDL-C goals

BURDEN OF EXPECTED EVENTS

- Subjects, on statin, **mildly** (80-100 mg/dl - 2.0-2.5 mmol/L) above LDL-C goals:
up to 3 to 5 extra CV events/100 pts over 10 yrs
- Subjects **moderately** (100-120 mg/dl - 2.5-3.0 mmol/L) above LDL-C goals:
up to 6 to 8 extra CV events/100 pts over 10 yrs
- In an **extremely high** CV risk conditions (3 vascular beds affected) LDL-C at 2.5 mmol/L (100 mg/dl) vs 1.4 (53), **up to 21 extra CV events/100 pts over 10 yrs**

SUMMARY

EXPECTED PRICE TO PAY*

- Both direct and indirect cost are bound to rise in the near future*
- **Direct healthcare costs** attributable to CVD will rise from a €81.1 billion in 2014, to **about 98.7 billion** by the end of the decade
- **Indirect cost** from premature mortality will rise from €19.6 to **22.3 billion** and from morbidity from €1.4 to **1.6 billion**.
- **Total costs** to the economies from CVD will **rise** from €102.1 billion in 2014 € to **122.6 billion** by the end of the decade, this is **an increase of €20.5 billion over six years.**

* CBER 2015 estimates for France, UK, Italy, Germany, Spain, Sweden

Knowing is not enough; we must apply

Willing is not enough; we must do

Goethe