Società Italiana dell'Ipertensione Arteriosa
Lega Italiana contro l'Ipertensione Arteriosa

EVENTO FORMATIVO INTERREGIONALE SIIA
PIEMONTE | LIGURIA | VALLE D'AOSTA
Torino, 12 ottobre 2024

AZIENDA OSPEDALIERO-UNIVERSITARIA
Città della Salute e della Scienza di Torino

UNIVERSITÀ DI TORINO

UPDATE-2

Approccio terapeutico all'ipertensione di difficile controllo

Franco Rabbia

ESC European Society of Cardiology
European Heart Journal (2024) 00, 1–107
https://doi.org/10.1093/eurheartj/ehae178

2024 ESC Guidelines for the management of elevated blood pressure and hypertension

Developed by the task force on the management of elevated blood pressure and hypertension of the European Society of Cardiology (ESC) and *endorsed by the European Society of Endocrinology (ESE) and the European Stroke Organisation (ESO)*

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ESH Guidelines

2023 ESH Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Hypertension

Endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA)

Authors/Task Force Members: Giuseppe Mancia (Chairperson)[a,*], Reinhold Kreutz (Co-Chair)[b,*], Mattias Brunström[c], Michel Burnier[d], Guido Grassi[e], Andrzej Januszewicz[f], Maria Lorenza Muiesan[g], Konstantinos Tsioufis[h], Enrico Agabiti-Rosei[i], Engi Abd Elhady Algharably[b], Michel Azizi[j,k], Athanase Benetos[l], Claudio Borghi[m], Jana Brguljan Hitij[n], Renata Cifkova[o,p], Antonio Coca[q], Veronique Cornelissen[r], J. Kennedy Cruickshank[s], Pedro G. Cunha[t,u], A.H. Jan Danser[v], Rosa Maria de Pinho[w], Christian Delles[x], Anna F. Dominiczak[y], Maria Dorobantu[z], Michalis Doumas[aa], María S. Fernández-Alfonso[bb,cc], Jean-Michel Halimi[dd,ee,ff], Zoltán Járai[gg], Bojan Jelakovic[hh], Jens Jordan[ii,jj], Tatiana Kuznetsova[kk], Stephane Laurent[ll], Dragan Lovic[mm], Empar Lurbe[nn,oo,pp], Felix Mahfoud[qq,rr], Athanasios Manolis[ss], Marius Miglinas[tt,uu], Krzystof Narkiewicz[vv], Teemu Niiranen[ww,xx], Paolo Palatini[yy], Gianfranco Parati[zz,aaa], Atul Pathak[bbb], Alexandre Persu[ccc], Jorge Polonia[ddd], Josep Redon[oo,eee,fff], Pantelis Sarafidis[ggg], Roland Schmieder[hhh], Bart Spronck[iii], Stella Stabouli[jjj], George Stergiou[kkk], Stefano Taddei[lll], Costas Thomopoulos[mmm],

IPERTENSIONE DI DIFFICILE CONTROLLO

INADEGUATO CONTROLLO PRESSORIO NONOSTANTE RIPETUTE ED ADEGUATE PRESCRIZIONI TERAPEUTICHE DA PARTE DEL MEDICO DI FAMIGLIA E DELLO SPECIALISTA

ESC European Society of Cardiology
European Heart Journal (2024) 00, 1–107
https://doi.org/10.1093/eurheartj/ehae178

2023 ESH Guidelines for the management of arterial hypertension

Prevalenza di ipertensione arteriosa controllata e non controllata

Italy

Hypertension profile

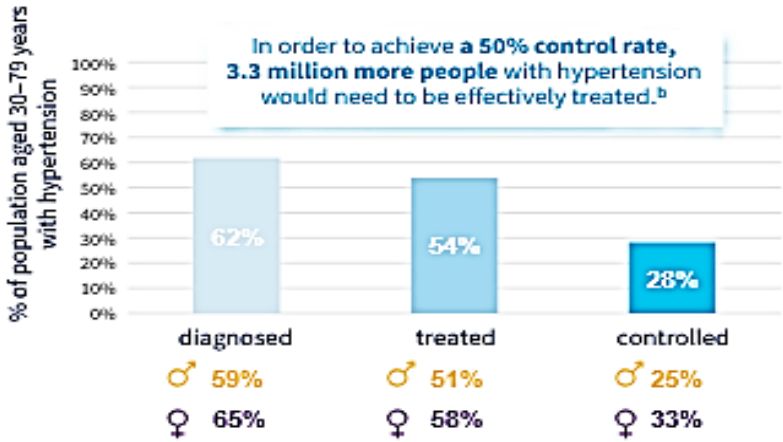
Total population (2019): 59 728 000

Total deaths (2019): 651 000

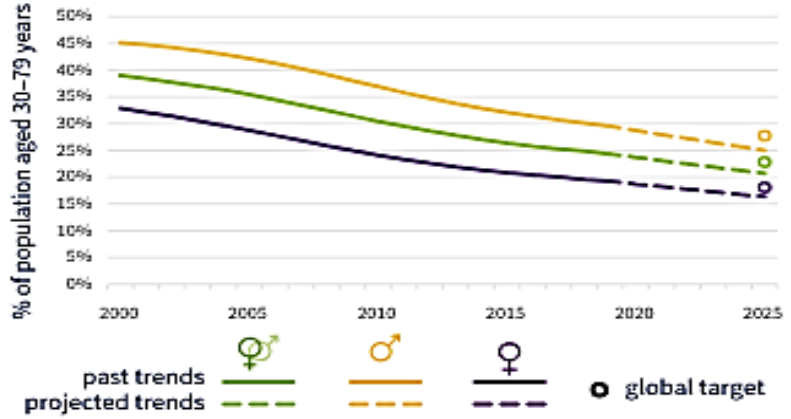
Age-standardized prevalence of hypertension among adults aged 30–79 years (2019)[a] ⚥ 34% ♂ 39% ♀ 29%

Prevalence of hypertension – global comparison (both sexes)[a]

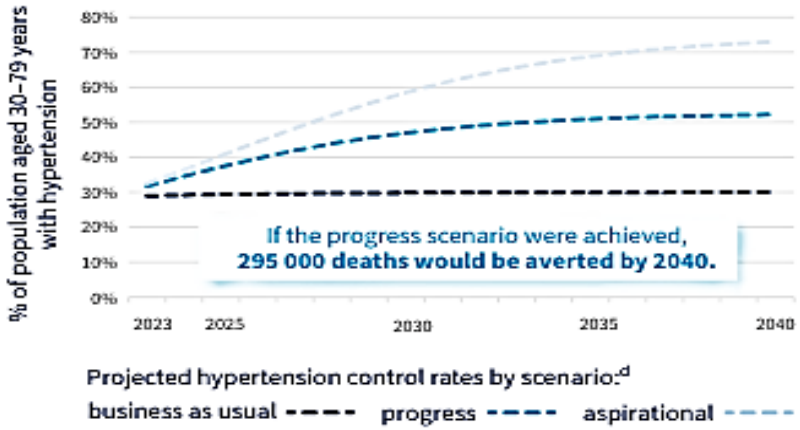
Of the **16.6 million** adults aged 30–79 years with hypertension:



Trends in uncontrolled hypertension in adults aged 30–79 years[c]

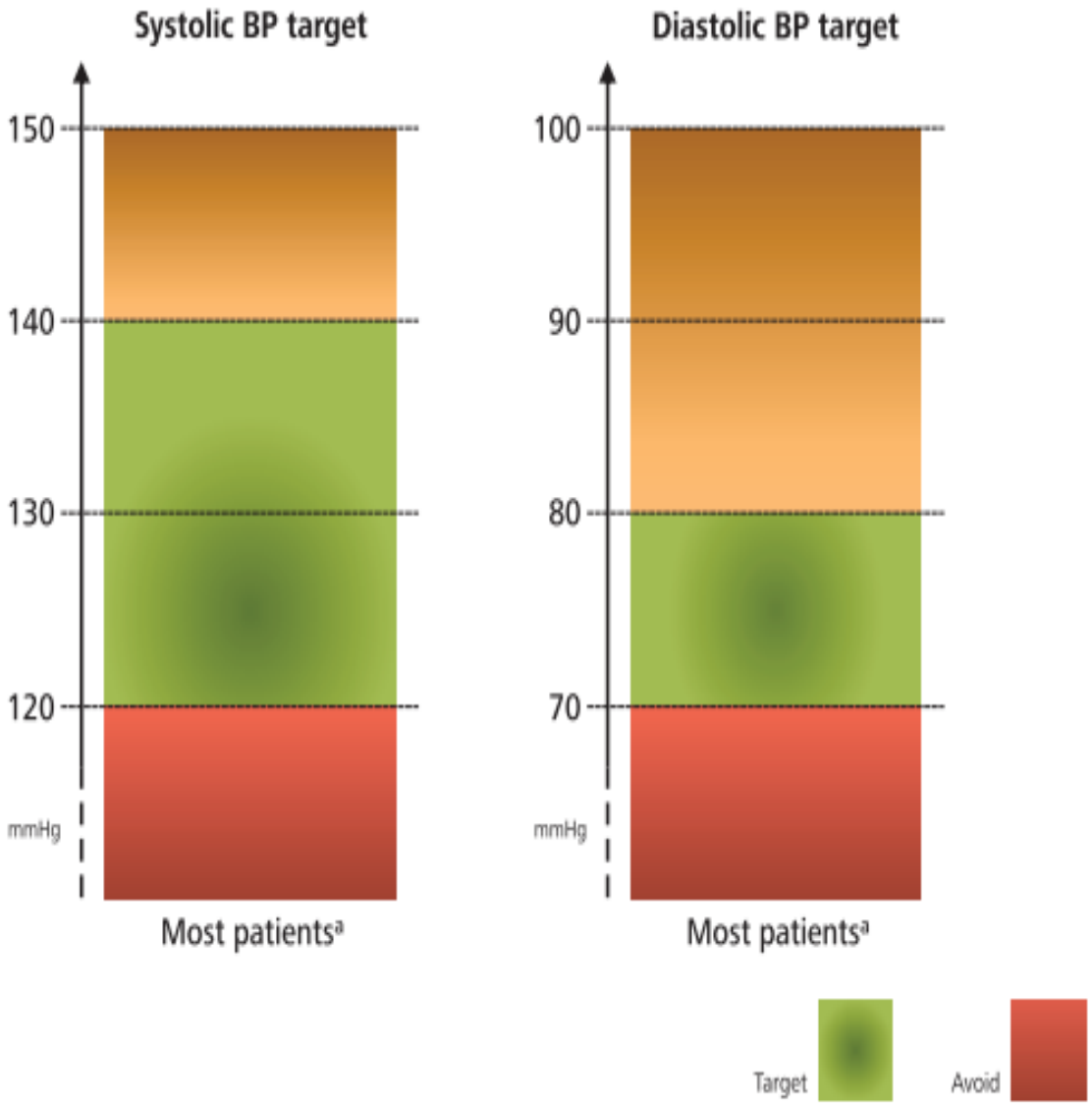


Hypertension control rate scenarios



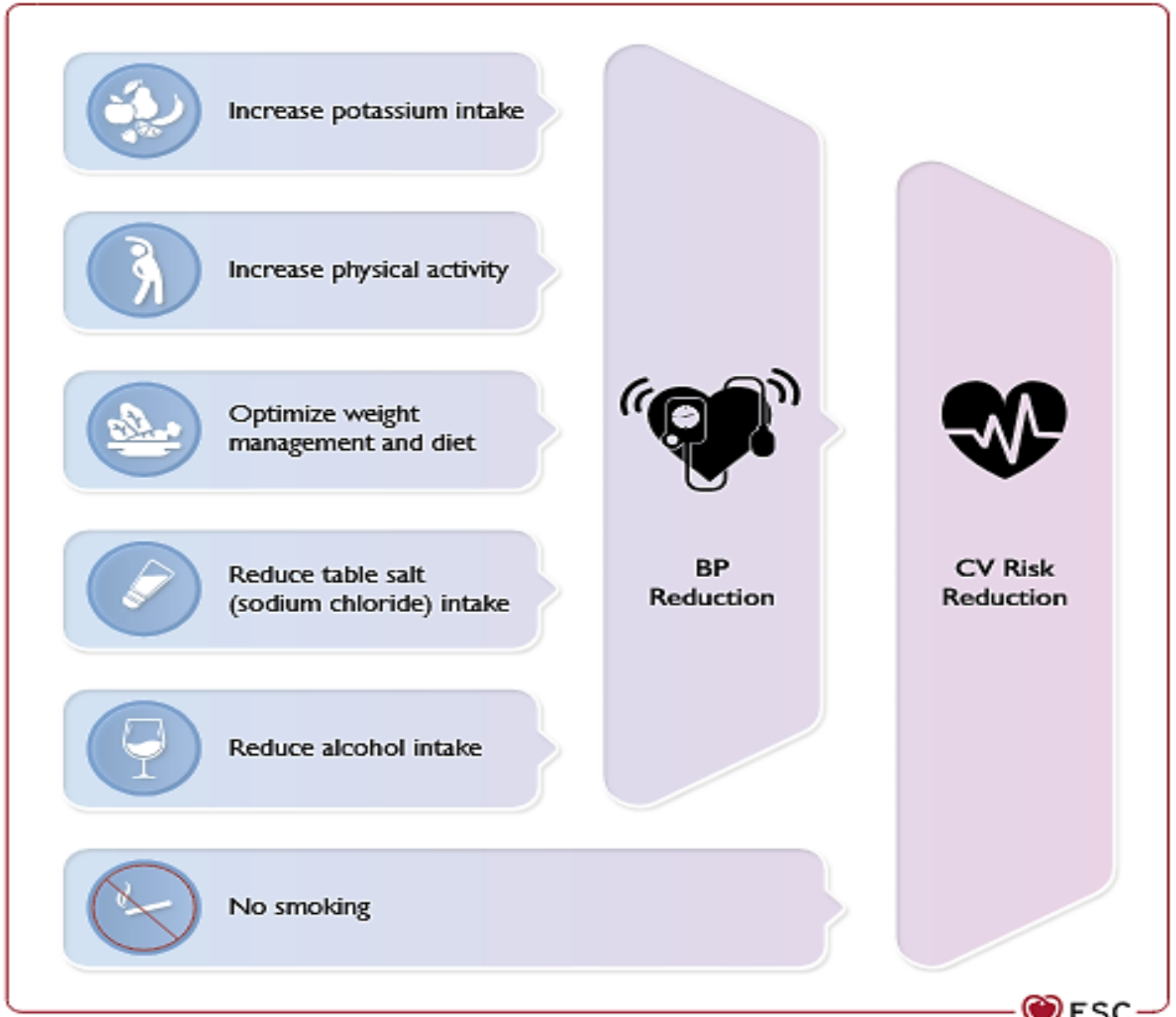
WHO 2023

2023 ESH Guidelines for the management of arterial hypertension



J Hypertens 2023

Trattamento non farmacologico



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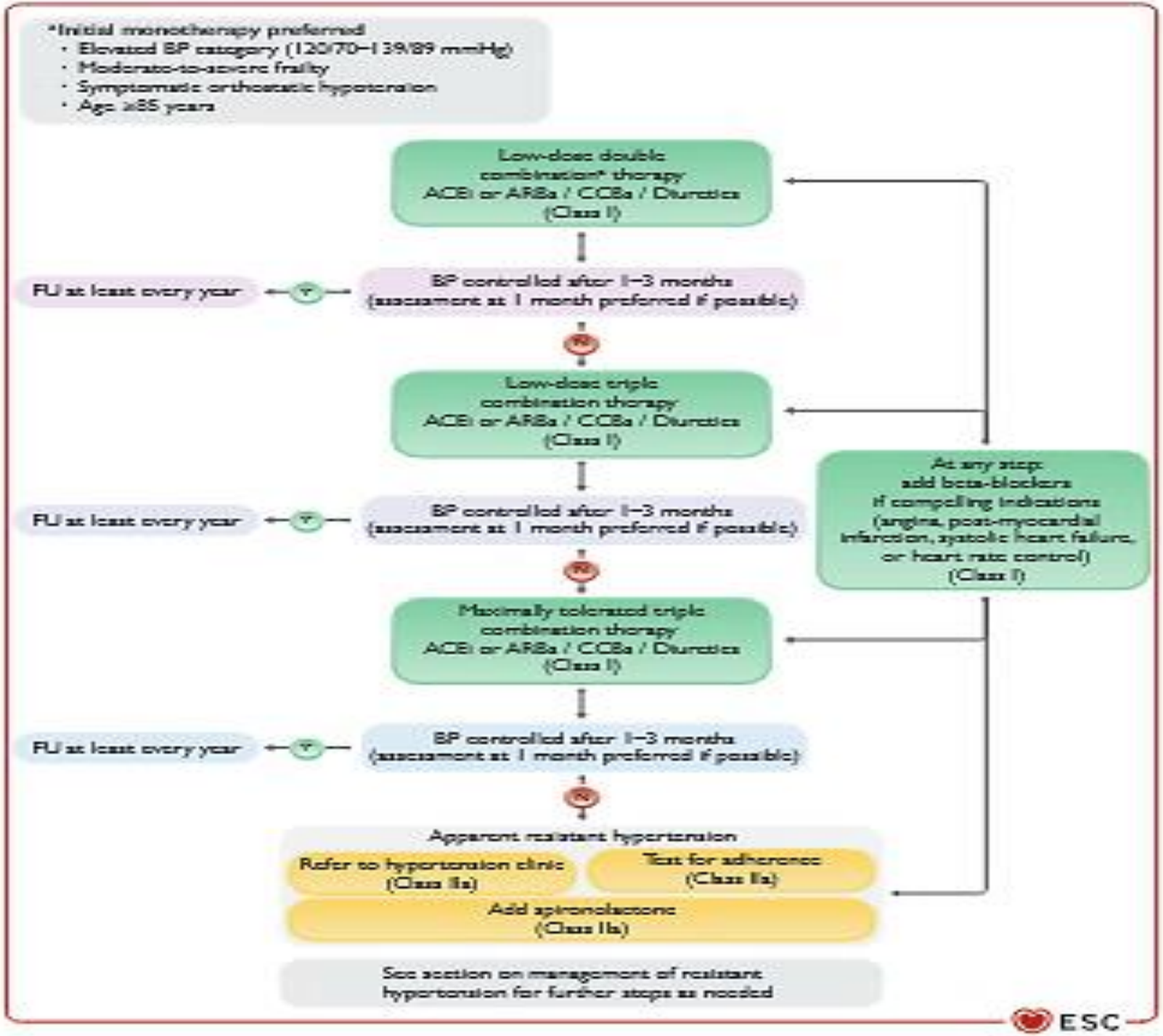
Trattamento farmacologico



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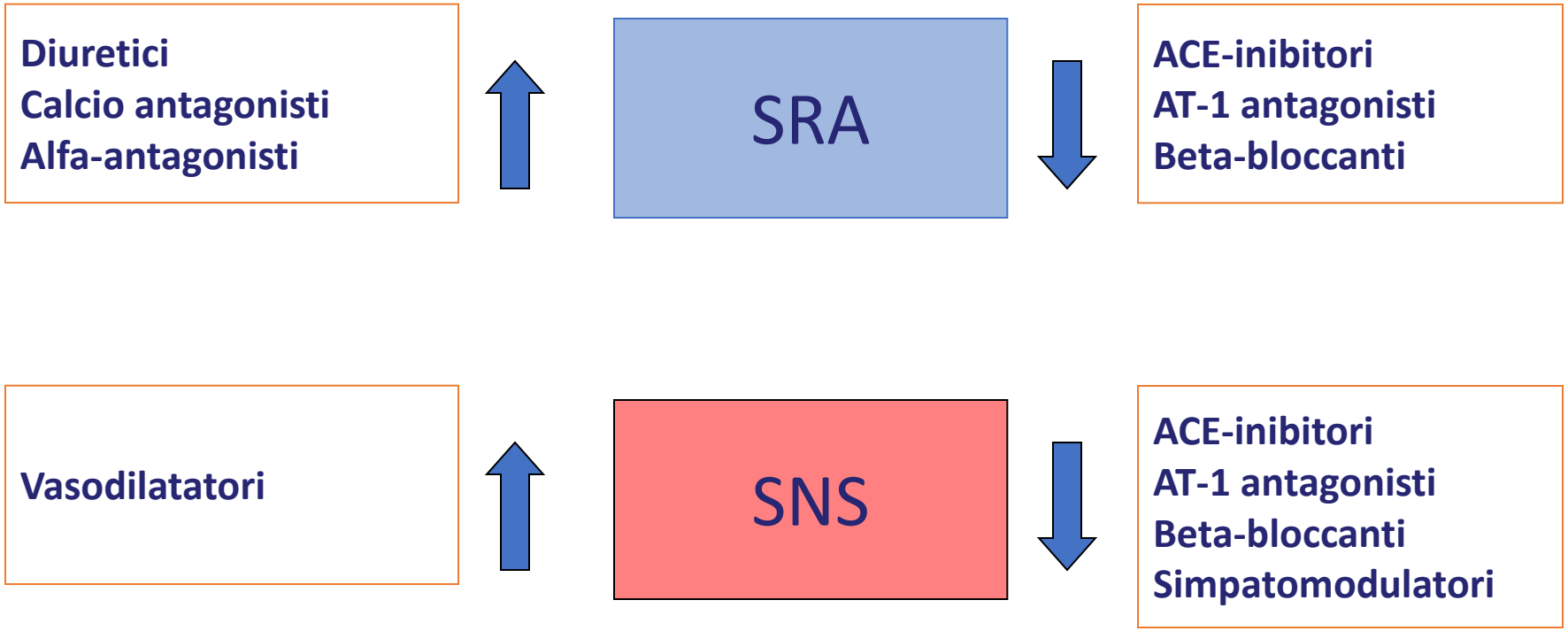
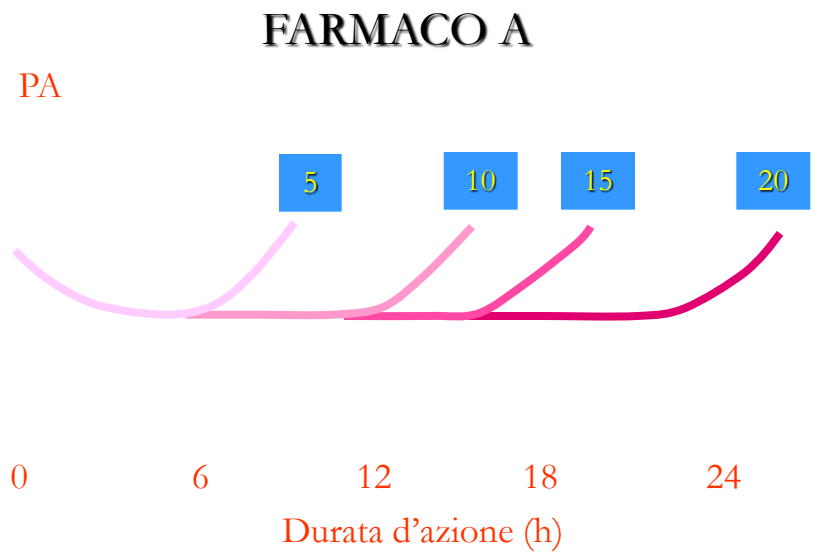
Associazioni Farmacodinamiche

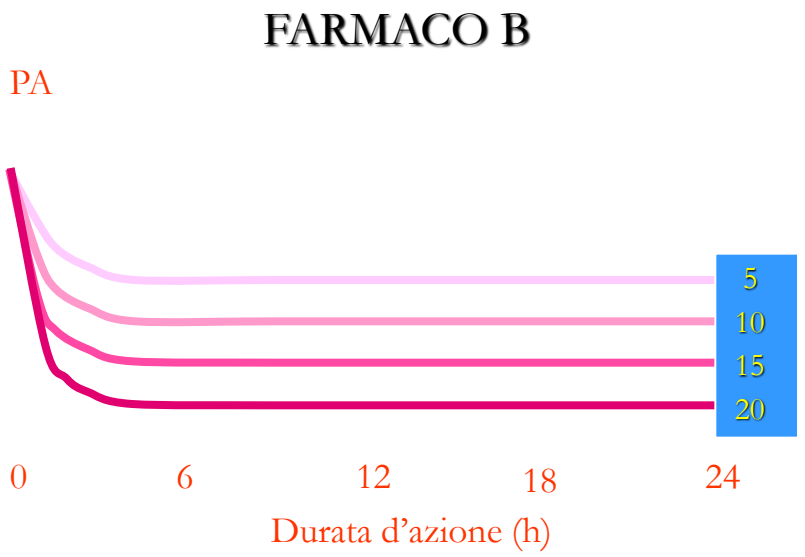


Integrazione della curva dose risposta Dose-Risposta dei Farmaci



Il farmaco di tipo A ha curva efficacia-durata

ACE-I
AIIRA

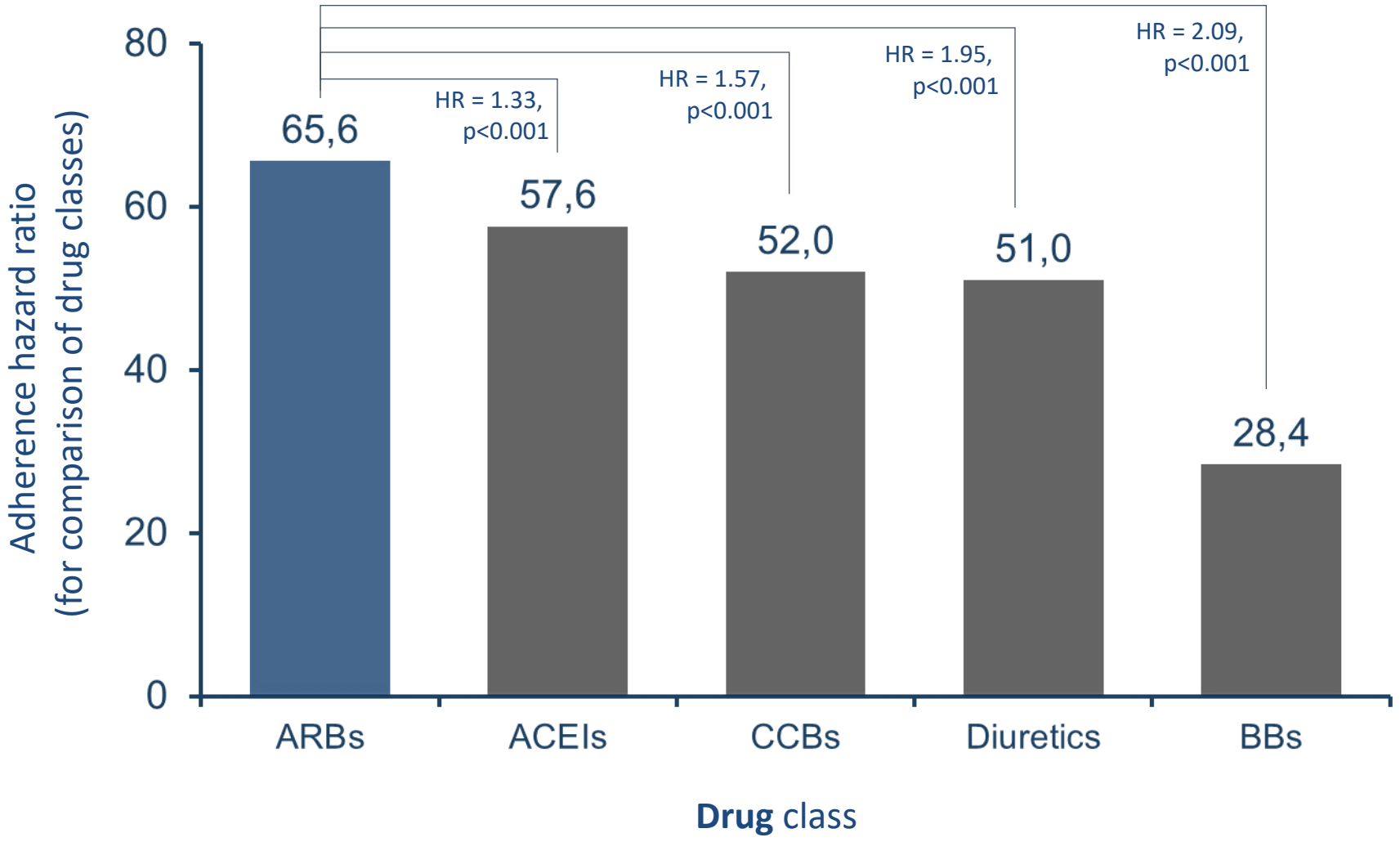


Il farmaco di tipo B ha curva dose-risposta

CCB
Diuretici
α-bloccanti
β-bloccanti

Fogari, J Hypertens, 1997

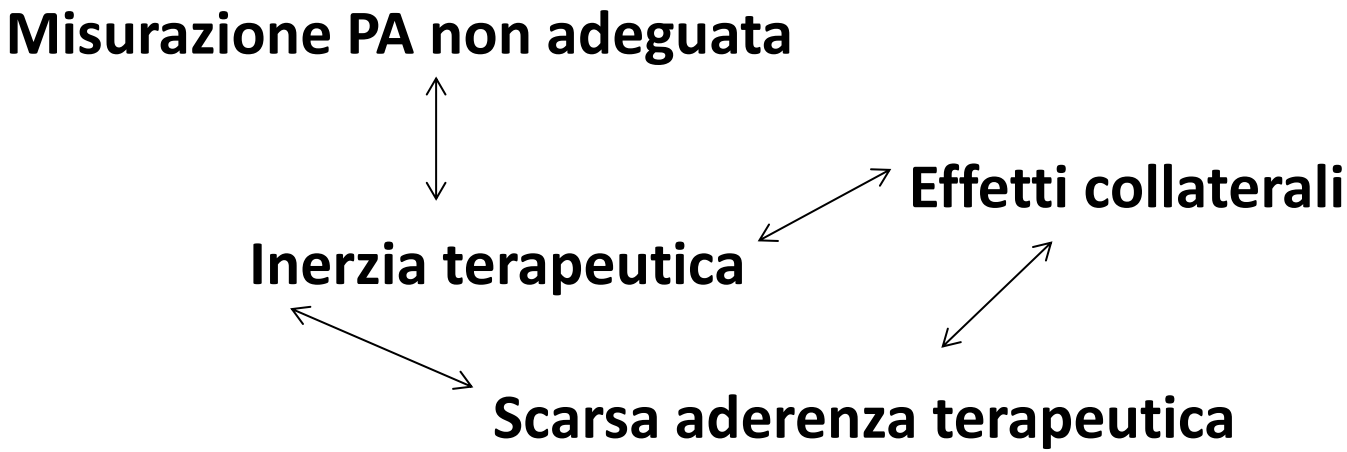
Persistenza con un farmaco antipertensivo



HR = hazard ratio
Meta-analysis of 17 studies

Kronish et al. *Circulation* 2011;123:1611–21

Perché un paziente presenta un ipertensione di difficile controllo?

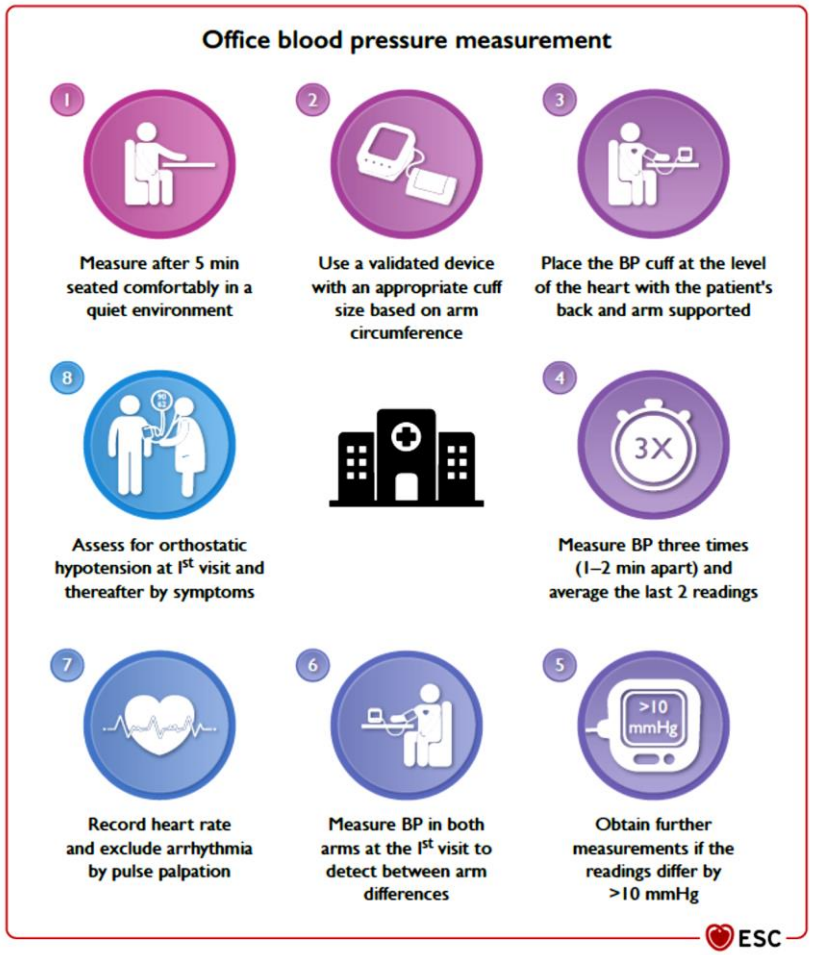


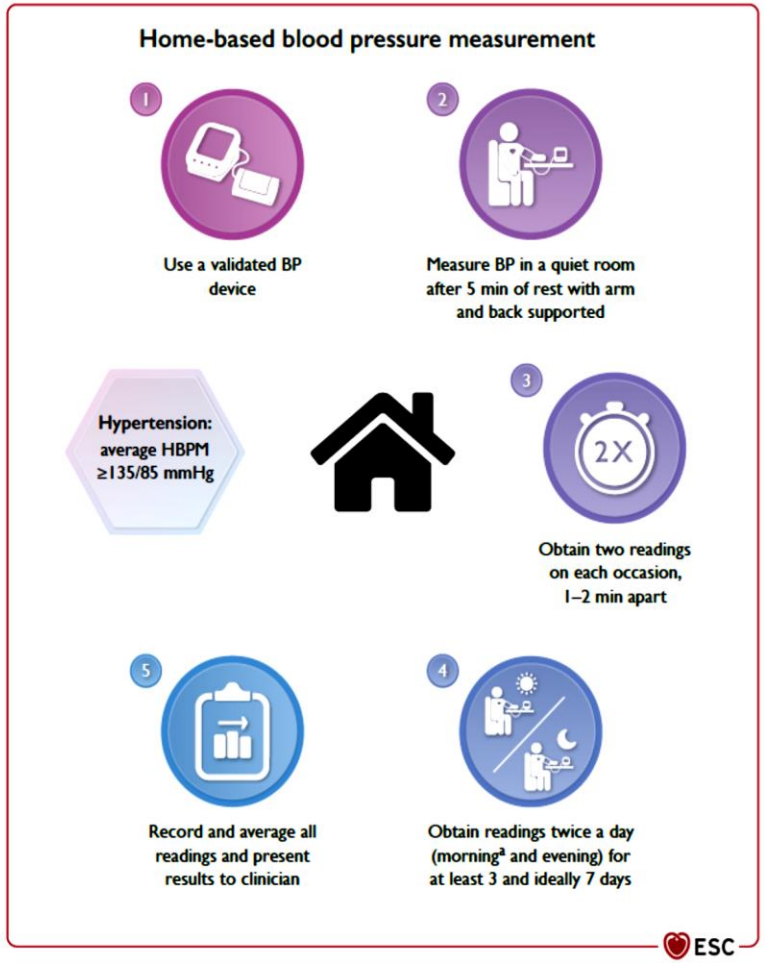
2023 ESH Guidelines for the management of arterial hypertension

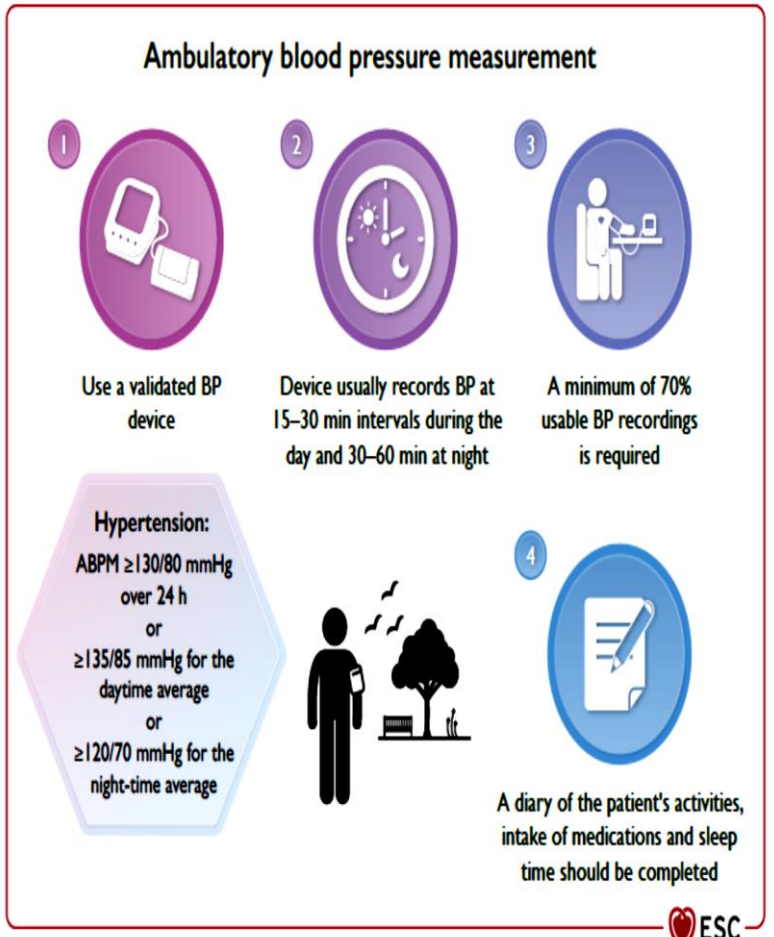
Esclusione di «pseudo ipertensione» di difficile controllo

Tecnica office

Tecniche out of office







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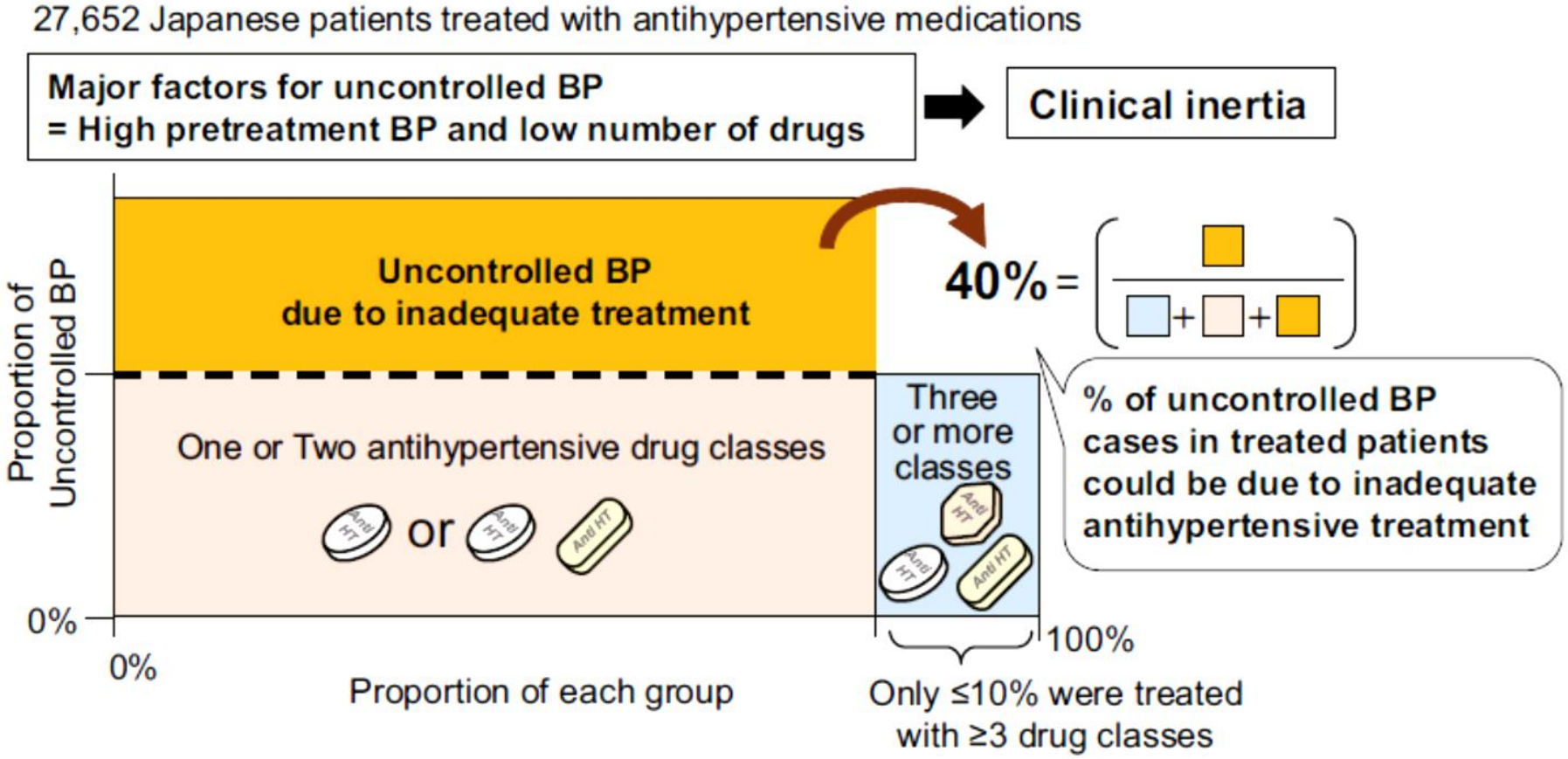
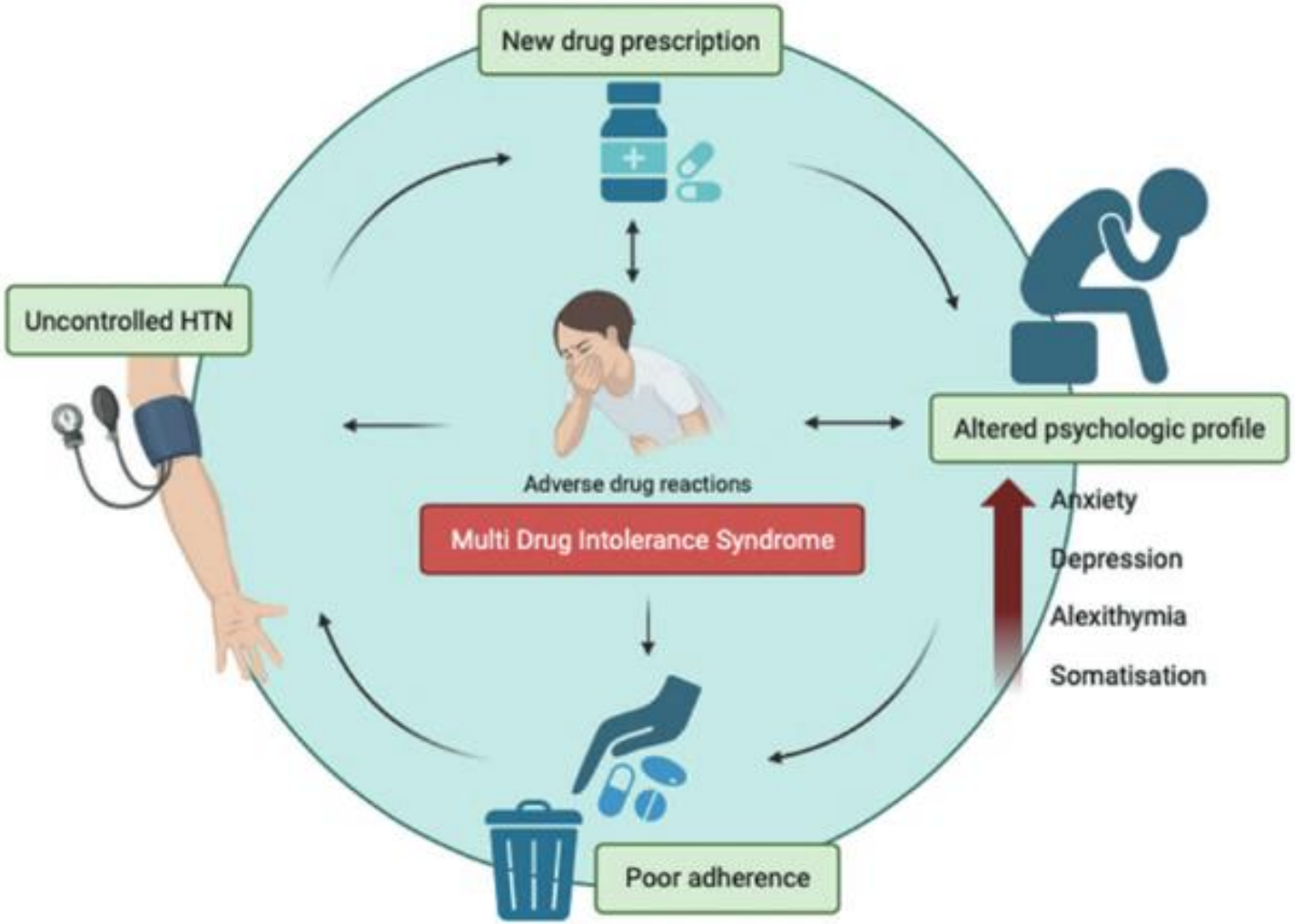
Inerzia Terapeutica= mancato inizio o adeguamento della terapia da parte degli operatori sanitari quando indicato dalle Linee Guida (O' Connor)

The impact of clinical inertia on uncontrolled blood pressure in treated hypertension: real-world, longitudinal data from Japan



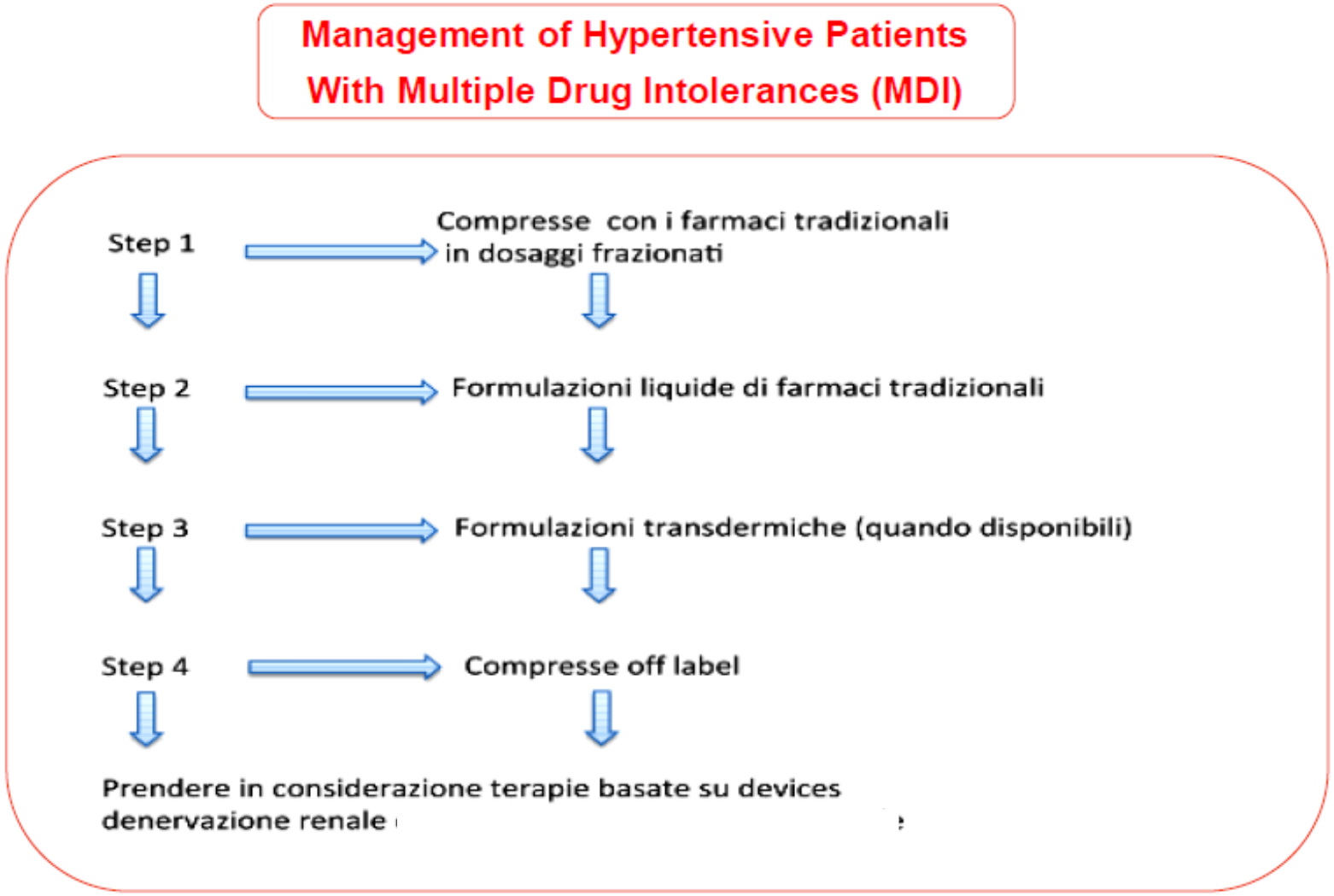
Satoh Hypertension Res 2024

EFFETTI COLLATERALI DA FARMACI ANTIPERTENSIVI



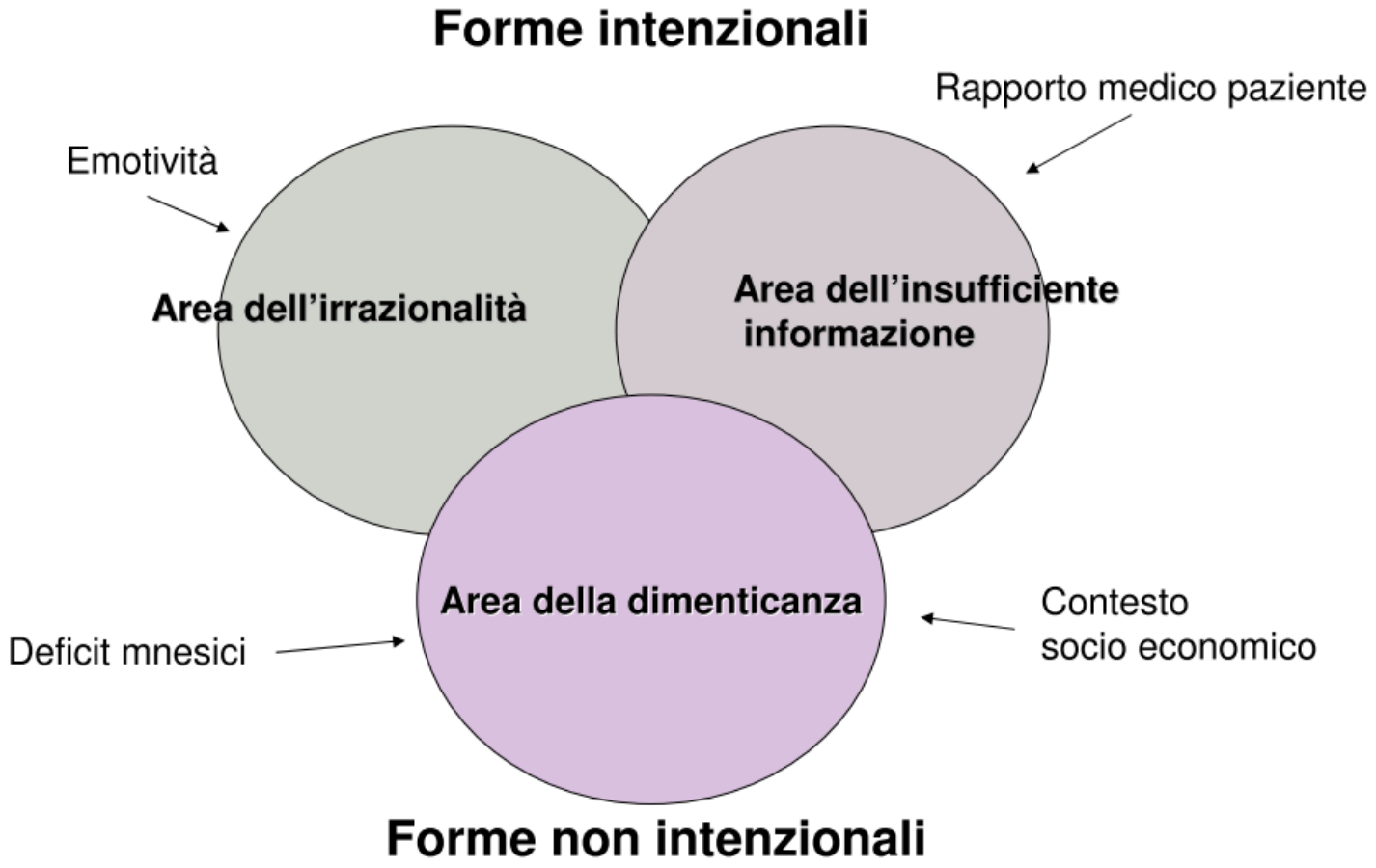
Pappaccogli, Hypertension 2024

Effetti collaterali

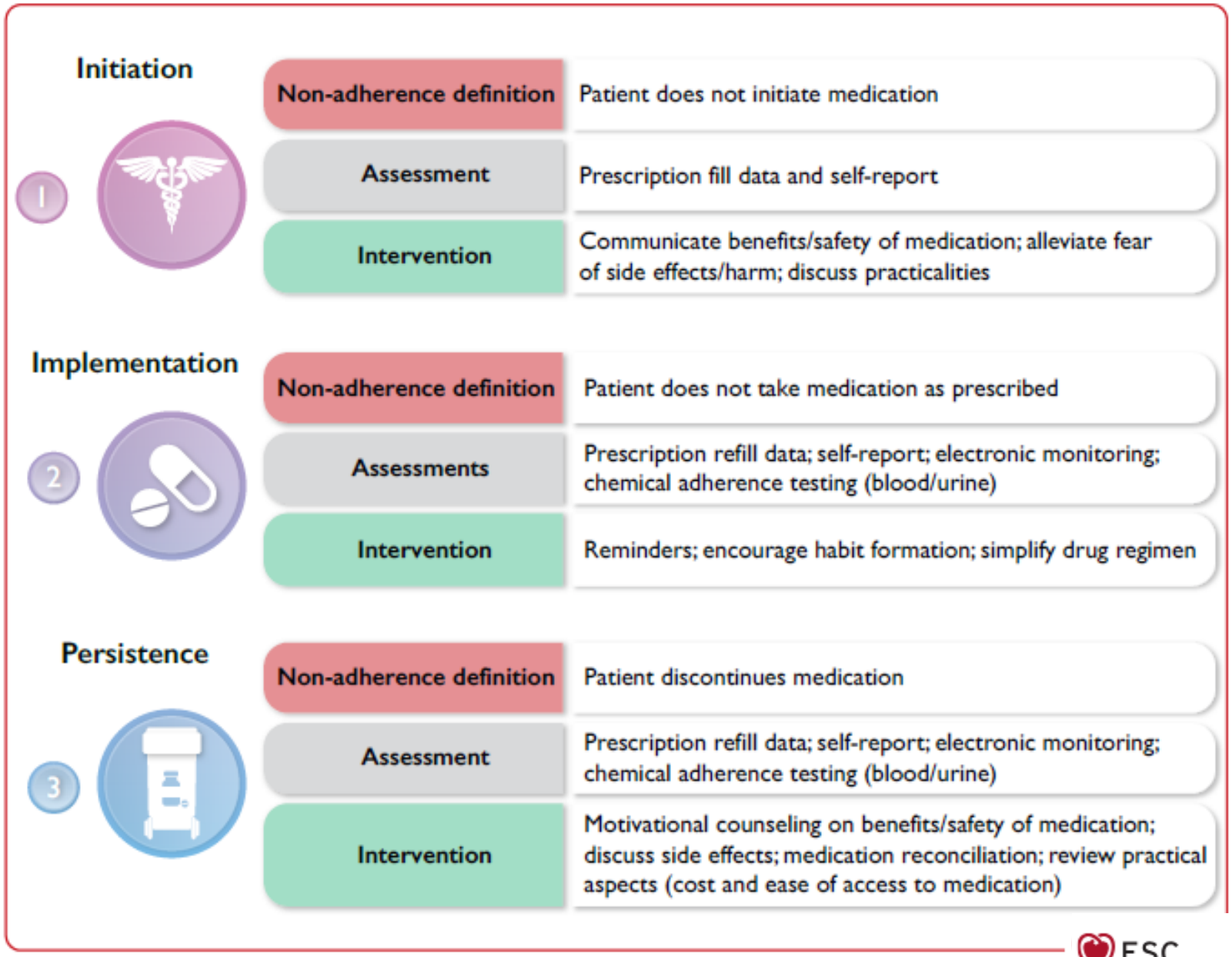


Mod . J Clin Hypertens, 2015

L’aderenza alla terapia è un comportamento individuale che comprende la **compliance** (assumere i farmaci ai dosaggi indicati e con la frequenza prescritta) e la **persistenza** (continuare la cura per il periodo di tempo consigliato).



Valutare sempre la potenziale non aderenza



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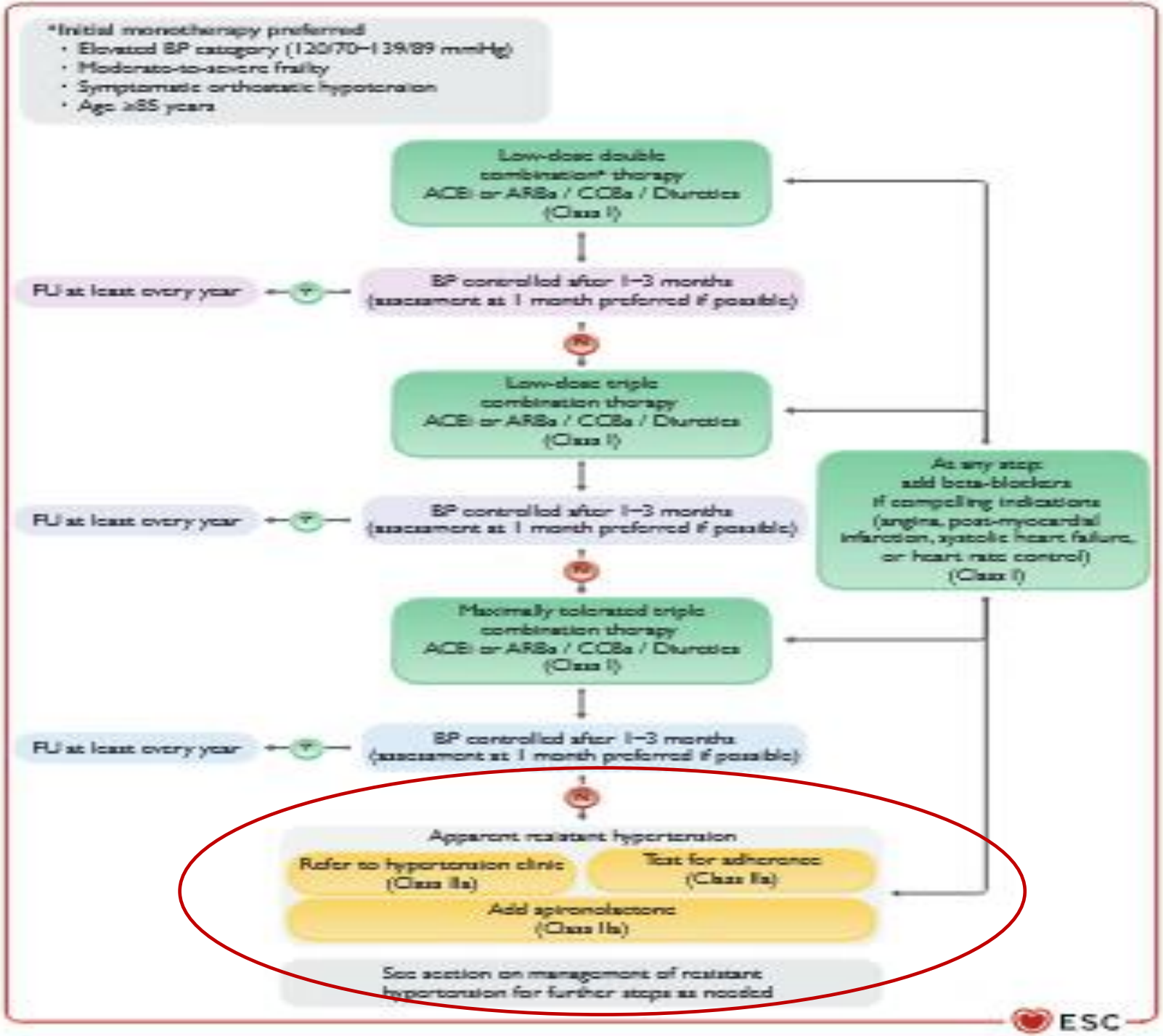

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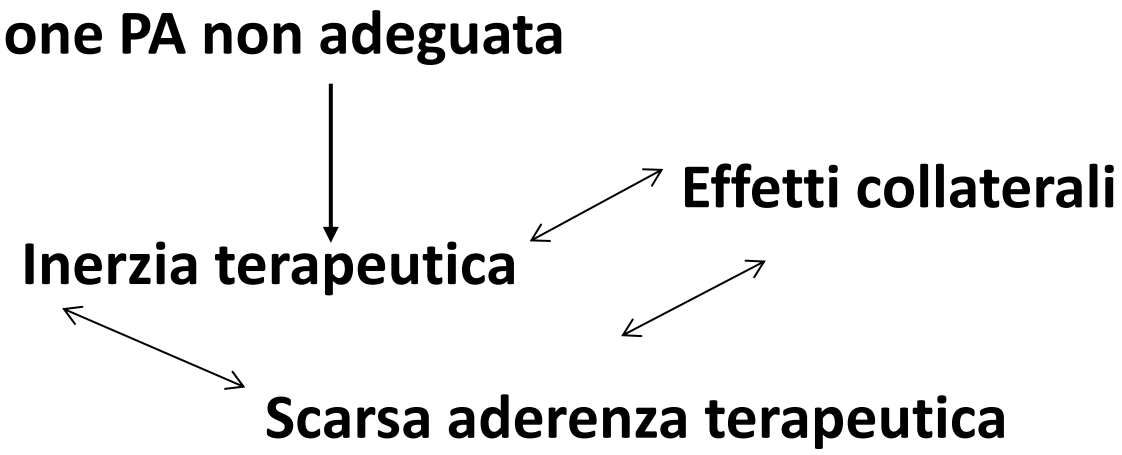
Perché un paziente presenta un ipertensione di difficile controllo?



Ipertensione secondaria

Uso di farmaci o sostanze che possono aumentare la pressione arteriosa

Comorbidità

2023 ESH Guidelines for the management of arterial hypertension

Un ipertensione secondaria per ogni età

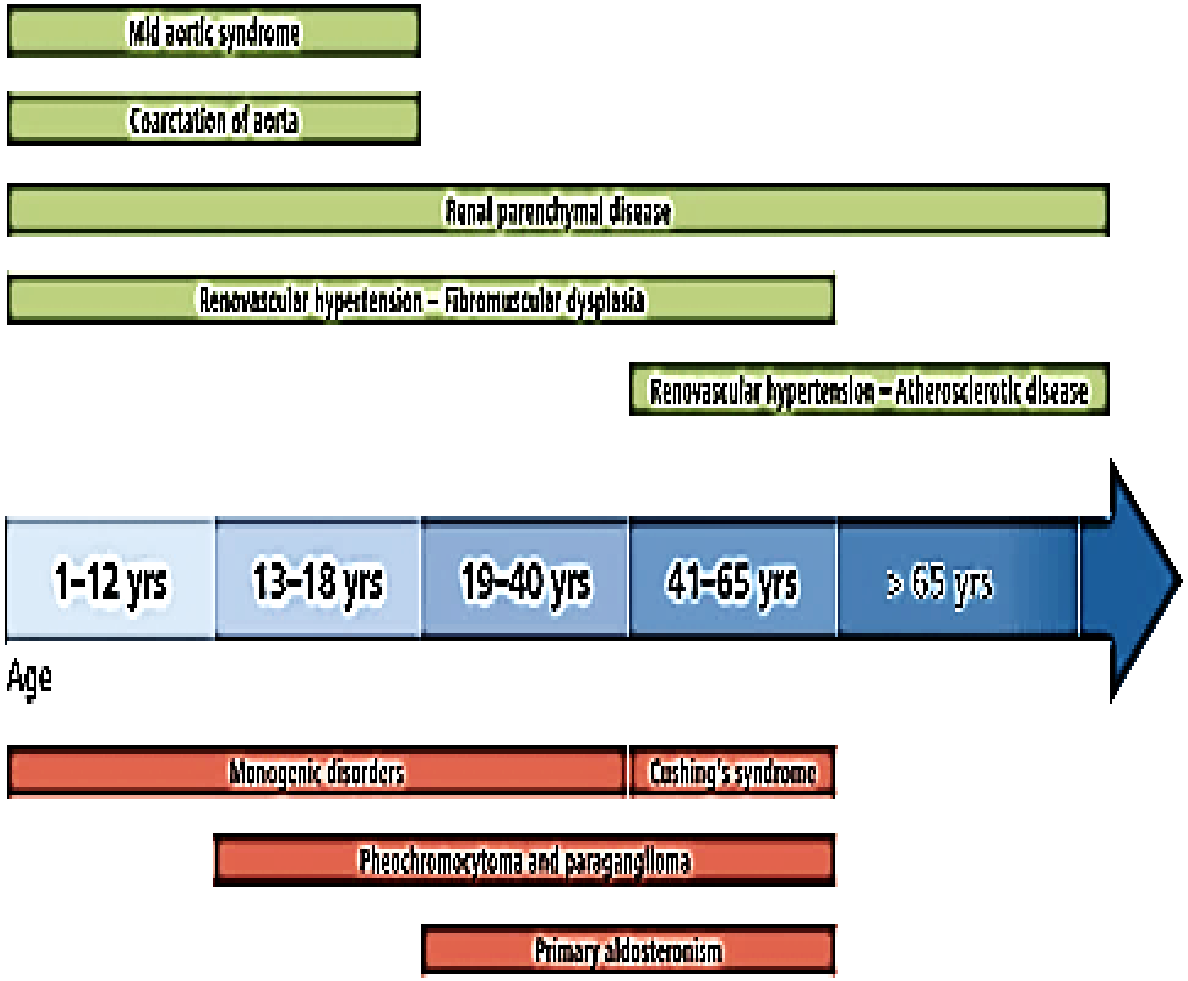


FIGURE 7 Incidence of selected forms of secondary hypertension according to age.

2023 ESH Guidelines for the management of arterial hypertension

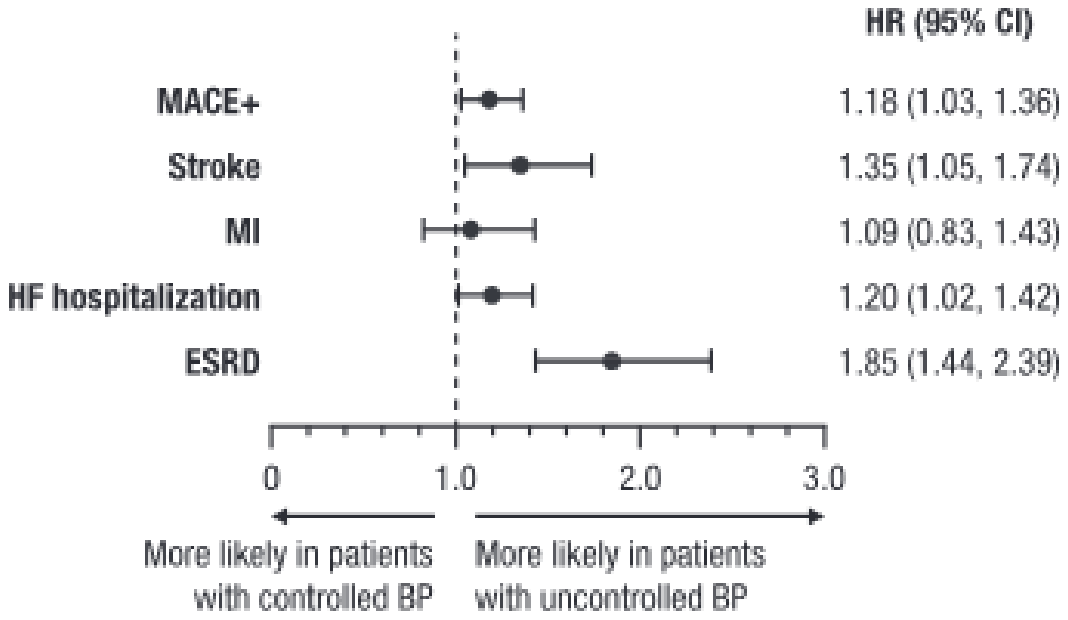
SOSTANZE CHE POSSONO CAUSARE SCARSO CONTROLLO DELLA PRESSIONE ARTERIOSA

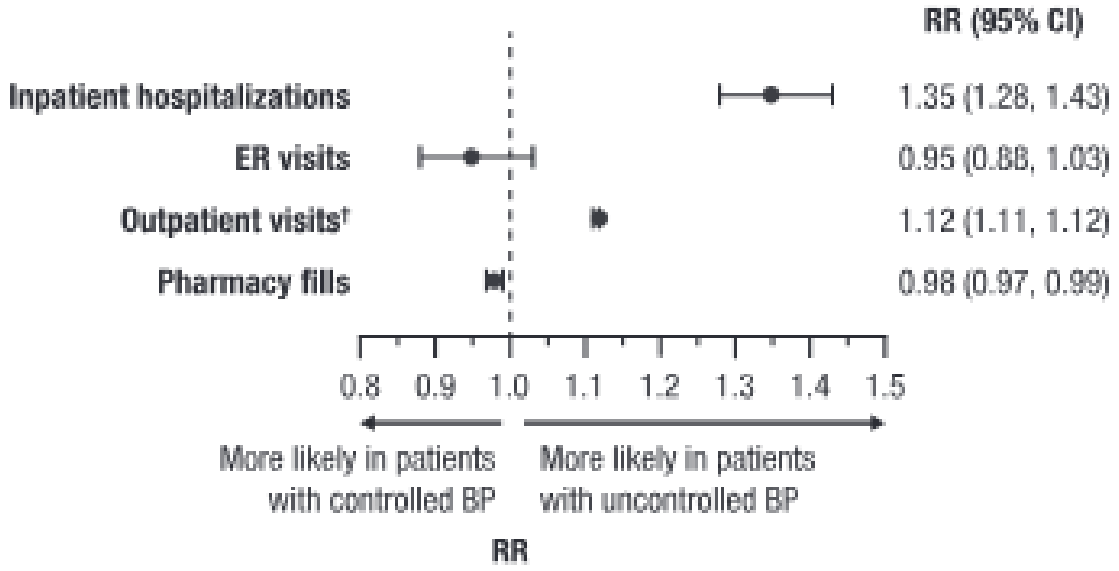
Medication/substance	Proposed mechanism	Comments
NSAIDs	Inhibition of COX-1 and 2, decreasing PG I2 and E2 synthesis with subsequent reduction in urinary Na excretion and an increased systemic vascular resistance	Mild, dose-dependent increase in BP. Increased risk with age, preexisting hypertension, salt-sensitive patients, patients with renovascular hypertension.
Paracetamol (acetaminophen)	Presumably via inhibition of cyclooxygenases and reduced production of prostaglandins.	Increased relative risk of 1.34 of hypertension with almost daily paracetamol use.
Oestrogens and progestins	Increased renin synthesis (by oestrogens) leading to RAS activation and subsequent Na and water retention.	Mild, sustained increase in BP (6/3 mmHg increase with high doses of oestrogen (>50 µg of oestrogen and 1–4 µg progestin) but can be severe, common in premenopausal women, cause hypertension in 5% of women.
Glucocorticoids	Enhanced Na reabsorption and fluid retention via stimulation of mineralocorticoid receptors. Increased systemic vascular resistance due to upregulation of AT1 receptors on vascular smooth muscle cells.	Dose-dependent, low doses have less effect on BP, more common in older patients, or with a family history of primary hypertension.
Calcineurin inhibitors	Reduced NO production, ET-1 over production, systemic and renal vasoconstriction, renal Na retention.	Dose-dependent, mild-to-moderate increase in BP. Severe hypertension has been reported. Increased risk with preexisting hypertension, elevated creatinine levels and maintenance therapy with corticosteroids.
Antidepressants SNRIs	Increased noradrenaline release causing adrenergic activation and increased SNS activity.	Dose-dependent, mild (2/1mmHg) increase in BP.
Nasal decongestants	Vasoconstriction due to stimulation of alpha-1 receptors on vascular smooth muscles.	Dose-dependent, sustained increase in BP
Erythropoietin-stimulating agents	Increased thromboxane, reduced prostacyclin levels and activation of the local RAS. Increased ET-1 production, decreased NO synthesis with subsequent vasoconstriction.	Dose-dependent, mild increase in BP, increased risk with preexisting hypertension, or when the initial haematocrit level is low
Stimulants -Modafinil -Amphetamines -Methylphenidate	Block noradrenaline or dopamine reuptake Promote release of catehcholamines	
VEGF inhibitors	Decreased NO production via VEGFR-2 antagonism and stimulation of ET-1 receptors promoting vasoconstriction	A class effect. The incidence of hypertension is dose related, risk is increased by preexisting hypertension, old age and overweight
Substances of abuse -MDMA -PCP -Methamphetamine -Cocaine -Alcohol	Increased release and inhibited reuptake of monoamine neurotransmitters with subsequent SNS activation. Increased CNS catecholamine release with decreased neuronal uptake. Cocaine induces acute sympathomimetic effects and chronic HMOD, i.e., an increase in arterial wall stiffness.	Cocaine induces both acute and chronic increase in BP. Alcohol causes a dose-dependent, sustained increase in BP.
Herbal products -Licorice -Ephedra -St. John's wort -Yohimbine -Ginseng (high doses) -Ma huang	Chronic excessive liquorice use mimics hyperaldosteronism by stimulating the mineralocorticoid receptor and inhibiting cortisol metabolism. Ephedra activates the alpha-1receptor, increasing SNS activity	Licorice. Dose-dependent, sustained increase in BP characterized by hypokalaemia, metabolic alkalosis and suppressed plasma renin activity and aldosterone levels. Yohimbine causes acute, dose-dependent increase in BP.
Diet pills -Sibutramine -Phenylpropanolamine	Increased levels of norepinephrine with subsequent activation of noradrenergic transmission	Mild increase in BP

2023 ESH Guidelines for the management of arterial hypertension

Comorbidità

Real-World Impact of Blood Pressure Control in Patients With Apparent Treatment-Resistant or Difficult-to-Control Hypertension and Stages 3 and 4 Chronic Kidney Disease





N: 1487 N: 2479

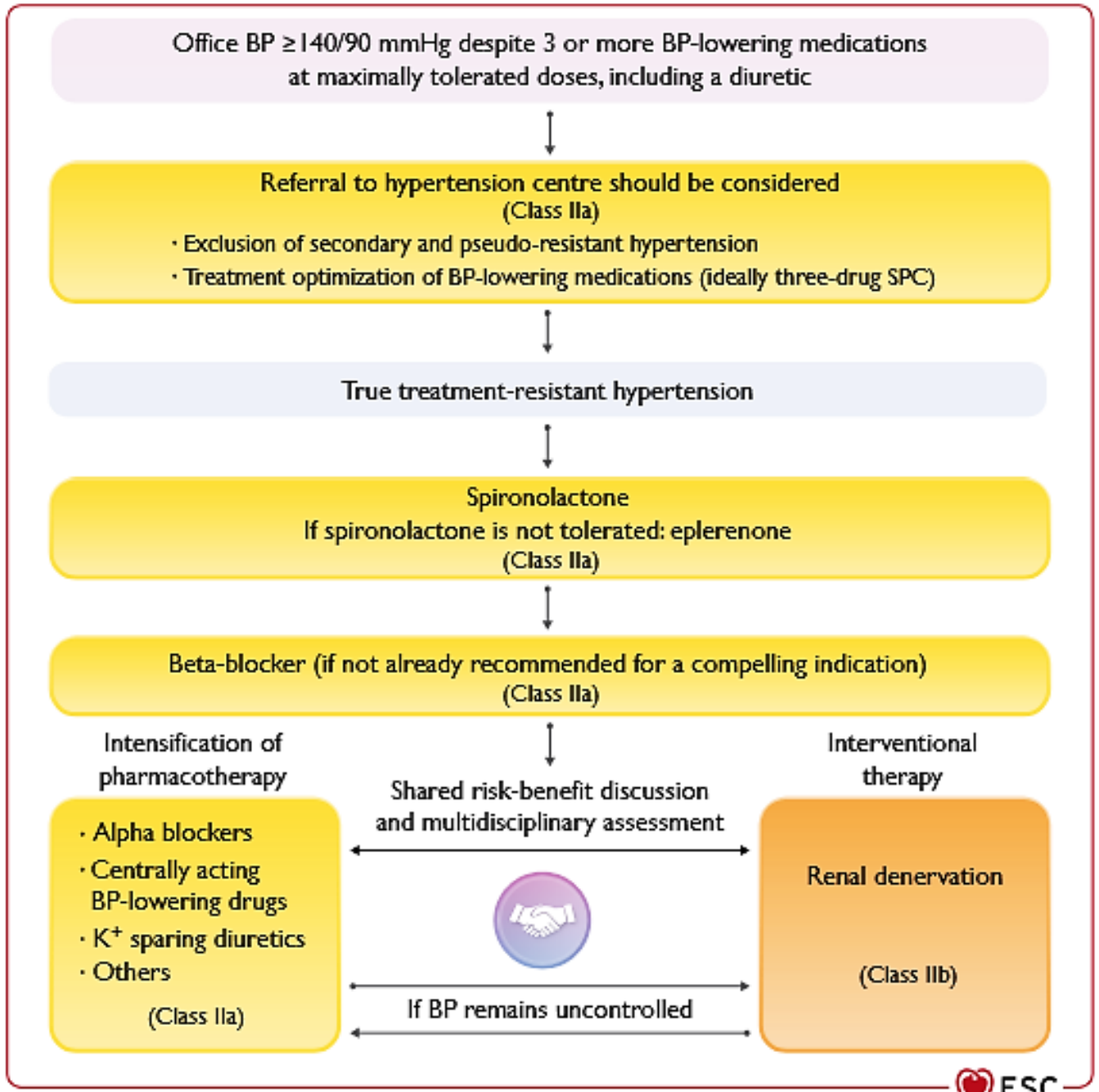
Bakris Am J Hypertens 2024

CLASSIFICAZIONE DELL'IPERTENSIONE RESISTENTE SU BASE FISIOPATOLOGICA

Types	Causes
True resistant essential hypertension [24]	Genetic factors
	Inappropriate aldosterone secretion
	Volume excess
	Endothelial dysfunction
	Sympathetic overactivity
	Insulin resistance
Secondary resistant hypertension	Primary aldosteronism
	Pheochromocytoma
	Cushing disease
	Renovascular disease
	Chronic kidney disease
	Aortic coarctation
	Obstructive sleep apnea
	Drugs and substances
Apparent treatment-resistant hypertension	No data for out-of-office BP measurement (ABPM or HBPM) or for medication adherence
Pseudoresistant hypertension	Undertreatment
	Medication nonadherence
	Clinical inertia
	Inadequate BP measurement technique
	White coat and masked effect

Veglio J Hypertens 2021

Strategia terapeutica dell'ipertensione resistente



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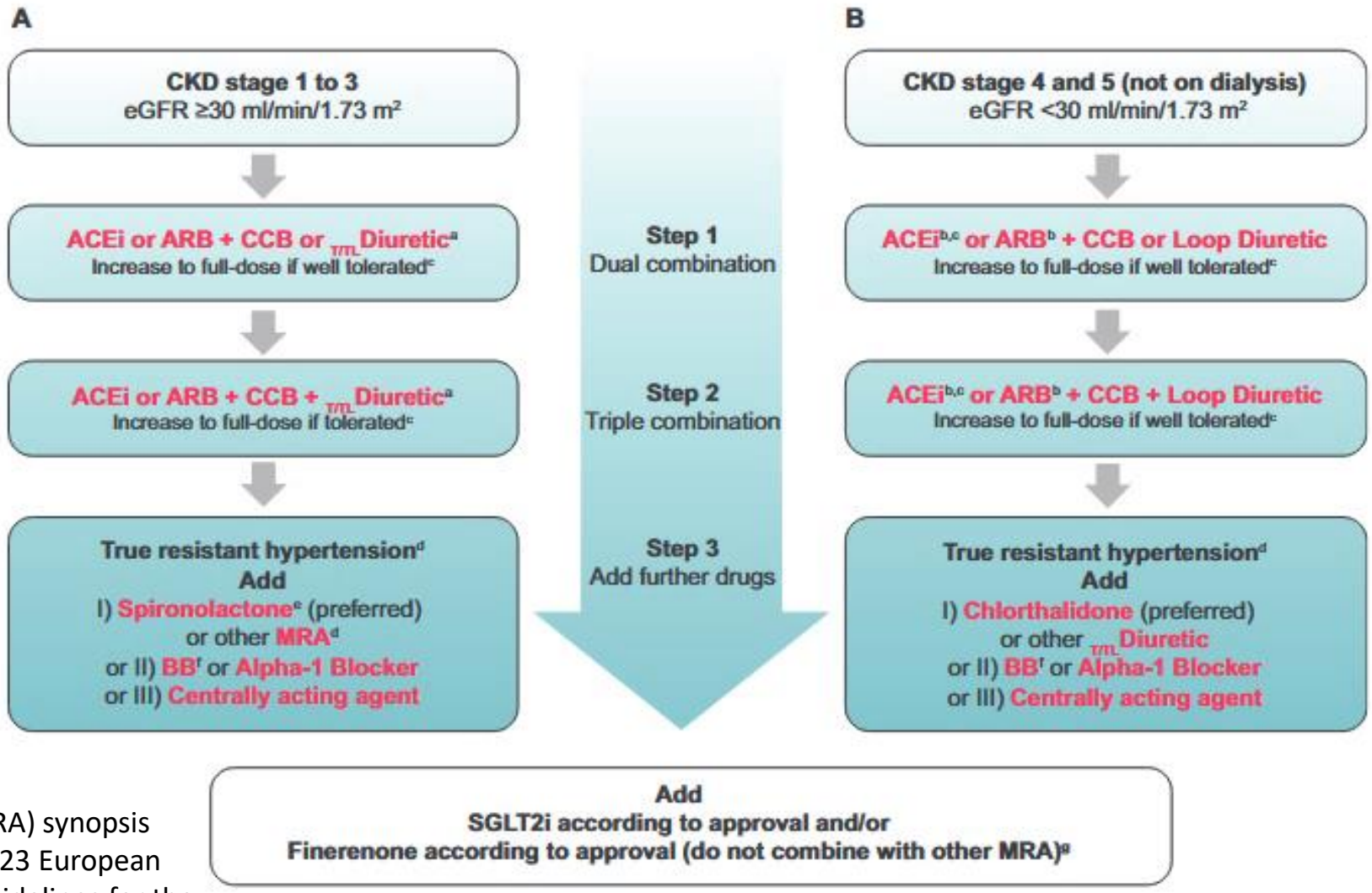
Gestione dell'ipertensione non controllata nell'iperteso con insufficienza renale



A European Renal Association (ERA) synopsis for nephrology practice of the 2023 European Society of Hypertension (ESH) Guidelines for the Management of Arterial Hypertension

Nephrol dial transpl 2024

ASSOCIAZIONI ANTIPERTENSIVI NON RAZIONALI

Effetto subaddittivo: 1+1> 1 ma < 2

Antagonismo: 1+1< 1

Associazione di Farmaci con Interazione Negativa sull'Effetto Ipotensivo

- **α_1-Bloccante+ Clonidina**

Associazione di Farmaci Antipertensivi Potenzialmente Pericolosa

- **β-Bloccante + Clonidina**
- **β-Bloccante + Ca-antagonista non DHP**

Renal Denervation (RDN)

Recommendations and statements	CoR	LoE
RDN can be considered as a treatment option in patients an eGFR>40 ml/min/1.73m2 who have uncontrolled BP despite the use of antihypertensive drug combination therapy, or if drug treatment elicits serious side effects and poor quality of life.	IIb	B
RDN can be considered as an additional treatment option in patients with resistant hypertension if eGFR is >40 ml/min/1.73m2	IIb	B
Selection of patients to whom RDN is offered should be done in a shared decision-making process after objective and complete patient's information.	I	C
Renal denervation should only be performed in experienced specialized centers to guarantee appropriate selection of eligible patients and completeness of the denervation procedure.	I	C

2023 ESH Guidelines for the management of arterial hypertension

Recommendation Table 20 — Recommendations for device-based treatment of hypertension (see Evidence Table 35)

Recommendations	Class[a]	Level[b]
To reduce BP, and if performed at a medium-to-high volume centre, catheter-based renal denervation may be considered for resistant hypertension patients who have BP that is uncontrolled despite a three BP-lowering drug combination (including a thiazide or thiazide-like diuretic), and who express a preference to undergo renal denervation after a shared risk-benefit discussion and multidisciplinary assessment.[564,566–568,586–590]	IIb	B
To reduce BP, and if performed at a medium-to-high volume centre, catheter-based renal denervation may be considered for patients with both increased CVD risk and uncontrolled hypertension on fewer than three drugs, if they express a preference to undergo renal denervation after a shared risk-benefit discussion and multidisciplinary assessment.[564,566–568,586–590]	IIb	A
Due to a lack of adequately powered outcomes trials demonstrating its safety and CVD benefits, renal denervation is not recommended as a first-line BP-lowering intervention for hypertension.	III	C
Renal denervation is not recommended for treating hypertension in patients with moderate-to-severely impaired renal function (eGFR <40 mL/min/1.73 m^2) or secondary causes of hypertension, until further evidence becomes available.	III	C

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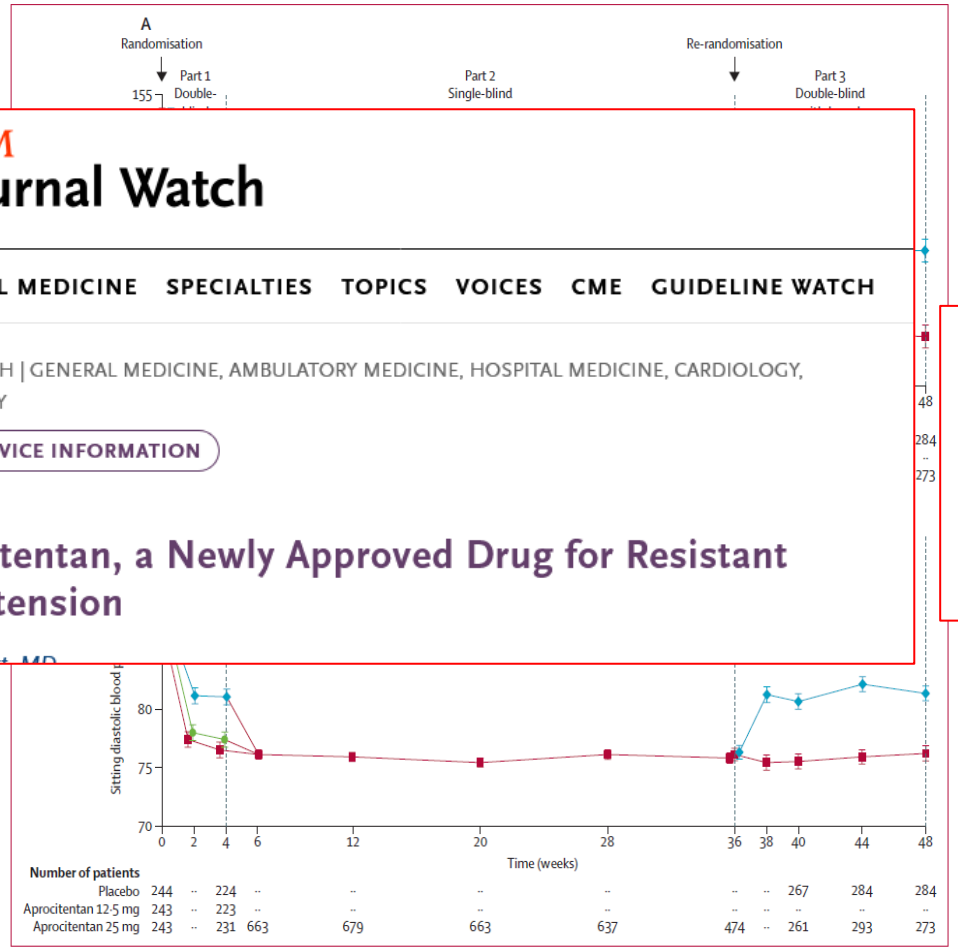
NUOVE PROPOSTE

Dual endothelin antagonist
Aprocitentan for resistant hypertension (PRECISION)



NEJM Journal Watch

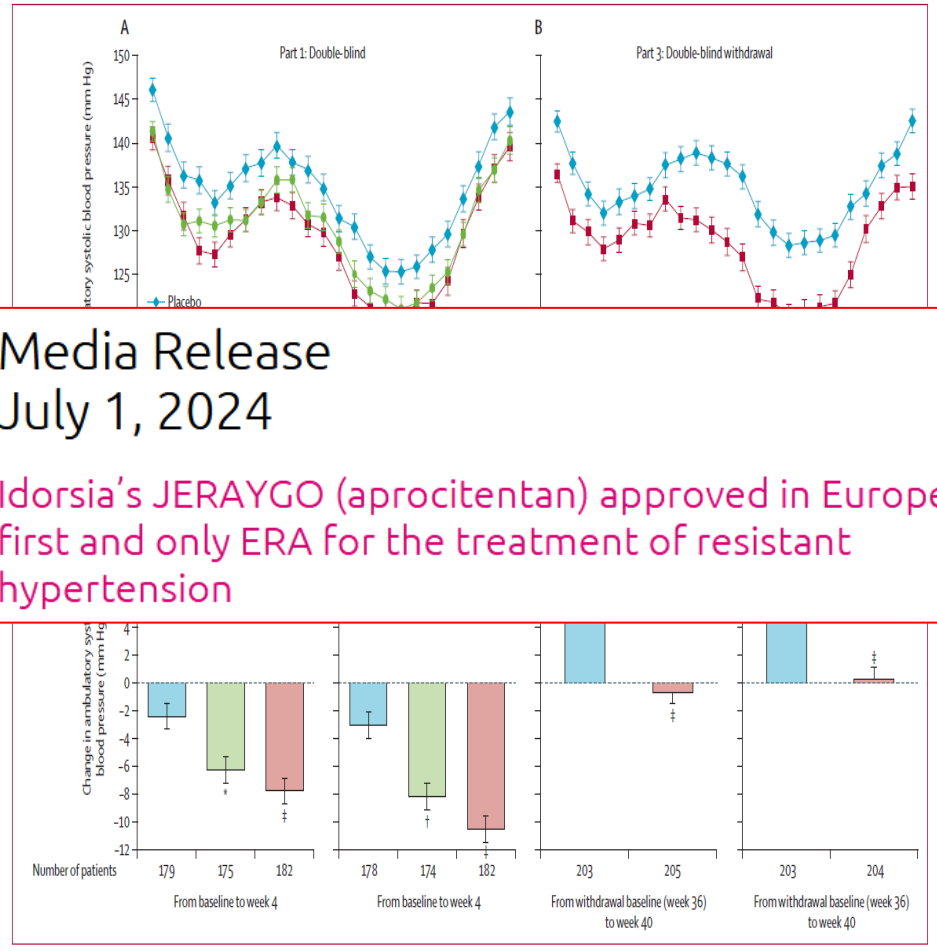
GENERAL MEDICINE SPECIALTIES TOPICS VOICES CME GUIDELINE WATCH

DRUG WATCH | GENERAL MEDICINE, AMBULATORY MEDICINE, HOSPITAL MEDICINE, CARDIOLOGY, NEUROLOGY

DRUG/DEVICE INFORMATION

April 11, 2024

Aprocitentan, a Newly Approved Drug for Resistant Hypertension



Media Release
July 1, 2024

Idorsia's JERAYGO (aprocitentan) approved in Europe as first and only ERA for the treatment of resistant hypertension

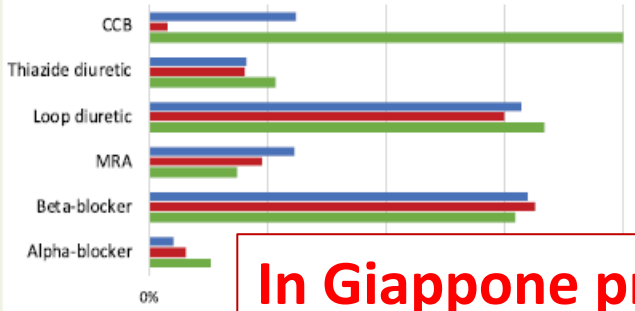
Schlaich, Lancet 2022

ARNI-SACUBITRIL-VALSARTAN

PARAGON STUDY

Apparent resistant hypertension in HFpEF

Baseline BP-lowering medications

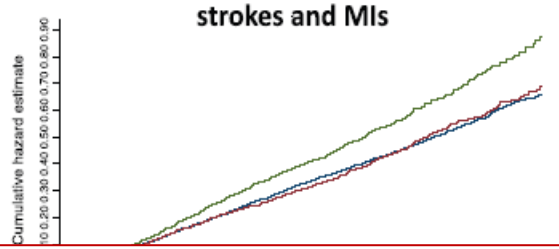


Controlled BP Non-resistant hypertension Apparent resistant hypertension

Present in **15%** of patients

More often White
Less often Asian
Higher BMI
More frequent diabetes

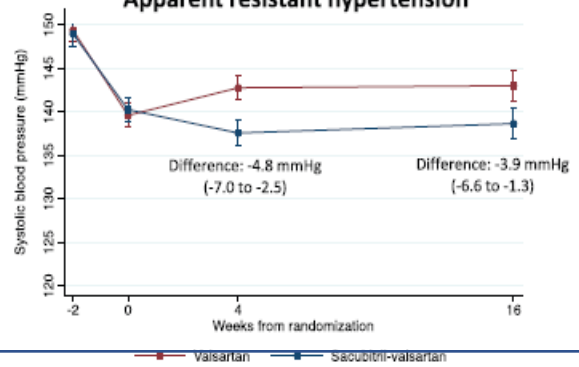
CV death, total HF hospitalizations, strokes and MIs



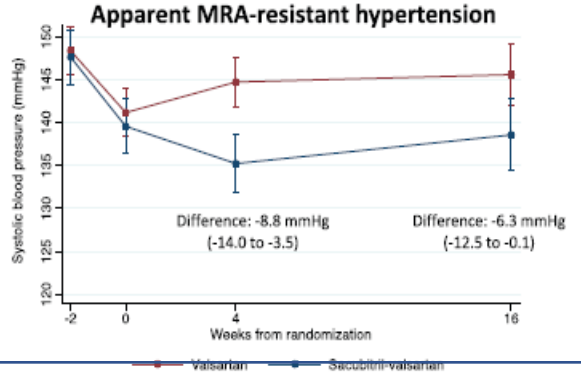
In Giappone prescrivibile per ipertensione resistente

SBP change with sacubitril-valsartan vs. valsartan

Apparent resistant hypertension



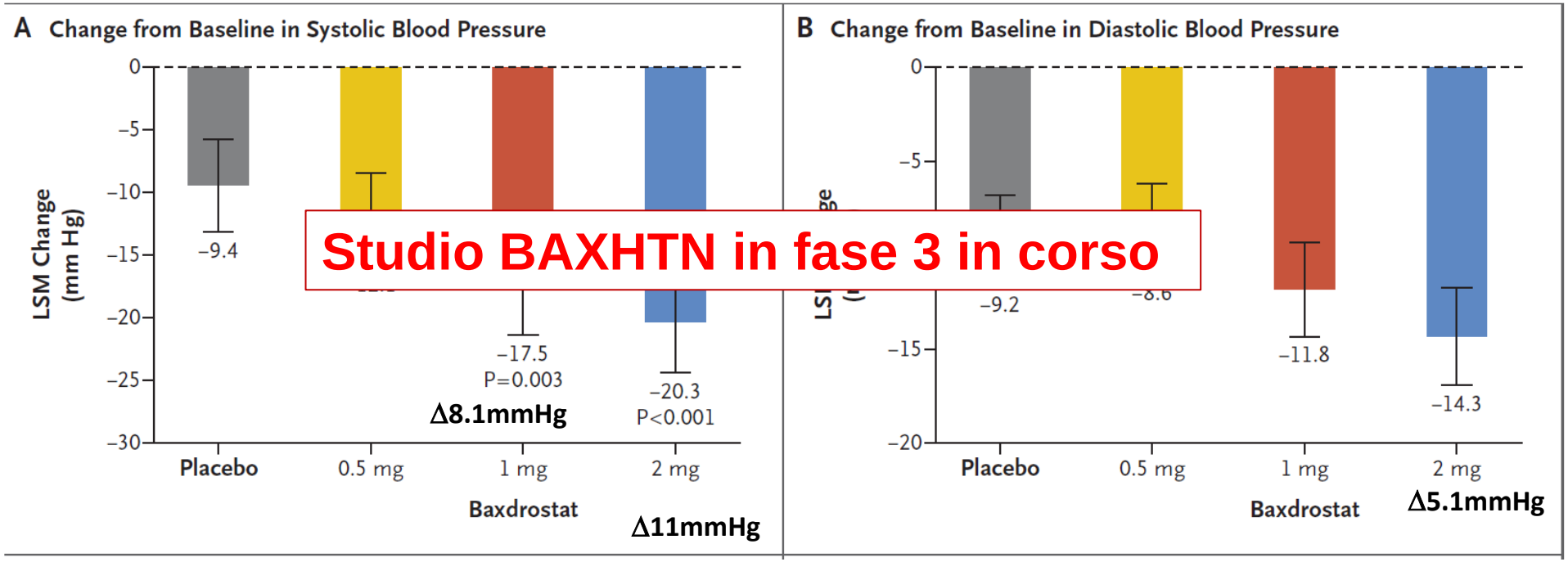
Apparent MRA-resistant hypertension



Jackson, Eur Heart Journal 2021

ALDOSTERONE SYNTHASE INHIBITOR

Baxdrostat for treatment-Resistant Hypertension



Studio BAXHTN in fase 3 in corso

Freeman, New Engl J Med ,2022

TAKE HOME MESSAGES

Gestione del paziente iperteso di difficile controllo

Conoscere

Cercare

Condividere

Motivare

Ascoltare

Razionalizzare

Ottimizzare

Dipartimento
Scienze Mediche

UNIVERSITÀ
DI TORINO

SIIA

Updating sulla Denervazione Renale nell'ipertensione arteriosa

Aula Roccia (Ex Palazzina Odonto), Molinette
Venerdi, 25 Ottobre 2024
h 14:00 – 17:00

Introduzione
F. Veglio

Fisiopatologia
F. Veglio

Denervazione renale: Linee guida ESH - ESC, selezione del paziente ideale e aspetti pratici della procedura
F. Rabbia

Insight sulla procedura
D. Rossato

Esperienza del centro: presentazione casi clinici
M. Pappaccogli

Tavola rotonda: discussione e confronto
Moderatore: *P. Mulatero*