Capitolo 5

La prevenzione cardiovascolare
e la nota 13

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European Guidelines

The 2012 European Guidelines on Cardiovascular Disease Prevention in Clinical Practice

Chairperson

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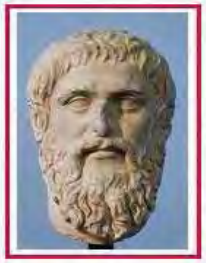
Guidelines based upon the five principles of teaching



Plato, 424-347 b. C.

1. **What** is CVD prevention.
2. **Why** is CVD prevention needed.
3. **Who** needs CVD prevention.
4. **How** is CVD prevention applied.
5. **Where** should CVD prevention be offered.

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What is CVD prevention?

"A coordinated set of actions, at public and individual level, aimed at eradicating, eliminating or minimizing the impact of cardiovascular diseases and their related disability.

The bases of prevention are rooted in cardiovascular epidemiology and evidence-based medicine"

A Dictionary of Epidemiology. 4th ed New York: Oxford University Press; 2001.

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Why is CVD prevention needed?

Atherosclerotic CVD, especially CHD, remains the leading cause of premature death worldwide.

CVD affects both men and women; of all deaths that occur before the age of 75 years in Europe, 42% are due to CVD in women and 38% in men.

Prevention works: over 50% of the reductions seen in CHD mortality relate to changes in risk factors, and 40% to improved treatments.

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Very high risk

- **Subjects with any of the following:**
  - Documented CVD by invasive or non-invasive testing (such as coronary angiography, nuclear imaging, stress echocardiography, carotid plaque on ultrasound), previous myocardial infarction, ACS, coronary revascularization (PCI, CABG) and other arterial revascularization procedures, ischaemic stroke, peripheral artery disease.
  - Diabetes mellitus (type 1 or type 2) with one or more CV riskfactors and/or target organ damage (such as microalbuminuria: 30-300 mg/24 h).
  - Severe chronic kidney disease (CKD) (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m^2).
  - A calculated SCORE ≥10%.

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Other risk groups

- **High risk:**
  - Markedly elevated single risk factors such as familial dyslipidaemias and severe hypertension,
  - Diabetes mellitus (type 1 or type 2) but without CV riskfactors or target organ damage,
  - Moderate chronic kidney disease (CKD) (estimated glomerular filtration rate [eGFR] 30-59 mL/min/1.73 m^2),
  - A calculated SCORE of ≥5% and <10% for 10-year risk of fatal CVD.
- **Moderate risk:**
  - Subjects are considered to be at moderate risk when their SCORE is ≥1 and <5% at 10 years. Many middle-aged subjects belong to this category.
- **Low risk:**
  - The low-risk category applies to individuals with a SCORE <1% and free of qualifiers that would put them at moderate risk.

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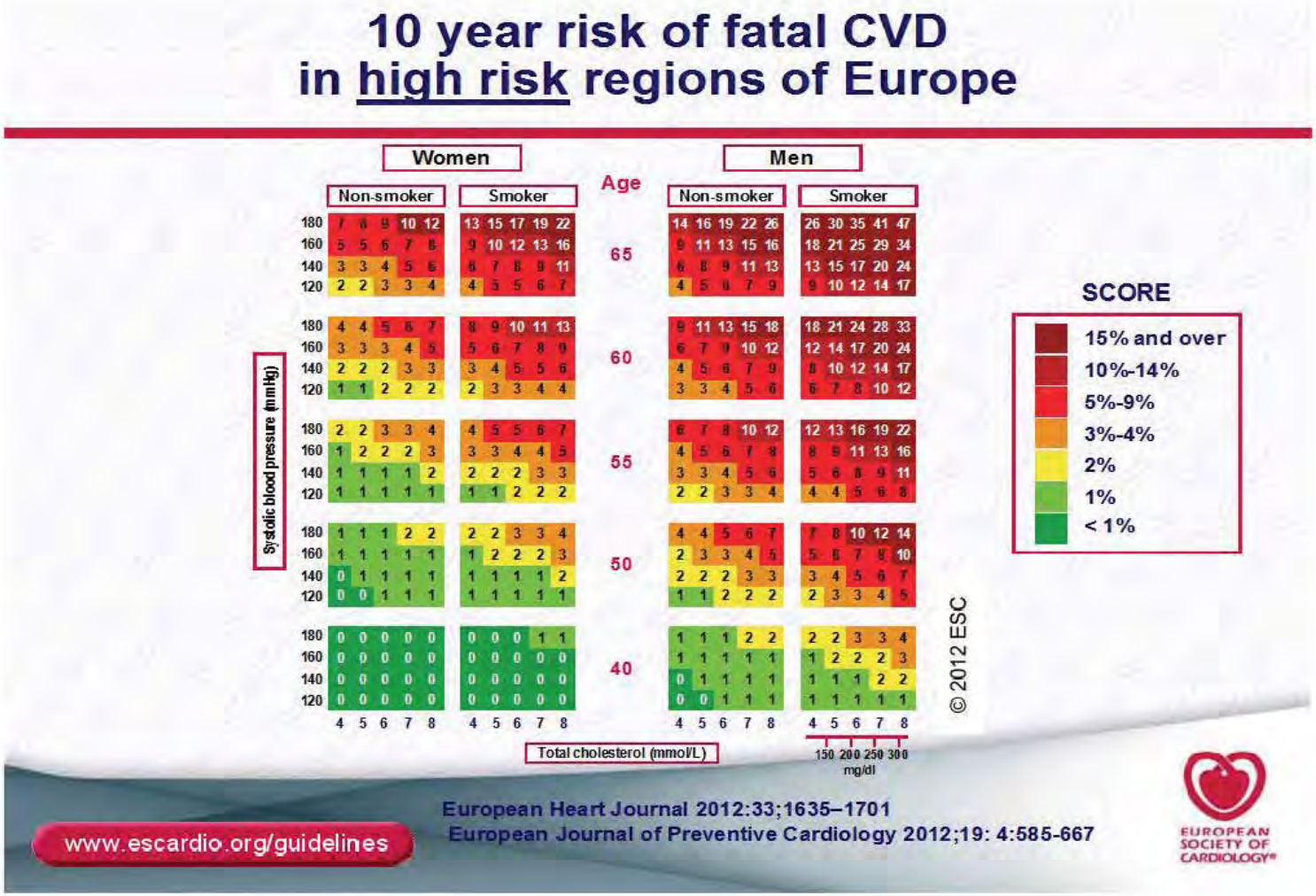

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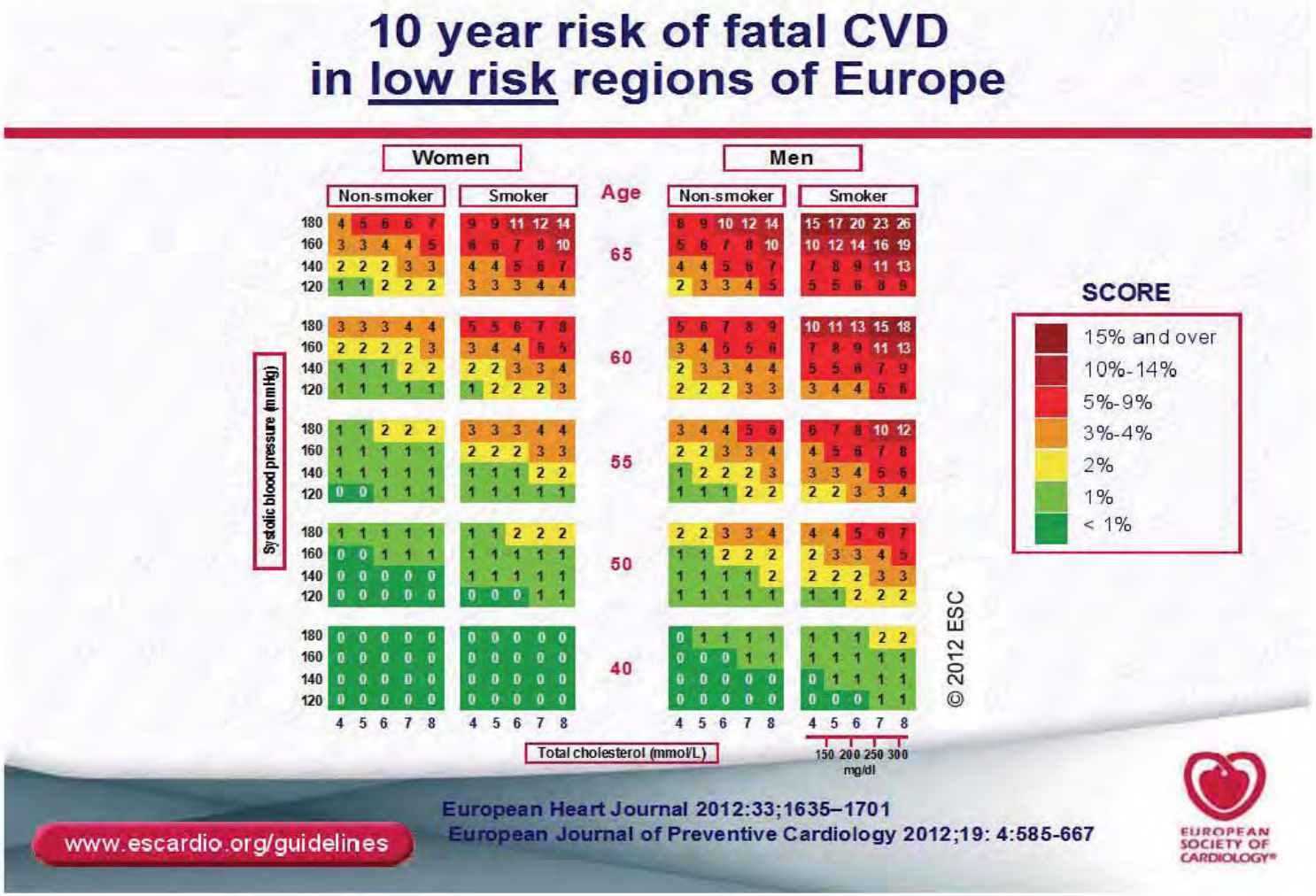

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Risk regions in Europe

- **Countries at low CVD risk:**
  - Based on age, sex, smoking, systolic blood pressure, total cholesterol:

    Andorra, Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Monaco, The Netherlands, Norway, Portugal, San Marino, Slovenia, Spain, Sweden, Switzerland, United Kingdom.

- **High CVD risk countries** are all those not listed under the low risk chart.
  - Of these, some are at **very high risk**, and the high-risk chart may under-estimate risk in these:

    Albania, Algeria, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Bulgaria, Croatia,Czech Republic, Egypt, Estonia, Georgia, Hungary, Kosovo, Latvia, Lebanon, Libya, Lithuania, Macedonia F.Y.R., Moldova, Montenegro, Morocco, Poland, Romania, Russia, Serbia, Slovakia, Syria, Tunisia,Turkey, Ukraine.

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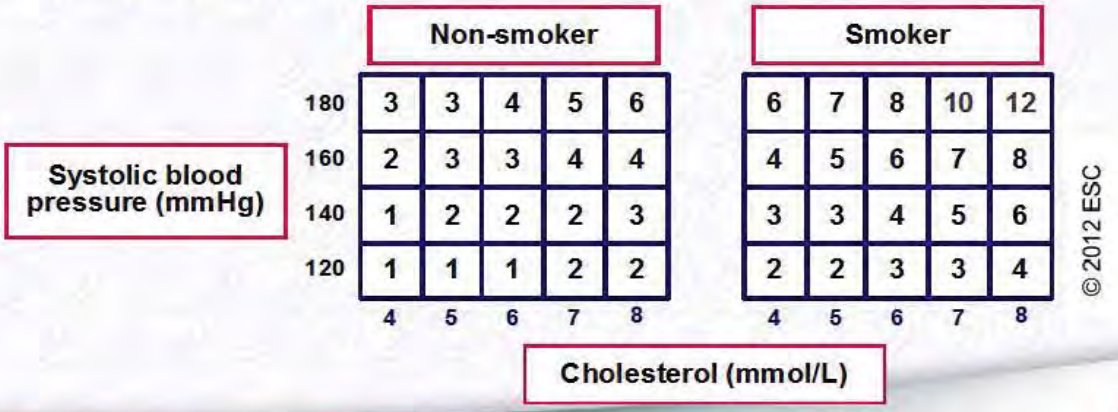
Relative risk chart

- This chart may be used to show younger people at low absolute risk that, relative to others in their age group, their risk may be many times higher than necessary.
- This may help to motivate decisions about avoidance of smoking, healthy nutrition and exercise, as well as flagging those who may become candidates for medication.



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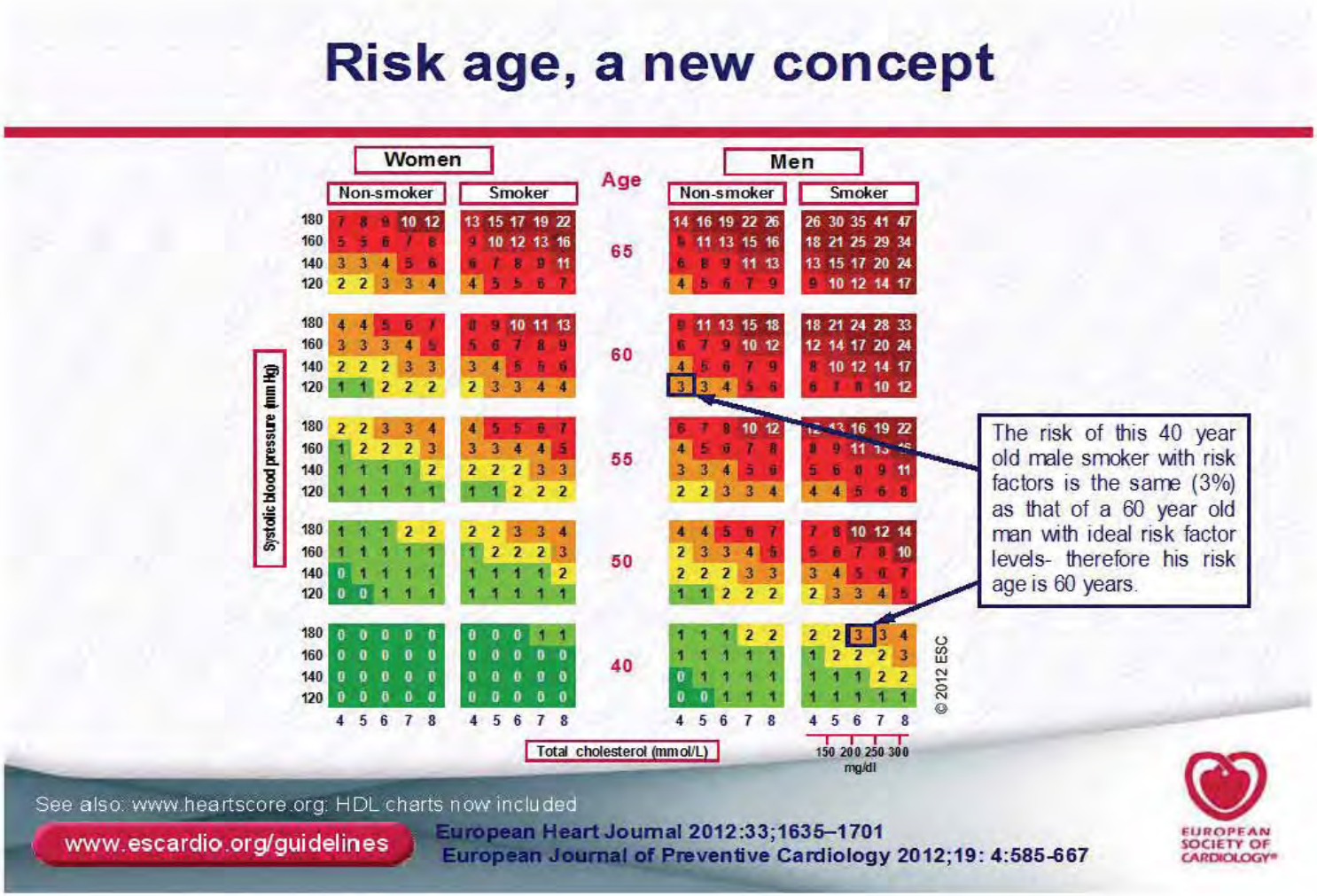

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Other risk recommendations

- Genetic testing has no place in CVD risk assessment (III, B, strong).
- Psychosocial factors should be taken into account in risk assessment (IIA, B, strong).
- Fibrinogen, high sensitivity CRP and/or homocysteine may be measured as part of refined risk assessment in patients with an unusual or moderate CVD risk profile (IIB, B, weak).
- In patients with a moderate CVD risk profile the use of carotid IMT, ABI (ankle-brachial index) (IIA, B, strong) or CT-scan calcium score (IIa, B, weak) may be considered.
- Risk assessement should be conducted in patients with sleep-apneic disease (IIA, A, strong), or those with erectile dysfunction (IIa, B, strong).

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The 'Five A's' for smoking cessation strategy for routine practice

A - ASK	Systematically inquire about smoking status at every opportunity.
A - ADVISE	Unequivocally urge all smokers to quit.
A - ASSESS	Determine the person's degree of addiction and readiness to quit.
A - ASSIST	Agree on a smoking-cessation strategy, including setting a quit date, behavioural counselling and pharmacological support.
A - ARRANGE	Arrange a schedule for follow-up.

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Regarding nutrition

	Class	Level	GRADE
A healthy diet is recommended as being the cornerstone of CVD prevention.	I	B	Strong

- Saturated fatty acids to account for <10% of total energy intake, through replacement by polyunsaturated fatty acids.
- Trans unsaturated fatty acids: as little as possible, preferably no intake from processed food, and <1% of total energy intake from natural origin.
- <5 g of salt per day.
- 30–45 g of fibre per day, from wholegrain products, fruits and vegetables.
- 200 g of fruit per day (2-3 servings).
- 200 g of vegetables per day (2-3 servings).
- Fish at least twice a week, one of which to be oily fish.
- Consumption of alcoholic beverages should be limited to 2 glasses per day (20 g/d of alcohol) for men and 1 glass per day (10 g/d of alcohol) for women.

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Regarding body weight

	Class	Level	GRADE
Weight reduction in overweight and obese people is recommended as this is associated with favourable effects on blood pressure and dyslipidaemia, which may lead to less CVD.	I	A	Strong

Key messages body weight

- Both overweight and obesity are associated with a risk of death in CVD.
- There is a positive linear association of BMI with all-cause mortality.
- All-cause mortality is lowest with a BMI of 20 to 25 kg/m^2.
- Further weight reduction cannot be considered protective against CVD.

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Physical activity

	Class	Level	GRADE
Healthy adults should spend 2.5-5 hours a week on physical activity or aerobic exercise training of at least moderate intensity, or 1-2.5 hours a week on intense exercise. Sedentary subjects should be strongly encouraged to start light-intensity exercise programmes.	I	A	Strong
Physical activity/aerobic exercise training should be performed in multiple bouts lasting ≥10 minutes and spread throughout the week.	IIa	A	Strong
Patients with previous acute myocardial infarction, CABG, PCI, stable angina pectoris or stable chronic heart failure should undergo moderate-to-vigorous intensity aerobic exercise training ≥ 3 times a week and 30 min per session. Sedentary patients should be strongly encouraged to start light-intensity exercise programmes after adequate exercise-related risk stratification.	I	A	Strong

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Management of psychosocial factors

	Class	Level	GRADE
Multimodal behavioural interventions, integrating health education, physical exercise and psychological therapy for psychosocial risk factors and coping with illness, should be prescribed.	I	A	Strong
In case of clinically significant symptoms of depression, anxiety and hostility, psychotherapy, medication or collaborative care should be considered. This approach can reduce mood symptoms and enhance health related quality of life, although evidence for a definite beneficial effect on cardiac endpoints is inconclusive.	IIa	A	Strong

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Blood pressure (1)

	Class	Level	GRADE
Lifestyle measures such as weight control, increased physical activity, alcohol moderation, sodium restriction, and increased consumption of fruits, vegetables, and low-fat dairy products are recommended in all patients with hypertension and in individuals with high normal BP.	I	B	Strong
All major antihypertensive drug classes (i.e. diuretics, ACE inhibitors, calcium antagonists, angiotensin receptor antagonists and beta-blockers) do not differ significantly in their BP-lowering efficacy and should be recommended for the initiation and maintenance of antihypertensive treatment.	I	A	Strong
Systolic BP should be lowered to <140 mmHg (and DBP <90 mmHg) in all hypertensive patients.	IIa	A	Strong

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Blood pressure (2)

	Class	Level	GRADE
Drug treatment is recommended to be initiated promptly in patients with grade 3 hypertension, as well as in patients with grade 1 or 2 hypertension who are at high or very high total cardiovascular risk.	I	C	Strong
In patients with grade 1 or 2 hypertension and at moderate total cardiovascular risk, drug treatment may be delayed for several weeks, and in grade 1 hypertensive patients without any other risk factor, for several months while trying lifestyle measures.	IIb	C	Weak
All hypertensive patients with established cardiovascular disease or with type 2 diabetes or with an estimated 10-year risk of cardiovascular death ≥5% (based on the SCORE chart) should be considered for statin therapy.	IIa	B	Strong

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Blood pressure (3)

	Class	Level	GRADE
Beta-blockers and thiazide diuretics are not recommended in hypertensive patients with multiple metabolic risk factors increasing the risk of new-onset diabetes.	III	A	Strong
In patients with diabetes, an ACE inhibitor or a renin-angiotensin receptor blocker is recommended.	I	A	Strong
Risk stratification using the SCORE risk chart isrecommended as a minimal requirement in each hypertensive patient.	I	B	Strong
However, as there is evidence that subclinical organ damage predicts cardiovascular death independently of SCORE, a search for subclinical organ damage should be encouraged, particularly in individuals at low or moderate risk.	IIa	B	Weak

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Definitions and classification of blood pressure levels

Category	Systolic BP (mmHg)		Diastolic BP (mmHg)
Optimal	<120	and	<80
Normal	120-129	and/or	80-84
High normal	130-139	and/or	85-89
Grade 1 hypertension	140-159	and/or	90-99
Grade 2 hypertension	160-179	and/or	100-109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension	≥140	and	<90

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Thresholds for definition of hypertension with different types of measurement

	SBP (mmHg)	DBP (mmHg)
Office or clinic	140	90
24-hour	125–130	80
Day	130–135	85
Night	120	70
Home	130–135	85

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Hyperlipidemia

	Class	Level	GRADE
The recommended target levels are <5 mmol/L (<~ 190 mg/dL) for total plasma cholesterol and <3 mmol/L (<~ 115 mg/dL) for LDL cholesterol for subjects at low or moderate risk.	I	A	Strong
In patients at high CVD risk, a LDL-cholesterol goal <2.5 mmol/L (<~ 100 mg/dL) is recommended.	I	A	Strong
In patients at very high CVD risk, the recommended LDL cholesterol target is <1.8 mmol/L (<~ 70 mg/dL) or a ≥50% LDL-cholesterol reduction when the target level cannot be reached.	I	A	Strong
All patients with familial hypercholesterolaemia must be recognized as high-risk patients and be treated with lipid-lowering therapy.	I	A	Strong
In patients with an ACS, statin treatment in high doses has to be initiated while the patients are in the hospital.	I	A	Strong

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Metodologia per la misurazione dei fattori di rischio

- Maschio / Femmina
- Pressione arteriosa sistolica
- Abitudine al fumo
- Colesterolemia (in mg / dl)

Le note AIFA non sono delle linee guida

- Le Linee Guida sono modelli comportamentali che propongono agli operatori le scelte professionali più appropriate.
- Le Linee guida per la pratica clinica descrivono un percorso utile per le raccomandazioni in campo diagnostico, terapeutico, organizzativo, ecc.

Le Note AIFA sono un obbligo per la rimborsabilità

Il rispetto delle Note AIFA è vincolante se il medico effettua la prescrizione a carico del SSN

Ultima modifica della Nota 13
(*determina AIFA del 14/11/2012*)

- L'ultima revisione della nota 13 nasce dalla necessità di adeguare la definizione del livello di rischio alle linee guida European Society of Cardiology (**ESC**) ed European Atherosclerosis Society (**EAS**), apparse in letteratura subito dopo la pubblicazione della precedente revisione della nota stessa.
- L'adeguamento a tali linee guida ha comportato la **reintroduzione delle relative carte di rischio**.

Ultima modifica della Nota 13
(*determina AIFA del 14/11/2012*)

- Le Carte del rischio sono un obbligo

- "Si confida sulla disponibilità della classe medica ad utilizzare questo strumento, peraltro di facile applicazione, al fine di tenere conto delle evidenze scientifiche più recenti".

AIFA – Agenzia Italiana del Farmaco

- Non rimborsabilità da parte del Servizio Sanitario Nazionale dei medicinali appartenenti alla classe «PUFA (acidi grassi polinsaturi) Omega 3» (13A01771) (GU n.50 del 28-2-2013)
- La Commissione Consultiva Tecnico Scientifica, in accordo a quanto previsto all'art. 11, comma 1, della legge 8 novembre 2012 n. 189, nella seduta del 5 dicembre 2012 ha disposto che, per le specialità medicinali appartenenti alla classe PUFA Omega 3, la prescrizione per la prevenzione secondaria nel paziente con pregresso infarto miocardico non è rimborsata dal Servizio Sanitario Nazionale.
- Restano rimborsate le indicazioni riportate in Nota 13 secondo le modalità ivi descritte.

PUFA-N3 rimborsabilità a carico SSN

Trattamento di 2° livello nelle dislipidemie familari:

- Iperlipemia familiare combinata
- Iperchilomicronemie
- Ipertrigliceridemie

Trattamento di 1^ scelta:

- Trigliceridi =/> 500 in IRC grave

Tutti i farmaci interessati dalla Nota 3

Fibrati:

- Bezafibrato,
- Fenofibrato,
- Gemfibrozil,
- Simfibrato

Altri:

- Omega-3-etilesteri
- Ezetimibe+simv.
- Ezetimibe monot.
- Sequestranti ac.Biliari **(solo per trattamento 3° liv. In alcune forme familiari)**

Statine:

- Simvastatina,
- Pravastatina,
- Atorvastatina,
- Rosuvastatina.

(Lovastatina,fluvastatina?)

La prescrizione a carico del SSN in prevenzione primaria

1. Ipercolesterolemia non corretta dalla sola dieta, seguita per almeno tre mesi
2. Ipercolesterolemia poligenica (*l'ipercolesterolemia poligenica è una malattia ad eziologia multifattoriale, causata da fattori ambientali quali dieta ad alto contenuto di grassi saturi e inattività fisica che agiscono in presenza di fattori genetici predisponenti; i deficit genetici riguardano probabilmente i meccanismi di feedback compromettendo così la capacità dell'organismo di compensare adeguatamente l'eccesso lipidico della dieta*)
3. Dislipidemie familiari. Tali pazienti sono da considerarsi a rischio alto e pertanto l'obiettivo terapeutico è un valore di LDL-C < 100mg/dl

La prescrizione a carico del SSN in prevenzione primaria

4. Iperlipidemie in pazienti con insufficienza renale cronica in stadio 3 e 4 (con filtrato glomerulare compreso tra 15 e 60). Tali pazienti sono da considerarsi a rischio molto alto e pertanto l'obiettivo terapeutico è un valore di LDL-C < 70mg/dl
5. Diabetici tipo 2
6. Diabetici di tipo 1 con markers di danno d'organo (come la microalbuminuria)

La prescrizione a carico del SSN in prevenzione secondaria

Prevenzione secondaria in Pazienti con:

- Malattia coronarica ,
- Stroke ischemico,
- Arteriopatie periferiche ,
- Pregresso infarto,
- Bypass aorto-coronarico

Metodologia per la misurazione dei fattori di rischio

- Maschio / Femmina
- Pressione arteriosa sistolica
- Abitudine al fumo
- Colesterolemia (in mg / dl)

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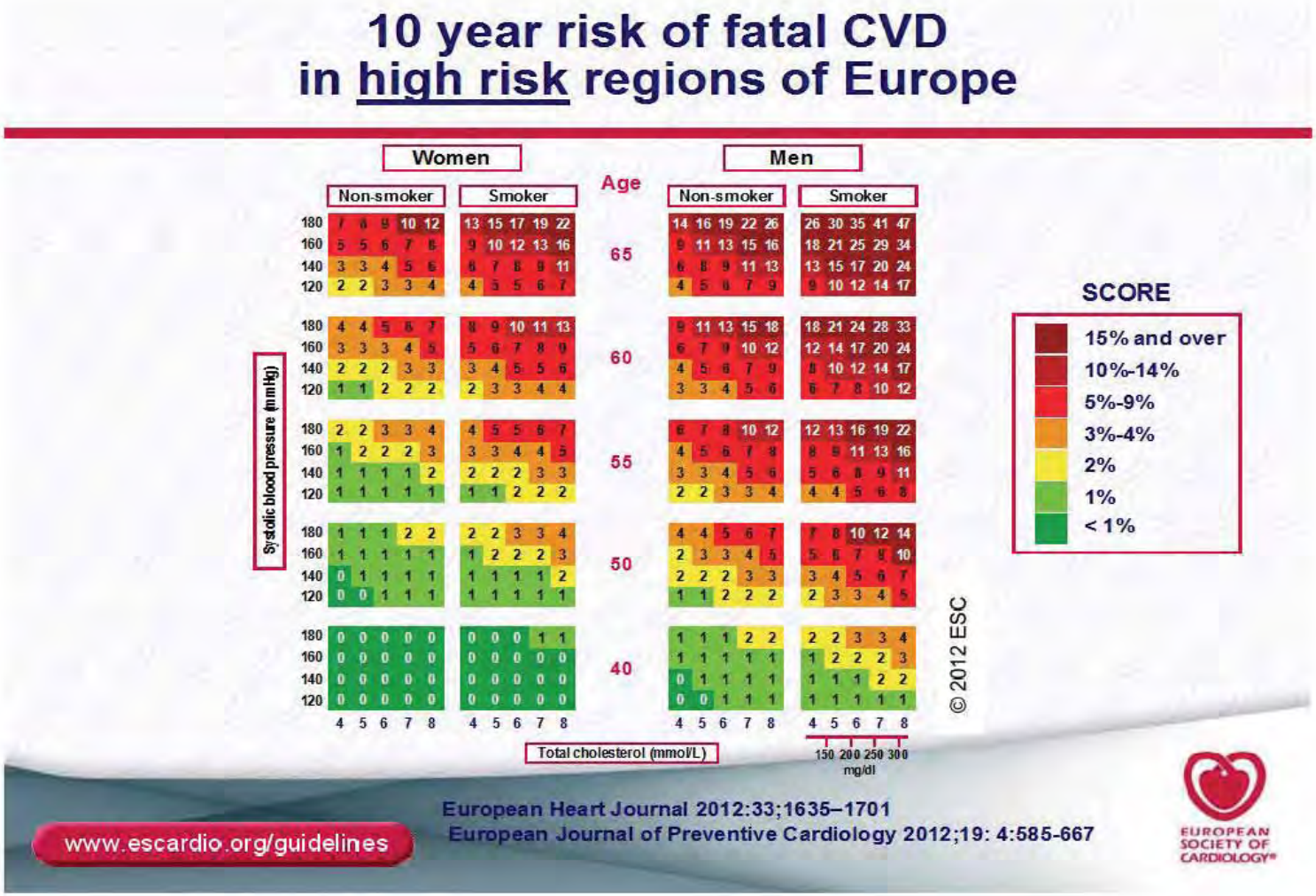

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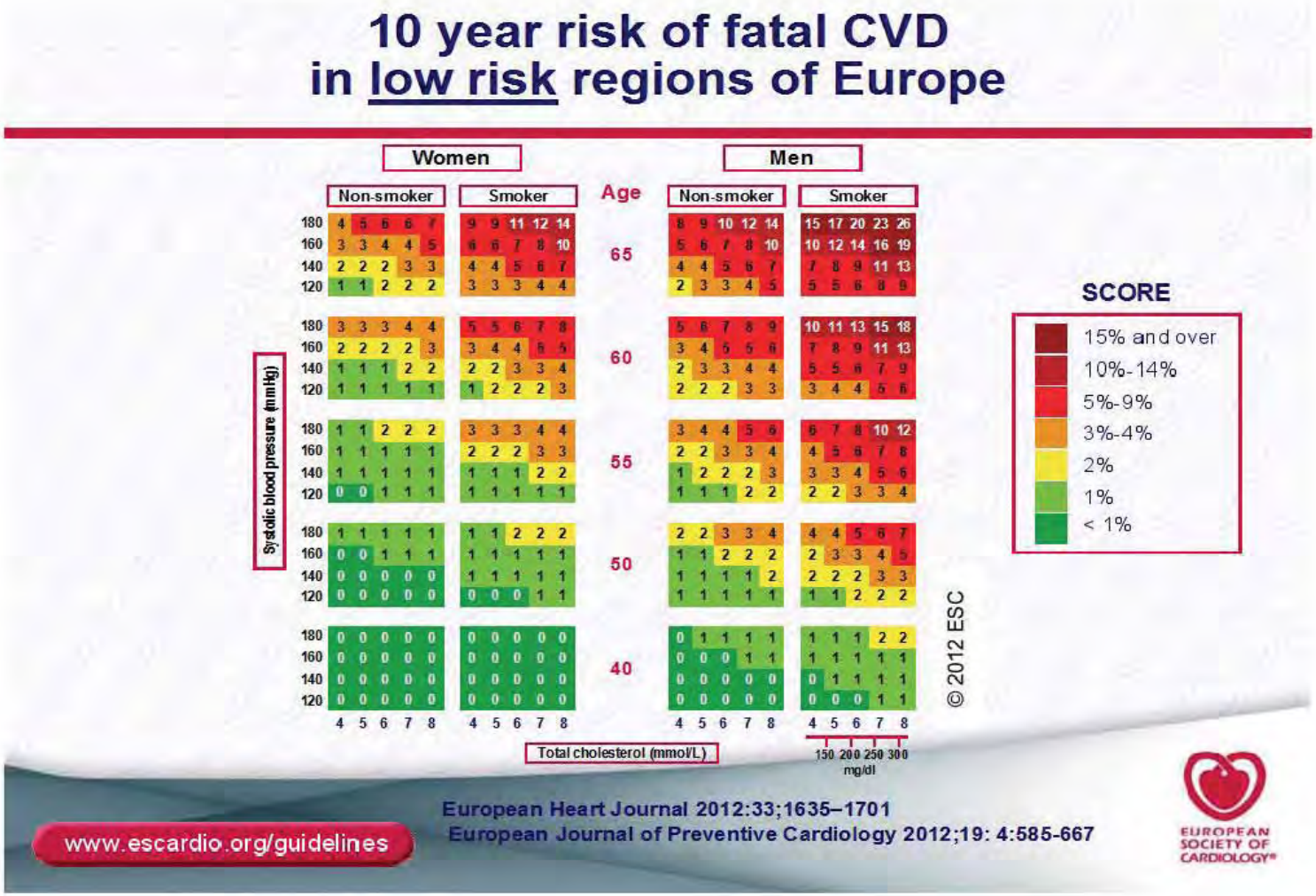

Calcolo del rischio a 10 anni

1. <1% rischio basso
2. 1% basso
3. 2% medio (cambiare stile di vita) LDL < 130
4. 3-4% medio (cambiare stile di vita) LDL < 130
5. 5-9 % moderato (pz con ipertensione severa, dislipidemie familiari) LDL <115 trattamento 1°liv.
6. 10-14 % alto LDL < 100 mg/dl 1° o 2° liv.
7. > 15% molto alto (pz con IRC 3° e 4° stadio)
   LDL <70% 1° o 2° liv.

Quando non si applicano le Carte del Rischio Cardio Vascolare

1. Dislipidemie familiari
2. In tutti i casi di Prevenzione secondaria
3. Nei diabetici

Prevenzione secondaria

- Pazienti con malattia coronarica , strokeischemico, arteriopatie periferiche, pregresso infarto, bypass aorto-coronarico,
- Diabetici tipo 2
- Diabetici di tipo 1 con markers di danno d'organo(come la microalbuminuria)
- Pazienti con IRC e filtrato glomerulare <60ml/min/ 1.73m2.100mg/dl≤
- **Target terapeutico**: riduzione del colesterolo LDL >50%

Pazienti diabetici

Per quanto riguarda i pazienti diabetici

- **le LDL sono impoverite in colesterolo e arricchite in trigliceridi**; pertanto il dosaggio del colesterolo LDL non fornisce una adeguata informazione sul suo reale valore e quindi anche sul TT che deve essere raggiunto.
- **in questi pazienti dovrebbe quindi essere considerato anche il dosaggio dell'ApoB** sia per stabilire il momento di inizio della terapia, sia per quanto riguarda il TT da raggiungere. L'ApoB infatti è indicativo del numero di particelle circolanti dato che ogni particella di LDL contiene una molecola di ApoB.
- Il dosaggio dell'ApoB sarebbe utile anche nei soggetti con sindrome metabolica e nei pazienti con insufficienza renale cronica.
- **la determinazione del colesterolo non HDL** può essere utile se non è possibile il dosaggio dell'Apo B, si calcola facilmente dal colesterolo totale (TC) meno col.HDL.

Pazienti con insufficienza renale cronica (IRC)

- Per il trattamento ipocolesterolemizzante dei pazienti con insufficienza renale (e GFR <60 ml/min/173m2) è necessario prestare attenzione alla scelta della terapia a seconda del grado di insufficienza renale.
- Le statine si sono dimostrate efficaci nel ridurre gli eventi cardiovascolari nei pazienti con insufficienza renale cronica, di ridurre la proteinuria e di rallentare la progressione della malattia renale.