

PLACE



PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

9^a Edizione

ROMA

MINICORSI E EVENTI
PRECONGRESSUALI

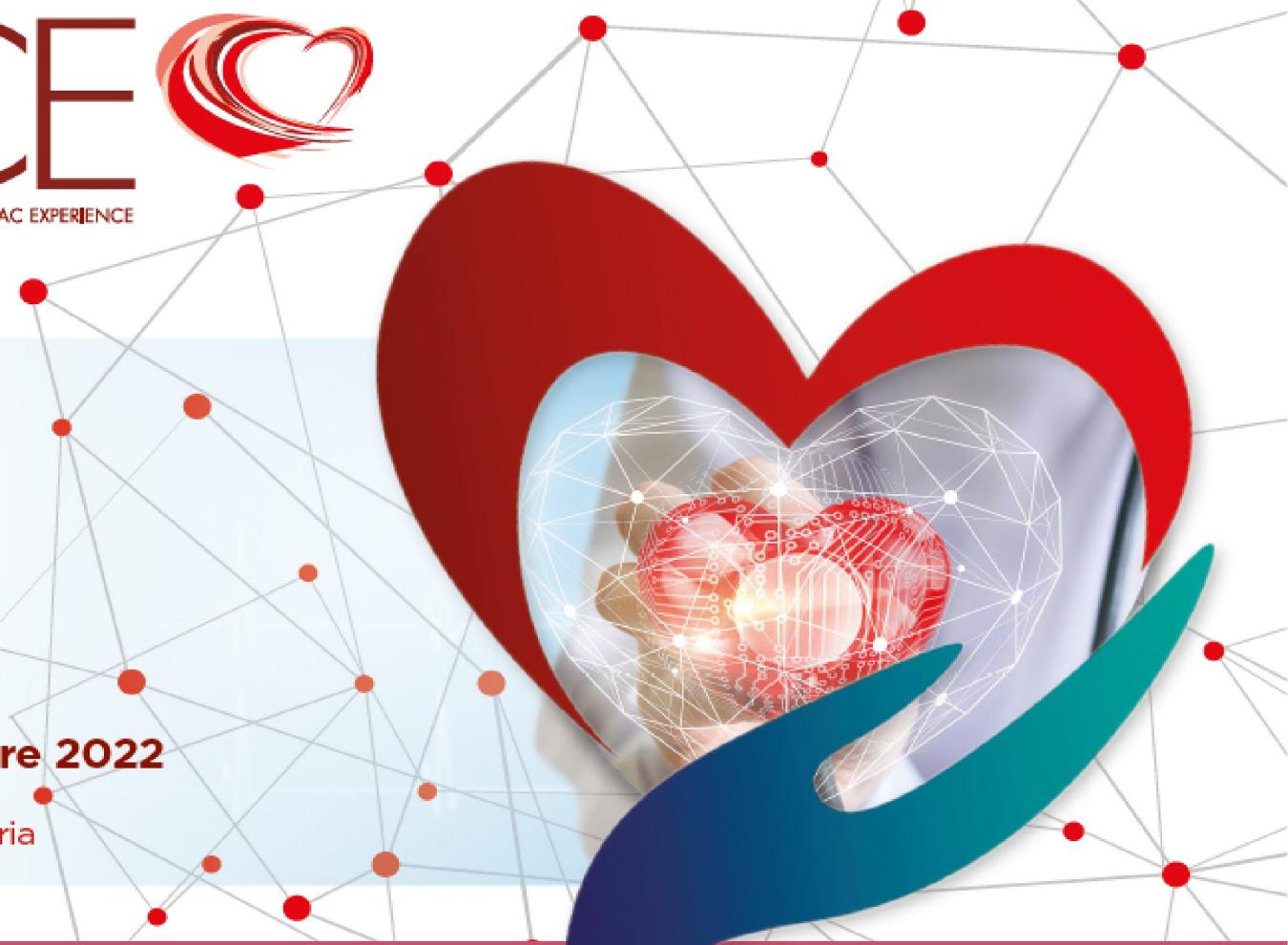
29 Settembre 2022

CONGRESSO

30 Settembre • 1 ottobre 2022

Centro Congressi di Confindustria

Auditorium della Tecnica



Flow chart nella diagnosi e nel trattamento delle forme di
ipercolesterolemia familiare
R. Volpe, Roma



Unità Prevenzione e Protezione
Consiglio Nazionale delle Ricerche



SIPREC
Società italiana
per la prevenzione
cardiovascolare

Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55 000 vascular deaths

Lancet 370, 1829, 2007

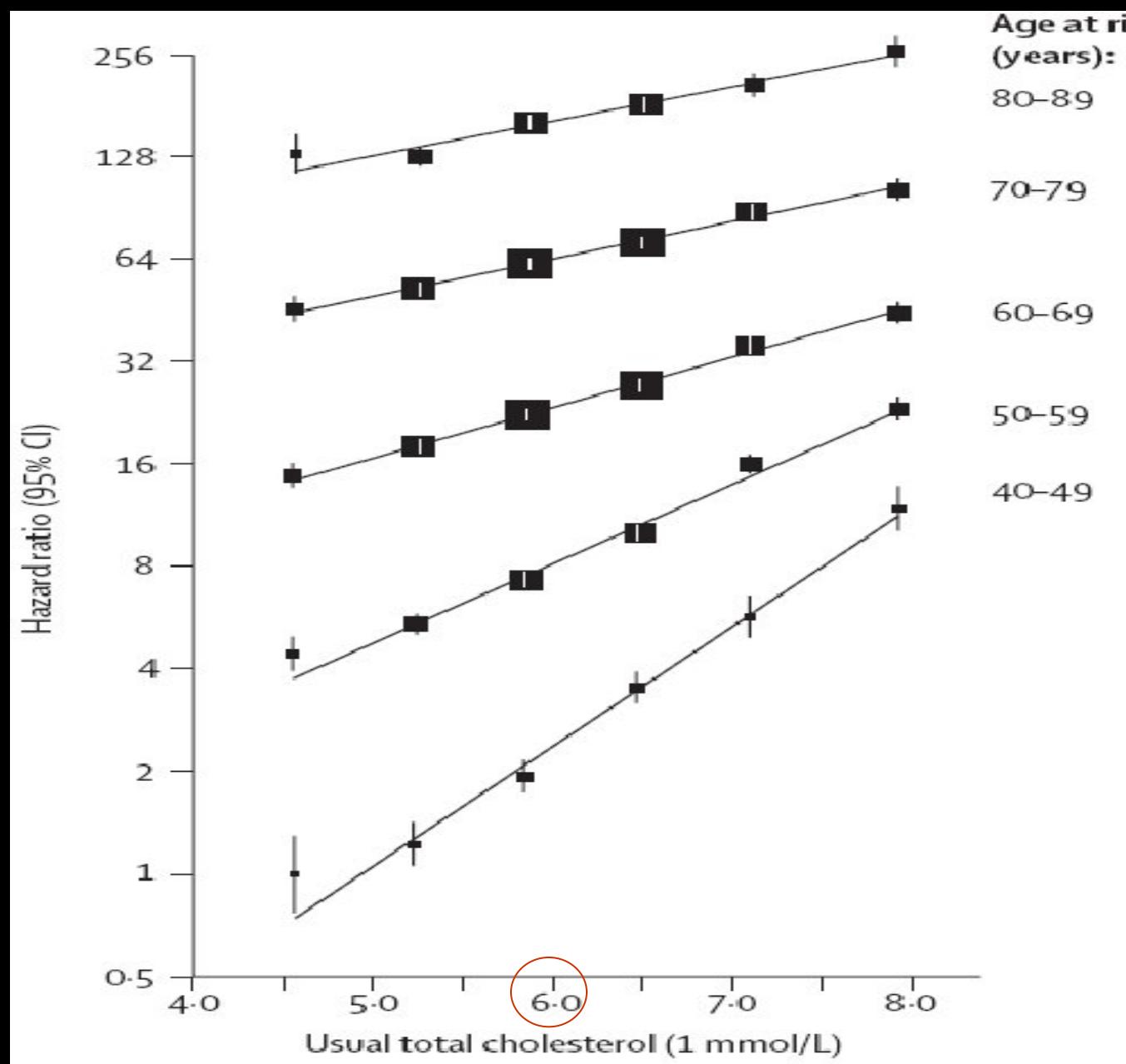
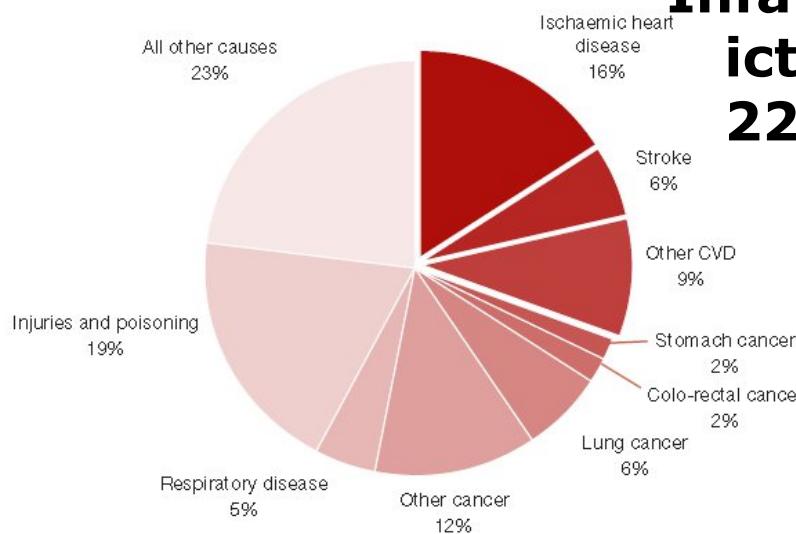


Figure 1.3a Deaths under 65 years by cause, males, latest available year, Europe

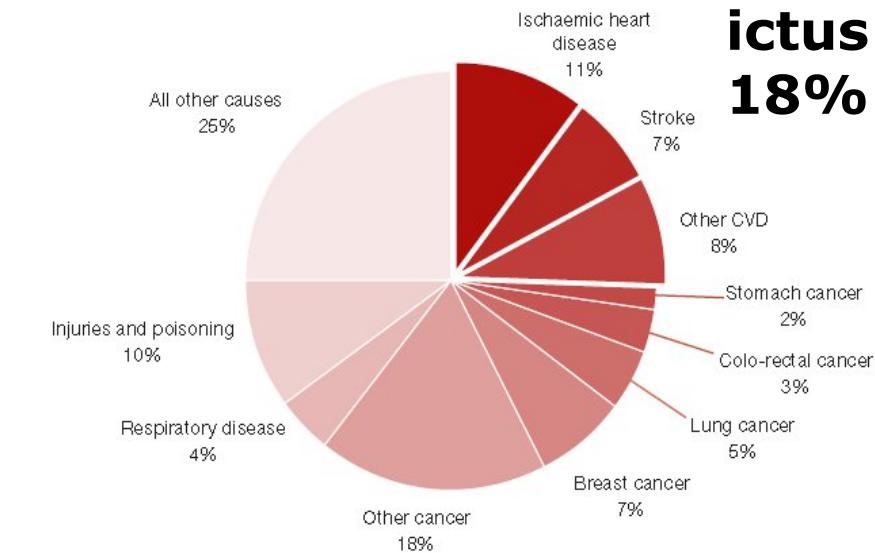


**Infarto+
ictus
22%**

European
Cardiovascular
Disease
Statistics
2017 edition



Figure 1.3b Deaths under 65 years by cause, females, latest available year, Europe



**Infarto+
ictus
18%**

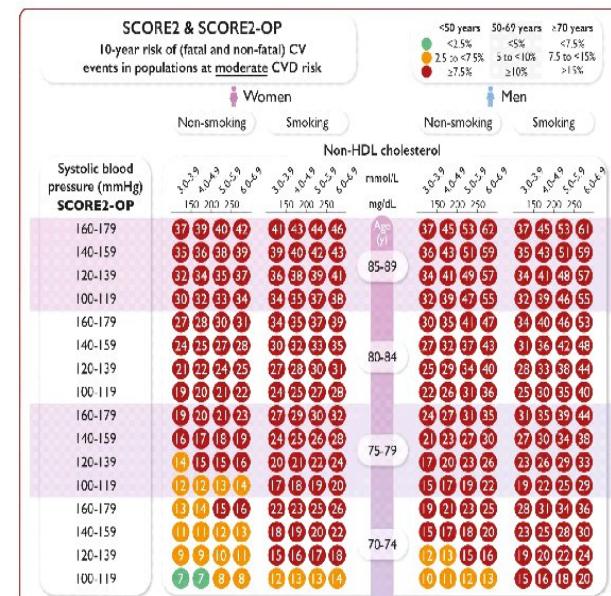
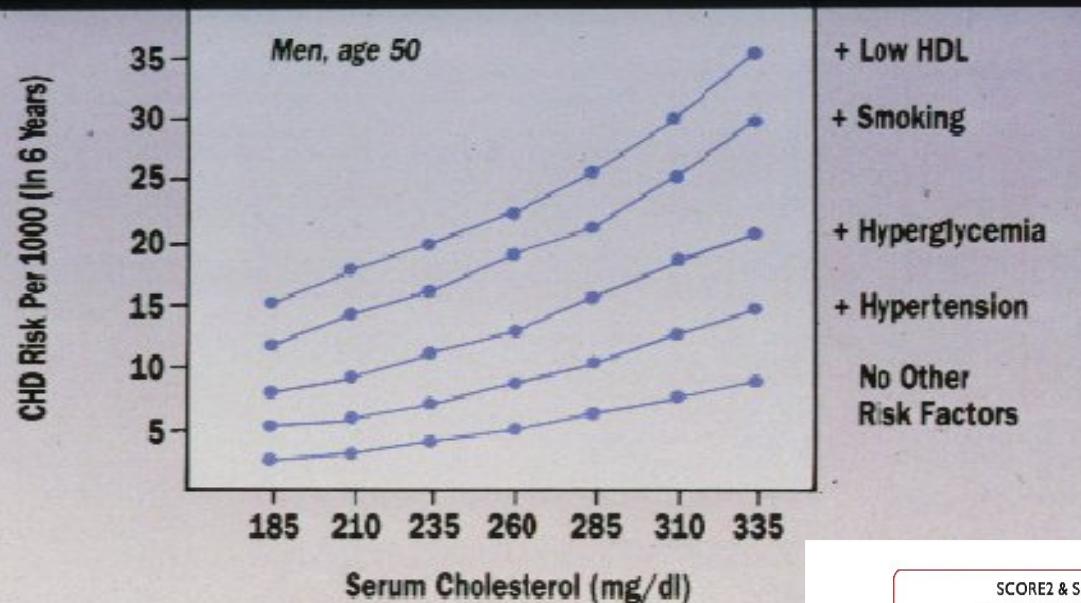
Coronaropatia prematura in soggetti con Ipercolesterolemia familiare (FH)



Studio	Pazienti (n.)	Prevalenza eventi coronarici	
		Donne	Uomini
Hirobe et al., 1982	52	27%	57%
Mabuchi et al., 1989	692	10%	22%
Hill et al., 1991	364	13%	31%
Hopkins et al., 2001	262	15%	41%
Alonso et al., 2002	819	12%	27%
		~15%	~36%

MRFIT, 1972-1998, uomini 35-57, prevenzione primaria

Stamler J, Neaton JD



SCORE2 and SCORE2-OP
risk chart for fatal and
non-fatal (MI, stroke)
ASCVD

Moderate CVD Risk (1)

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies

With the special contribution of the European Association of Preventive Cardiology (EAPC)

Authors/Task Force Members: Frank L.J. Visseren* (Chairperson) (Netherlands), François Mach* (Chairperson) (Switzerland), Yvo M. Smulders† (Task Force Coordinator) (Netherlands), David Carballo† (Task Force Coordinator) (Switzerland), Konstantinos C. Koskinas (Switzerland), Maria Bäck (Sweden), Athanase Benetos⁸ (France), Alessandro Biffi^{7,10} (Italy), José-Manuel Boavida⁹ (Portugal), Davide Capodanno (Italy), Bernard Cosyns (Belgium), Carolyn Crawford (Northern Ireland), Constantinos H. Davos (Greece), Iléana Desormais (France), Emanuele Di Angelantonio (United Kingdom), Oscar H. Franco (Switzerland), Sigrun Halvorsen (Norway), F. D. Richard Hobbs¹³ (United Kingdom), Monika Hollander (Netherlands), Ewa A. Jankowska (Poland), Matthias Michal¹¹ (Germany), Simona Sacco⁶ (Italy), Naveed Sattar (United Kingdom), Lale Tokgozoglu² (Turkey), Serena Tonstad (Norway), Konstantinos P. Tsiofiris⁵ (Greece), Ineke van Dis³ (Netherlands), Isabelle C. van Gelder (Netherlands), Christoph Wanner⁴ (Germany), Bryan Williams (United Kingdom), ESC Scientific Document Group

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

ESC European Society of Cardiology European Heart Journal (2019) 00, 1–78 doi:10.1093/eurheartj/ehz455

ESC/EAS GUIDELINES
25 YEARS

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

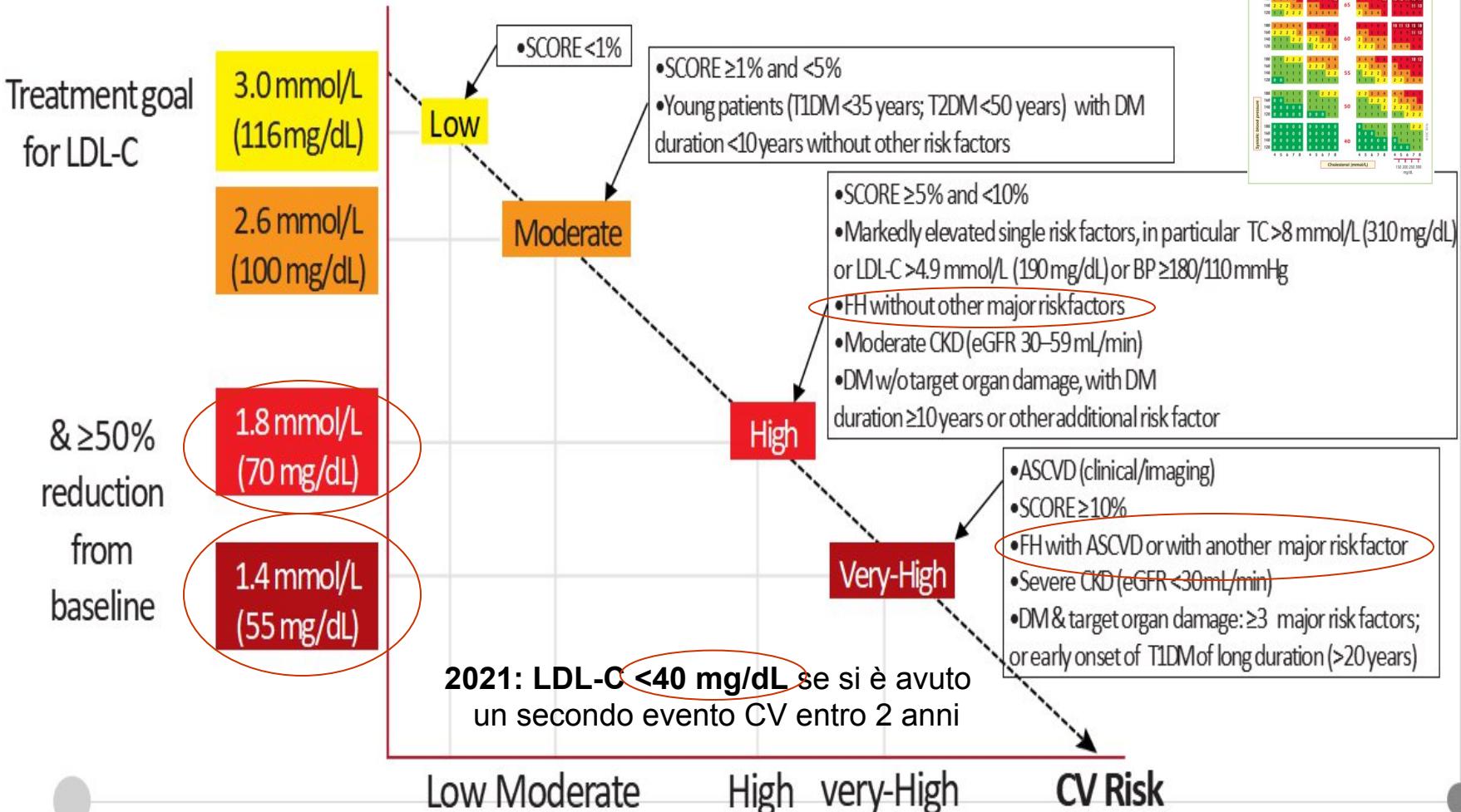
The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

Authors/Task Force Members: François Mach^{1*} (Chairperson) (Switzerland), Colin Baigent^{2*} (Chairperson) (United Kingdom), Alberico L. Catapano^{1*}

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 maximum tolerated statin-based therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) is recommended

Treatment goals for low-density lipoprotein cholesterol (LDL-C) across categories of total cardiovascular disease risk



The Nobel Prize in Physiology or Medicine 1985



Photo from the Nobel Foundation archive.

Michael S. Brown

Prize share: 1/2

Photo from the Nobel Foundation archive.

Joseph L. Goldstein

Prize share: 1/2

A Receptor-Mediated Pathway for Cholesterol Homeostasis

MICHAEL S. BROWN AND JOSEPH L. GOLDSTEIN

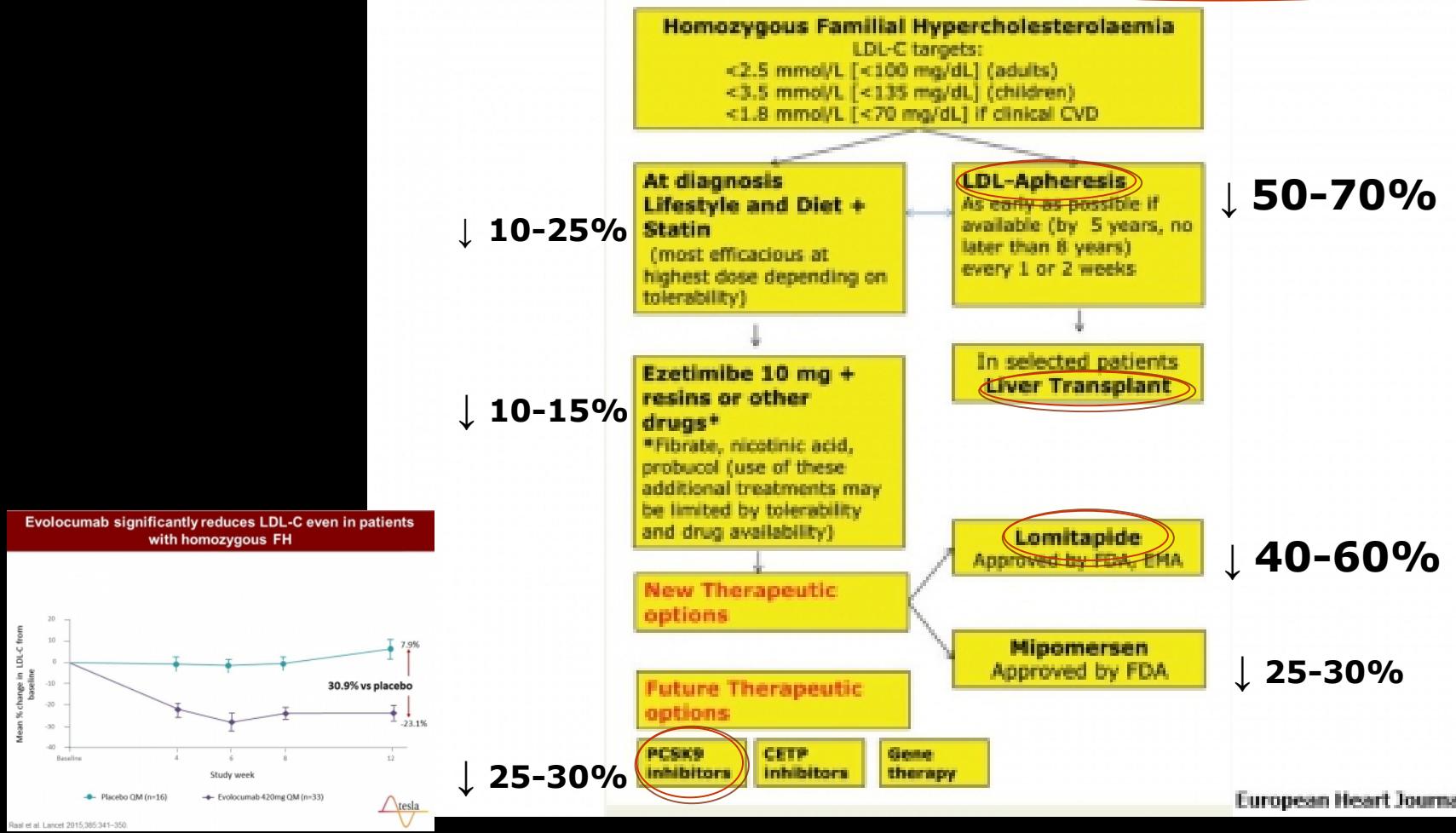
The LDL-receptor studies lend experimental support to the epidemiologists' suggestion that the levels of plasma cholesterol usually seen in Western industrialized societies are inappropriately high (9). This support derives from knowledge of the affinity of the LDL receptor for LDL. The receptor binds LDL optimally when the lipoprotein is present at a cholesterol concentration of 2.5 mg/dl (28). In view of the 10-to-1 gradient between concentrations of LDL in plasma and interstitial fluid, a level of LDL-cholesterol in plasma of 25 mg/dl would be sufficient to nourish body cells with cholesterol (118). This is roughly one-fifth of the level usually seen in Western societies (Fig. 16) (119). Several lines of evidence suggest that plasma levels of LDL-cholesterol in the range of 25 to 60 mg/dl (total plasma cholesterol of 110 to 150 mg/dl) might indeed be physiologic for human beings.

Intensity of lipid-lowering treatment	
Treatment	Average LDL-C reduction
Moderate-intensity statin	≈30%
High-intensity statin	≈50%
High-intensity statin plus ezetimibe	≈65%
PCSK9 inhibitor	≈60%
PCSK9 inhibitor plus high-intensity statin	≈75%
PCSK9 inhibitor plus high-intensity statin plus ezetimibe	≈85%

Expected low-density lipoprotein cholesterol reductions for combination therapies



Suggested algorithm for management of homozygous familial hypercholesterolaemia



EDUCATION & DEBATE

BMJ VOLUME 304

15 FEBRUARY 1992

For Debate

Should There be a Moratorium on the use of Cholesterol Lowering Drugs?

George Davey Smith, Juha Pekkanen

Trials of primary prevention of CHD by reducing cholesterol concentrations

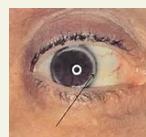
	No of particip.		No of deaths from CHD		No of deaths from causes other than CHD				All causes		Years of follow-up				
	I	C	I	C	All	Cancer	Injury	Other	I	C					
WHO study	5331	5296	36	34	92	53	42	25	18	15	32	13	128	87	5
Colestipol-Upjohn Study	548	546	9	22	8	5	2	2	2	0	4	3	17	27	2
UpIid Research Clinics	1906	1900	32	44	38	27	16	15	11	4	9	8	68	71	7
Helsinki heart Study	2051	2030	14	19	31	23	11	11	10	4	10	8	45	42	5
Extended follow-up			16	28	43	27	na	na	na	na	59	55			6.5

I = Intervention, C = control.

Dutch Lipid Clinic Network: criteri per la diagnosi di ipercolesterolemia familiare eterozigote

(Marks D, Atherosclerosis 2002)

	Punti
Storia familiare	
a) Parenti di primo grado con coronaropatia (CHD) prematura (<55 anni negli uomini; <60 anni nelle donne)	1
b) Parenti di primo grado con colesterolo >8 mmol/L ($\geq 310 \text{ mg/dL}$) (o >95° percentile del Paese)	1
c) Parenti di primo grado con xantomi tendinei e/o arco corneale	2
d) Bambini <18 anni con colesterolo >6 mmol/L ($\geq 230 \text{ mg/dL}$) (o >95° percentile del Paese)	2
Storia clinica	
a) Soggetto con CHD prematura (<55 anni negli uomini; <60 anni nelle donne)	2
b) Soggetto con malattia vascolare cerebrale o periferica prematura (<55 anni negli uomini; <60 anni nelle donne)	1
Esame fisico	
a) Xantoma tendineo	6
b) Arco corneale in un soggetto con <45 anni	4
Risultati biochimici (colesterolo LDL)	
>8,5 mmol/L ($>325 \text{ mg/dL}$)	8
6,5-8,4 mmol/L (251-325 mg/dL)	5
5,0-6,4 mmol/L (191-250 mg/dL)	3
4,0-4,9 mmol/L (155-190 mg/dL)	1
Analisi del DNA	
a) Mutazione causativa nota nei geni (LDLR, ApoB, PCSK9)	8



Analisi del DNA

- a) Mutazione causativa nota nei geni (LDLR, ApoB, PCSK9)

8

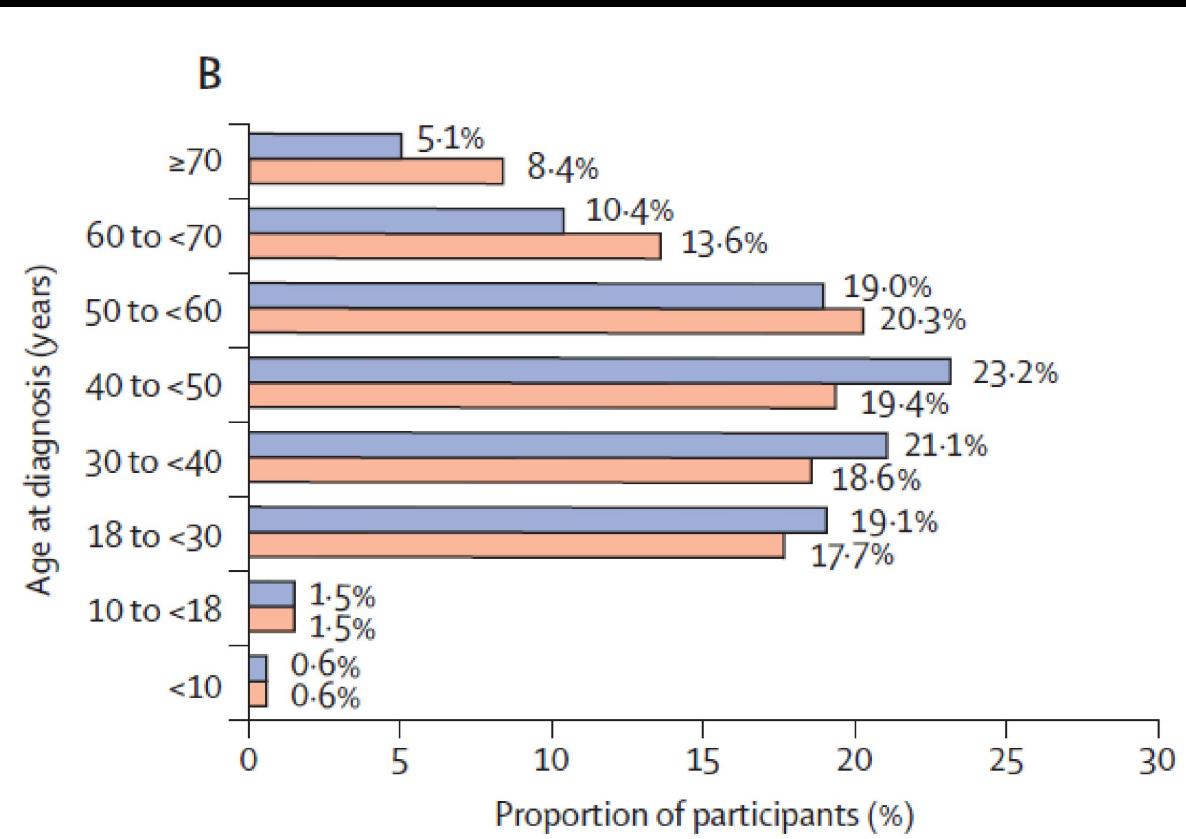
Diagnosi "certa" con un punteggio >8 punti. Diagnosi "probabile" con un punteggio tra 6 e 8 punti. Diagnosi "possibile" con un punteggio tra 3 e 5 punti. Diagnosi "improbabile" con un punteggio tra 0 e 2 punti.

Global perspective of familial hypercholesterolaemia: a cross-sectional study from the EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC)

EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC)*

Lancet 2021; 398: 1713-25

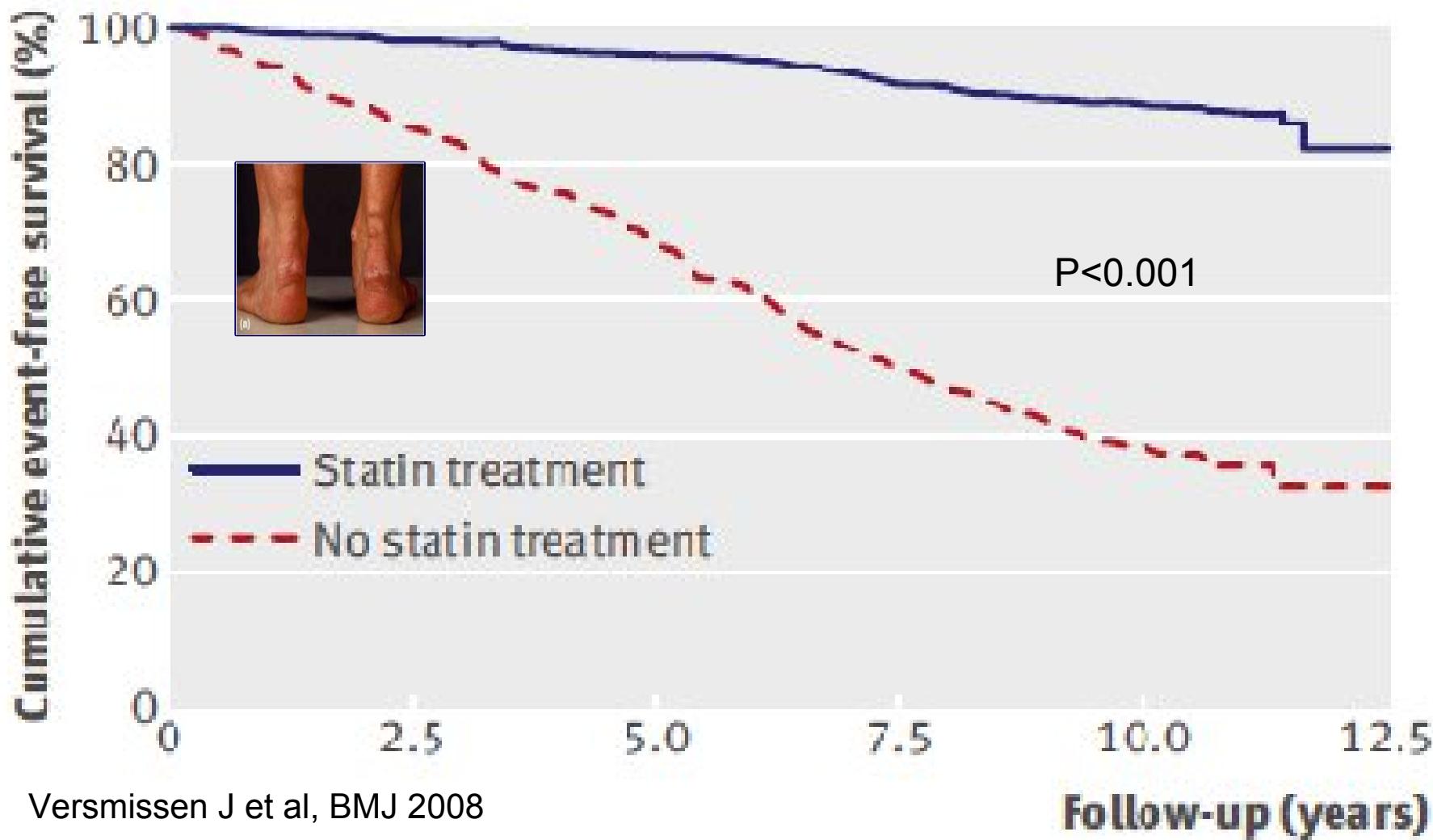
42167 soggetti FH adulti di 56 paesi
75.6% diagnosticati con DLCN



**La diagnosi di FH avviene
ad un'età media di 50 anni,
quando circa 1/3 dei pazienti
M e circa 1/7 dei pazienti F
ha già avuto un evento
coronarico!**

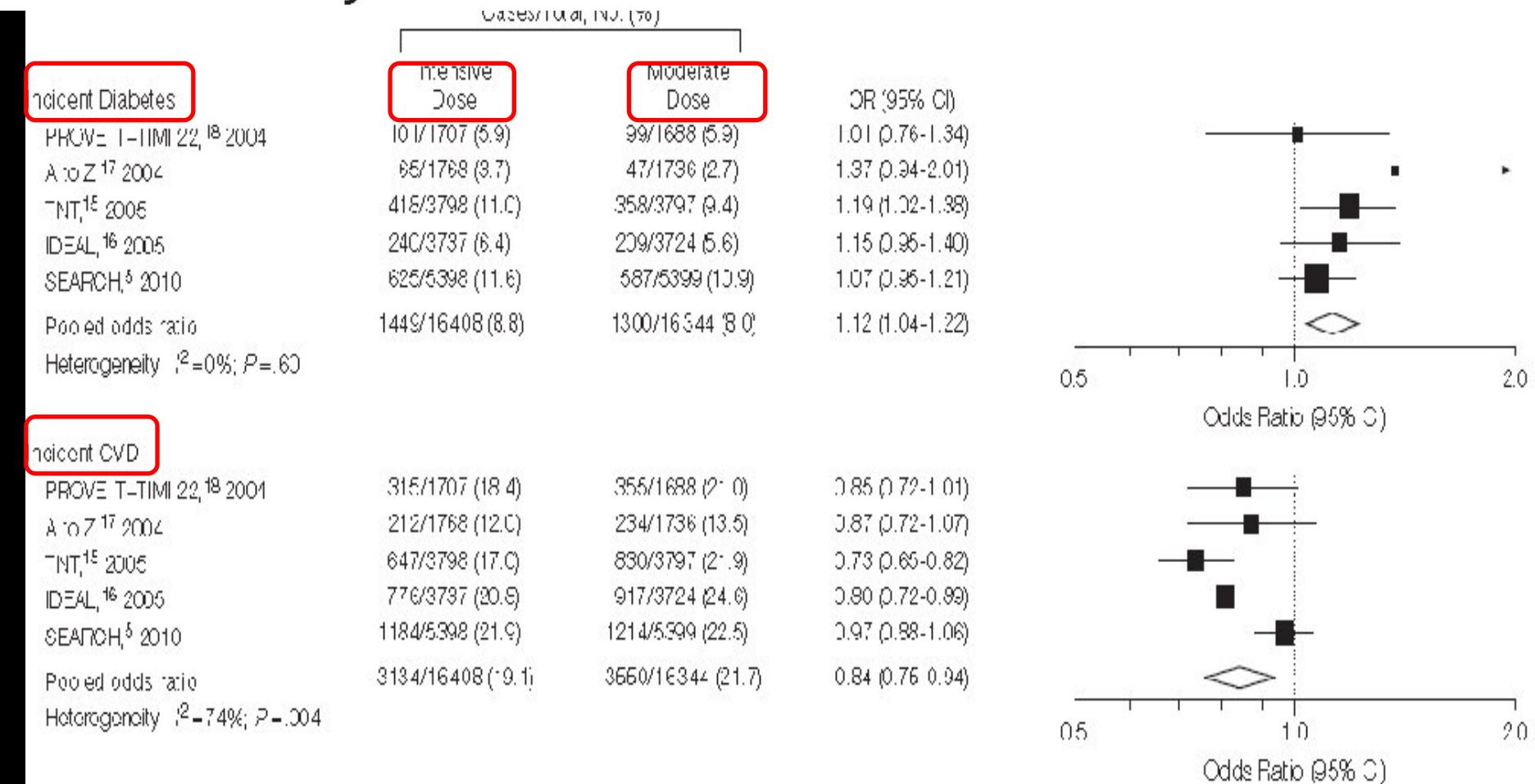
Studio	Pazienti (n.)	Prevalenza eventi coronarici	
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Hopkins et al., 2001	262	15%	41%
Alonso et al., 2002	819	12%	27%

Cumulative CHD-free survival among patients with familial hypercholesterolaemia according to statin therapy



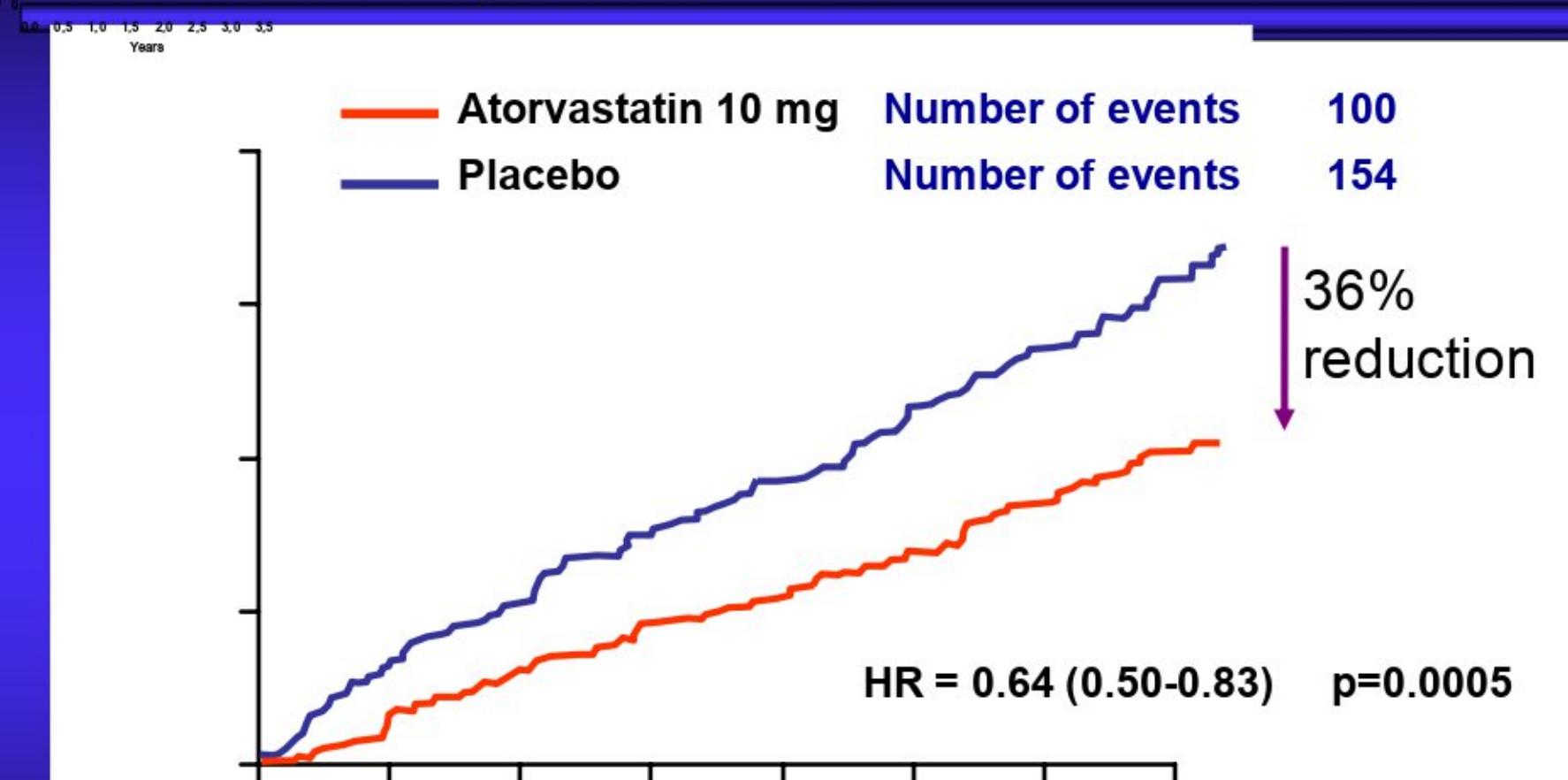
Risk of Incident Diabetes With Intensive-Dose Compared With Moderate-Dose Statin Therapy

A Meta-analysis

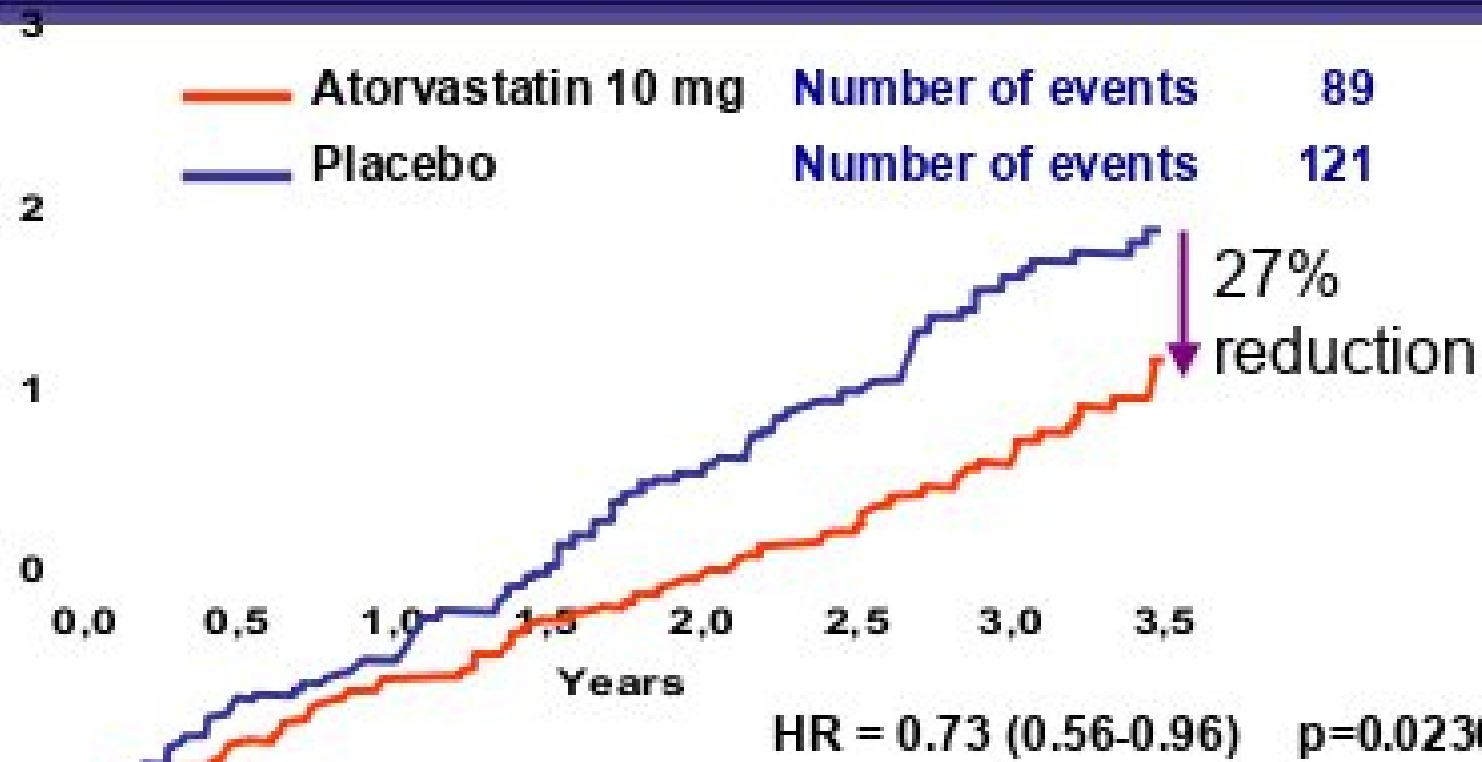


As compared with moderate-dose statin therapy, the number needed to harm per year for moderate-dose statin therapy was 498 for new-onset diabetes while the number needed to treat per year for intensive-dose statin therapy was 155 for cardiovascular events.

ENDPOINT PRIMARIO: IM non-fatale, CHD fatale



ENDPOINT SECONDARIO: ICTUS FATALE E NON-FATALE



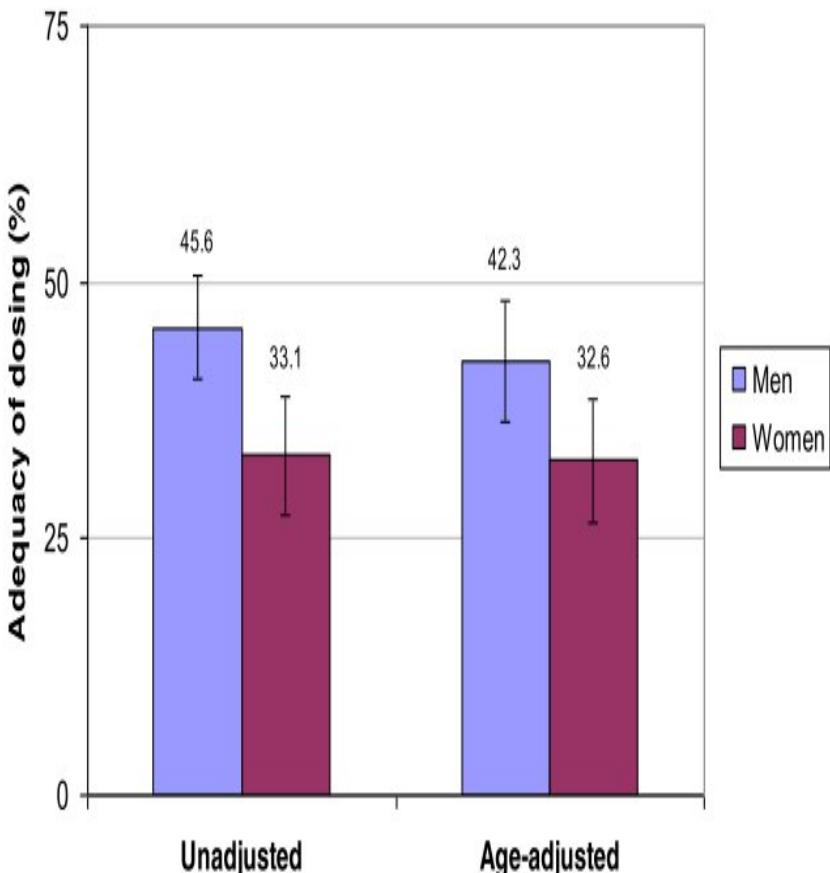


Fig. 1 Crude and age-adjusted gender differences in the proportion of subjects prescribed with adequate statin dose, calculated in the group of patients who received at least one statin prescription

Table 22 Management of dyslipidaemia in women

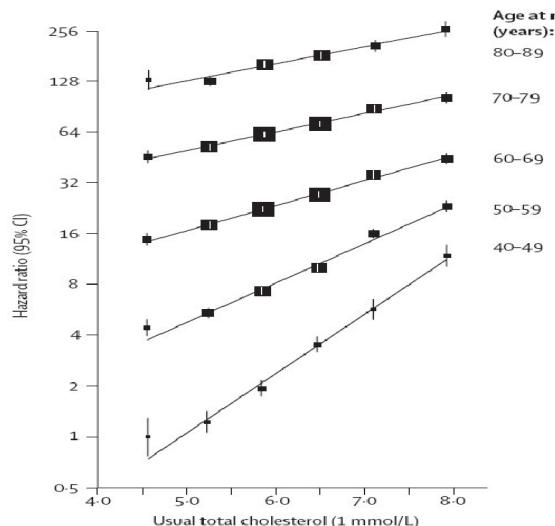
- Statin treatment is recommended for primary prevention of CAD in high risk women.¹⁶
- Statins are recommended for secondary prevention in women with the same indications and targets as in men.^{15, 164}
- Lipid-lowering drugs should not be given when pregnancy is planned, during pregnancy or during the breast feeding period.



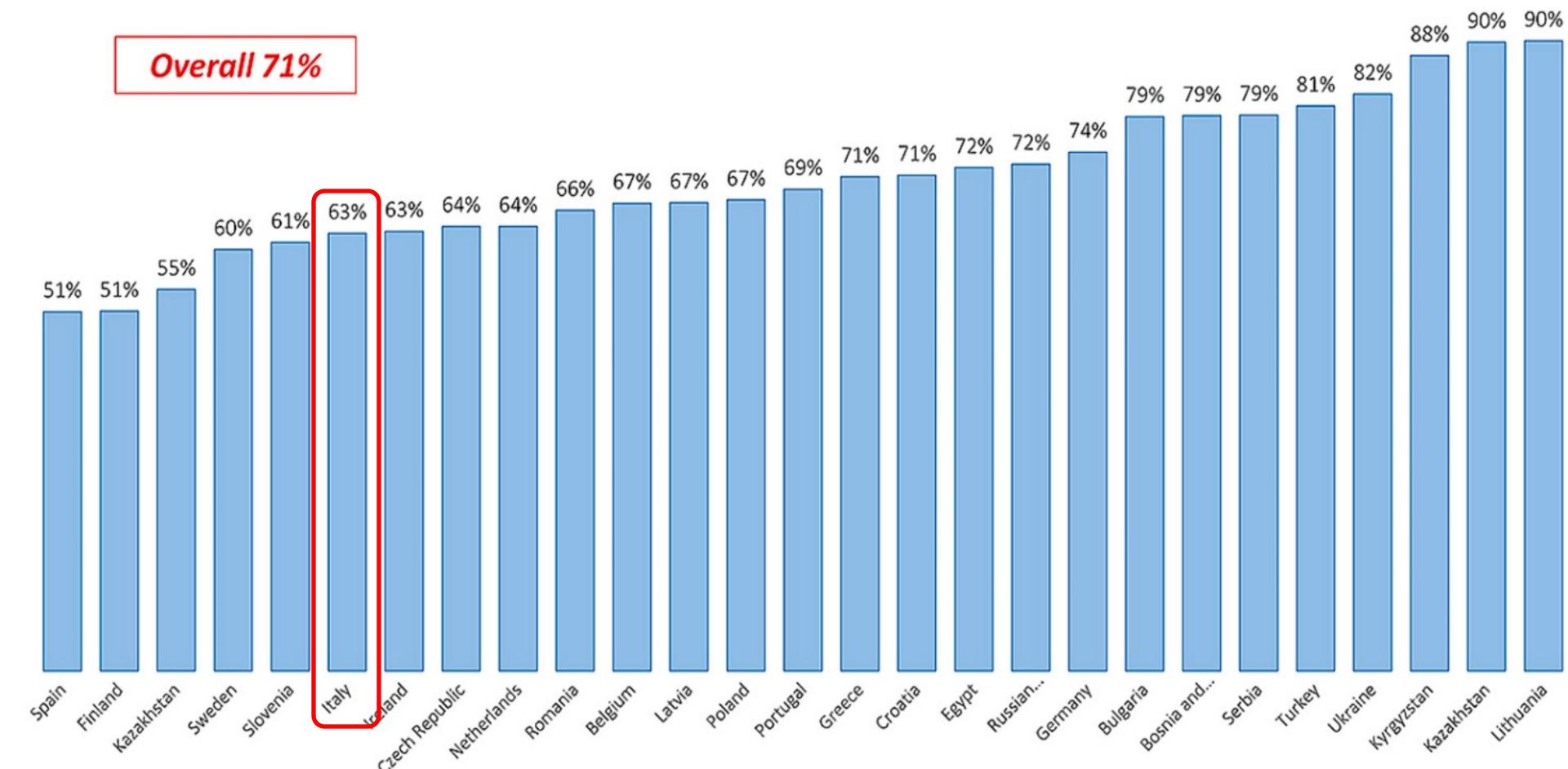
In conclusion, in a population of patients discharged with a diagnosis of chronic HF, female gender was independently associated with lower statin prescription rates and higher probability of inadequate dose. Statin therapy in these subjects was associated with improved 1-year survival in both men and women. This prognostic benefit was not affected by gender.

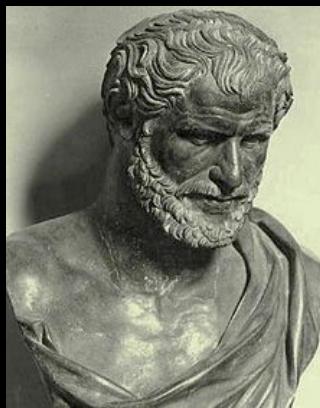
Recommendations for the treatment of dyslipidaemias in older people (>70 years)

Recommendations	Class	Level
Treatment with statins is recommended for older people with ASCVD in the same way as for younger patients.	I	A
Initiation of statin treatment for primary prevention in older people aged ≥ 70 may be considered, if at high risk or above.	IIb	B
It is recommended that the statin is started at a low dose if there is significant renal impairment and/or the potential for drug interactions.	I	C



**2019 The EUROASPIRE V Study - $LDL-C \geq 1.8 \text{ mmol/L}$
($>70 \text{ mg/dL}$)**





Democrito
(460-370 aC):

**“Nelle loro preghiere,
gli uomini domandano aiuto agli dei,
ma non sanno che il potere è nelle loro mani.”**