

LDL come target per il controllo della dislipidemia HIV-correlata

EU vs USA: dove sta la verità?

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8° WORKSHOP NAZIONALE CISAI

PERUGIA, 30 - 31 MARZO 2017

**Prevenzione e gestione
delle co-morbidity associate all'infezione da HIV**

LINEE GUIDA EUROPEE ESH/ESC

Recommendations for cardiovascular risk assessment

Recommendations	Class ^a	Level ^b
Systematic CV risk assessment is recommended in individuals at increased CV risk, i.e. with family history of premature CVD, familial hyperlipidaemia, major CV risk factors (such as smoking, high BP, DM or raised lipid levels) or comorbidities increasing CV risk.	I	C
It is recommended to repeat CV risk assessment every 5 years, and more often for individuals with risks close to thresholds mandating treatment.	I	C
Systematic CV risk assessment may be considered in men >40 years of age and in women >50 years of age or post-menopausal with no known CV risk factors.	IIb	C
Systematic CV risk assessment in men <40 of age and women <50 years of age with no known CV risk factors is not recommended.	III	C

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Eur Heart J 2016;37;2315--81

CATEGORIE DI RISCHIO

Very high-risk

Subjects with any of the following:

- Documented CVD, clinical or unequivocal on imaging. Documented clinical CVD includes previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Unequivocally documented CVD on imaging includes significant plaque on coronary angiography or carotid ultrasound. It does NOT include some increase in continuous imaging parameters such as intima-media thickness of the carotid artery.
- DM with target organ damage such as proteinuria or with a major risk factor such as smoking or marked hypercholesterolaemia or marked hypertension.
- Severe CKD (GFR <30 mL/min/1.73 m²).
- A calculated SCORE ≥10%.

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CATEGORIE DI RISCHIO

High-risk

Subjects with:

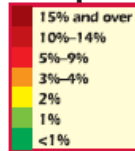
- Markedly elevated single risk factors, in particular cholesterol >8 mmol/L (>310 mg/dL) (e.g. in familial hypercholesterolaemia) or BP $\geq 180/110$ mmHg.
- Most other people with DM (with the exception of young people with type 1 DM and without major risk factors that may be at low or moderate risk).
- Moderate CKD (GFR 30–59 mL/min/1.73 m²).
- A calculated SCORE $\geq 5\%$ and $< 10\%$.

CATEGORIE DI RISCHIO

Moderate-risk	SCORE is $\geq 1\%$ and $< 5\%$ at 10 years. Many middle-aged subjects belong to this category.
Low-risk	SCORE $< 1\%$.



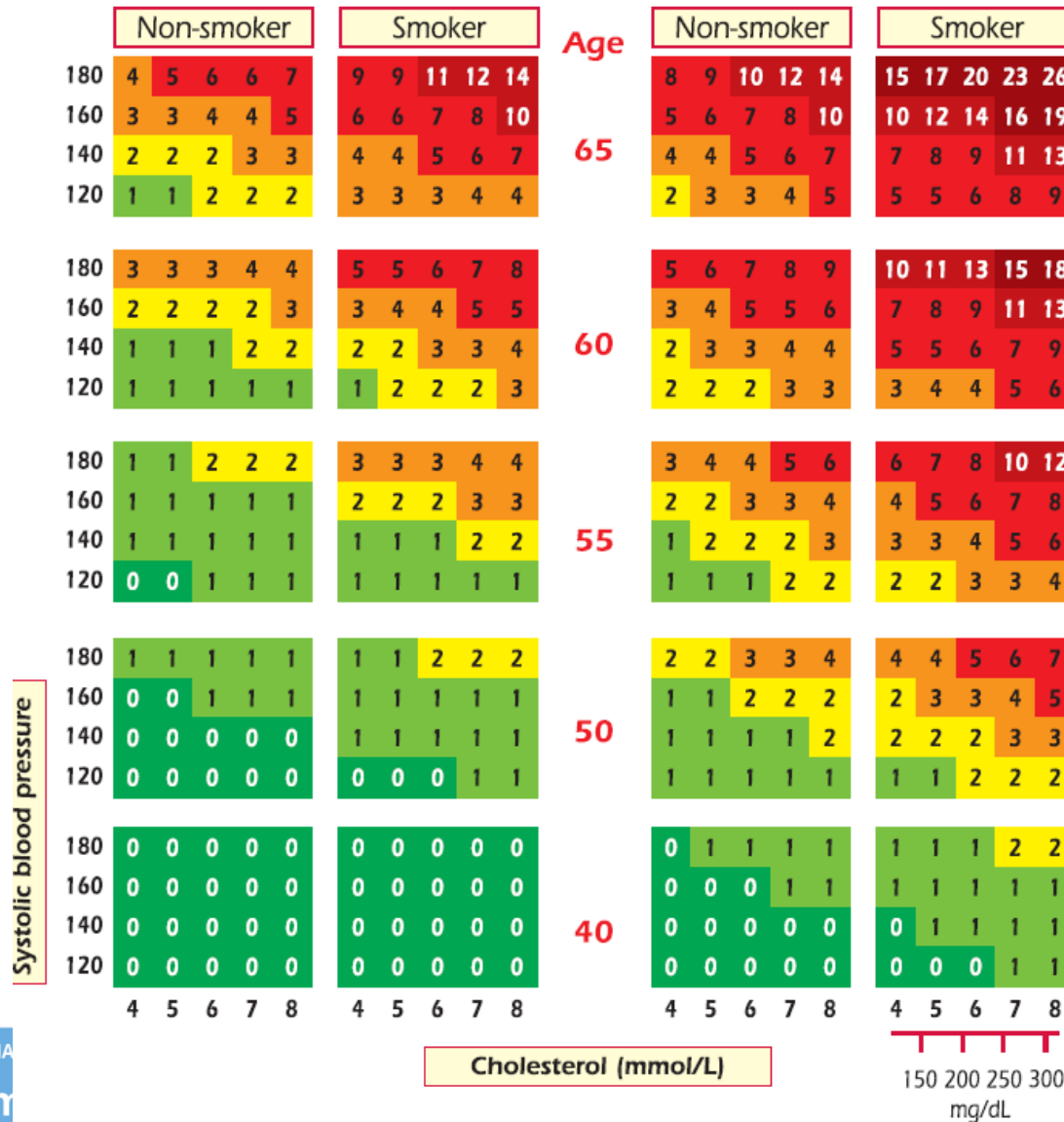
SCORE



10-year risk of fatal CVD in populations at low CVD risk

WOMEN

MEN



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delle co-m

Table 6 Risk factor goals and target levels for important cardiovascular risk factors

Smoking	No exposure to tobacco in any form.
Diet	Low in saturated fat with a focus on wholegrain products, vegetables, fruit and fish.
Physical activity	At least 150 minutes a week of moderate aerobic PA (30 minutes for 5 days/week) or 75 minutes a week of vigorous aerobic PA (15 minutes for 5 days/week) or a combination thereof.
Body weight	BMI 20–25 kg/m ² . Waist circumference <94 cm (men) or <80 cm (women).
Blood pressure	<140/90 mmHg ^a
Lipids^b LDL ^c is the primary target	Very high-risk: <1.8 mmol/L (<70 mg/dL) , or a reduction of at least 50% if the baseline is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL) ^d High-risk: <2.6 mmol/L (<100 mg/dL) , or a reduction of at least 50% if the baseline is between 2.6 and 5.1 mmol/L (100 and 200 mg/dL) Low to moderate risk: <3.0 mmol/L (<115 mg/dL).
HDL-C	No target but >1.0 mmol/L (>40 mg/dL) in men and >1.2 mmol/L (>45 mg/dL) in women indicate lower risk.
Triglycerides	No target but <1.7 mmol/L (<150 mg/dL) indicates lower risk and higher levels indicate a need to look for other risk factors.
Diabetes	HbA1c <7%. (<53 mmol/mol)

Table 13 Possible intervention strategies as a function of total cardiovascular risk and low-density lipoprotein cholesterol level

Total CV risk (SCORE) %	LDL-C levels				
	<70 mg/dL <1.8 mmol/L	70 to <100 mg/dL 1.8 to <2.6 mmol/L	100 to <155 mg/dL 2.6 to <4.0 mmol/L	155 to <190 mg/dL 4.0 to <4.9 mmol/L	≥190 mg/dL ≥4.9 mmol/L
<1	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle advice, consider drug if uncontrolled
Class ^a /Level ^b	I/C	I/C	I/C	I/C	IIa/A
≥1 to <5	Lifestyle advice	Lifestyle advice	Lifestyle advice, consider drug if uncontrolled	Lifestyle advice, consider drug if uncontrolled	Lifestyle advice, consider drug if uncontrolled
Class ^a /Level ^b	I/C	I/C	IIa/A	IIa/A	I/A
≥5 to <10, or high-risk	Lifestyle advice	Lifestyle advice, consider drug if uncontrolled	Lifestyle advice and drug treatment for most	Lifestyle advice and drug treatment	Lifestyle advice and drug treatment
Class ^a /Level ^b	IIa/A	IIa/A	IIa/A	I/A	I/A
≥10 or very high-risk	Lifestyle advice, consider drug	Lifestyle advice and concomitant drug treatment	Lifestyle advice and concomitant drug treatment	Lifestyle advice and concomitant drug treatment	Lifestyle advice and concomitant drug treatment
Class ^a /Level ^b	IIa/A	IIa/A	I/A	I/A	I/A

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Neil J. Stone, Jennifer Robinson, Alice H. Lichtenstein, C. Noel Bairey Merz, Conrad B. Blum, Robert H. Eckel, Anne C. Goldberg, David Gordon, Daniel Levy, Donald M. Lloyd-Jones, Patrick McBride, J. Sanford Schwartz, Susan T. Shero, Sidney C. Smith, Jr, Karol Watson and Peter W.F. Wilson

Circulation. 2014;129:S1-S45

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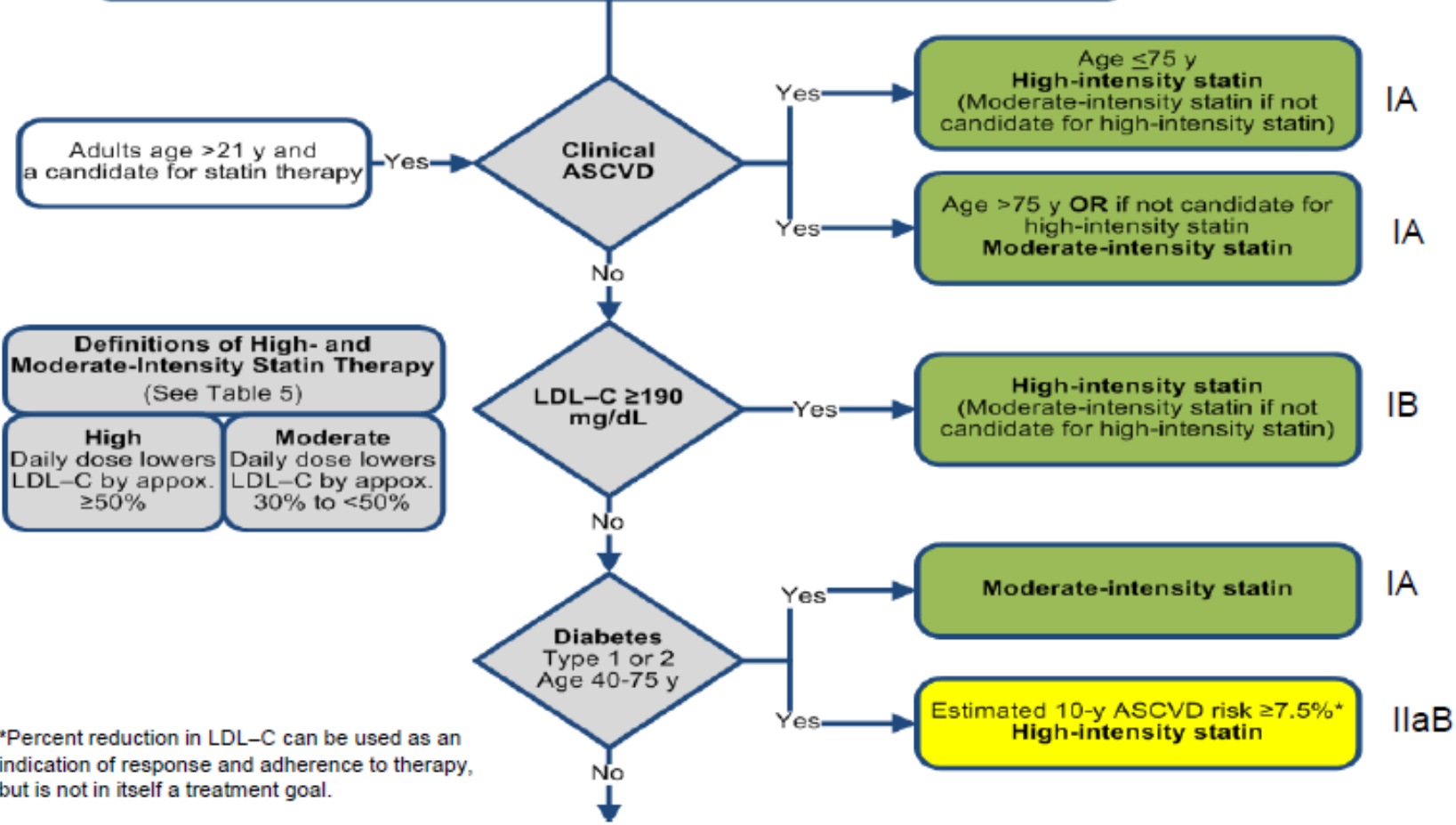
**Prevenzione e gestione
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4 Statin Benefit Groups

- 1- Individui con evidenze cliniche di malattia cardiovascolare aterosclerotica:
infarto miocardico, stroke, SCA, arteriopatia obliterante periferica, storia di rivascolarizzazione in distretti arteriosi → PREVENZIONE SECONDARIA
- 2- Individui con aumento primario del c-LDL oltre 190 mg/dL
Valore molto alto che spesso sono paziente con dislipidemie familiari considerati ad alto rischio
- 3- Diabetici nella fascia di età 40-75 anni e con c-LDL > 70 mg/dL senza evidenze cliniche di ASCVD → rischio almeno alto
- 4- Individui senza ASCVD o diabete, con c-LDL >70mg/dL e rischio stimato di ASCVD a 10 anni $\geq 7,5\%$

Circulation. 2014;129:S1-S45

ASCVD Statin Benefit Groups
 Heart healthy lifestyle habits are the foundation of ASCVD prevention. In individuals not receiving cholesterol-lowering drug therapy, recalculate estimated 10-y ASCVD risk every 4-6 y in individuals aged 40-75 y without clinical ASCVD or diabetes and with LDL-C 70-189 mg/dL.

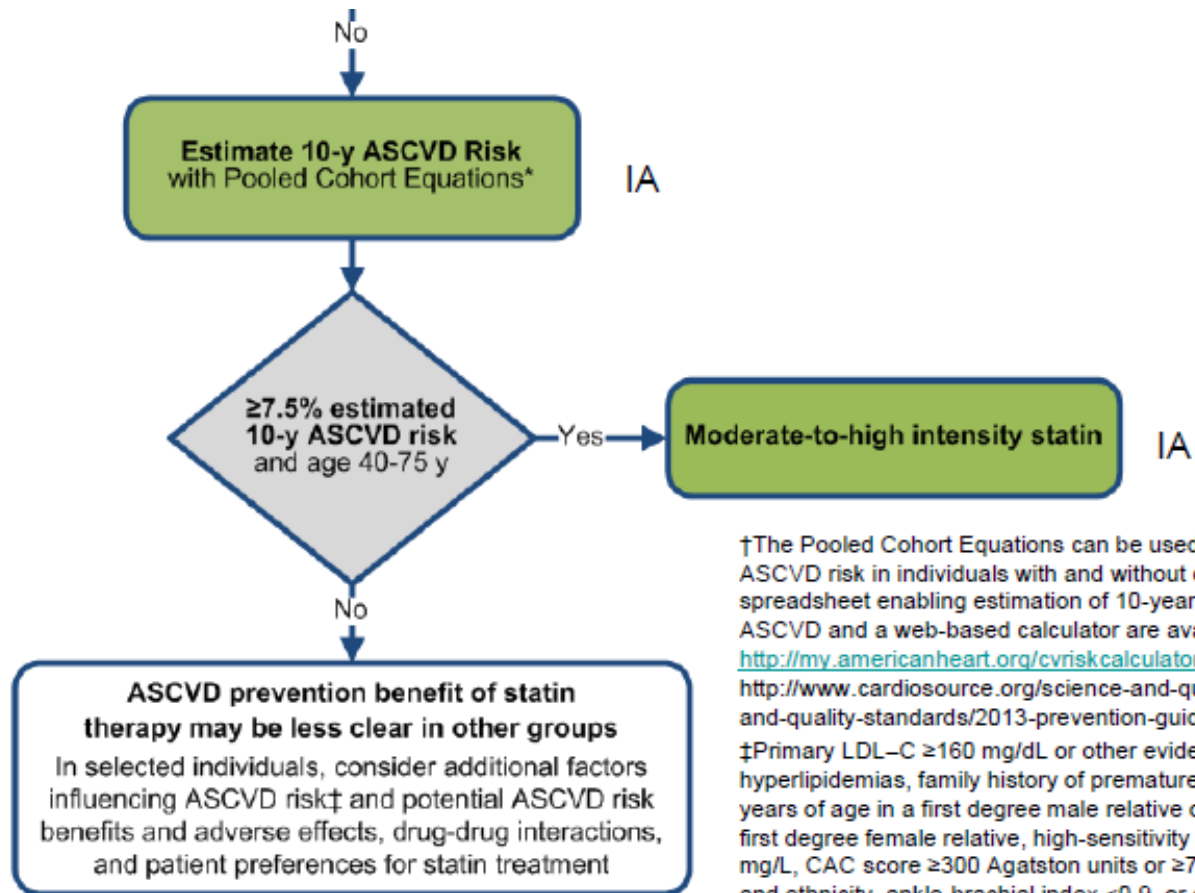


Definitions of High- and Moderate-Intensity Statin Therapy
 (See Table 5)

High Daily dose lowers LDL-C by approx. ≥50%	Moderate Daily dose lowers LDL-C by approx. 30% to <50%
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*Percent reduction in LDL-C can be used as an indication of response and adherence to therapy, but is not in itself a treatment goal.





†The Pooled Cohort Equations can be used to estimate 10-year ASCVD risk in individuals with and without diabetes. A downloadable spreadsheet enabling estimation of 10-year and lifetime risk for ASCVD and a web-based calculator are available at <http://my.americanheart.org/cvriskcalculator> and <http://www.cardiosource.org/science-and-quality/practice-guidelines-and-quality-standards/2013-prevention-guideline-tools.aspx>.

‡Primary LDL-C ≥160 mg/dL or other evidence of genetic hyperlipidemias, family history of premature ASCVD with onset <55 years of age in a first degree male relative or <65 years of age in a first degree female relative, high-sensitivity C-reactive protein ≥2 mg/L, CAC score ≥300 Agatston units or ≥75 percentile for age, sex, and ethnicity, ankle-brachial index <0.9, or elevated lifetime risk of ASCVD.



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Circulation. 2014;129:S1-S45

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INTENSITA' STATINE

Table 5. High-, Moderate-, and Low-Intensity Statin Therapy (Used in the RCTs Reviewed by the Expert Panel)*

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL-C, on average, by approximately $\geq 50\%$	Daily dose lowers LDL-C, on average, by approximately 30% to $< 50\%$	Daily dose lowers LDL-C, on average, by $< 30\%$
Atorvastatin (40†)–80 mg Rosuvastatin 20 (40) mg	Atorvastatin 10 (20) mg Rosuvastatin (5) 10 mg Simvastatin 20–40 mg‡ Pravastatin 40 (80) mg Lovastatin 40 mg Fluvastatin XL 80 mg Fluvastatin 40 mg BID Pitavastatin 2–4 mg	Simvastatin 10 mg Pravastatin 10–20 mg Lovastatin 20 mg Fluvastatin 20–40 mg Pitavastatin 1 mg

Circulation. 2014;129:S1-S45



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- In those not clearly in 1 of 4 statin benefit groups, additional factors may inform treatment decision-making:
 - *Family history of premature ASCVD*
 - *Elevated lifetime risk of ASCVD*
 - *LDL-C ≥ 160 mg/dL*
 - *hs-CRP ≥ 2.0 mg/L*
 - *Subclinical atherosclerosis*
 - *CAC score ≥ 300 or ABI < 0.9*
- Discussion of potential for ASCVD risk reduction benefit, potential for adverse effects, drug-drug interactions, and patient preferences



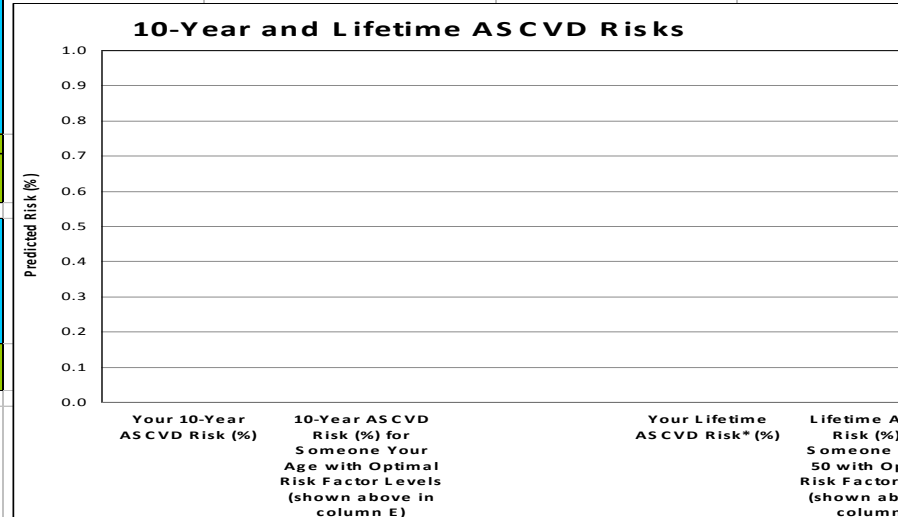
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RISK CALCULATOR

Risk Factor	Units	Enter patient values in this column	Acceptable range of values	Optimal values
Sex		M (for males) or F (for females)	M or F	
Age	years		20-79	
Race		AA (for African Americans) or WH (for whites or others)	AA or WH	
Total Cholesterol	mg/dL		130-320	170
HDL-Cholesterol	mg/dL		20-100	50
Systolic Blood Pressure	mm Hg		90-200	110
Treatment for High Blood Pressure		Y (for yes) or N (for no)	Y or N	N
Diabetes		Y (for yes) or N (for no)	Y or N	N
Smoker		Y (for yes) or N (for no)	Y or N	N

Your 10-Year ASCVD Risk (%)	This calculator only provides 10-year risk estimates for individuals 40 to 79 years of age Enter M or F for Gender Enter WH or AA for race Enter 130-320 for TC value Enter 20-100 for HDL value Enter 90-200 for SBP value Enter Y or N for treatment for hypertension Enter Y or N for Diabetes Enter Y or N for Smoker
10-Year ASCVD Risk (%) for Someone Your Age with Optimal Risk Factor Levels (shown above in column E)	Enter M or F for Gender This calculator only provides 10-year risk estimates for individuals 40 to 79 years of age Enter WH or AA for race
Your Lifetime ASCVD Risk* (%)	This calculator only provides lifetime risk estimates for individuals 20 to 59 years of age Enter M or F for Gender Enter 130-320 for TC value Enter 90-200 for SBP value Enter Y or N for treatment for Hypertension Enter Y or N for Diabetes Enter Y or N for Smoker
Lifetime ASCVD Risk (%) for Someone at Age 50 with Optimal Risk Factor Levels (shown above in column E)	Enter M or F for gender



*This is the lifetime ASCVD risk for an individual at age 50 years with your risk factor levels. In rare cases, 10-year risks may exceed lifetime risks given that the estimates come from different approaches. While 10-year risk estimates are derived from methods and data using continuous variables, the reported estimate of lifetime risk is based on assigning each person into one of 5 mutually exclusive sex-specific groups, as per Lloyd-Jones et al., Circulation 2006; 113(6):791-8. Within each of the 5 groups, each person receives the same lifetime risk estimate. In other words, using this approach, there are only 5 possible lifetime risk estimates reported for men and only 5 possible lifetime risk estimates reported for women. In some cases, the average risk for the group will underestimate the individual's true lifetime risk. This feature of lifetime risk estimation will result in the estimated lifetime risk being less than the estimated 10-year risk. In these cases, the 10-year risk should be the primary focus for the risk discussion and risk reduction efforts. As further data becomes available

For patients and the public: *This is the lifetime risk of cardiovascular diseases, including stroke, for an individual at age 50 years with your risk factor levels. In rare cases, 10-year risks may exceed lifetime risks given that the estimates come from different mathematical approaches. If this is the case, the 10-year risk should be the primary focus for your risk discussion with your provider and for your efforts to reduce your risk.

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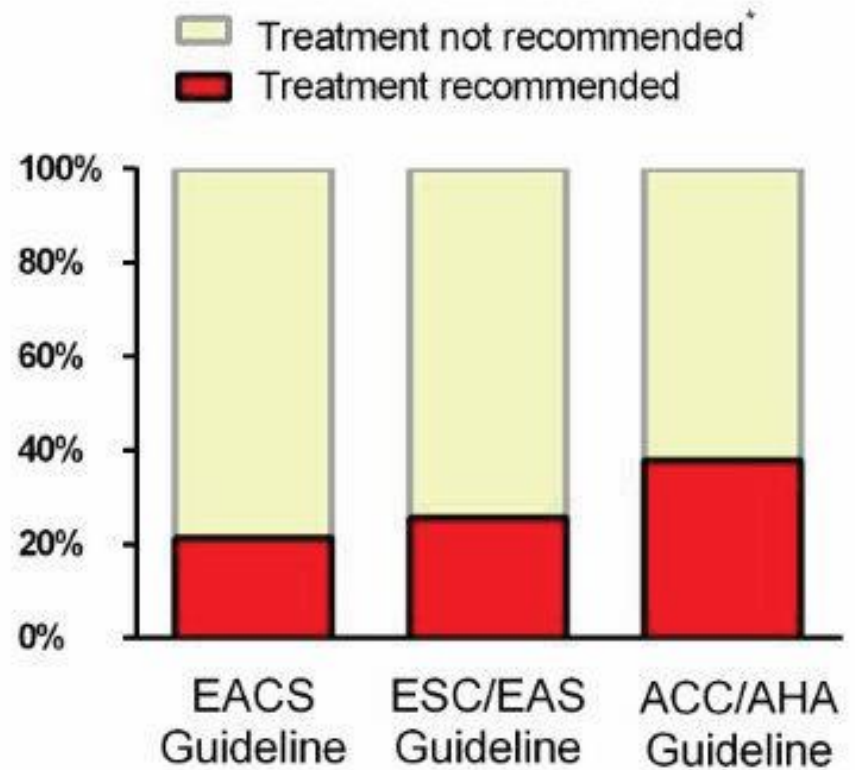
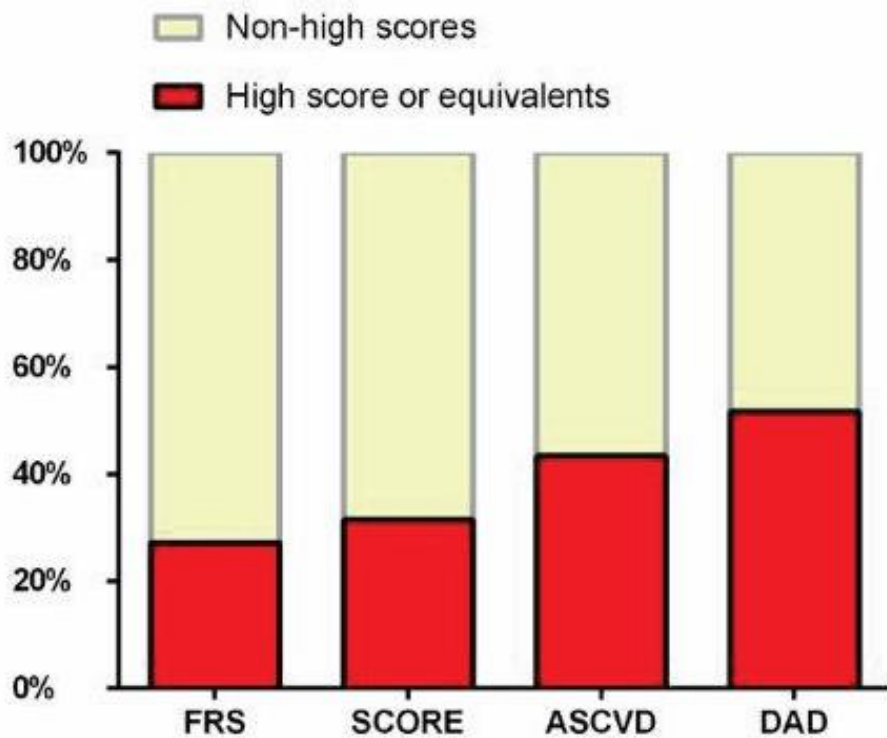
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Prevenzione e gestione delle co-morbidity associate all'infezione da HIV

Tabella: Somiglianze e differenze nella terapia farmacologica tra il documento 2011 ESC-EAS Management of Dyslipidaemias Guidelines e quello 2013 ACC/AHA Guidelines on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk

	EAS/ESC	AHA/ACC
Prevenzione secondaria	Target c-LDL <70 mg/dL (1,8 mmol/L) o almeno una riduzione del 50%. Se il target non può essere raggiunto con la statina, può essere considerata una combinazione di farmaci.	Terapia intensiva con statine. Se non si raggiunge una riduzione del 50%, può essere considerata una combinazione di farmaci.
Intolleranza alle statine in prevenzione secondaria	Ridurre la dose di statina, considerare la terapia di combinazione.	Statina a dose bassa o moderata, considerare la terapia di combinazione.
Prevenzione primaria in soggetti con c-LDL >190 mg/dL (4,9 mmol/L)	Target LDL-C <100 mg/dL (2,5 mmol/L). Se non si riesce a raggiungere il target, perseguire la massima riduzione del c-LDL utilizzando appropriate combinazioni di farmaci a dosi tollerate.	Terapia intensiva con statine, per raggiungere almeno una riduzione del 50% del c-LDL. Se non si riesce a raggiungere una riduzione del 50%, considerare una terapia aggiuntiva.
Prevenzione primaria in soggetti diabetici	Diabete con altri fattori di rischio o danno d'organo: Target c-LDL <70 mg/dL (1,8 mmol/L) o almeno una riduzione del 50%. Diabete non complicato: Target c-LDL <100 mg/dL (2,5 mmol/L)	Diabete e alto rischio: terapia intensiva con statine. Diabete e basso rischio: terapia con statine a moderata intensità.
Prevenzione primaria in soggetti ad alto rischio	Rischio di CVD fatali SCORE $\geq 5\%$: Target c-LDL <100 mg/dL (2,5 mmol/L)	Rischio totale di eventi CV >7,5%: terapia con statine a intensità moderata-alta. Rischio di eventi CV 5-7,5%: terapia con statine a intensità moderata.



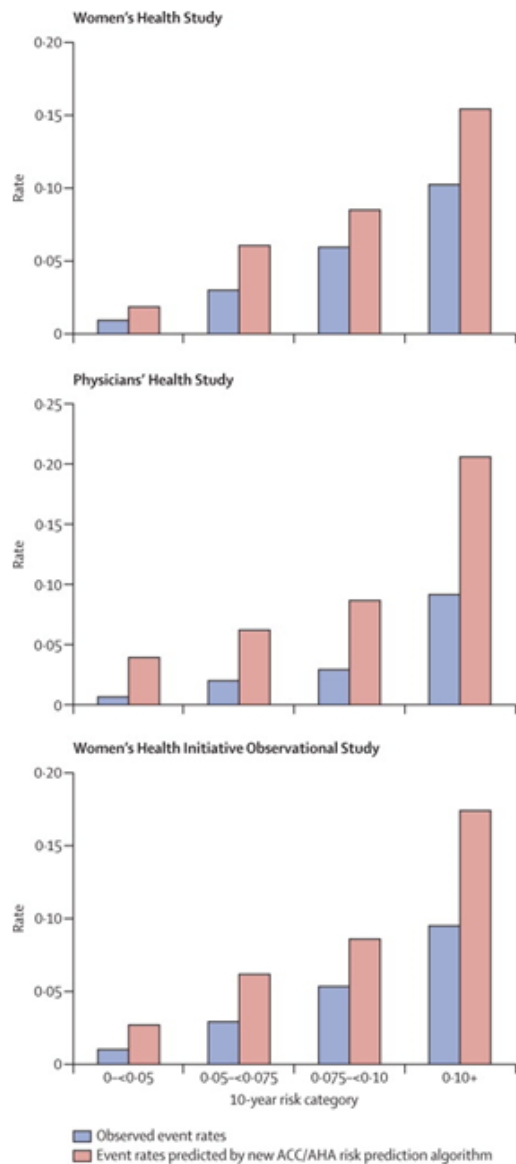


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Croat Med J. 2015;56:14-23



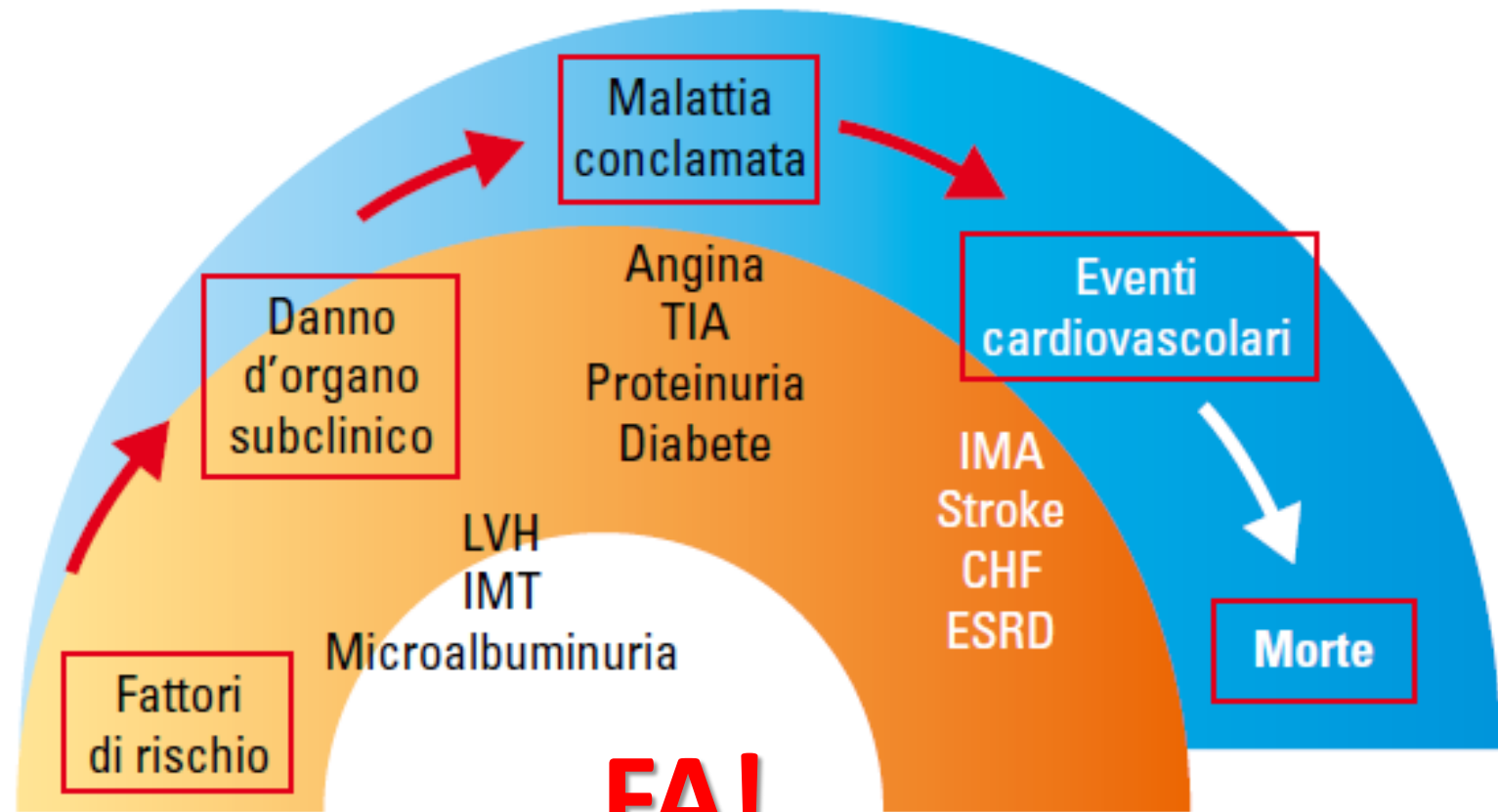
Lancet. 2013;382(9907):1762-5

Figure 1. Comparison of observed event rates with event rates predicted by new ACC/AHA risk prediction algorithm in three external validation primary prevention cohorts: the Women's Health Study, the Physicians' Health Study, and the Women's Health Initiative ...

Table 2. Treatment Recommendations Based on Different Guidelines

Treatment Categories	Guideline ^a		
	ACC/AHA ⁵	ATP-III ⁴	ESC ⁶
Men (n = 1894)^b			
Treatment recommended	96.4 (95.4-97.1)	52.0 (49.8-54.3)	66.1 (64.0-68.3)
Treatment considered	3.3 (2.6-4.2)	14.2 (12.6-15.8)	31.6 (29.5-33.7)
No treatment	0.3 (0.1-0.7)	33.8 (31.7-35.9)	2.3 (1.6-2.9)
Women (n = 2315)^b			
Treatment recommended	65.8 (63.8-67.7)	35.5 (33.5-37.5)	39.1 (37.1-41.2)
Treatment considered	14.2 (12.8-15.7)	14.1 (12.7-15.6)	51.4 (49.3-53.4)
No treatment	20.0 (18.3-21.6)	50.4 (48.4-52.5)	9.5 (8.3-10.8)

Il continuum cardiovascolare



FA!

Iperensione
Diabete
LDL elevate, ecc.

CHF: Scompenso cardiaco
ESRD: Malattia renale allo stadio terminale
LVH: Ipertrofia ventricolare sinistra
IMT: Spessore media intimale

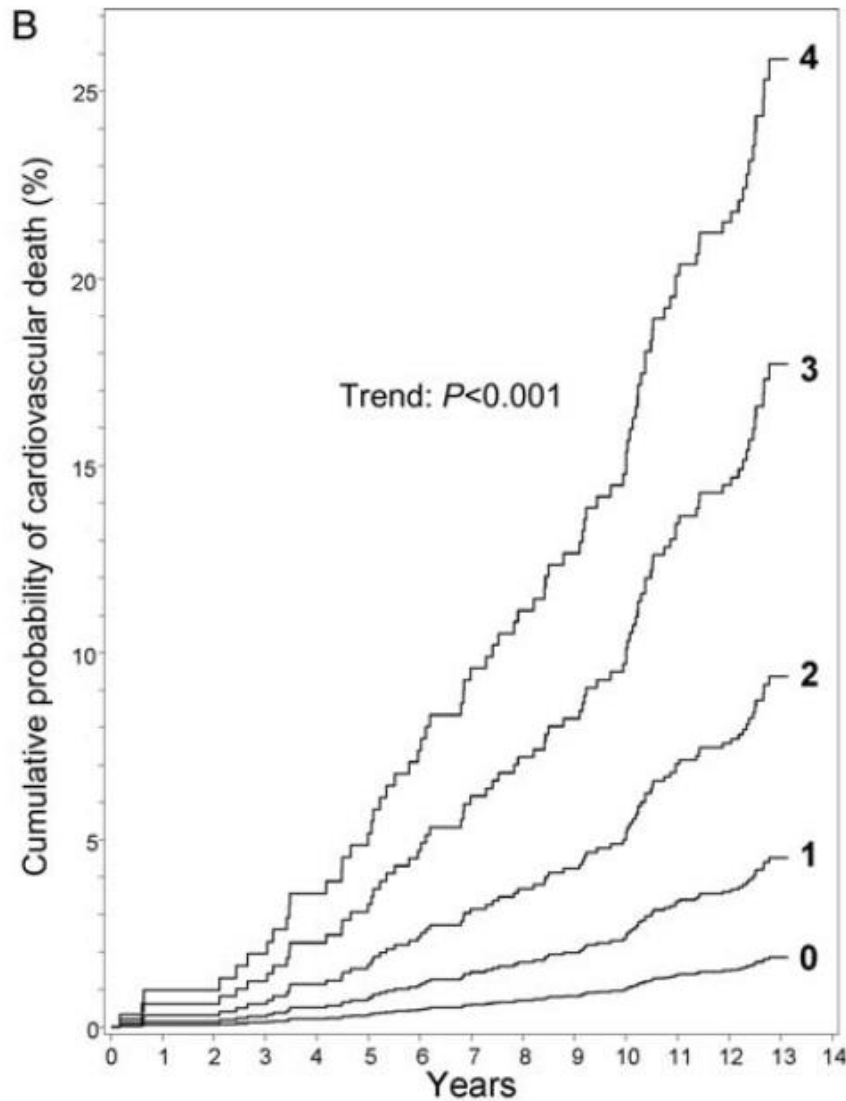
Risk prediction is improved by adding markers of subclinical organ damage to SCORE

Table 2 Hazard ratios for cardiovascular death for markers of subclinical organ damage in multiple Cox regression models

Model		Hazard ratio	95% CI	P-value
Each marker separately, adjusted for age and gender				
LV hypertrophy (n = 101)		2.2	(1.2–4.0)	0.01
Atherosclerotic plaques (n = 440)		2.1	(1.3–3.3)	0.003
PWV > 12 m/s (n = 464)		2.0	(1.2–3.5)	0.008
UACR ≥ 90th percentile (n = 198)		2.4	(1.4–4.0)	0.0009
SCORE plus each marker separately				
	SCORE			
LV hypertrophy	≥5%	2.2	(1.2–4.1)	0.02
	<5%	1.9	(1.3–13.9)	0.01
Atherosclerotic plaques	≥5%	2.1	(1.2–3.6)	0.007
	<5%	3.9	(1.7–9.2)	0.002
PWV > 12 m/s ^a	≥5%	1.9	(1.1–3.3)	0.03
	<5%	7.3	(3.2–16.4)	<0.001
UACR ≥ 90th percentile	≥5%	2.2	(1.2–4.0)	0.008
	<5%	3.4	(1.3–9.3)	0.01

LV hypertrophy, left ventricular hypertrophy; PWV, pulse wave velocity; UACR, urine/albumin creatinine ratio.

^aOnly PWV had an significant interaction with SCORE ($P = 0.008$).



European Heart Journal (2010) **31**, 883–891

Number of subclinical organ damage	0 (<i>n</i> =1127)	1 (<i>n</i> =563)	2 (<i>n</i> =206)	3 (<i>n</i> =60)	4 (<i>n</i> =12)
Hazard ratios (95%CI)	1	2.6 (1.3–5.1)	5.7 (2.9–11.4)	11.4 (5.2–25.0)	18.3 (5.9–57.1)
Adjusted for SCORE					

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delle co-morbidity as

IN SINTESI

LA MESSA A PUNTO DI UNA ADEGUATA STRATEGIA DI PREVENZIONE CARDIOVASCOLARE NON POTRA' MAI ESSERE LA SEMPLICE APPLICAZIONE DI UNO SCHEMA (PUR IMPORTANTE),

MA NON DOVRA' MAI PRESCINDERE DA UNA ATTENTA E TENDENZIALMENTE COMPLETA VALUTAZIONE DEL GRADO DI COMPROMISSIONE D'ORGANO DEL PAZIENTE, SOPRATTUTTO NEI SOGGETTI IN PREVENZIONE PRIMARIA.

