European Society of Hypertension

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Isabel Muinelo Voces

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ESC European Society of Cardiology
European Heart Journal (2021) 42, 3227–3337
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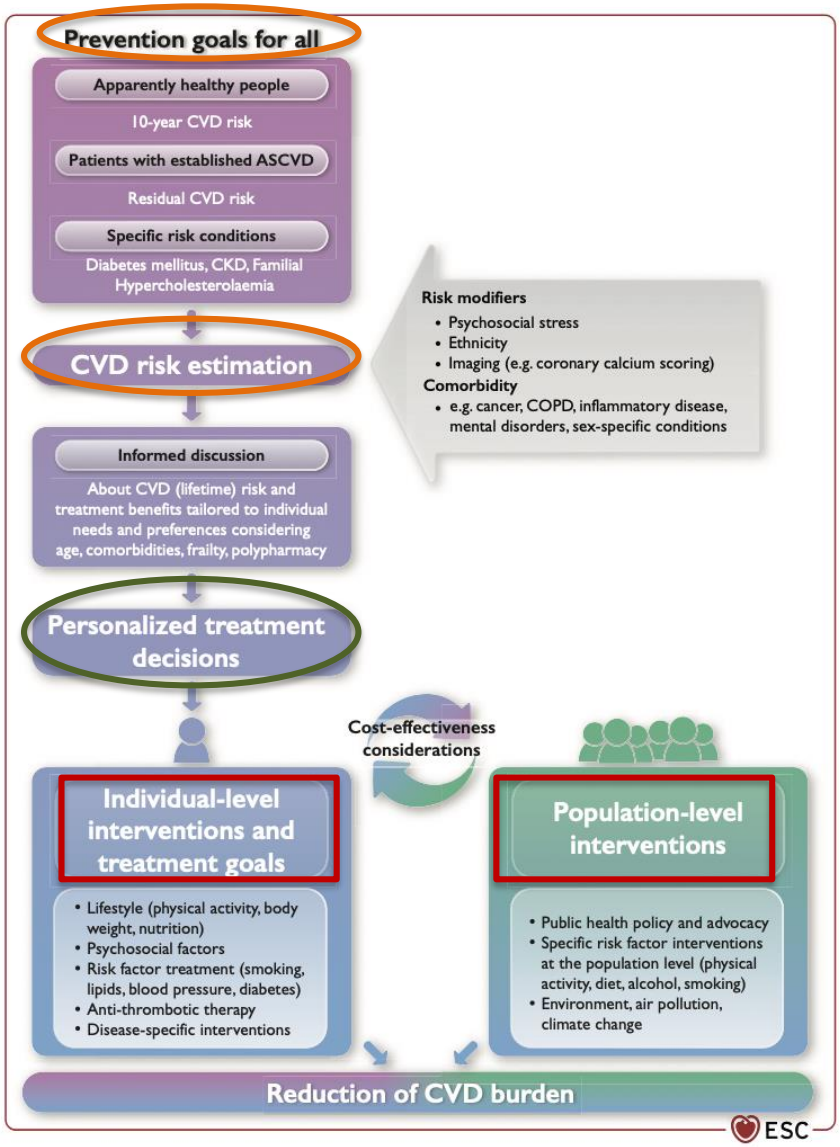
2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

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)



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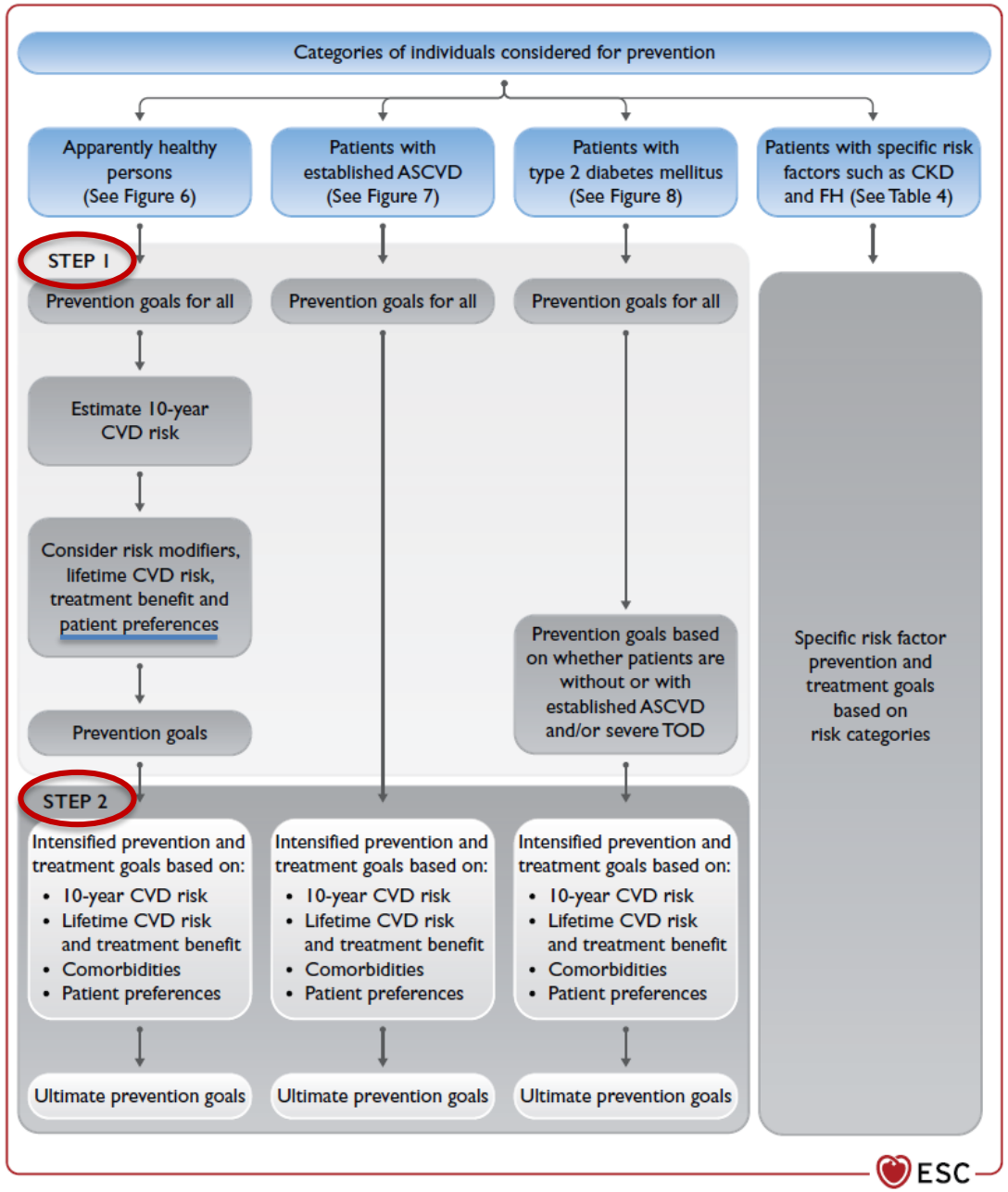
Patient category	Subgroups	Risk categories	CVD risk and therapy benefit estimation
Apparently healthy persons			
Persons without established ASCVD, diabetes mellitus, CKD, Familial Hypercholesterolemia	<50 years	Low- to high-risk	10-year CVD risk estimation (SCORE2). Lifetime risk and benefit estimation of risk factor treatment (e.g. with the LIFE-CVD lifetime model) to facilitate the communication of CVD risk and treatment benefits.
	50-69 years	Low- to very high-risk	10-year CVD risk estimation (SCORE2). Lifetime benefit estimation of risk factor treatment (e.g. with the LIFE-CVD lifetime model) to facilitate the communication of treatment benefits.
	≥70 years	Low- to very high-risk	10-year CVD risk estimation (SCORE2-OP). Lifetime benefit estimation of risk factor treatment (e.g. with the LIFE-CVD lifetime model) to facilitate the communication of treatment benefits.
Patients with CKD			
CKD without diabetes or ASCVD	Moderate CKD (eGFR 30–44 mL/min/1.73 m^2 and ACR <30 **or** eGFR 45–59 mL/min/1.73 m^2 and ACR 30–300 **or** eGFR ≥60 mL/min/1.73 m^2 and ACR >300)	High-risk	N/A
	Severe CKD (eGFR<30 mL/min/1.73 m^2 **or** eGFR 30–44 mL/min/1.73 m^2 and ACR >30)	Very high-risk	N/A
Familial Hypercholesterolemia			
Associated with markedly elevated cholesterol levels	N/A	High-risk	N/A
Patients with type 2 diabetes mellitus			
Patients with type 1 DM above 40 years of age may also be classified according to these criteria	Patients with well controlled short-standing DM (e.g. <10 years), no evidence of TOD and no additional ASCVD risk factors	Moderate-risk	N/A
	Patients with DM without ASCVD and/or severe TOD, and not fulfilling the moderate risk criteria.	High-risk	Residual 10-year CVD risk estimation after general prevention goals (e.g. with the ADVANCE risk score or DIAL model). Consider lifetime CVD risk and benefit estimation of risk factor treatment (e.g. DIAL model).
	Patients with DM with established ASCVD and/or severe TOD:[87,93-95] • eGFR <45 mL/min/1.73 m^2 irrespective of albuminuria • eGFR 45-59 mL/min/1.73 m^2 and microalbuminuria (ACR 30 -300 mg/g) • Proteinuria (ACR >300 mg/g) • Presence of microvascular disease in at least 3 different sites (e.g. microalbuminuria plus retinopathy plus neuropathy)	Very high-risk	Residual 10-year CVD risk estimation after general prevention goals (e.g. with the SMART risk score for established CVD or with the ADVANCE risk score or with the DIAL model). Consider lifetime CVD risk and benefit estimation of risk factor treatment (e.g. DIAL model).
Patients with established ASCVD			
Documented ASCVD, clinical or unequivocal on imaging. Documented clinical ASCVD includes previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Unequivocally documented ASCVD on imaging includes plaque on coronary angiography or carotid ultrasound or on CTA. It does NOT include some increase in continuous imaging parameters such as intima–media thickness of the carotid artery.	N/A	Very high-risk	Residual CVD risk estimation after general prevention goals (e.g. 10-year risk with the SMART risk score for patients with established CVD or 1- or 2-year risk with EUROASPIRE risk score for patients with CHD). Consider lifetime CVD risk and benefit estimation of risk factor treatment (e.g. SMART-REACH model; or DIAL model if diabetes).

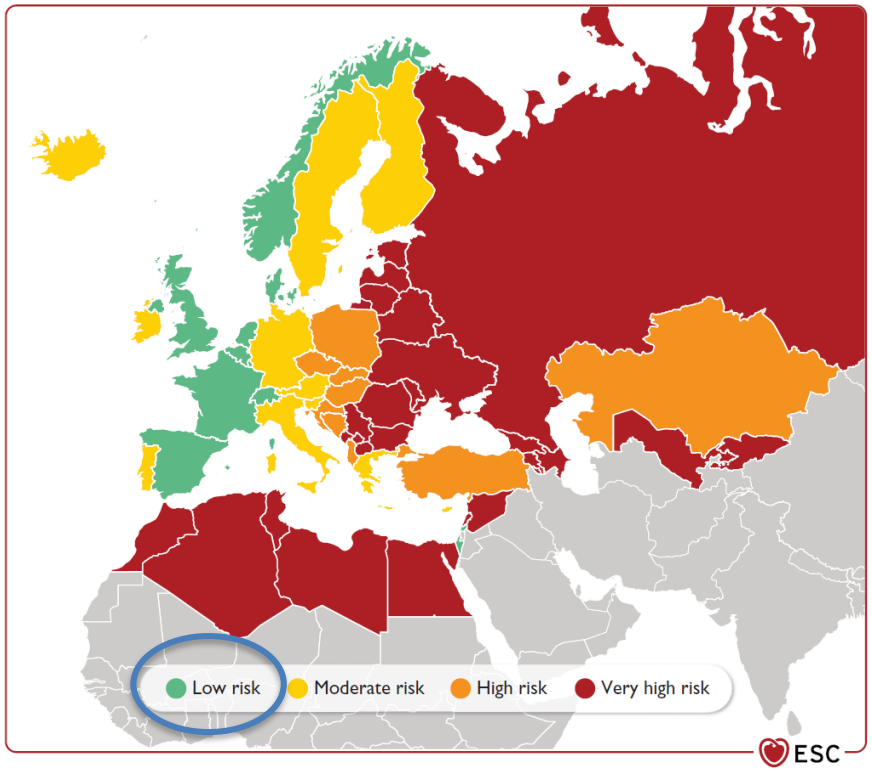

Categories of individuals considered for prevention
Apparently healthy persons (See Figure 6)
Patients with established ASCVD (See Figure 7)
Patients with type 2 diabetes mellitus (See Figure 8)
Patients with specific risk factors such as CKD and FH (See Table 4)
STEP 1
Prevention goals for all
Prevention goals for all
Prevention goals for all
Estimate 10-year CVD risk
Consider risk modifiers, lifetime CVD risk, treatment benefit and patient preferences
Prevention goals
Prevention goals based on whether patients are without or with established ASCVD and/or severe TOD
Specific risk factor prevention and treatment goals based on risk categories
STEP 2
Intensified prevention and treatment goals based on:
• 10-year CVD risk
• Lifetime CVD risk and treatment benefit
• Comorbidities
• Patient preferences
Intensified prevention and treatment goals based on:
• 10-year CVD risk
• Lifetime CVD risk and treatment benefit
• Comorbidities
• Patient preferences
Intensified prevention and treatment goals based on:
• 10-year CVD risk
• Lifetime CVD risk and treatment benefit
• Comorbidities
• Patient preferences
Ultimate prevention goals
Ultimate prevention goals
Ultimate prevention goals
ESC

GRUPO “APARENTEMENTE SANOS” PERO CON FRCV

2 nuevas tablas (RCV a 10 años)

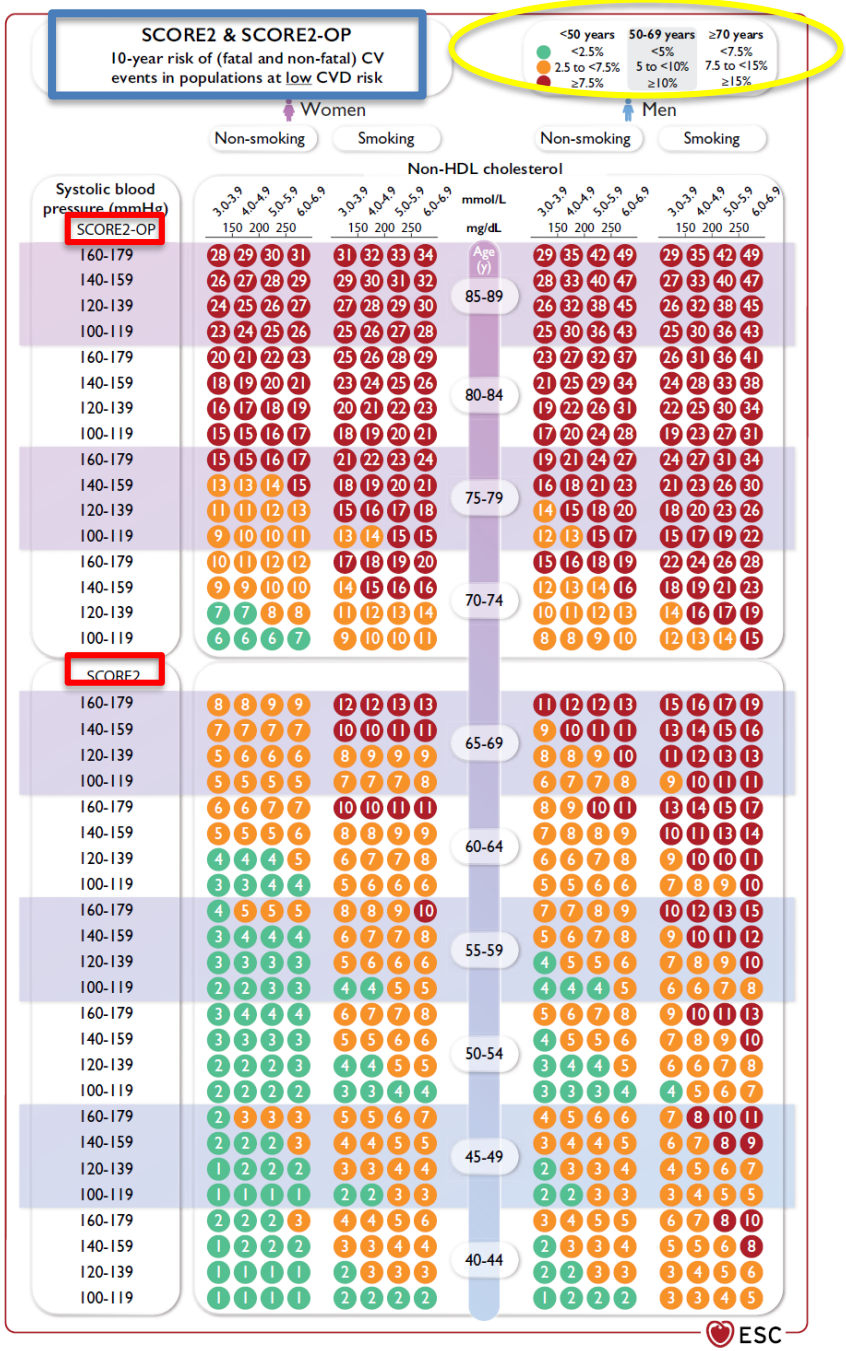
- **SCORE2** 40 - 69 años, que amplía el cálculo de riesgo a la morbilidad y no solo a la mortalidad

- **SCORE2-OP** 70 - 89 años, teniendo en cuenta consideraciones específicas de edades avanzadas y llevando a cabo una valoración a 5 y 10 años



REGIÓN

SEXO
EDAD
TABACO
NO cHDL
PAS



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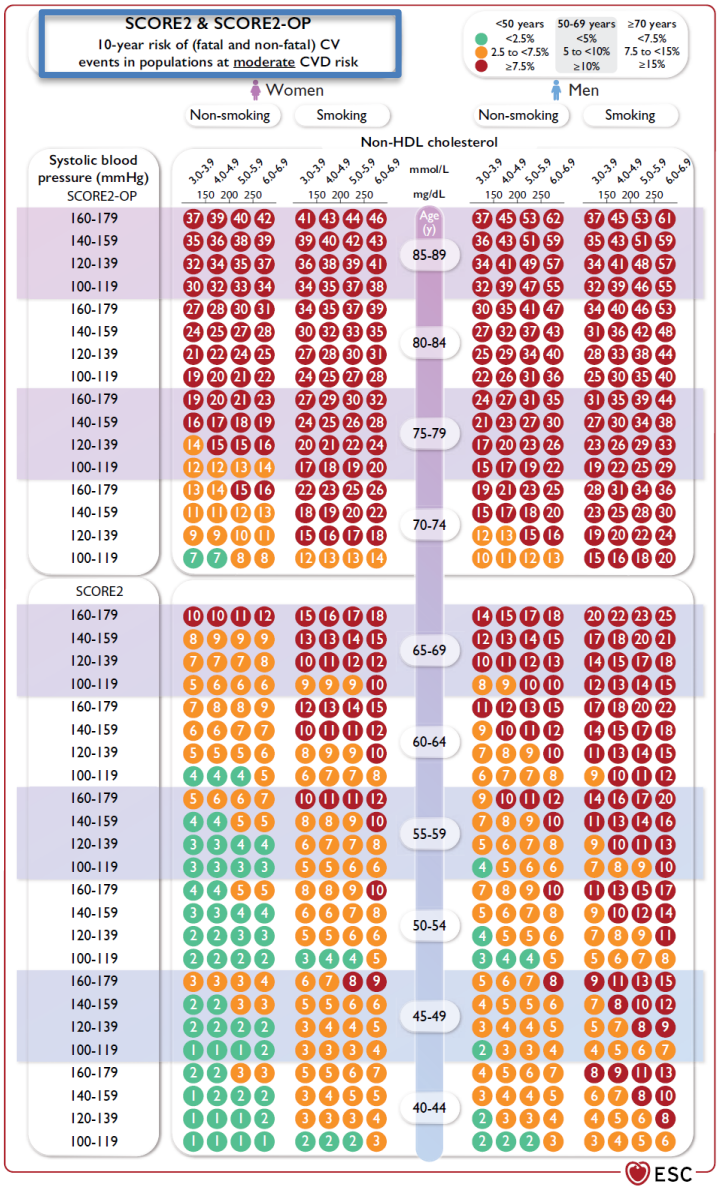

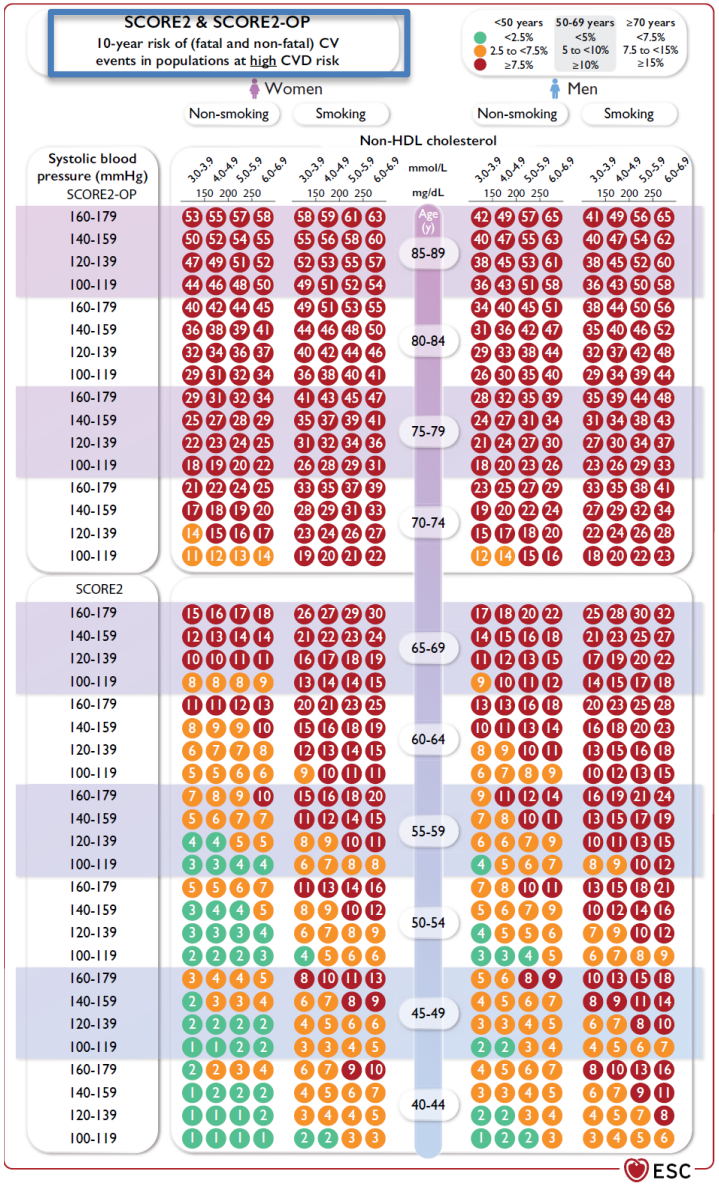

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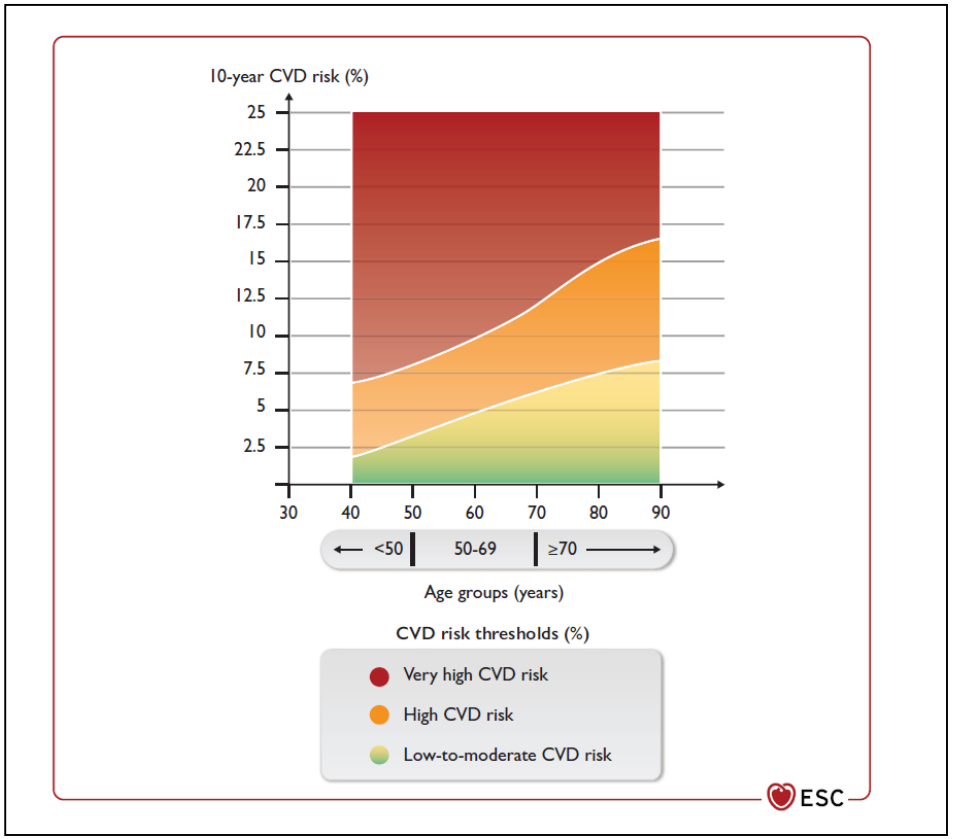
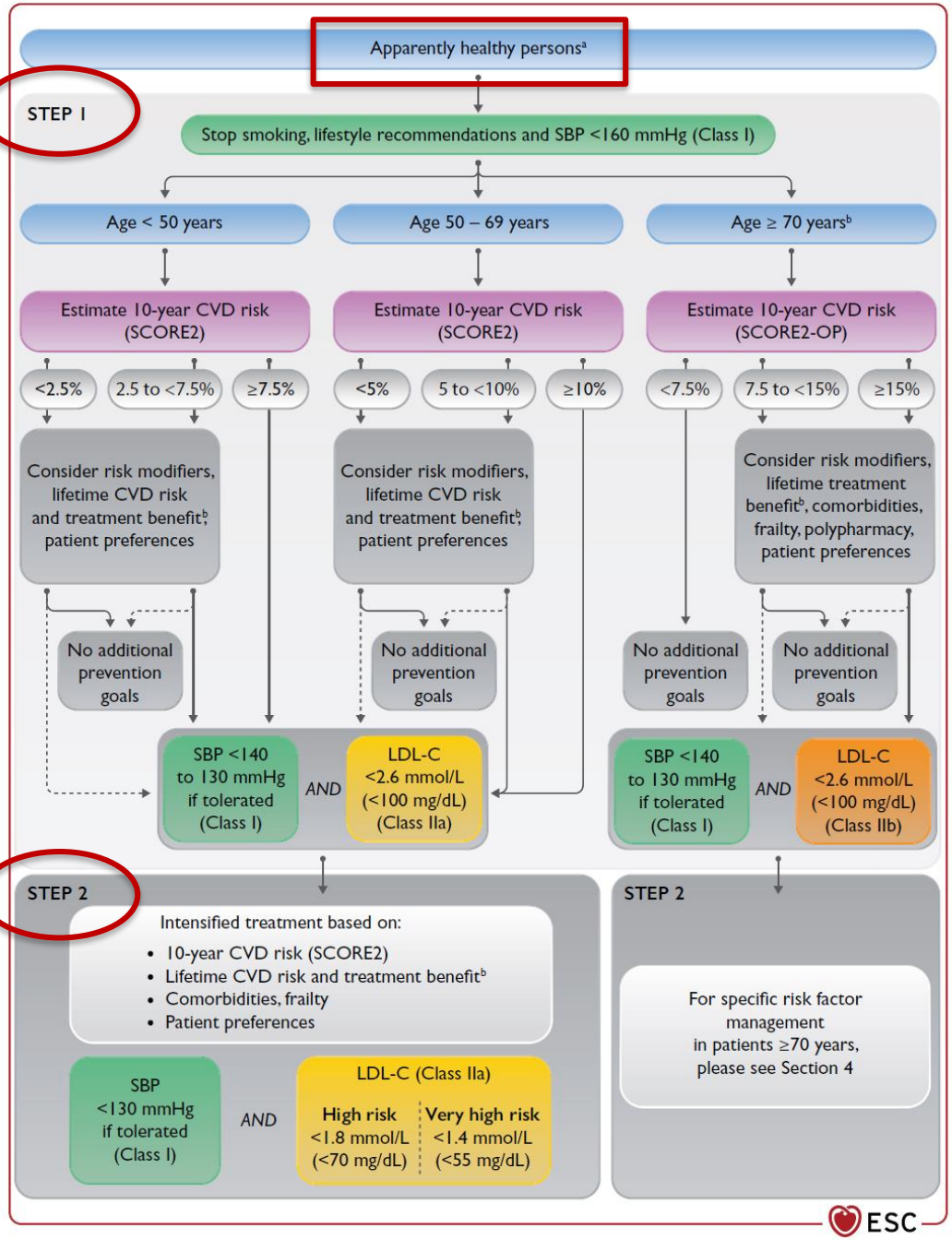
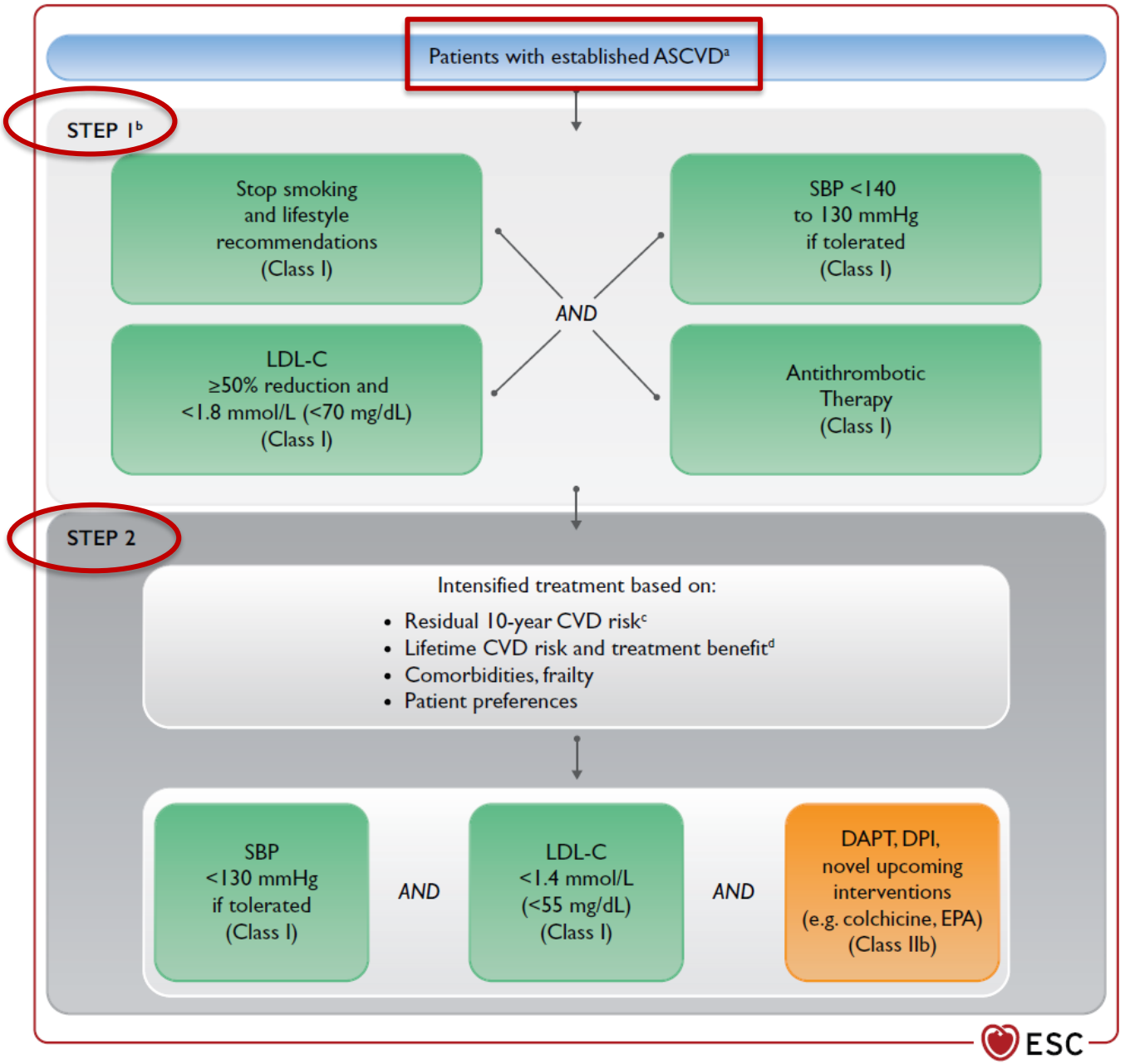
	<50 years	50–69 years	≥70 years[a]
Low-to-moderate CVD risk: risk factor treatment generally not recommended	<2.5%	<5%	<7.5%
High CVD risk: risk factor treatment should be considered	2.5 to <7.5%	5 to <10%	7.5 to <15%
Very high CVD risk: risk factor treatment generally recommended[a]	≥7.5%	≥10%	≥15%



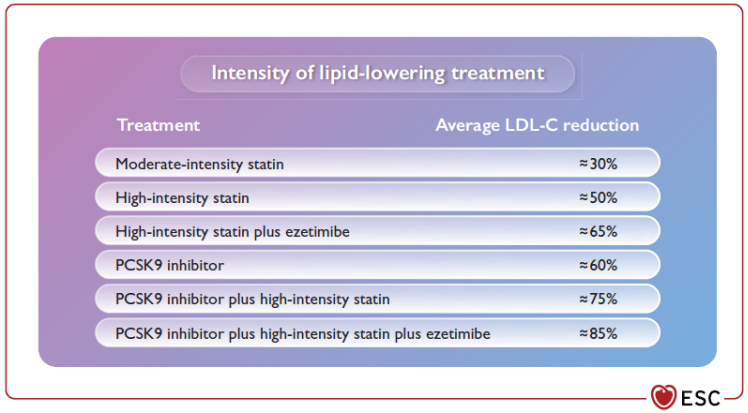

Apparently healthy persons[a]
STEP 1
Stop smoking, lifestyle recommendations and SBP <160 mmHg (Class I)
Age < 50 years
Age 50 – 69 years
Age ≥ 70 years[b]
Estimate 10-year CVD risk (SCORE2)
Estimate 10-year CVD risk (SCORE2)
Estimate 10-year CVD risk (SCORE2-OP)
<2.5%
2.5 to <7.5%
≥7.5%
<5%
5 to <10%
≥10%
<7.5%
7.5 to <15%
≥15%
Consider risk modifiers, lifetime CVD risk and treatment benefit[b], patient preferences
Consider risk modifiers, lifetime CVD risk and treatment benefit[b], patient preferences
Consider risk modifiers, lifetime treatment benefit[b], comorbidities, frailty, polypharmacy, patient preferences
No additional prevention goals
No additional prevention goals
No additional prevention goals
No additional prevention goals
SBP <140 to 130 mmHg if tolerated (Class I)
AND
LDL-C <2.6 mmol/L (<100 mg/dL) (Class IIa)
SBP <140 to 130 mmHg if tolerated (Class I)
AND
LDL-C <2.6 mmol/L (<100 mg/dL) (Class IIb)
STEP 2
Intensified treatment based on:
• 10-year CVD risk (SCORE2)
• Lifetime CVD risk and treatment benefit[b]
• Comorbidities, frailty
• Patient preferences
SBP <130 mmHg if tolerated (Class I)
AND
LDL-C (Class IIa)
High risk <1.8 mmol/L (<70 mg/dL)
Very high risk <1.4 mmol/L (<55 mg/dL)
STEP 2
For specific risk factor management in patients ≥70 years, please see Section 4


Patients with established ASCVD[a]
STEP 1[b]
Stop smoking and lifestyle recommendations (Class I)
SBP <140 to 130 mmHg if tolerated (Class I)
AND
LDL-C ≥50% reduction and <1.8 mmol/L (<70 mg/dL) (Class I)
Antithrombotic Therapy (Class I)
STEP 2
Intensified treatment based on:
• Residual 10-year CVD risk[c]
• Lifetime CVD risk and treatment benefit[d]
• Comorbidities, frailty
• Patient preferences
SBP <130 mmHg if tolerated (Class I)
AND
LDL-C <1.4 mmol/L (<55 mg/dL) (Class I)
AND
DAPT, DPI, novel upcoming interventions (e.g. colchicine, EPA) (Class IIb)
ESC

LÍPIDOS *Guías ESC/EAS 2019*

cLDL <70 mg/dl y reducción ≥50 % en RCV alto
cLDL <55 mg/dl y reducción ≥50 % en RCV muy alto.

Recommendations	Class[a]	Level[b]
It is recommended that a high-intensity statin is prescribed up to the highest tolerated dose to reach the LDL-C goals set for the specific risk group.[21,520,521]	I	A
An ultimate[c] LDL-C goal of <1.4 mmol/L (55 mg/dL) and LDL-C reduction of ≥50% from baseline should be considered in apparently healthy persons <70 years at very high risk.[21,22,522]	IIa	C
An ultimate[c] LDL-C goal of <1.8 mmol/L (70 mg/dL) and LDL-C reduction of ≥50% from baseline should be considered in apparently healthy persons <70 years at high risk.[21,22,522]	IIa	C
In patients with established ASCVD, lipid-lowering treatment with an ultimate[c] LDL-C goal of <1.4 mmol/L (55 mg/dL) and a ≥50% reduction in LDL-C vs. baseline is recommended.[21,508,515–517,522]	I	A
If the goals are not achieved with the maximum tolerated dose of a statin, combination with ezetimibe is recommended.[515]	I	B
For primary prevention patients at very high risk, but without FH, if the LDL-C goal is not achieved on a maximum tolerated dose of a statin and ezetimibe, combination therapy including a PCSK9 inhibitor may be considered.	IIb	C



For secondary prevention patients not achieving their goals on a maximum tolerated dose of a statin and ezetimibe, combination therapy including a PCSK9 inhibitor is recommended.[516,517]	I	A
For very-high-risk FH patients (that is, with ASCVD or with another major risk factor) who do not achieve their goals on a maximum tolerated dose of a statin and ezetimibe, combination therapy including a PCSK9 inhibitor is recommended.	I	C
If a statin-based regimen is not tolerated at any dosage (even after rechallenge), ezetimibe should be considered.[515,523–525]	IIa	B
If a statin-based regimen is not tolerated at any dosage (even after rechallenge), a PCSK9 inhibitor added to ezetimibe may be considered.[523,524,526]	IIb	C
If the goal is not achieved, statin combination with a bile acid sequestrant may be considered.	IIb	C
Statin therapy is not recommended in premenopausal female patients who are considering pregnancy or are not using adequate contraception.	III	C

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

Recommendations	Class[a]	Level[b]
Treatment with statins is recommended for older people with ASCVD in the same way as for younger patients.[538,539]	I	A
Initiation of statin treatment for primary prevention in older people aged ≥70 may be considered, if at high risk or above.[538,539]	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

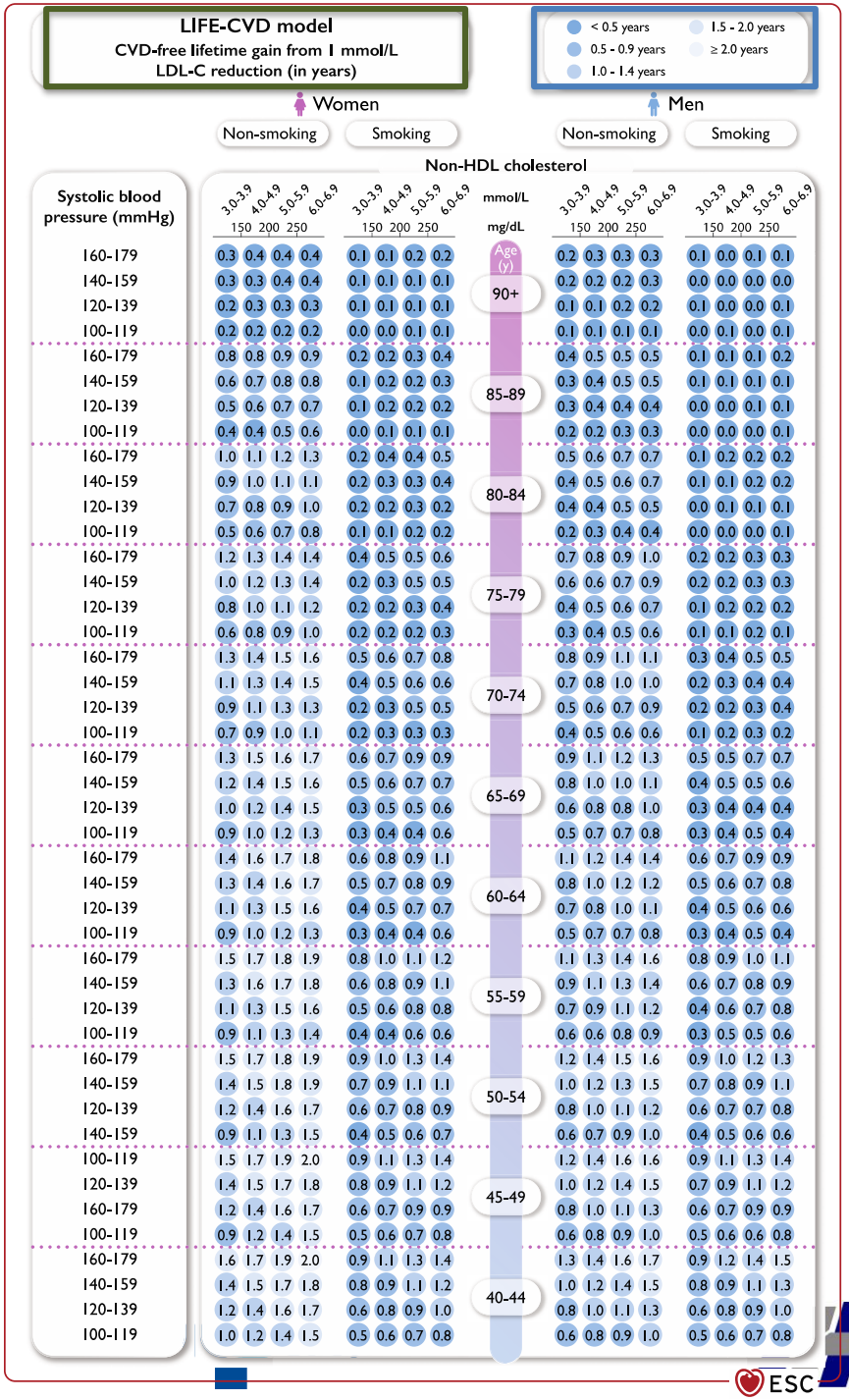
Although 5-10% of patients receiving statins complain of myalgia, in most cases it is not attributable to statins.

Bempedoic acid, an oral cholesterol synthesis inhibitor, has recently been approved in several countries. Usage is mainly intended in combination with ezetimibe in patients with statin intolerance.

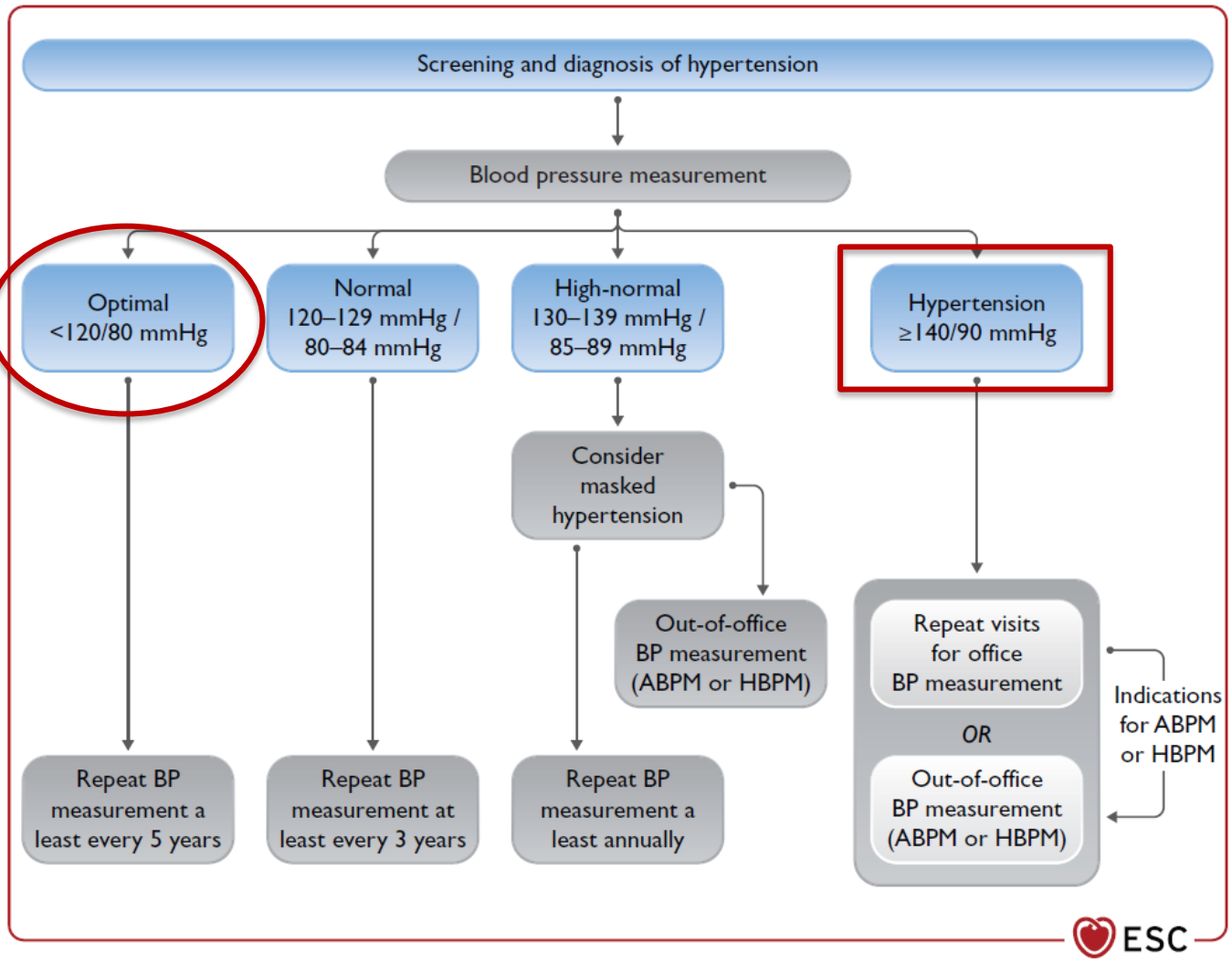
Inclisiran, a new small interfering ribonucleic acid, has shown to reduce LDL-C by 50-55% when applied subcutaneously twice a year.

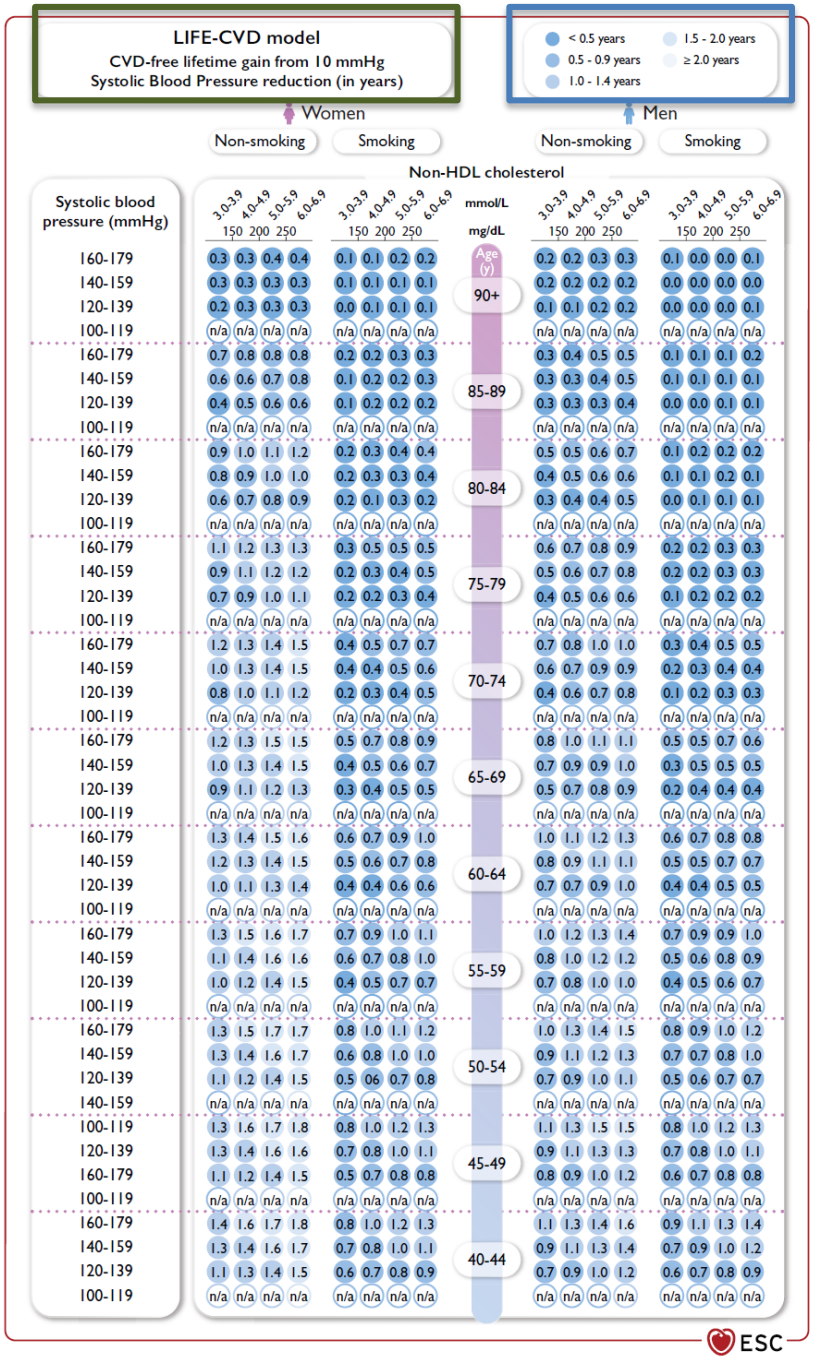
No objetivos cHDL
TG < 150 mg/dl menor riesgo

Recommendations	Class[a]	Level[b]
Statin treatment is recommended as the first drug of choice for reducing CVD risk in high-risk individuals with hypertriglyceridaemia [triglycerides >2.3 mmol/L (200 mg/dL)].[533]	I	A
In patients taking statins who are at LDL-C goal with triglycerides >2.3 mmol/L (200 mg/dL), fenofibrate or bezafibrate may be considered.[534–536]	IIb	B
In high-risk (or above) patients with triglycerides >1.5 mmol/L (135 mg/dL) despite statin treatment and lifestyle measures, n-3 PUFAs (icosapent ethyl 2 × 2 g/day) may be considered in combination with a statin.[84]	IIb	B



Ganancia en años libre de eventos CV


Screening and diagnosis of hypertension
Blood pressure measurement
Optimal
<120/80 mmHg
Normal
120–129 mmHg /
80–84 mmHg
High-normal
130–139 mmHg /
85–89 mmHg
Hypertension
≥140/90 mmHg
Consider
masked
hypertension
Out-of-office
BP measurement
(ABPM or HBPM)
Repeat visits
for office
BP measurement
OR
Out-of-office
BP measurement
(ABPM or HBPM)
Indications
for ABPM
or HBPM
Repeat BP
measurement a
least every 5 years
Repeat BP
measurement at
least every 3 years
Repeat BP
measurement a
least annually
ESC



Ganancia en años libre de eventos CV

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Age group	Office SBP treatment target ranges (mmHg)				
	Hypertension	+ DM	+ CKD	+ CAD	+ Stroke/TIA
18 – 69 years	120–130	120–130	<140–130	120–130	120–130
	Lower SBP acceptable if tolerated				
≥70 years	**<140 mmHg, down to 130 mmHg if tolerated** *Lower SBP acceptable if tolerated*				
DBP treatment target (mmHg)	<80 for all treated patients				

CAD = coronary artery disease; CKD = chronic kidney disease; DBP = diastolic blood pressure; DM = diabetes mellitus; SBP = systolic blood pressure; TIA = transient ischaemic attack.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

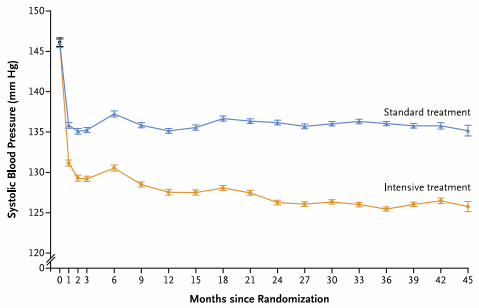
Trial of Intensive Blood-Pressure Control in Older Patients with Hypertension

Weili Zhang, M.D., Ph.D., Shuyuan Zhang, Ph.D., Yue Deng, Ph.D., Shouling Wu, M.D., Jie Ren, M.D., Gang Sun, M.D., Jinfeng Yang, M.D., Yinong Jiang, M.D., Xinjuan Xu, M.D., Tzung-Dau Wang, M.D., Ph.D., Youren Chen, M.D., Yufeng Li, M.D., Lianchen Yao, M.D., Dianfang Li, M.D., Lixin Wang, M.D., Xiaomei Shen, M.D., Xinhua Yin, M.D., Wei Liu, M.D., Xiaoyang Zhou, M.D., Bingpo Zhu, M.D., Zihong Guo, M.D., Hualing Liu, M.D., Xiaoping Chen, M.D., Yingqing Feng, M.D., Gang Tian, M.D., Xiuyin Gao, B.Sc., Kazuomi Kario, M.D., Ph.D., and Jun Cai, M.D., Ph.D., for the STEP Study Group*

N Engl J Med 2021;385:1268-79.

Ensayo clínico multicéntrico
60-80 años.
PAS 140-190
- TTO intensivo PAS 110-130
- TTO estándar PAS 130-150

Sgto 4 años
PA medida por AMPA. App
Edad media 66,2 ± 4,8



No. with Data								
Standard treatment	4268	4139	4086	4092	4072	3954	3857	1885
Intensive treatment	4243	4128	4086	4049	4050	3969	3894	1850
Mean No. of Medications								
Standard treatment	1.4	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Intensive treatment	1.5	1.7	1.8	1.8	1.9	1.9	1.9	1.9

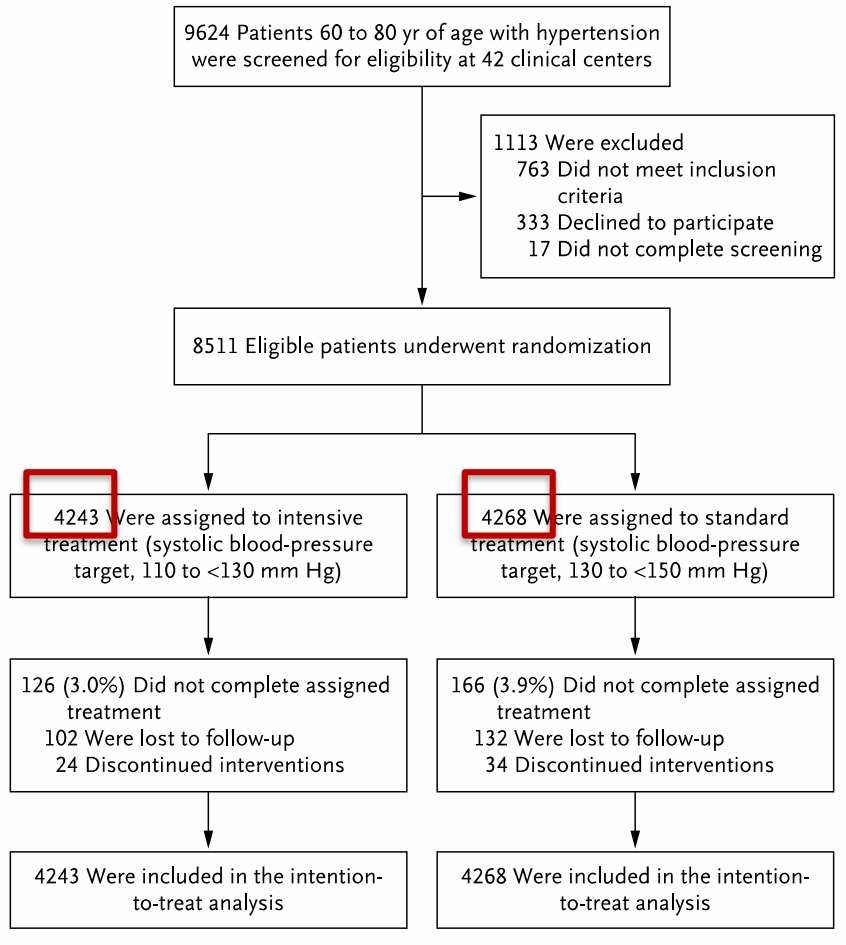


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Table 2. Hazard Ratios for the Primary and Secondary Outcomes.*

Outcome	Intensive Treatment (N=4243)		Standard Treatment (N=4268)		Hazard Ratio (95% CI)	P Value
	no. of patients (%)	*% with event per year*	*no. of patients (%)*	*% with event per year*		
Primary outcome†	147 (3.5)	1.0	196 (4.6)	1.4	0.74 (0.60–0.92)	0.007
Secondary outcomes						
Components of primary outcome						
Stroke	48 (1.1)	0.3	71 (1.7)	0.5	0.67 (0.47–0.97)	—
Acute coronary syndrome	55 (1.3)	0.4	82 (1.9)	0.6	0.67 (0.47–0.94)	—
Acute decompensated heart failure	3 (0.1)	0.03	11 (0.3)	0.09	0.27 (0.08–0.98)	—
Coronary revascularization	22 (0.5)	0.1	32 (0.7)	0.2	0.69 (0.40–1.18)	—
Atrial fibrillation	24 (0.6)	0.2	25 (0.6)	0.2	0.96 (0.55–1.68)	—
Death from cardiovascular causes	18 (0.4)	0.1	25 (0.6)	0.2	0.72 (0.39–1.32)	—
Death from any cause	67 (1.6)	0.5	64 (1.5)	0.5	1.11 (0.78–1.56)	—
Major adverse cardiac events‡	100 (2.4)	0.7	138 (3.2)	1.0	0.72 (0.56–0.93)	—

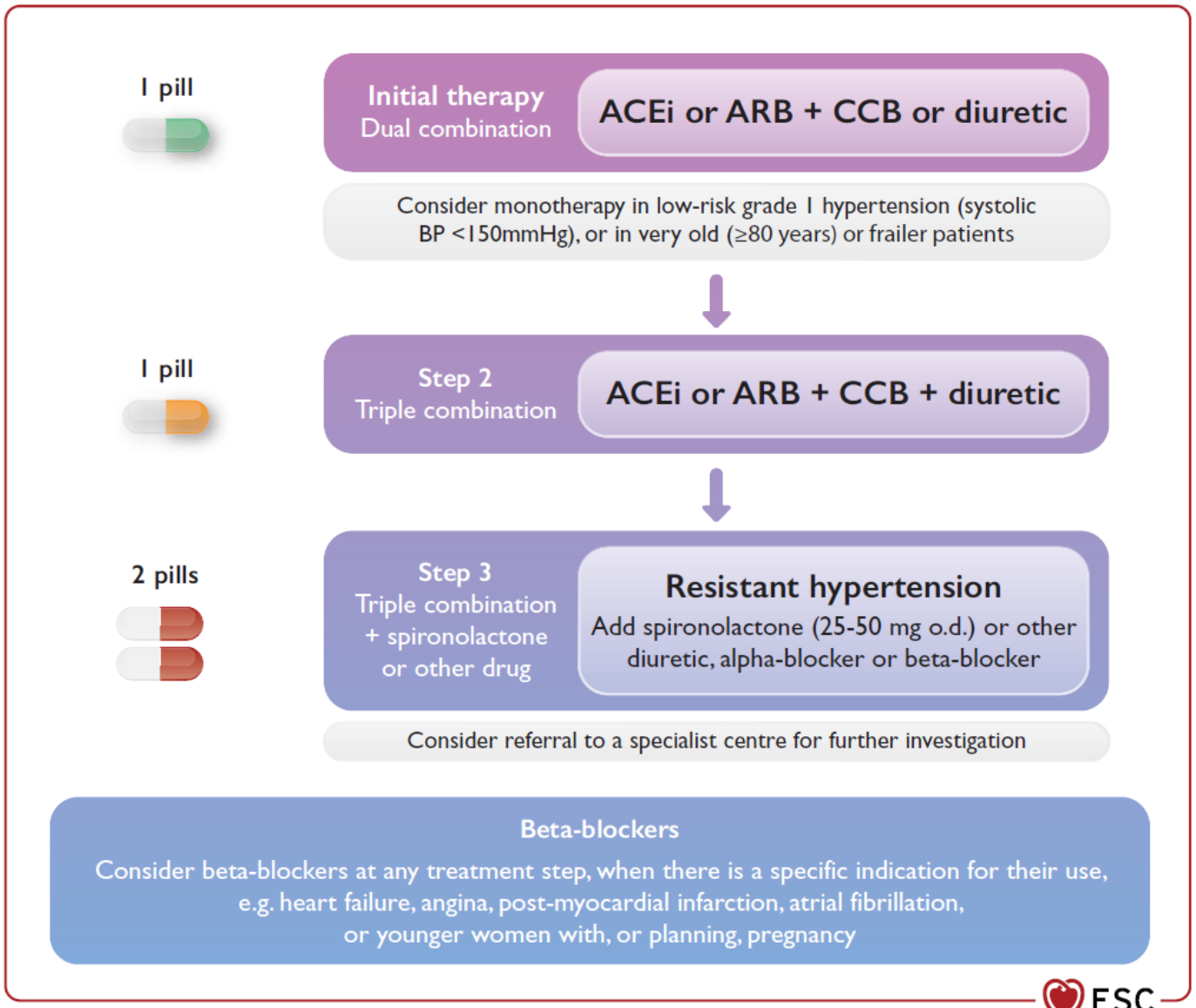
* For the primary outcome and secondary outcomes except for death from any cause, the hazard ratios, 95% confidence intervals, and P value were calculated with the use of the Fine–Gray subdistribution hazard model for the competing risk of death. For death from any cause, the Cox regression model was used. All models were adjusted for clinical center.

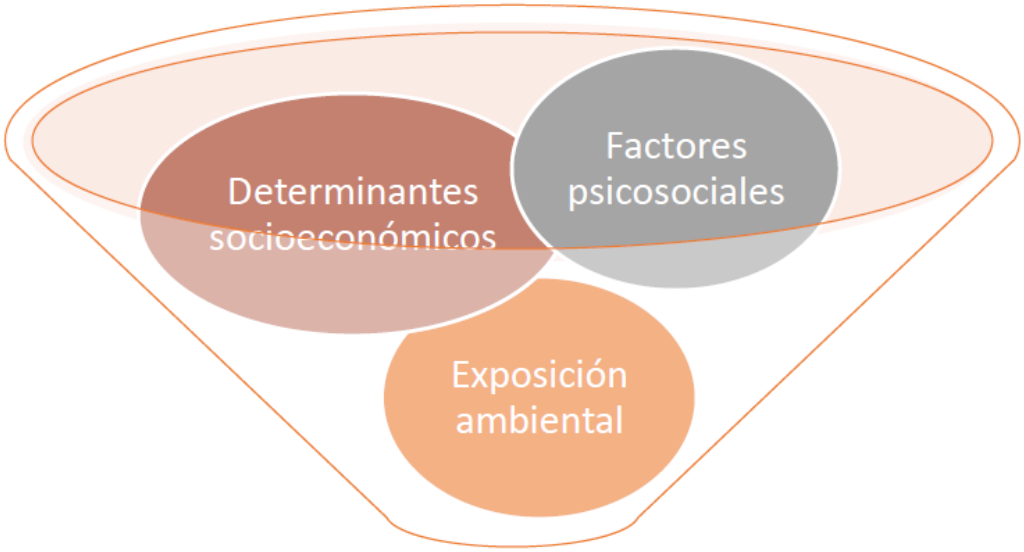
† The primary outcome was a composite of stroke, acute coronary syndrome, acute decompensated heart failure, coronary revascularization, atrial fibrillation, or death from cardiovascular causes.

‡ The secondary outcome of major adverse cardiac events was a composite of the individual components of the primary outcome except for stroke.

En pacientes mayores el tratamiento antihipertensivo con objetivo de PAS 110-130 mmHg y control por AMPA reduce la incidencia de eventos cardiovasculares frente al tratamiento estándar.

No hubo diferencias significativas entre ambos grupos en cuanto al objetivo de seguridad que evaluó la aparición de mareos, síncopes y fracturas; ni variaciones significativas de la función renal





Estrés laboral, Depresión
Inseguridad alimentaria, obesidad
Pobre adherencia
Tabaquismo

Modificaciones al estilo de vida

The DASH (Dietary Approaches to Stop Hypertension)/Dieta Mediterránea

Adopt a more plant- and less animal-based food pattern
Saturated fatty acids should account for <10% of total energy intake, through replacement by PUFAs, MUFAs, and carbohydrates from whole grains
Trans unsaturated fatty acids should be minimized as far as possible, with none from processed foods
<5 g total salt intake per day
30–45 g of fibre of per day, preferably from wholegrains
≥200 g of fruit per day (≥2–3 servings)
≥200 g of vegetables per day (≥2–3 servings)
Red meat should be reduced to a maximum of 350 - 500 g a week, in particular processed meat should be minimized
Fish is recommended 1–2 times per week, in particular fatty fish
30 g unsalted nuts per day
Consumption of alcohol should be limited to a maximum of 100 g per week
Sugar-sweetened beverages, such as soft drinks and fruit juices, must be discouraged

MUFA = monounsaturated fatty acid; PUFA = polyunsaturated fatty acid.

Bariatric surgery for obese high-risk individuals should be considered when lifestyle change does not result in maintained weight loss.[455]	IIa	B	

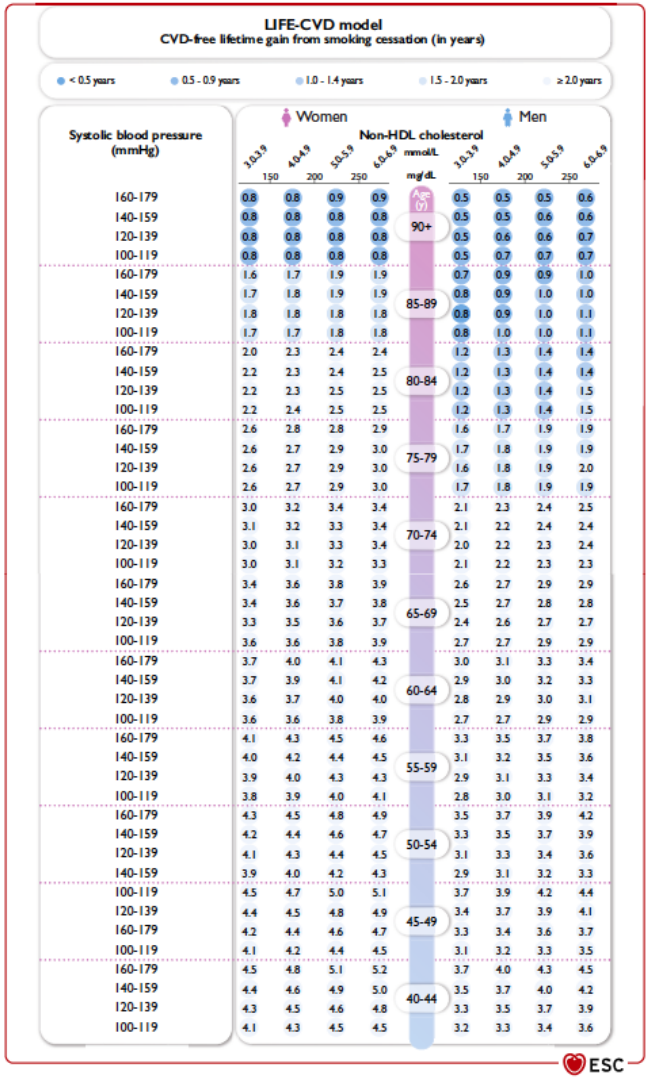
Medicación aprobada Europa: Orlistat, naltrexona/bupropion, Liraglutide

Salud Mental

Recommendations	Class[a]	Level[b]
Patients with mental disorders need intensified attention and support to improve adherence to lifestyle changes and drug treatment.[3,465]	I	C
In ASCVD patients with mental disorders, evidence-based mental healthcare and interdisciplinary cooperation are recommended.[100,113,466]	I	B
ASCVD patients with stress should be considered for referral to psychotherapeutic stress management to improve CV outcomes and reduce stress symptoms.[467–469]	IIa	B
Patients with CHD and moderate-to-severe major depression should be considered for antidepressive treatment with an SSRI.[470,471]	IIa	B
In patients with HF and major depression, SSRIs, SNRIs, and tricyclic antidepressants are not recommended.[472,473] c	III	B

Tabaco

Recommendations	Class[a]	Level[b]
All smoking of tobacco should be stopped, as tobacco use is strongly and independently causal of ASCVD.[487,488]	I	A
In smokers, offering follow-up support, nicotine replacement therapy, varenicline, and bupropion individually or in combination should be considered.[489–494]	IIa	A
Smoking cessation is recommended regardless of weight gain, as weight gain does not lessen the ASCVD benefits of cessation.[495]	I	B



Ganancia en años libre de eventos CV

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Ejercicio

Recommendations	Class[a]	Level[b]
It is recommended for adults of all ages to strive for at least 150 - 300 min a week of moderate-intensity or 75 - 150 min a week of vigorous-intensity aerobic PA, or an equivalent combination thereof, to reduce all-cause mortality, CV mortality, and morbidity.[371,372]	I	A
It is recommended that adults who cannot perform 150 min of moderate-intensity PA a week should stay as active as their abilities and health condition allow.[373,374]	I	B
It is recommended to reduce sedentary time to engage in at least light activity throughout the day to reduce all-cause and CV mortality and morbidity.[375–377]	I	B
Performing resistance exercise, in addition to aerobic activity, is recommended on 2 or more days per week to reduce all-cause mortality.[378,379]	I	B
Lifestyle interventions, such as group or individual education, behaviour-change techniques, telephone counselling, and use of consumer-based wearable activity trackers, should be considered to increase PA participation.[380–382]	IIa	B

Fragilidad
Factores socio-económicos
Enf inflamatorias. AR
SAHS
EPOC

Exposición Ambiental

Recommendations	Class[a]	Level[b]
Patients at (very) high risk for CVD may be encouraged to try to avoid long-term exposure to regions with high air pollution.	IIb	C
In regions where people have long-term exposure to high levels of air pollution, (opportunistic) CVD risk screening programmes may be considered.	IIb	C

Putting in place measures to reduce air pollution, including reducing PM emission and gaseous pollutants, reducing the use of fossil fuels, and limiting carbon dioxide emissions, are recommended, to reduce CVD mortality and morbidity.	I	C

GLOBAL HEART

Taking a Stand Against Air Pollution – The Impact on Cardiovascular Disease

A Joint Opinion from the World Heart Federation, American College of Cardiology, American Heart Association, and the European Society of Cardiology

2021; 16(1): 8.

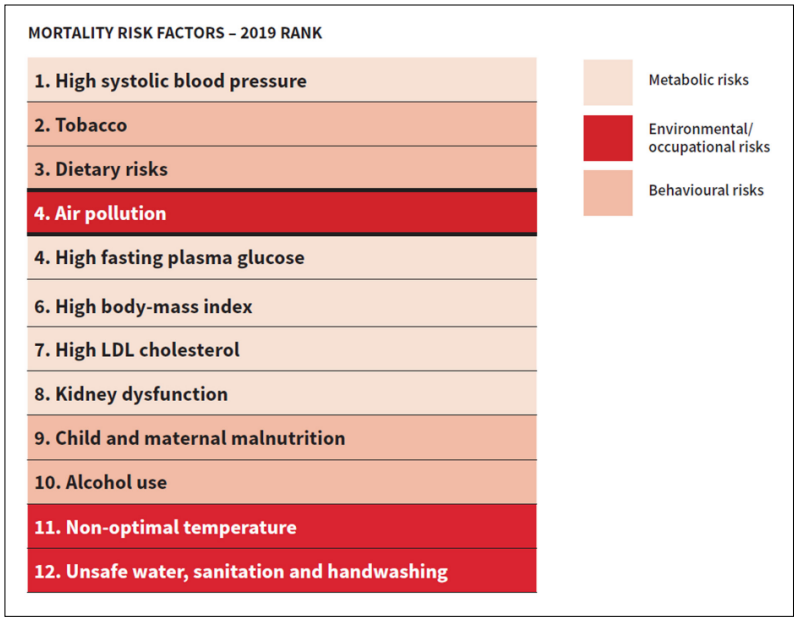

Figure 1: Ranking of air pollution relative to other leading risk factors for global mortality. Mortality Risk Factors, Both sexes, all ages, 2019. Institute for Health Metrics and Evaluation. (Adapted from Institute for Health Metrics and Evaluation, 2020).

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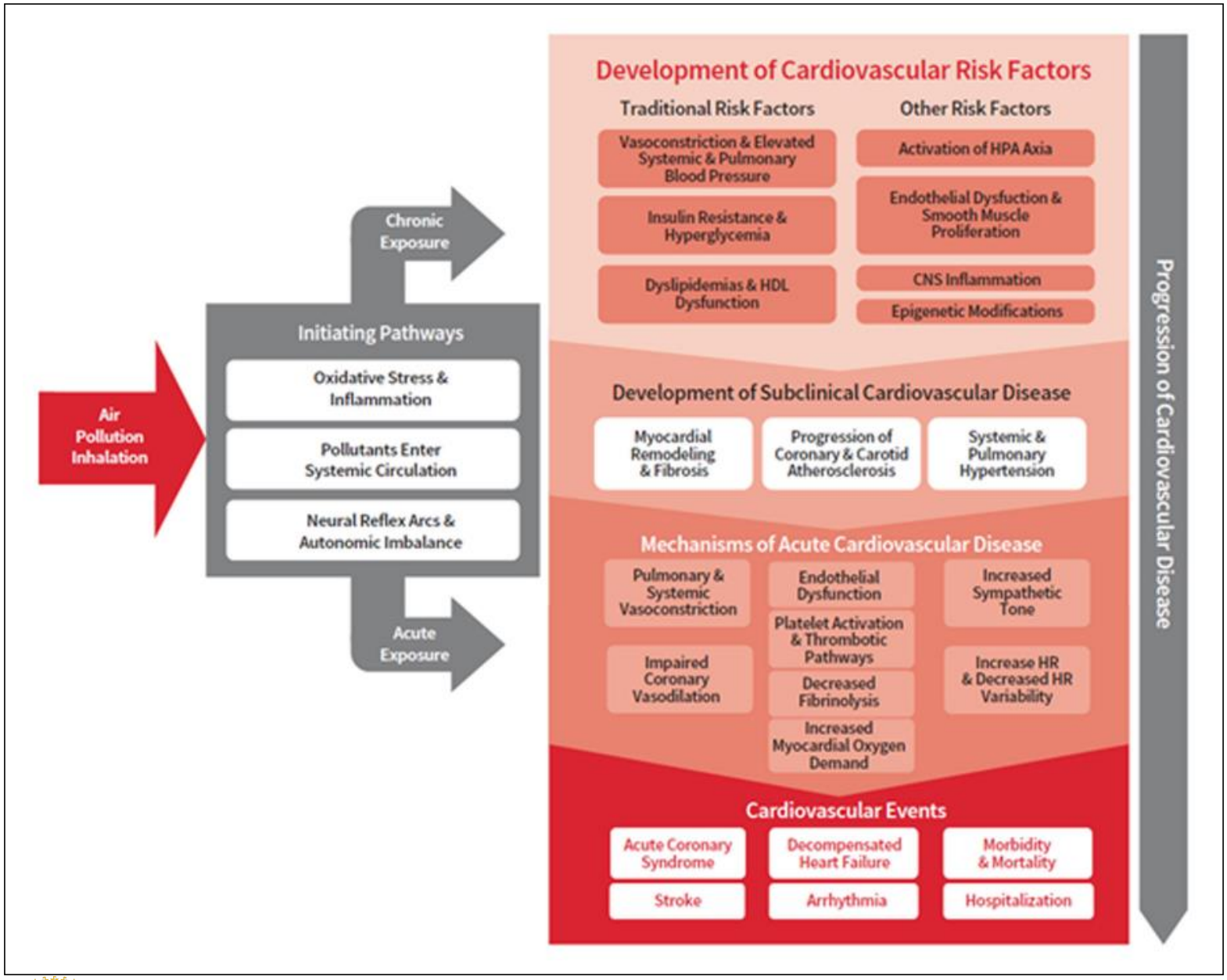

Air Pollution Inhalation
Chronic Exposure
Initiating Pathways
Oxidative Stress & Inflammation
Pollutants Enter Systemic Circulation
Neural Reflex Arcs & Autonomic Imbalance
Acute Exposure
Development of Cardiovascular Risk Factors
Traditional Risk Factors
Vasoconstriction & Elevated Systemic & Pulmonary Blood Pressure
Insulin Resistance & Hyperglycemia
Dyslipidemias & HDL Dysfunction
Other Risk Factors
Activation of HPA Axia
Endothelial Dysfuction & Smooth Muscle Proliferation
CNS Inflammation
Epigenetic Modifications
Development of Subclinical Cardiovascular Disease
Myocardial Remodeling & Fibrosis
Progression of Coronary & Carotid Atherosclerosis
Systemic & Pulmonary Hypertension
Mechanisms of Acute Cardiovascular Disease
Pulmonary & Systemic Vasoconstriction
Endothelial Dysfunction
Increased Sympathetic Tone
Platelet Activation & Thrombotic Pathways
Impaired Coronary Vasodilation
Decreased Fibrinolysis
Increase HR & Decreased HR Variability
Increased Myocardial Oxygen Demand
Cardiovascular Events
Acute Coronary Syndrome
Decompensated Heart Failure
Morbidity & Mortality
Stroke
Arrhythmia
Hospitalization
Progression of Cardiovascular Disease

European Society of Hypertension

Scientific Newsletter
Update on Hypertension Management
2021, 26, nr. 79

AN UPDATE OF THE GUIDELINES FOR DIAGNOSIS AND MANAGEMENT OF PRIMARY ALDOSTERONISM

Gian Paolo Rossi

Hypertension Unit , Dept. of Medicine - DIMED – University of Padova, Italy

Aprox 6% de los hipertensos

Hasta el 20% HTA en centros especializados en HTA

Actualmente poco frecuente la presentación HTA reciente dx + hipoK

Subtipo	Prevalencia
Hiperplasia adrenal bilateral [a]	65%
Hiperplasia adrenal unilateral [a]	<1%
Adenoma productor de aldosterona	35%
Carcinoma productor de aldosterona	<1%
Hiperaldosteronismos familiares • tipo I o sensible a glucocorticoides (síndrome de Sutherland) • tipo II (mutaciones en CLCN2) • tipo III (mutaciones en KCNJ5) • tipo IV (mutaciones en CACNA1H)	<1%

[a] La hiperplasia adrenal también se denomina hiperaldosteronismo idiopático, fundamentalmente cuando en las pruebas de imagen no hay alteraciones anatómicas significativas en las glándulas suprarrenales.

Ares J, Goicoechea Diezandino M, Gorostidi M. Nefrología al día. Hiperaldosteronismo primario.

Recomendaciones para la determinación del cociente aldosterona / renina, ARR
1. Corregir la hipopotasemia y dar una dieta de al menos 5 gramos de sal; valorar la ingesta de sal midiendo el sodio en orina de 24 horas
2. Establecer un valor mínimo de ARP de 0,2 ng/mL/h o de CRD de 2 mU/L
3. Se debe extraer la muestra después de que el paciente permanezca tumbado o sentado durante 60 minutos
4. El transporte de las muestras es diferente si se mide ARP, en este caso la muestra se debe transportar inmediatamente al laboratorio y en hielo para bloquear la generación de angiotensina I y el consumo de angiotensinógeno, o si se va a medir CRD, en este caso la muestra se puede transportar a temperatura ambiente
5. Fármacos: inicialmente se pueden mantener los fármacos necesarios para controlar la presión arterial e hipopotasemia, teniendo en cuenta su influencia sobre la concentración de aldosterona y renina; si el valor no es concluyente, se deberían suspender los fármacos y repetir la determinación
6. Existe una aplicación, la App-ARR, para calcular el cociente aldosterona/renina en las unidades de medidas correctas

- Siempre corregir antes hipoK
- Ingesta libre de sal
- Suspender siempre antes espironolactona, eplerenona, antagonistas de la renina
- Tener en cuenta las interacciones de otros fármacos. Utilizar preferentemente fármacos que no modifican los niveles

ALDOSTERONA > 15-20 ng/dl
ARP > 30

Fármaco o situación	Aldosterona	Renina	Cociente A/R
IECA y ARA II	Disminuye ↓	Aumenta ↑↑	Disminuye ↓↓ *
Diuréticos	Aumenta o igual	Aumenta ↑↑	Disminuye ↓ *
ARM	Aumenta ↑	Aumenta ↑↑	Disminuye ↓ *
Betabloqueantes	Disminuye ↓	Disminuye ↓↓	Aumenta ↑ **
Calcioantagonistas dihidropiridínicos	Disminuye o igual	Aumenta	Disminuye ↓ *
Antiinflamatorios no esteroideos	Disminuye ↓	Disminuye ↓	Aumenta ↑ **
Hipopotasemia	Disminuye ↓	Aumenta o igual	Disminuye ↓ *
Dieta hiposódica	Aumenta ↑	Aumenta ↑	Disminuye ↓ *

Fármaco	Dosis	Observaciones
Verapamilo	Habitual 240 mg/día, máxima 480 mg/día	
Doxazosina	Dosis inicial 1 mg/día al acostarse, aumentar a 2 mg/día al cabo de una semana si es preciso, aumentar a 4 mg/día al cabo de 1-2 semanas más si es preciso y completar la dosis a 8 mg/día al cabo de 1-2 semanas más si es preciso	Cuando se pauten 4 u 8 mg/día se utilizarán formulaciones Neo o de liberación prolongada para evitar hipotensión ortostática
Terazosina	Dosis inicial 1 mg/día al acostarse, aumentar a 2 mg/día al cabo de una semana si es preciso, aumentar a 4 mg/día al cabo de 1-2 semanas más si es preciso, etc. hasta dosis máxima de 20 mg/día	Riesgo de ortostatismo al aumentar la dosis
Prazosina	Misma pauta que Terazosina	Riesgo de ortostatismo al aumentar la dosis
Hidralazina	Dosis inicial 12,5 mg cada 6-12 h durante los 2-4 primeros días, aumentando después a 25 mg cada 6 h en la primera semana y a 50 mg cada 6 h posteriormente si es preciso En el periodo de mantenimiento la dosis debe ajustarse al nivel más bajo. La dosis máxima diaria de Hidralazina es de 200 mg al día.	Iniciar antes Verapamilo para evitar taquicardia refleja

Test confirmatorio	Método	Valores diagnósticos
Test de infusión de solución salina	Solución salina 0,9% 500 mL/h IV durante 4 horas	Concentración plasmática de aldosterona >5 ng/dL
Test de sobrecarga oral de sal	Dieta de >6 g/día de sal durante 3 días *	Aldosterona urinaria >12 ng/24 h
Test de supresión con Fludrocortisona	Fludrocortisona 0,4 mg/día VO durante 4 días	Concentración plasmática de aldosterona >5 ng/dL
Test de supresión con Captopril	Captopril 25 mg VO	Disminución a las 2 horas <30% de la concentración de aldosterona plasmática

* Comprobar que la eliminación urinaria de sodio sobrepasa los 100 mE/24 h, idealmente >200 mE/24 h.

IV, intravenosa; VO, vía oral.

Algorithm for The Work-up of PA

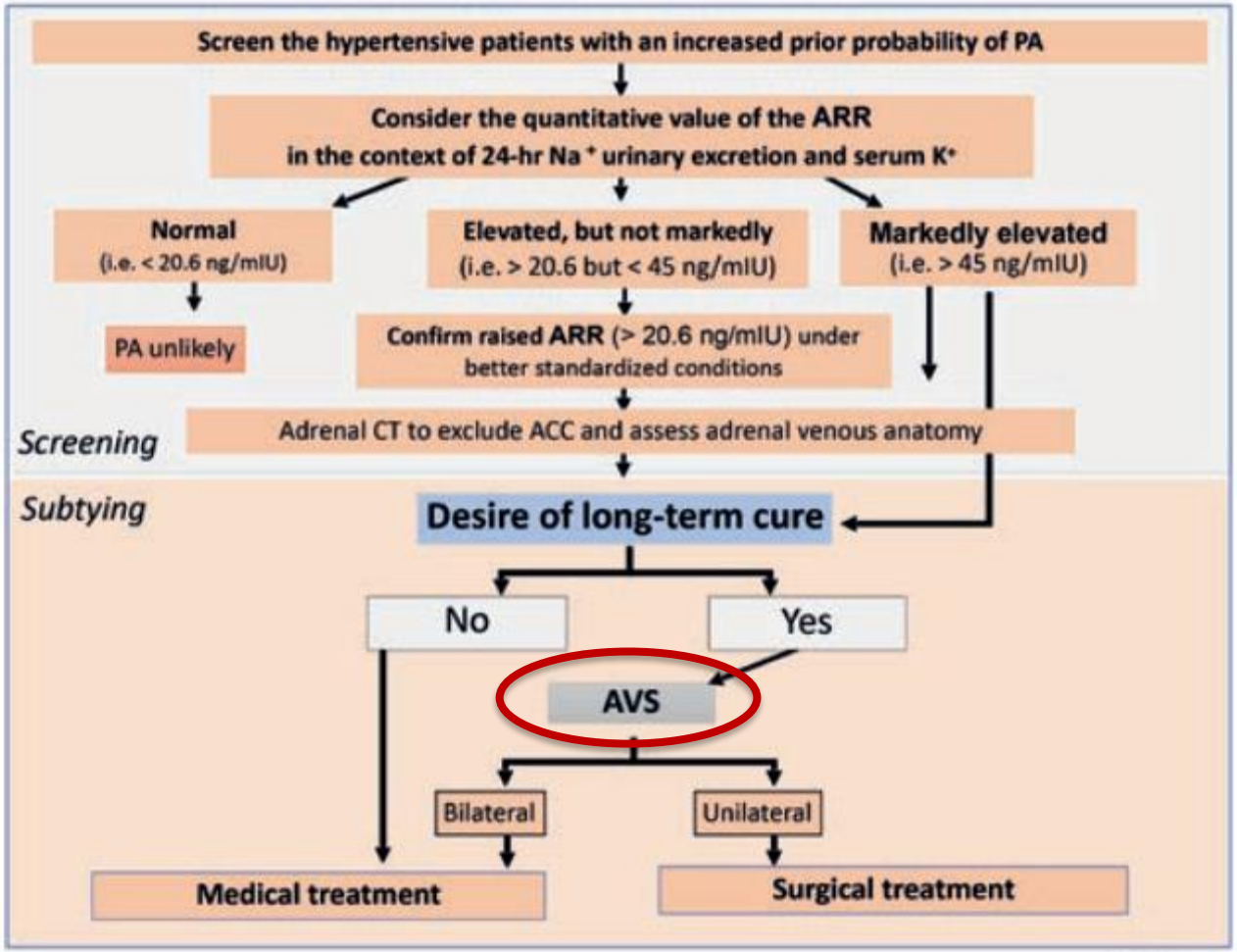
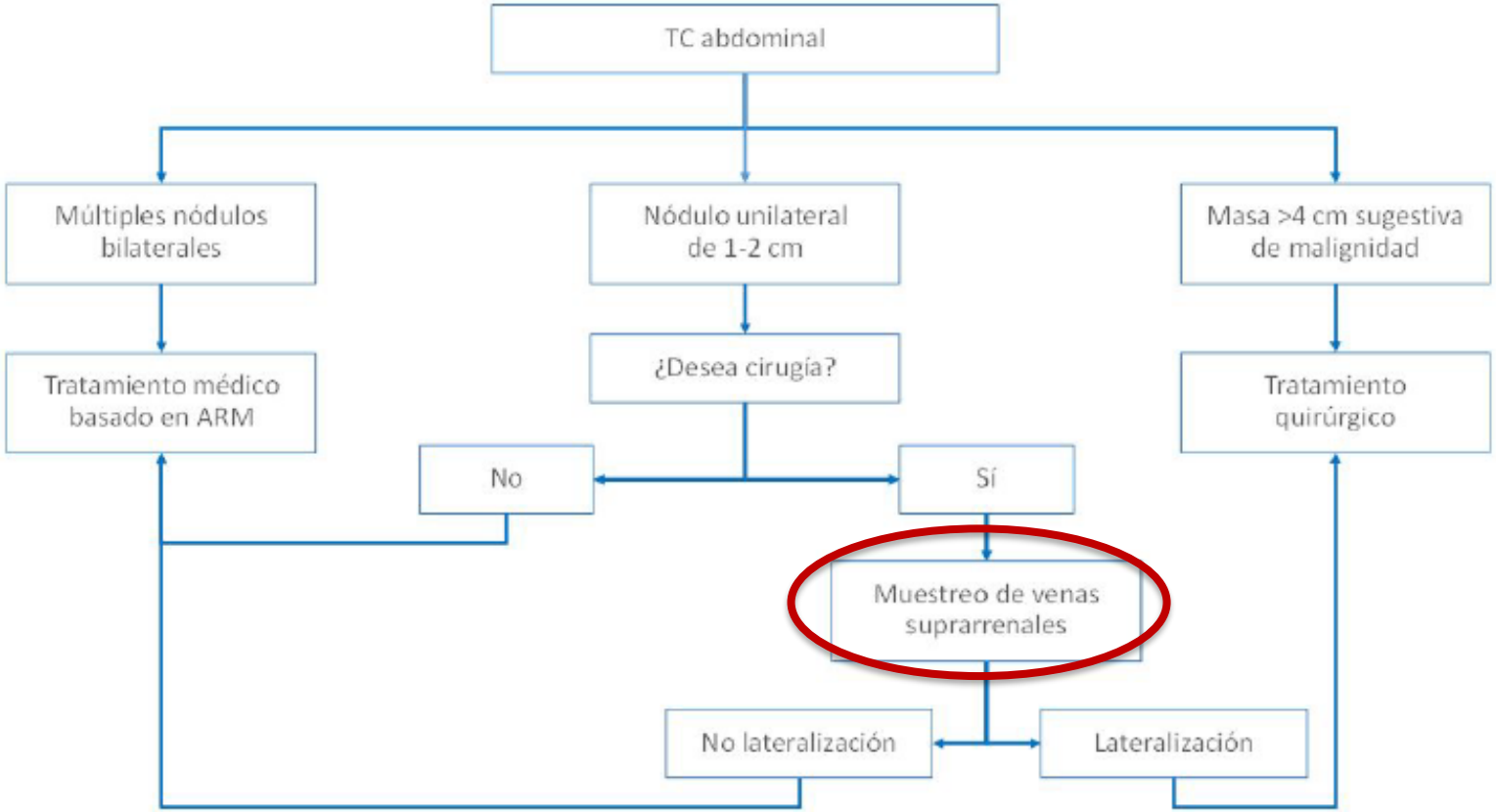


Figura 3. Algoritmo para el diagnóstico de los subtipos de hiperaldosteronismo primario.



TC, tomografía computarizada; ARM, antagonista de los receptores mineralcorticoides.
En pacientes jóvenes con cociente aldosterona/renina muy elevado, hipopotasemia y TC compatible con adenoma se puede optar por cirugía directamente sin el muestreo de venas suprarrenales.

AVS

Indicaciones

- Hiperaldosteronismo primario

    - Firmar consentimiento
    - No contraindicación para cirugía

NO indicado:

• <40 años con nódulo SR único hipodenso > 1 cm con SR contralateral normal en TAC (mayoría de los protocolos)

• Cirugía ya indicada por sospecha de carcinoma suprarrenal

AVS

- Acceso a través de vena femoral común
- Localización de ambas venas suprarrenales
- Toma de muestras de:
  - Vena suprarrenal derecha
  - Vena suprarrenal izquierda
  - Vena cava inferior
  - Vena periférica
- Determinación de relación Aldosterona/Cortisol
- Con o sin estímulo ACTH

Con/sin estimulación con ACTH (Synacthen®, Cosyntropin®)

- Sin estímulo (basal)
  Precisa toma simultánea y a primera hora de la mañana
- Tras bolus 0.25 mg iv
  Permite cualquier hora, pero precisa toma simultánea
- Durante infusión continua 50 µg/h
  Permite toma secuencial y a cualquier hora

PROTOCOLO TÉCNICA CAULE

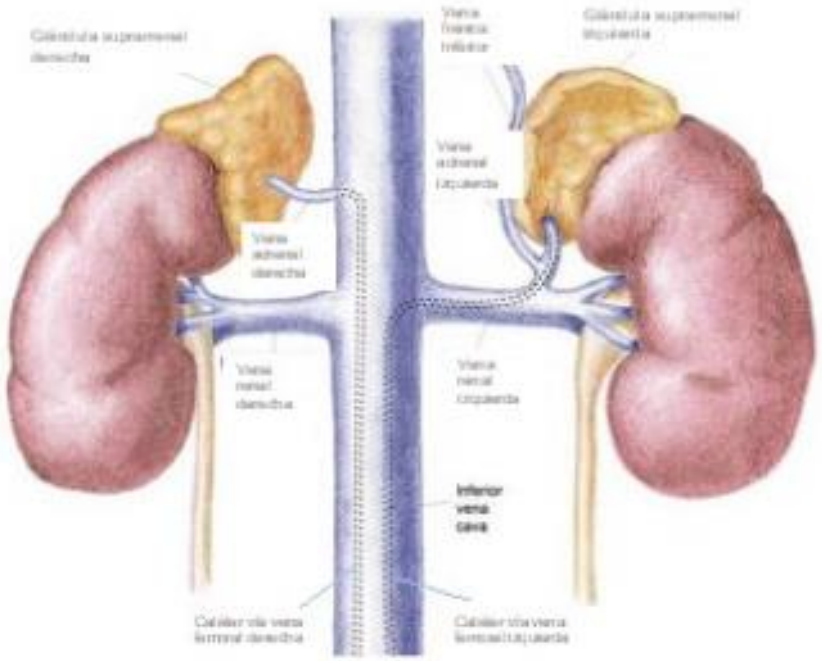
1. Se debe permanecer **en ayuno desde la noche anterior**. El paciente debe tener una vía venosa de acceso periférico calibre 18 en el antebrazo derecho.
2. **3 horas antes del procedimiento el paciente permanecerá en reposo absoluto y decúbito supino.**
3. **30 minutos antes de empezar el procedimiento recibirá ACTH (0,25 mg en bolo).**
4. El procedimiento se realiza bajo anestesia local/sedación consciente en la sala de Radiología Vascular e Intervencionista.
5. Se administra un bolo de 5.000 unidades de heparina sódica iv por vena periférica justo antes de cateterizar las venas suprarrenales.
6. Se realiza punción de ambas venas femorales comunes. Se colocan dos introductores 6F
7. Dos catéteres Cobra 5F (uno de ellos hidrofílico) y un microcatéter ≤2.8F.
8. Navegamos hasta la **vena suprarrenal derecha** con el catéter cobra y lo dejamos situado. Es la cateterización más compleja
9. Navegamos hasta la **vena suprarenal izquierda** con el catéter cobra (en ocasiones es mejor utilizar un catéter hidrofílico). Utilizamos un microcatéter ≤2.8F (con su lavado) para buscar el tronco común vena suprarrenal izq – frénica inferior. Si no logramos acceder a la suprarrenal se puede extraer desde el tronco.
10. Una vez que los catéteres estén colocados, se realiza lavado del contraste y se espera cinco minutos para minimizar la influencia del estrés.
11. A continuación, se realiza la **toma de muestras simultánea de los 4 accesos para las determinaciones**. Se recomienda una aspiración lenta e intermitente de las venas suprarrenales para evitar su colapso. Además, es muy conveniente que para cada catéter haya una persona encargada de su extracción y otra de recoger las muestras en los tubos correspondientes. Accesos:

» VSRD
» VSRI
» VCI por el introductor
» Vena periférica en antebrazo derecho.

12. Los tubos se deben rotular con anterioridad con su respectivo nombre, localización y momento de obtención, por ejemplo, “VSRD” (vena suprarrenal derecha), “VSRI” (vena suprarrenal izquierda), “VCI” (vena cava inferior), “VP” (vena periférica).

13. Una vez tomadas las muestras, se retiran los catéteres, y se realiza compresión manual para obtener una adecuada hemostasia antes del traslado del paciente a la sala de recuperación.
14. Se observa el paciente, quien debe estar **bajo estricto reposo en cama durante cuatro horas**. El **alta será 24h después**. HBPM dosis profiláctica el tiempo del ingreso: Enoxaparina (Clexane) 40 mg/24h o Bemiparina (Hibor) 2500 uds/24h. Independizar según el tipo de paciente.

AVS



Índice de selectividad (IS)

Cortisol VA / Cortisol VP

Indica canulación correcta de VA

Índice de lateralización (IL)

(Aldosterona/Cortisol) ipsilateral /
(Aldosterona/Cortisol) contralateral

Mide la lateralización de la síntesis de aldosterona

Tasa de inhibición contralateral (TCL)

(Aldosterona/Cortisol) contralateral /
(Aldosterona/Cortisol) VP

Inhibición de la síntesis de aldosterona por la glándula adrenal contralateral (≤ 1)

- Criterio de validez del procedimiento:
  - Indice de selectividad

$$IS = \frac{\text{[cortisol] vena suprarrenal}}{\text{[cortisol] vena cava inferior}}$$

- Criterio de lateralización:
  - Indice de lateralización

$$IL = \frac{\text{[aldosterona] / [cortisol] vena suprarrenal dominante}}{\text{[aldosterona] / [cortisol] vena suprarrenal NO dominante}}$$

- Criterio de supresión de la VSR no dominante:
  - Indice de supresión contralateral

$$ISup = \frac{\text{[aldosterona] / [cortisol] vena suprarrenal NO dominante}}{\text{[aldosterona] / [cortisol] vena cava inferior}}$$

IS > 2 sin estímulo; > 3 con estímulo
IL > 3 sin estímulo; > 4 con estímulo

IS: Para comprobar la correcta cateterización es preciso que la ratio Aldosterona/Cortisol de cada vena suprarrenal respecto a la ratio en periferia sea superior a 2-3.

IL: Una ratio Aldosterona/Cortisol de vena suprarrenal dominante respecto a la contralateral superior a 2-3 se considera indicativo de lateralidad (adenoma).
En la hiperplasia bilateral, los ratios de ambas suprarrenales deberían ser elevados comparados con la sangre periférica

Tratamiento

- **Adrenalectomía por Laparoscopia** (ELECCIÓN)
- ANTAGONISTAS RECEPTORES MINERALOCORTICOIDES

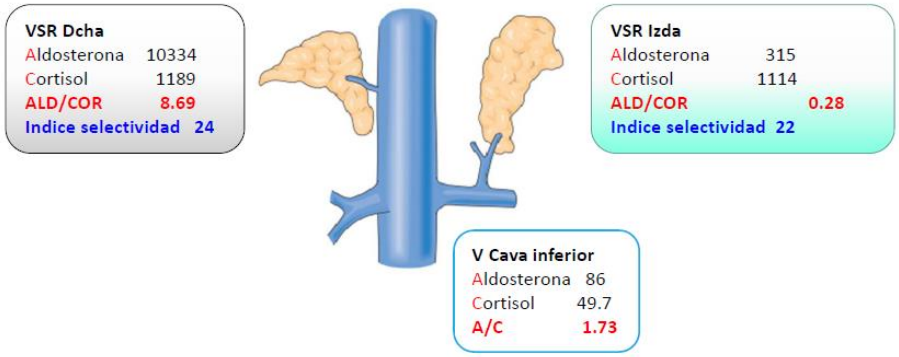
  Espironolactona.

  Eplerenona no aprobada para esta indicación por FDA ni EMA

CASO CLÍNICO

Varón 48 años
HTA Grado 2 tto BSRAA-HCTZDA-ACC sin LOD ni ECV establecida

Aldosterona 38 ng/dl
ALD/ARP 140
TC: Adenoma suprarrenal derecho



Indice lateralización dcha/izda (A/C dcha/ A/C izda): 30,7
Indice supresión izda/ periférica (A/C VSRI/ A/C VCI): 0.16

- Criterio de lateralización:
  - Indice de lateralización

$$IL = \frac{\text{[aldosterona] / [cortisol] vena suprarrenal dominante}}{\text{[aldosterona] / [cortisol] vena suprarrenal NO dominante}}$$

Suprarrenalectomía derecha laparoscópica

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