IPERTENSIONE E CARDIOPATIA ISCHEMICA CRONICA

Dr. Guglielmo Gallone

Division of Cardiology, Città della Salute e della Scienza Hospital
Department of Medical Sciences, University of Turin

HYPERTENSION AND ISCHEMIC HEART DISEASE

Scale of the problem

Hypertension

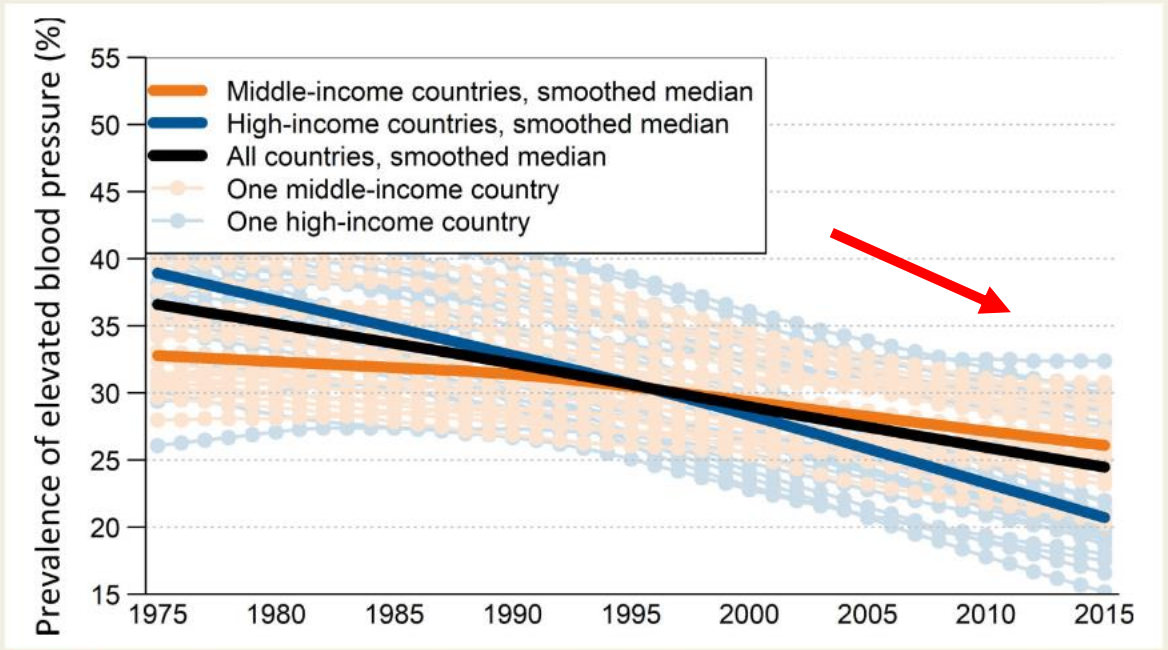


Figure 23 Time series: age-standardized prevalence of elevated blood pressure in European Society of Cardiology member countries (1975–2015).

Age-standardized prevalence in Europe 25.0%

Ischemic heart disease

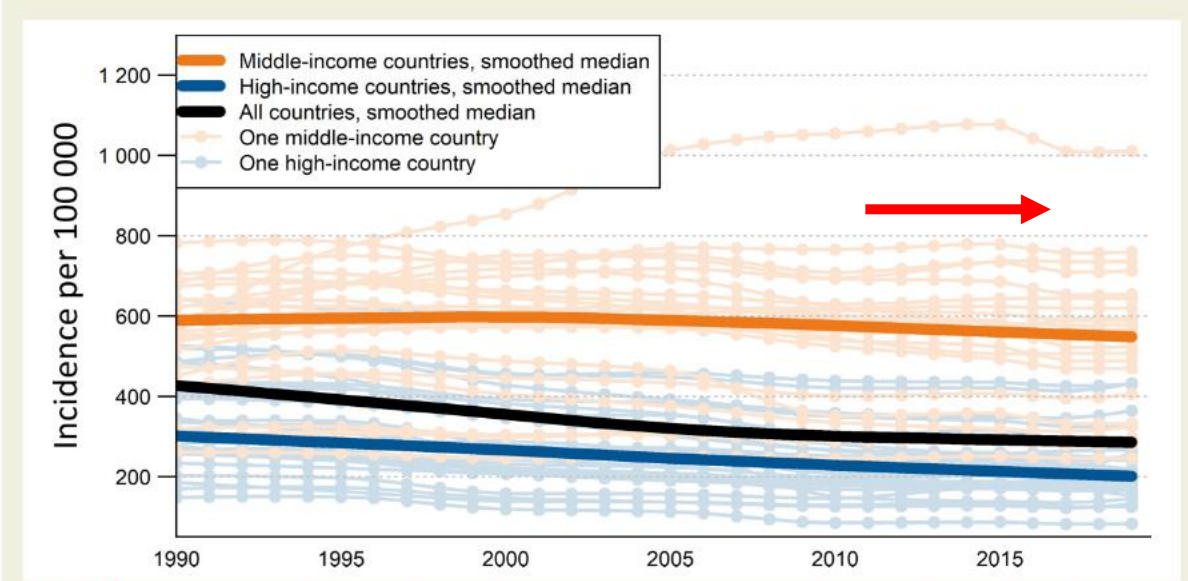


Figure 35 Time series: age-standardized incidence of ischaemic heart disease in European Society of Cardiology member countries (1990–2019).

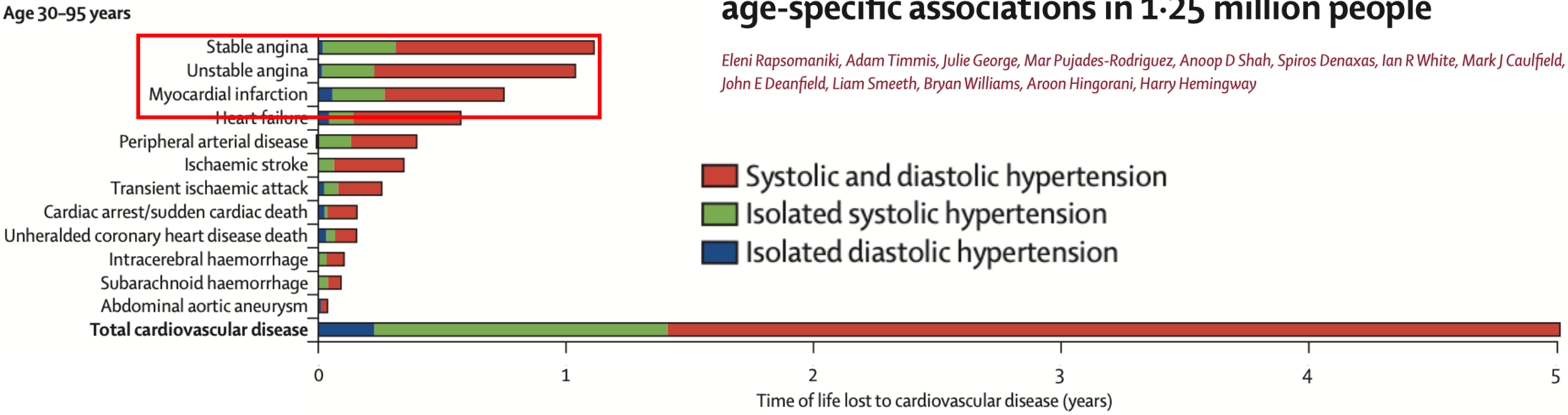
Age-standardized prevalence in Europe 2.8%

HYPERTENSION AND ISCHEMIC HEART DISEASE

A Dangerous Relationship

Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people

Eleni Rapsomaniki, Adam Timmis, Julie George, Mar Pujades-Rodriguez, Anoop D Shah, Spiros Denaxas, Ian R White, Mark J Caulfield, John E Deanfield, Liam Smeeth, Bryan Williams, Aroon Hingorani, Harry Hemingway



CAD accounts for 43% of the CVD-free years of life lost due to HTN

Rapsomaniki et al. Lancet 2014; 383: 1899–911

HYPERTENSION AND ISCHEMIC HEART DISEASE

A dangerous Relationship

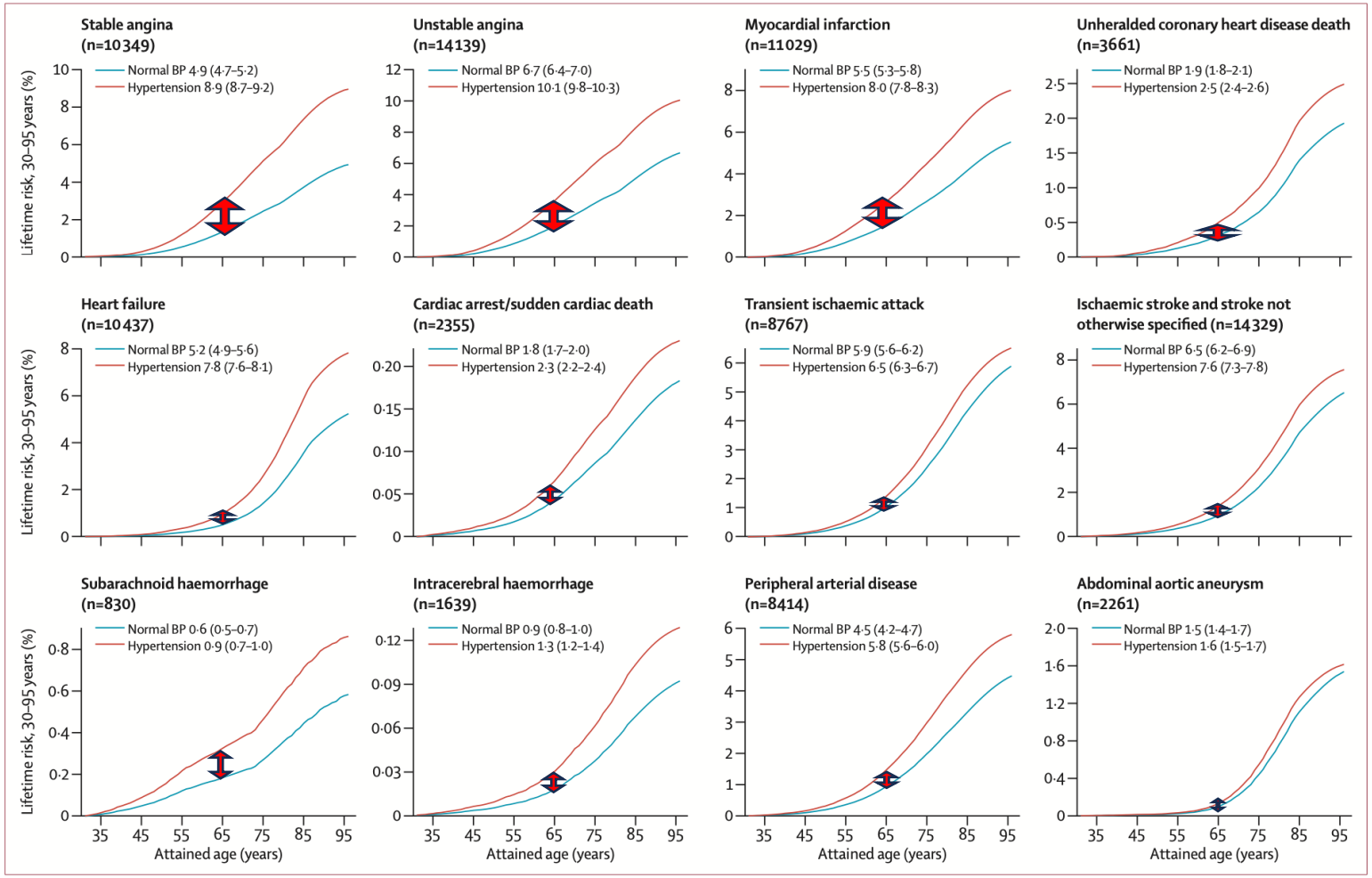


Figure 5: **Lifetime risk (95% CI) of 12 different cardiovascular diseases in people with hypertension or normal BP from index age 30 years**
Hypertension was defined as systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg or use of BP-lowering treatments or physician-recorded diagnosis at baseline. BP=blood pressure.

Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people

Eleni Rapsomaniki, Adam Timmis, Julie George, Mar Pujades-Rodriguez, Anoop D Shah, Spiros Denaxas, Ian R White, Mark J Caulfield, John E Deanfield, Liam Smeeth, Bryan Williams, Aroon Hingorani, Harry Hemingway

Among CVD complications of HTN, CAD occurr earlier!

Rapsomaniki et al. Lancet 2014; 383: 1899–911

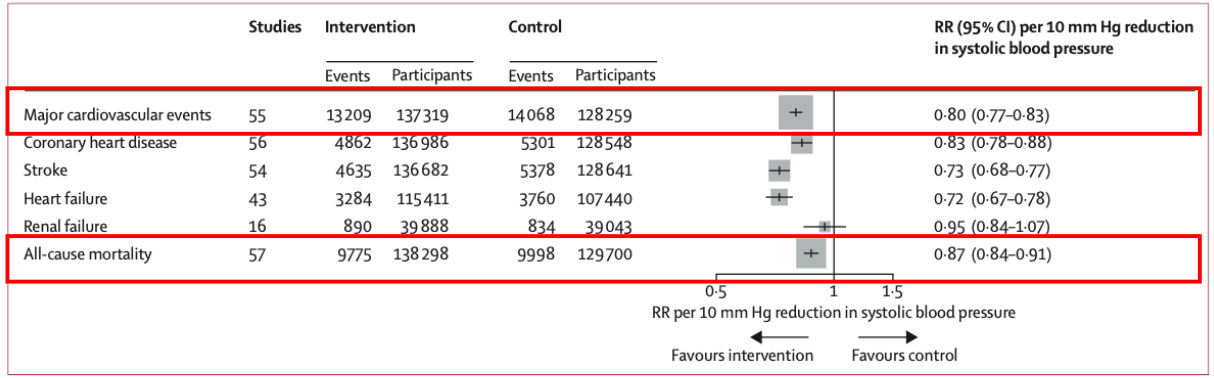
HYPERTENSION AND ISCHEMIC HEART DISEASE

Impact of BP lowering on ischemic heart disease events

Overall population

Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis

Dena Ettehad, Connor A Emdin, Amit Kiran, Simon G Anderson, Thomas Callender, Jonathan Emberson, John Chalmers, Anthony Rodgers, Kazem Rahimi



	Studies	Intervention Events	Intervention Participants	Control Events	Control Participants	RR (95% CI) per 10 mm Hg reduction in systolic blood pressure
Major cardiovascular events	55	13209	137319	14068	128259	0·80 (0·77–0·83)
Coronary heart disease	56	4862	136986	5301	128548	0·83 (0·78–0·88)
Stroke	54	4635	136682	5378	128641	0·73 (0·68–0·77)
Heart failure	43	3284	115411	3760	107440	0·72 (0·67–0·78)
Renal failure	16	890	39888	834	39043	0·95 (0·84–1·07)
All-cause mortality	57	9775	138298	9998	129700	0·87 (0·84–0·91)

Figure 3: Standardised effects of a 10 mm Hg reduction in systolic blood pressure

CAD population

Association of Blood Pressure Lowering With Mortality and Cardiovascular Disease Across Blood Pressure Levels
A Systematic Review and Meta-analysis

Mattias Brunström, MD; Bo Carlberg, MD, PhD

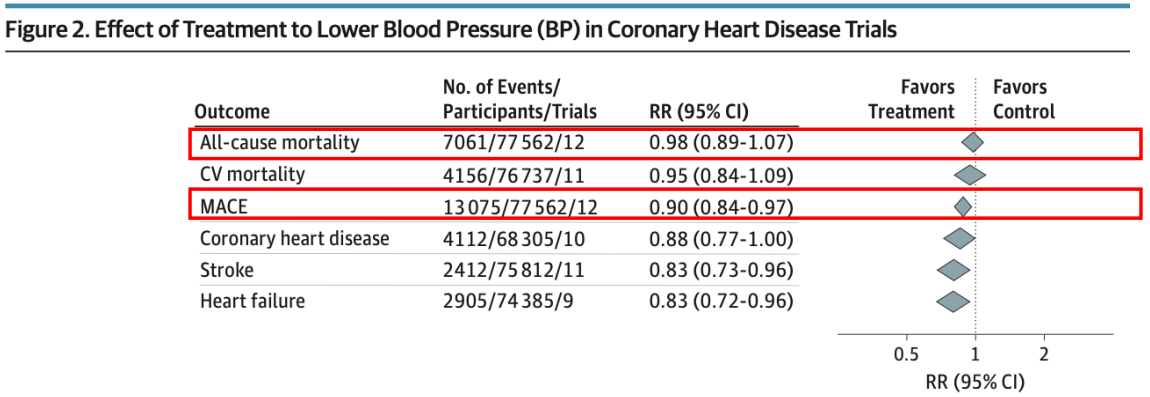


Figure 2. Effect of Treatment to Lower Blood Pressure (BP) in Coronary Heart Disease Trials

Outcome	No. of Events/ Participants/Trials	RR (95% CI)
All-cause mortality	7061/77 562/12	0.98 (0.89-1.07)
CV mortality	4156/76 737/11	0.95 (0.84-1.09)
MACE	13 075/77 562/12	0.90 (0.84-0.97)
Coronary heart disease	4112/68 305/10	0.88 (0.77-1.00)
Stroke	2412/75 812/11	0.83 (0.73-0.96)
Heart failure	2905/74 385/9	0.83 (0.72-0.96)

Greater relative CV risk reduction in the overall population than in patients who already developed CAD, suggesting the importance of early aggressive BP control

HYPERTENSION AND ISCHEMIC HEART DISEASE

The guidelines perspective: when to treat?

9. ANTIHYPERTENSIVE DRUG TREATMENT INITIATION

9.1 Should treatment initiation be based on total CV risk?

The above data and considerations support earlier in-life treatment of hypertension as well as treatment implementation also when CV risk is still low-to-moderate. Although total CV risk provides clinically important information and should

Recommendations and statements	CoR	LoE
In patients 18 to 79 years, the recommended office threshold for initiation of drug treatment is 140 mmHg for SBP and/or 90 mmHg for DBP.	I	A
In adult patients with a history of CVD, predominantly CAD, drug treatment should be initiated in the high-normal BP range (SBP ≥130 or DBP ≥80 mmHg).	I	A

HYPERTENSION AND ISCHEMIC HEART DISEASE

Blood pressure control in IHD: how to achieve it?

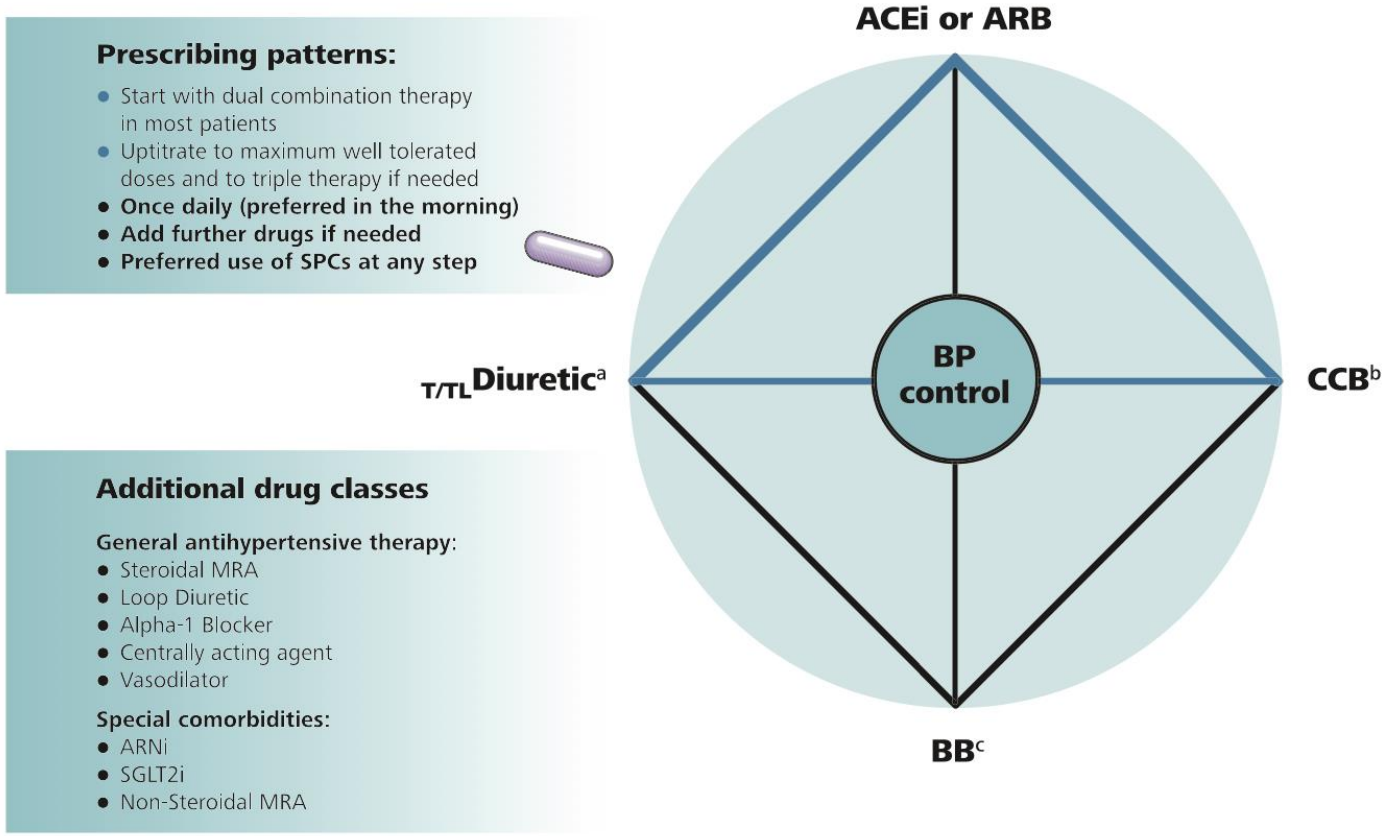
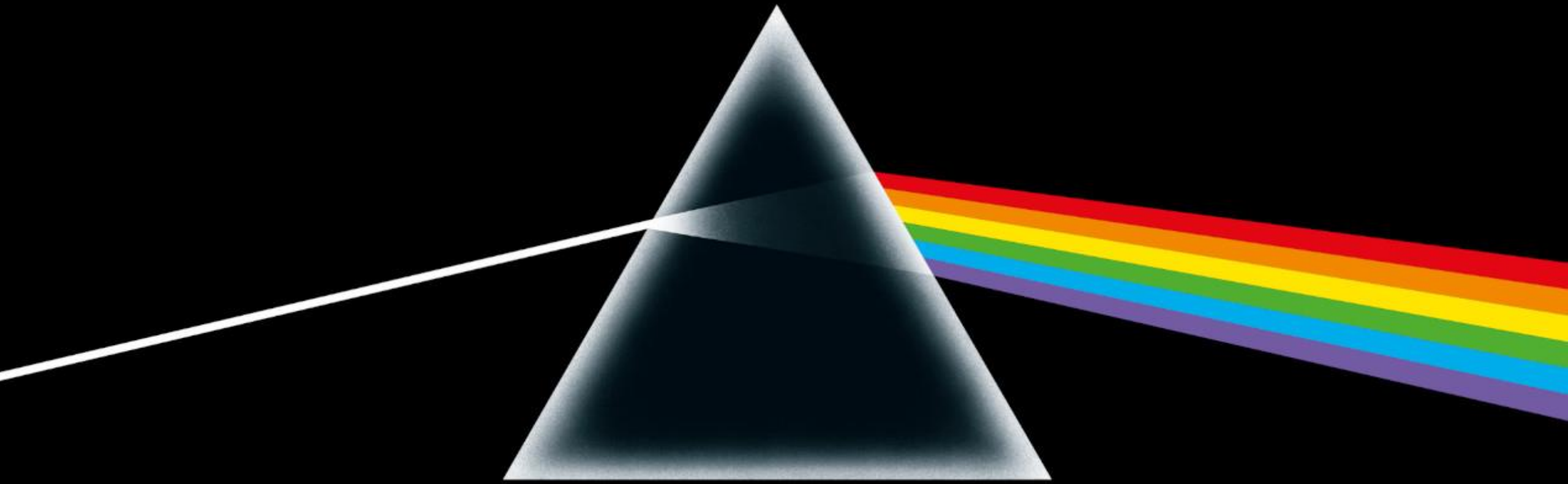


FIGURE 11 Drug classes for BP-lowering therapy.(a) Use of Diuretics: Consider transition to Loop Diuretic if eGFR is between 30 to 45 ml/min/1.73 m^2. If eGFR <30 ml/min/1.73 m^2 use Loop Diuretic. (b) Non-DHP CCB should not be combined with BB. (c) BB should be used as guideline directed medical therapy in respective indications or considered in several other conditions (Table 16). Start with dual combination therapy including a RAS-blocker (either ACEi or ARB) plus a T/TL Diuretic or a CCB is recommended (thick blue lines). Triple therapy includes a combination of the three classes as indicated by the blue lines.

Recommendations and statements	
BP lowering should be prioritized over the selection of specific antihypertensive drug classes because treatment benefit largely originates from BP reduction.	
CoR	**LoE**
I	A

PINK FLOYD



THE DARK SIDE OF THE MOON

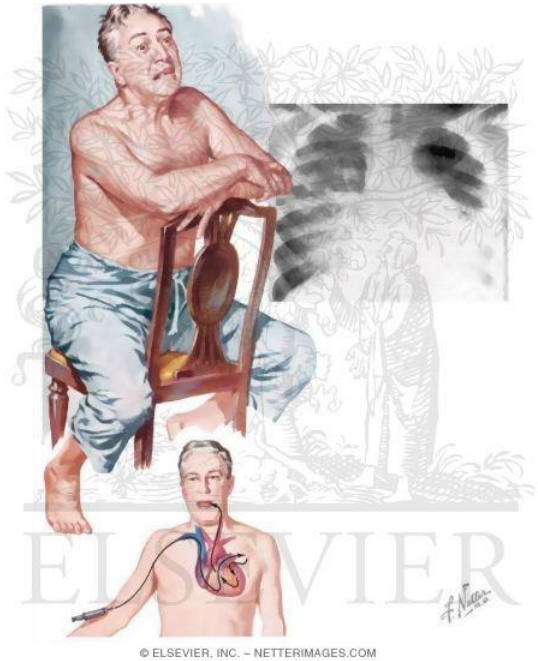
HYPERTENSION AND ISCHEMIC HEART DISEASE

Heart failure: a pandemic without vaccines?

European Heart Journal (2015) **36**, 395–397
doi:10.1093/eurheartj/ehv004

Heart failure: the cardiovascular epidemic of the 21st century

Thomas F. Lüscher, MD, FESC



Prevalence

Prevalence 1-3% in general adult population

Overall prevalence ↑

Prevalence in HFrEF ↔

Prevalence In HFpEF ↑

Mortality

Mortality remains high

30-day Mortality	~2-3%
1-year Mortality	~15-30%
3-year Mortality	~30-50%
5-year Mortality	~50-75%

CVD HFreF ↓ Non-CVD HFpeF ↑

Costs

Annual health care costs up to €25,500 per year

Increasing due to major demographic changes (>65 years)

Main cost drivers:
- Directs costs (~70%)
- Non-CVD comorbidities
- Invasive procedures
- Medications/Diagnostics
- Outpatient visits

HYPERTENSION AND ISCHEMIC HEART DISEASE

Heart failure: the dark side of the moon

Trends in prevalence of comorbidities in heart failure clinical trials

Muhammad Shahzeb Khan[1†], Ayman Samman Tahhan[2†], Muthiah Vaduganathan[3], Stephen J. Greene[4], Alaaeddin Alrohaibani[1], Stefan D. Anker[5], Orly Vardeny[6], Gregg C. Fonarow[7], and Javed Butler[8*]

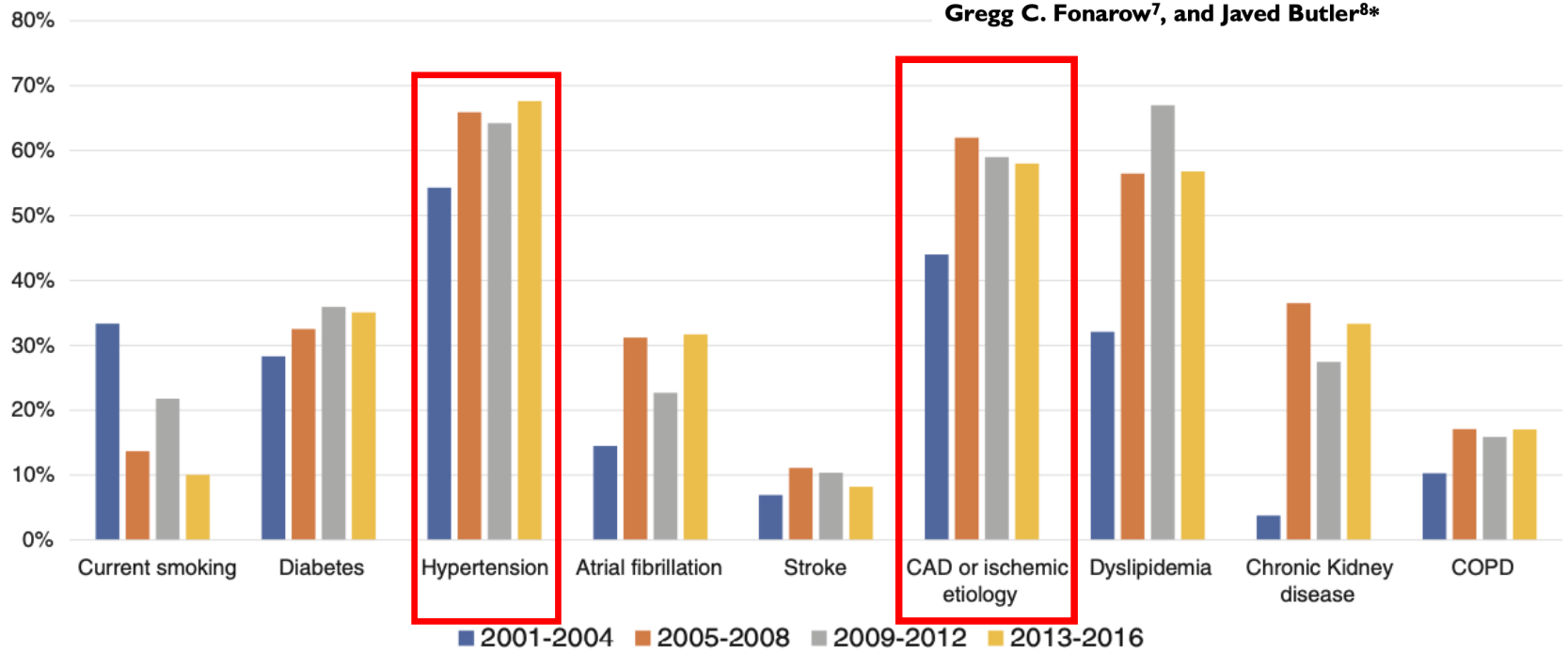


Figure 1 Trends of key comorbidities across all clinical trials of heart failure. The prevalence of smoking decreased over time while the prevalence of cardio-metabolic comorbidities increased. CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease.

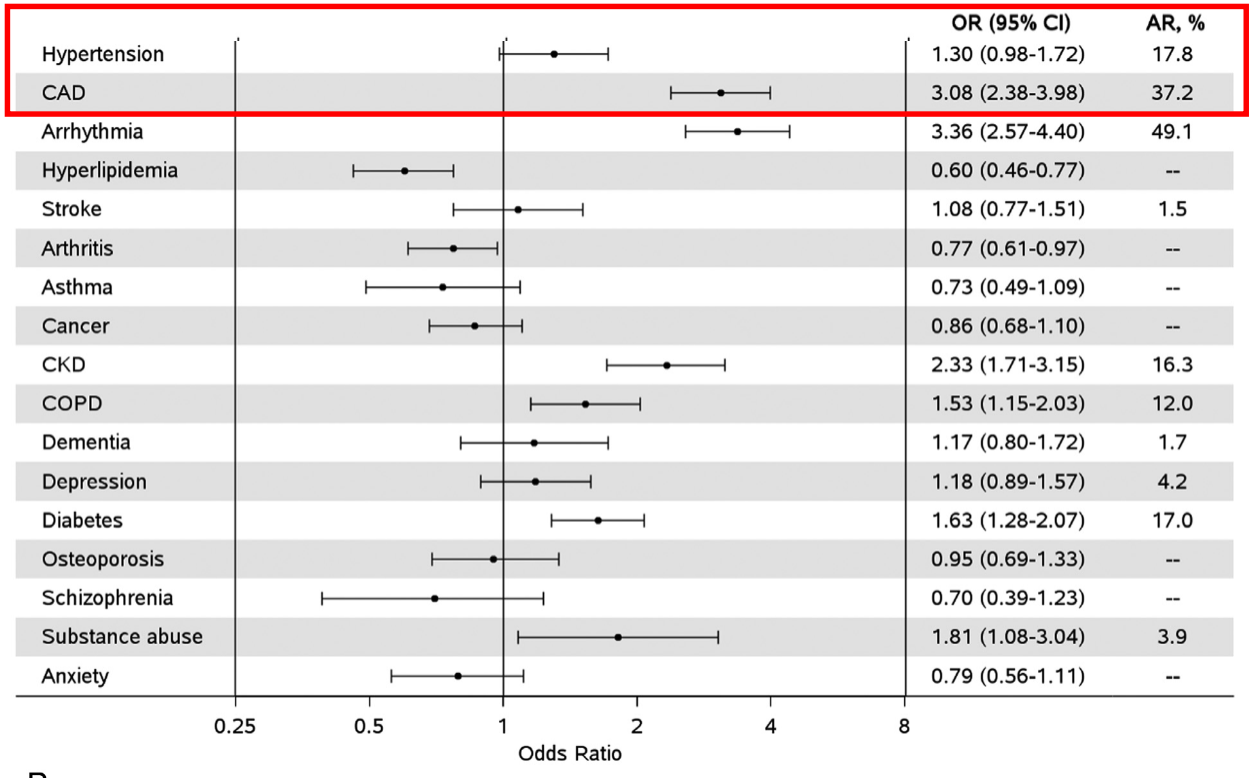
Khan et al. European Journal of Heart Failure (2020) 22, 1032–1042

HYPERTENSION AND ISCHEMIC HEART DISEASE

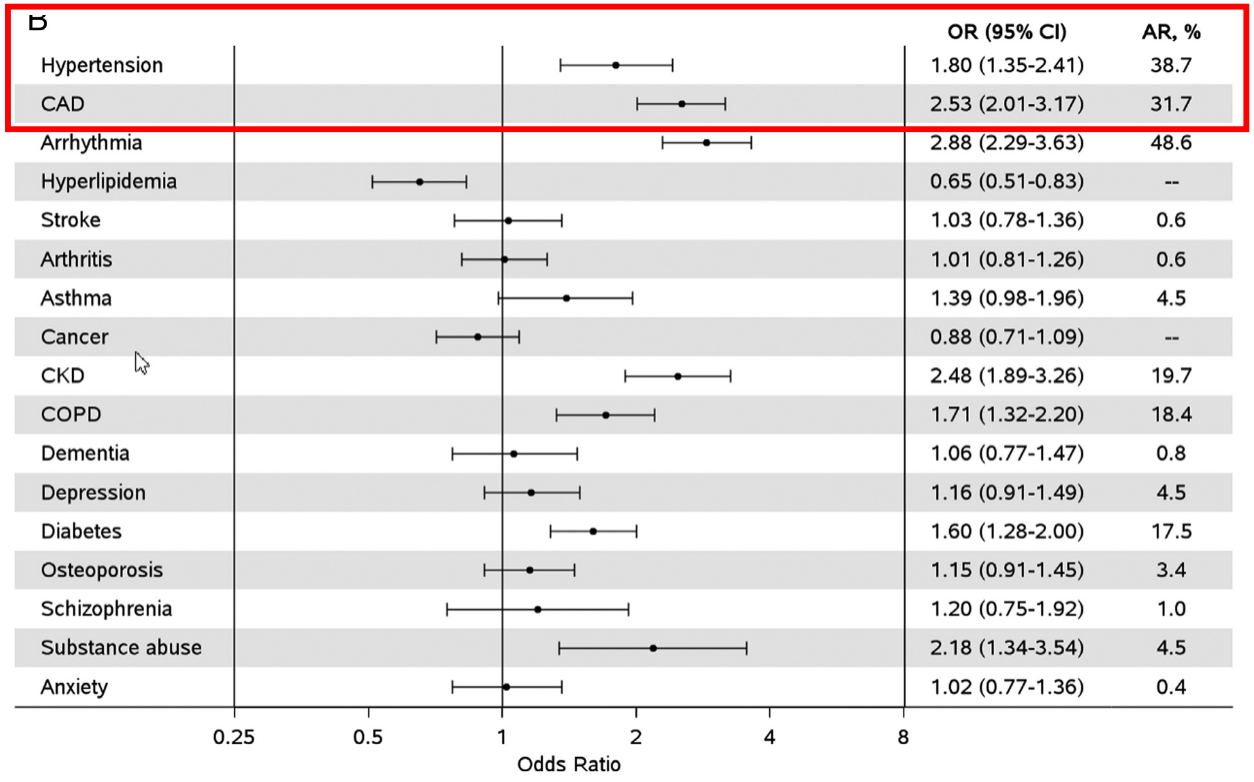
Heart failure, HT and IHD: a complex relationship

Risk Factors for Heart Failure in the Community: Differences by Age and Ejection Fraction

Alanna M. Chamberlain, PhD, MPH,[a] Cynthia M. Boyd, MD, MPH,[b] Sheila M. Manemann, MPH,[a] Shannon M. Dunlay, MD, MS,[c] Yariv Gerber, PhD,[d] Jill M. Killian, BS,[a] Susan A. Weston, MS,[a] Véronique L. Roger, MD, MPH[a,c]



HF with reduced ejection fraction

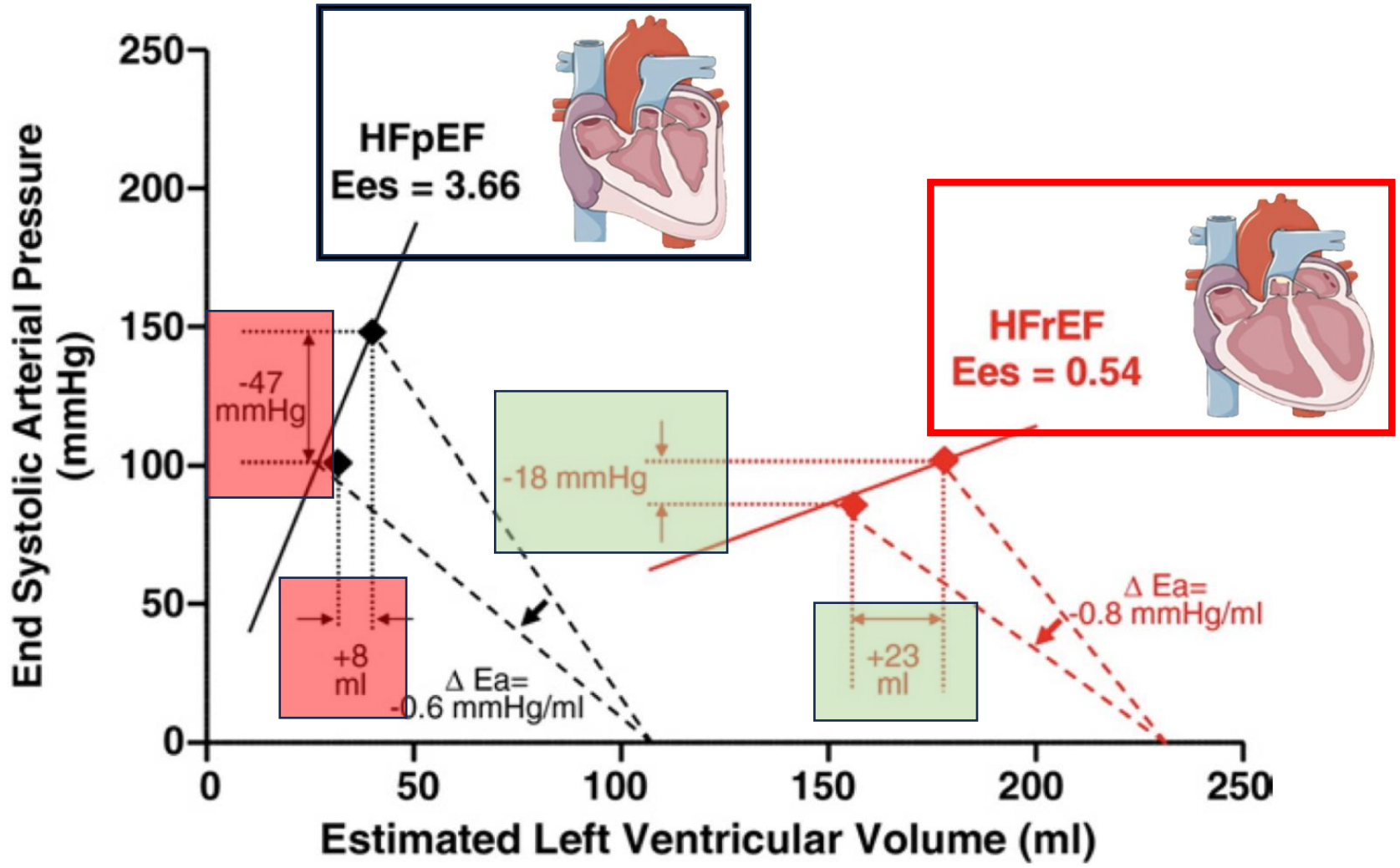


HF with preserved ejection fraction

Chamberlain et al. The American Journal of Medicine (2020) 133:e237–e248

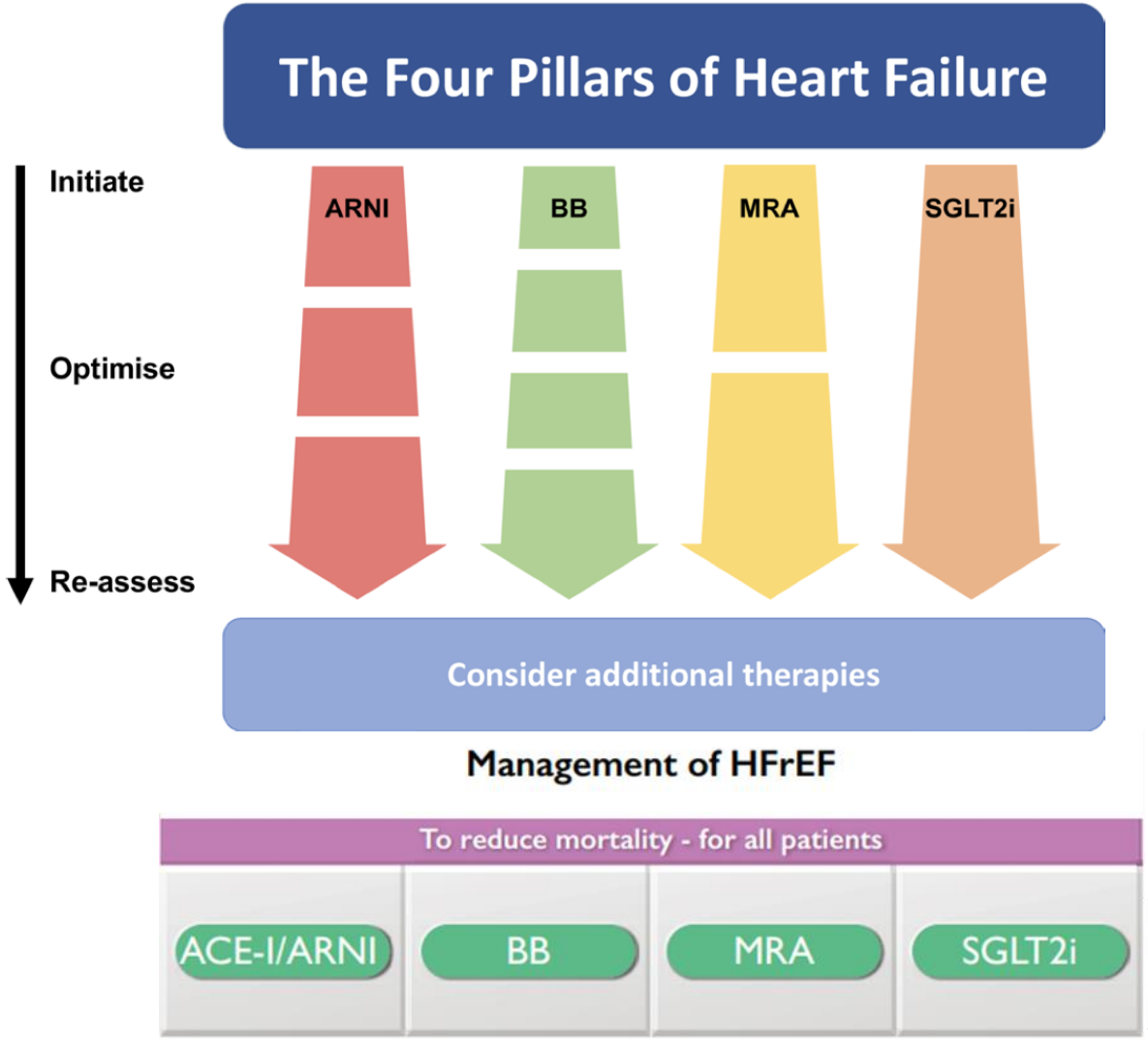
HYPERTENSION AND ISCHEMIC HEART DISEASE

HFrEF, HFpEF and blood pressure: a pathophysiological perspective



HYPERTENSION AND ISCHEMIC HEART DISEASE

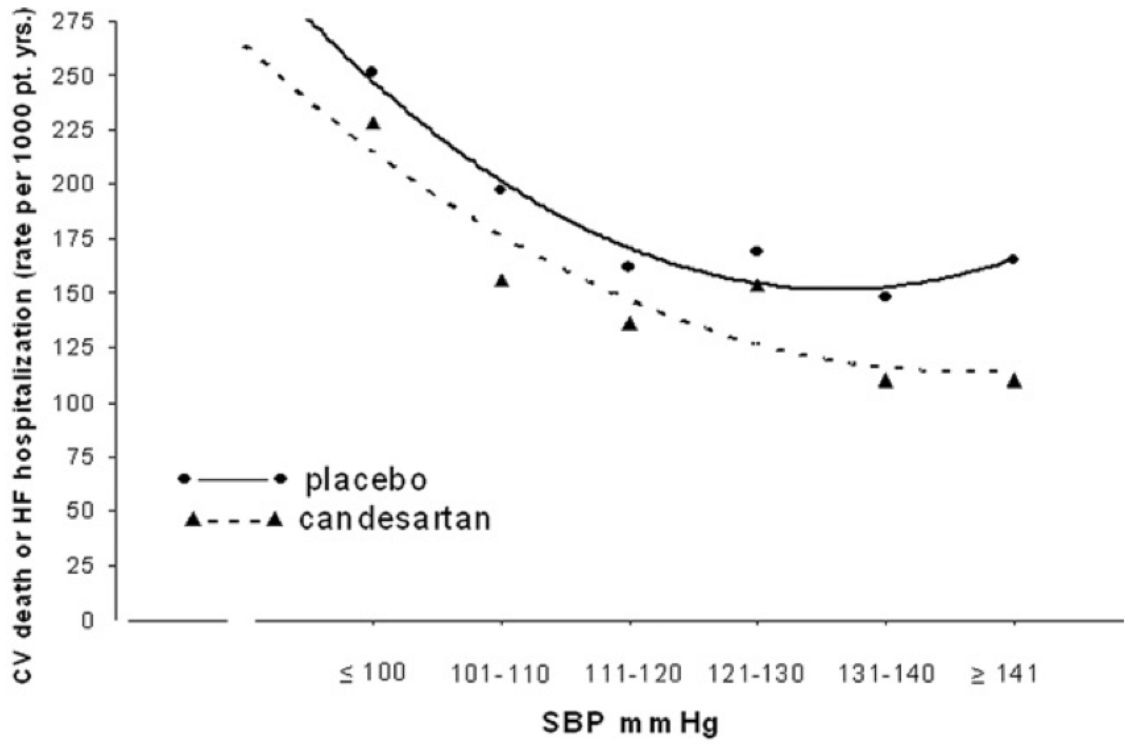
HFrEF prognostic drugs and blood pressure: what matters?



Additional safety recommendations		
Do not aim to target office SBP below 120 mmHg or DBP below 70 mmHg during drug treatment.	III	C

HYPERTENSION AND ISCHEMIC HEART DISEASE

Prognostic benefit of HFrEF drugs and blood pressure



Risk of CV Death or HF Hospitalization According to Baseline SBP in the Randomized Placebo and Candesartan Treatment Groups

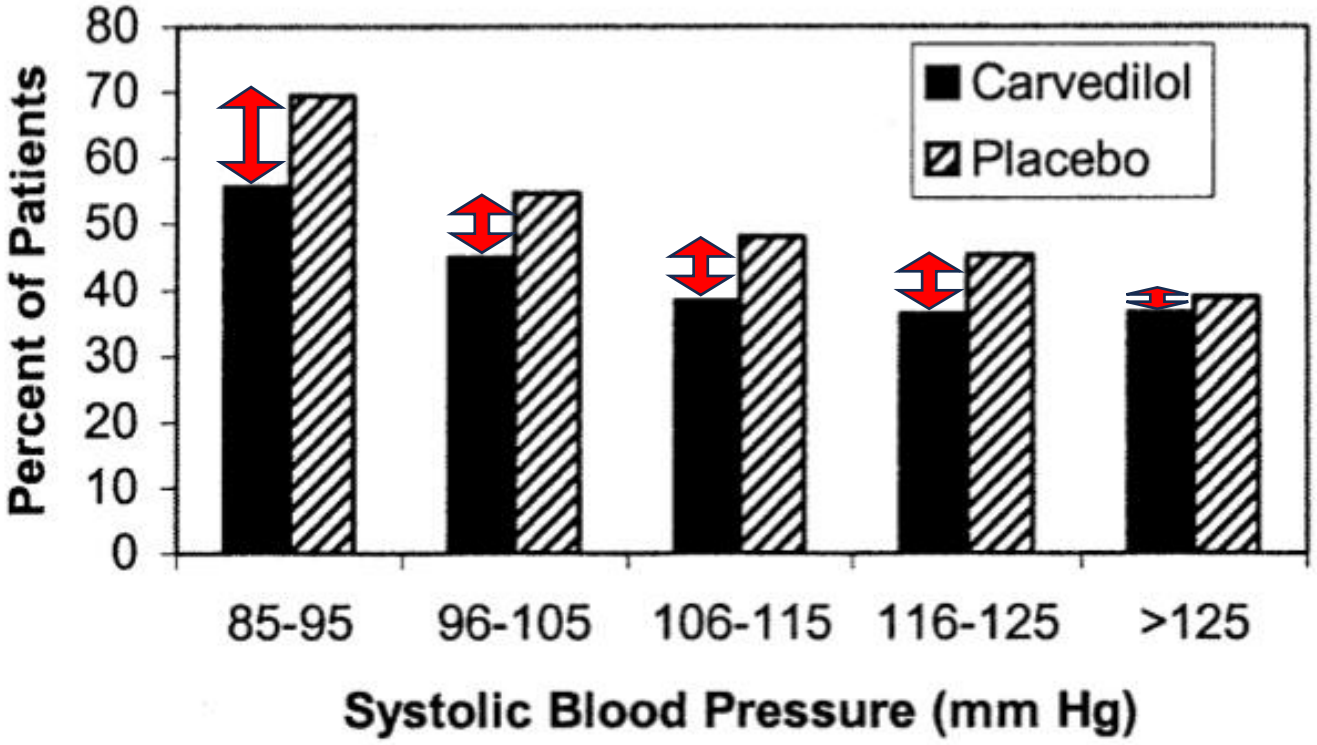
CV = cardiovascular; HF = heart failure; SBP = systolic blood pressure.

Clinical Outcomes According to Baseline Blood Pressure in Patients With a Low Ejection Fraction in the CHARM (Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity) Program

Preserved RAASi prognostic benefit regardless of blood pressure

HYPERTENSION AND ISCHEMIC HEART DISEASE

Prognostic benefit of HFrEF drugs and blood pressure



Influence of Pretreatment Systolic Blood Pressure on the Effect of Carvedilol in Patients With Severe Chronic Heart Failure

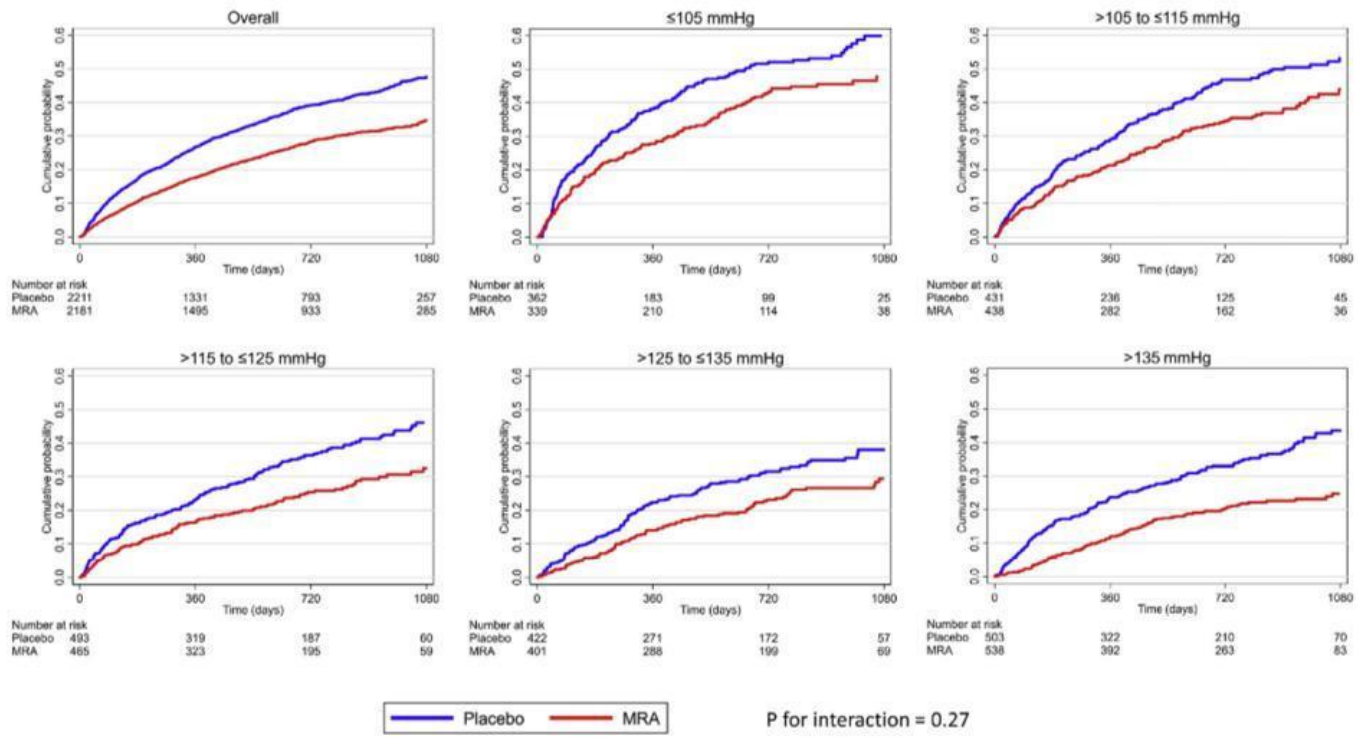
The Carvedilol Prospective Randomized Cumulative Survival (COPERNICUS) Study

Greatest relative and absolute MACE reduction at lower baseline blood pressures with carvedilol vs placebo

HYPERTENSION AND ISCHEMIC HEART DISEASE

Prognostic benefit of HFrEF drugs and blood pressure

FIGURE 2 Cumulative Incidence of Cardiovascular Death or Hospitalization for Heart Failure According to Baseline SBP Categories



Kaplan-Meier curves for cardiovascular death or hospitalization for heart failure, overall, and in each SBP category. The p value is for interaction between baseline SBP categories and treatment effect. The risk table below the graphs shows the number at risk of the event of interest. MRA denotes mineralocorticoid receptor antagonist. Abbreviations as in Figure 1.

Mineralocorticoid Receptor Antagonists, Blood Pressure, and Outcomes in Heart Failure With Reduced Ejection Fraction

Matteo Serenelli, MD,[a,b] Alice Jackson, MBChB,[a] Pooja Dewan, MBBS,[a] Pardeep S. Jhund, MBChB, PhD,[a] Mark C. Petrie, MBChB,[a] Patrick Rossignol, MD, PhD,[c] Gianluca Campo, MD,[b,d] Bertram Pitt, MD,[e] Faiez Zannad, MD, PhD,[c] João Pedro Ferreira, MD, PhD,[a,c] John J.V. McMurray, MD[a]

Preserved MRA prognostic benefit regardless of blood pressure

HYPERTENSION AND ISCHEMIC HEART DISEASE

So what?

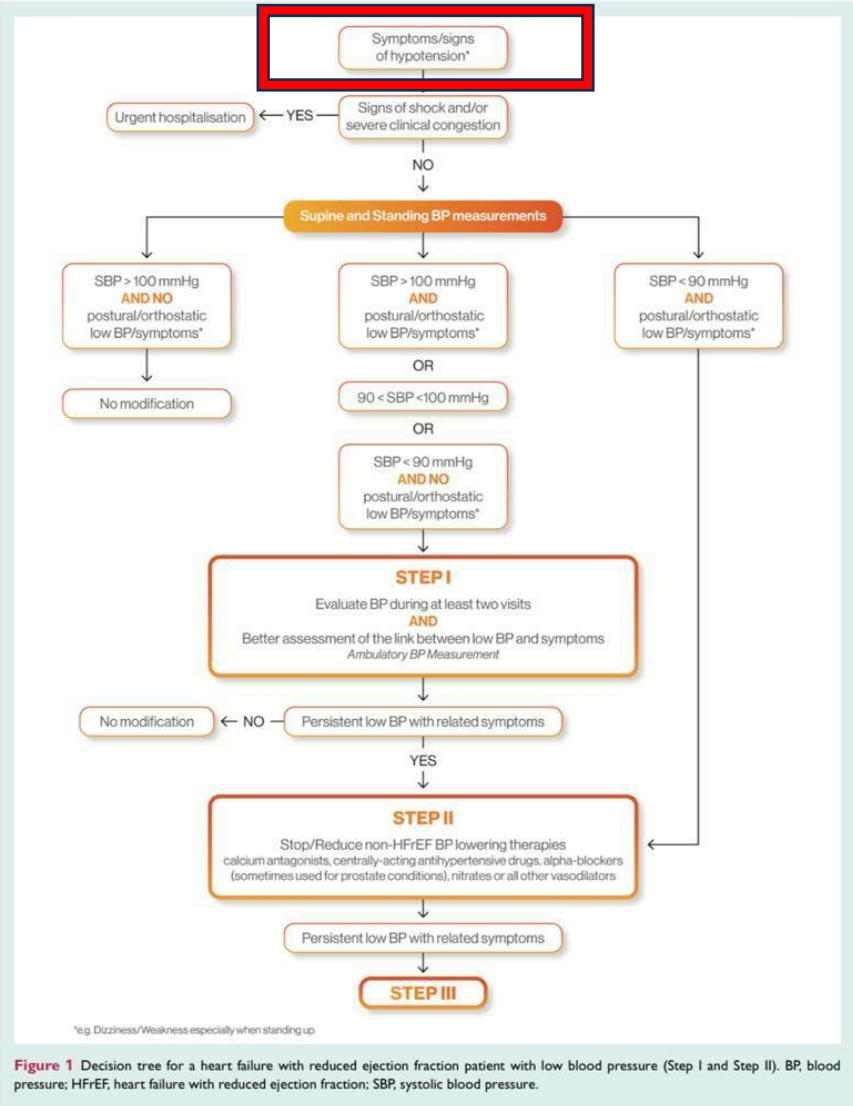


Figure 1 Decision tree for a heart failure with reduced ejection fraction patient with low blood pressure (Step I and Step II). BP, blood pressure; HFrEF, heart failure with reduced ejection fraction; SBP, systolic blood pressure.

ESC European Society of Cardiology

European Journal of Heart Failure (2020) **22**, 1357–1365
doi:10.1002/ejhf.1835

REVIEW

Management of low blood pressure in ambulatory heart failure with reduced ejection fraction patients

Jennifer Cautela[1†], Jean-Michel Tartiere[2†], Alain Cohen-Solal[3],

HYPERTENSION AND ISCHEMIC HEART DISEASE

So what?

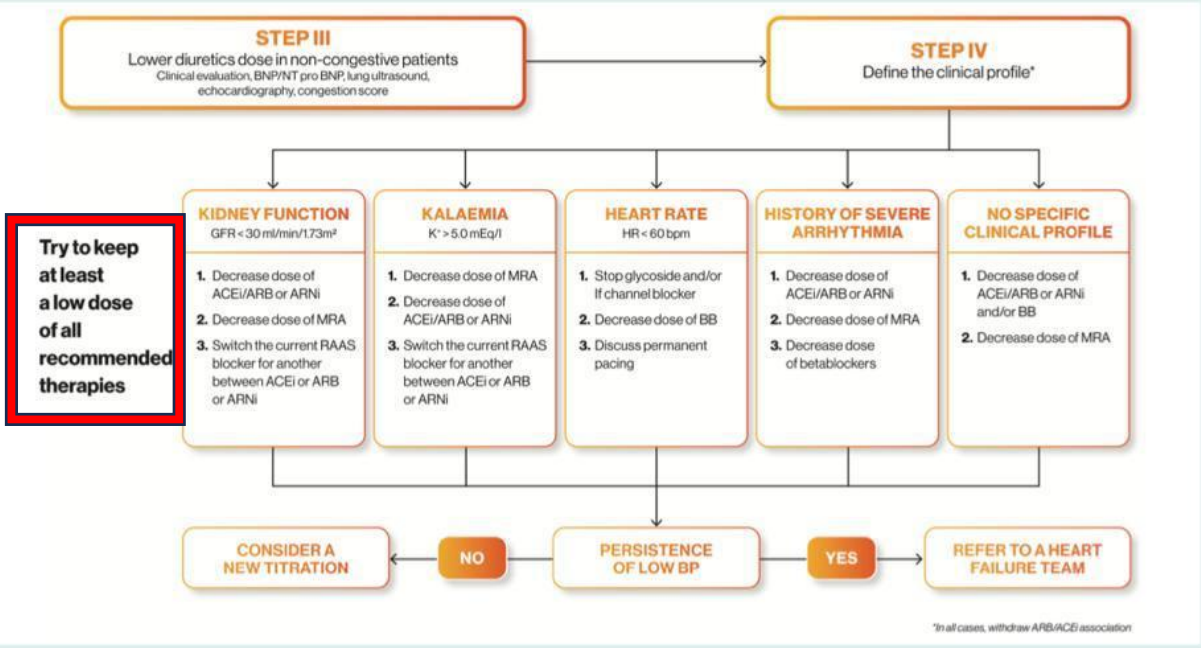


Figure 2 Decision tree for a heart failure with reduced ejection fraction patient with low blood pressure (Step III and Step IV). ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor–neprilysin inhibitor; BB, beta-blocker; BNP, B-type natriuretic peptide; BP, blood pressure; GFR, glomerular filtration rate; HR, heart rate; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal B-type natriuretic peptide; RAAS, renin–angiotensin–aldosterone system.

ESC European Society of Cardiology

European Journal of Heart Failure (2020) **22**, 1357–1365
doi:10.1002/ejhf.1835

REVIEW

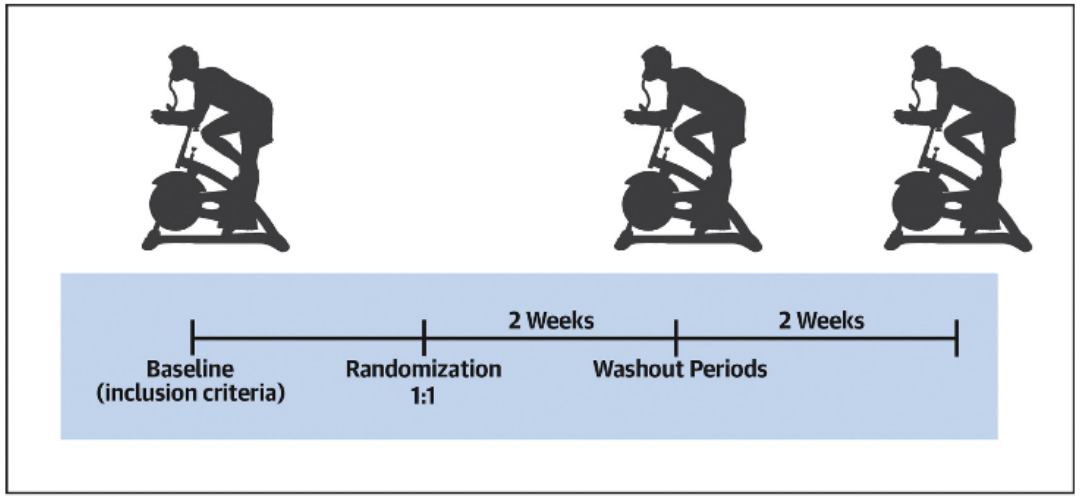
Management of low blood pressure in ambulatory heart failure with reduced ejection fraction patients

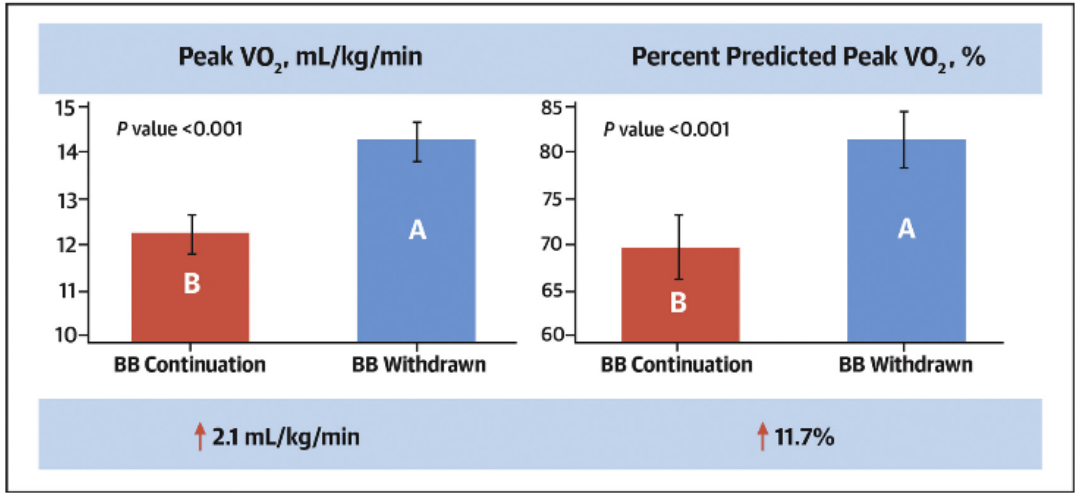
Jennifer Cautela[1†], Jean-Michel Tartiere[2†], Alain Cohen-Solal[3],

HFrEF treatments in routine practice. In patients with signs of shock and/or severe congestion, hospitalization is advised. However, in the very frequent cases of non-severe and asymptomatic hypotension observed while taking drugs with a class I indication in HFrEF, European and US guidelines recommend maintaining the same drug dosage. In instances of symptomatic or severe persistent hypotension (systolic blood pressure < 90 mmHg), it is recommended to first decrease blood pressure reducing drugs not indicated in HFrEF as well as the loop diuretic dose in the absence of associated signs of congestion. Unless the management of hypotension appears urgent, a HF specialist should then be sought rather than stopping or decreasing drugs with a class I indication in HFrEF. If symptoms or severe hypotension persist, no recommendations exist. Our HF group reviewed available evidence and proposes certain steps to follow in such situations in order to

HYPERTENSION AND ISCHEMIC HEART DISEASE

HFpEF and blood pressure: beta-blockers





Palau, P. et al. J Am Coll Cardiol. 2021;78(21):2042-2056.

Effect of β-Blocker Withdrawal on Functional Capacity in Heart Failure and Preserved Ejection Fraction

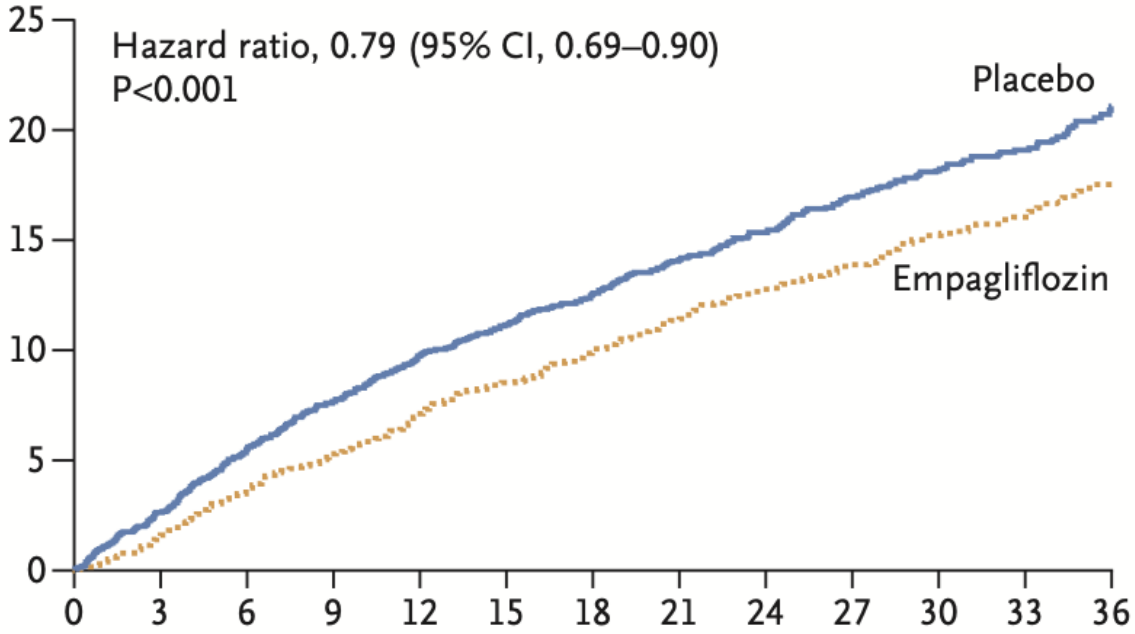
Avoid beta-blockers as anti-hypertensive agents in HFpEF, unless indicated for other reasons (AF, AMI)

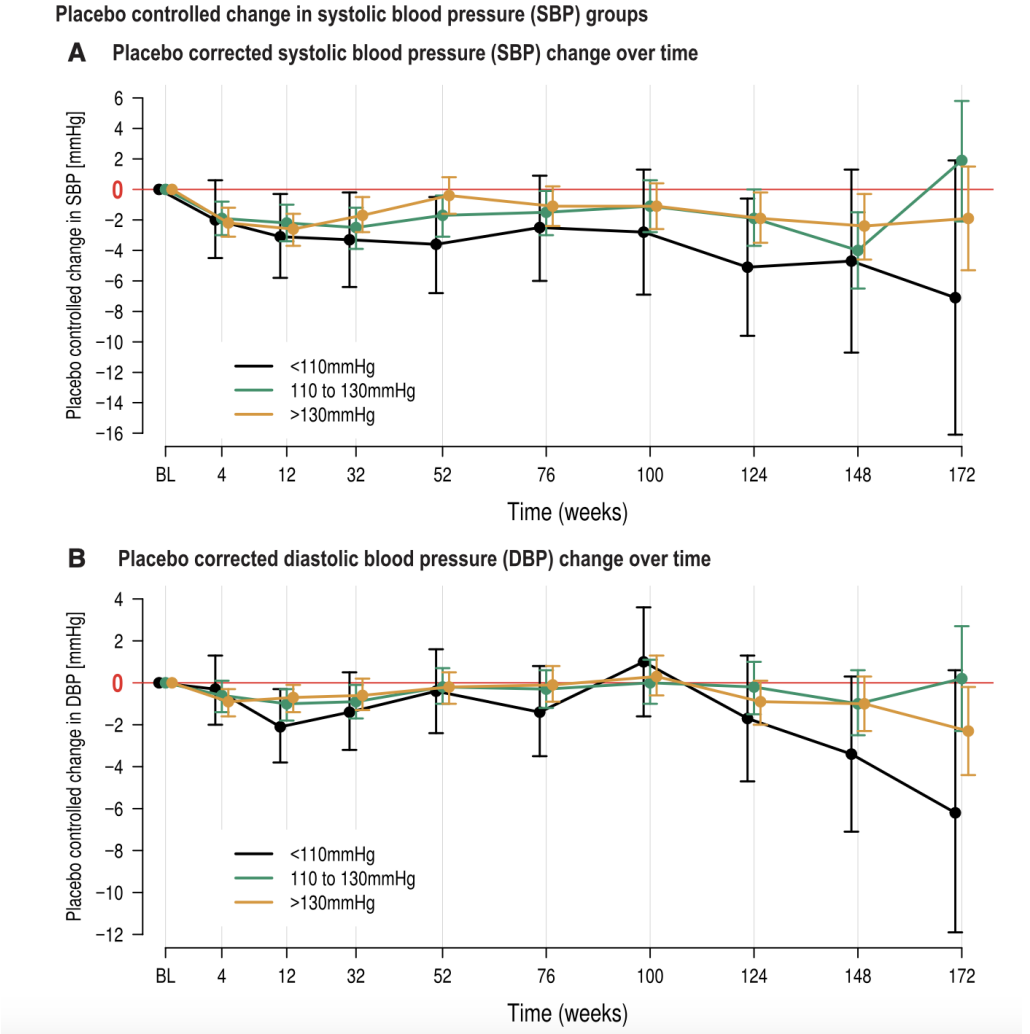
HYPERTENSION AND ISCHEMIC HEART DISEASE

HFpEF and blood pressure: prognostic drugs firt

Empagliflozin in Heart Failure with a Preserved Ejection Fraction

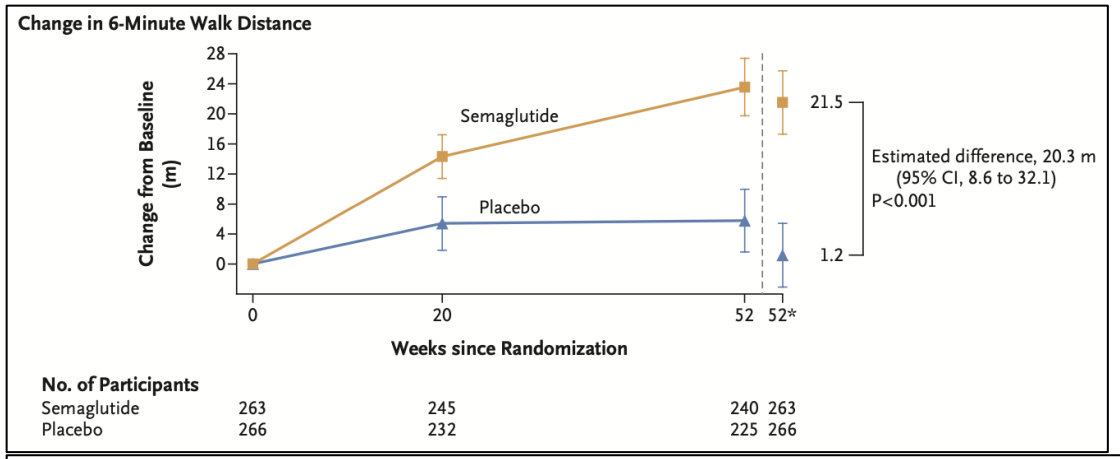
S.D. Anker, J. Butler, G. Filippatos, J.P. Ferreira, E. Bocchi, M. Böhm, H.-P. Brunner–La Rocca, D.-J. Choi, V. Chopra, E. Chuquiure-Valenzuela, N. Giannetti, J.E. Gomez-Mesa, S. Janssens, J.L. Januzzi, J.R. Gonzalez-Juanatey, B. Merkely, S.J. Nicholls, S.V. Perrone, I.L. Piña, P. Ponikowski, M. Senni, D. Sim, J. Spinar, I. Squire, S. Taddei, H. Tsutsui, S. Verma, D. Vinereanu, J. Zhang, P. Carson, C.S.P. Lam, N. Marx, C. Zeller, N. Sattar, W. Jamal, S. Schnaidt, J.M. Schnee, M. Brueckmann, S.J. Pocock, F. Zannad, and M. Packer, for the EMPEROR-Preserved Trial Investigators*

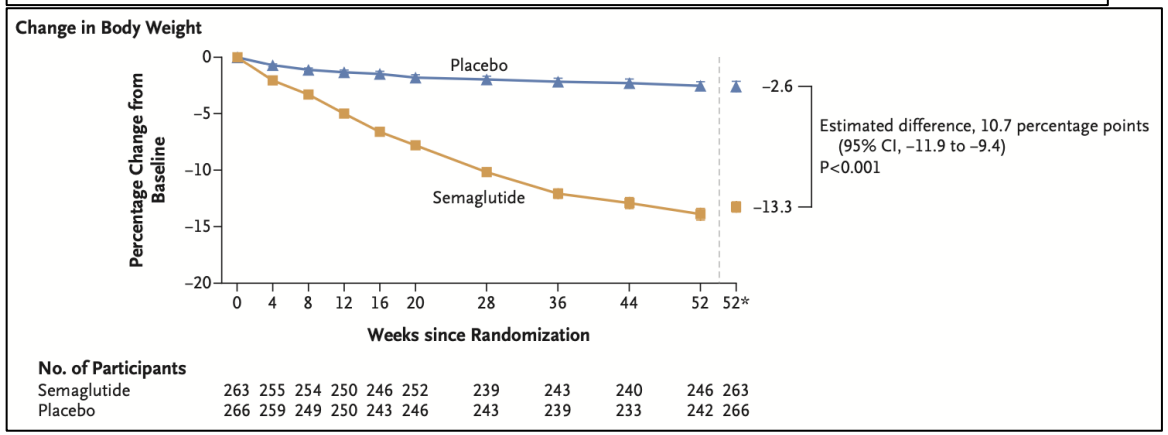




HYPERTENSION AND ISCHEMIC HEART DISEASE

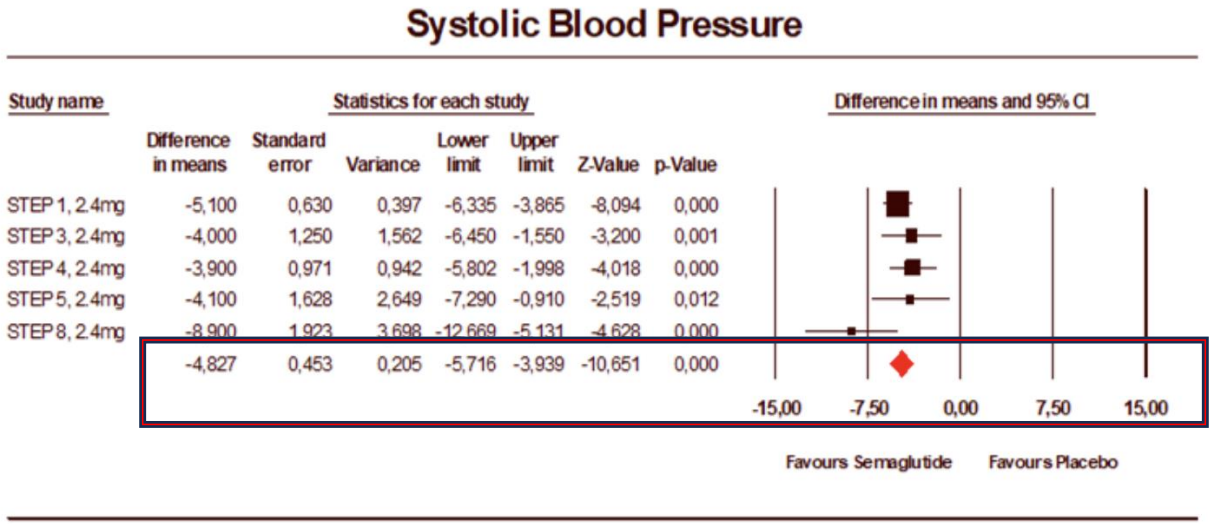
HFpEF and blood pressure: prognostic drugs first





Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity

M.N. Kosiborod, S.Z. Abildstrøm, B.A. Borlaug, J. Butler, S. Rasmussen, M. Davies, G.K. Hovingh, D.W. Kitzman, M.L. Lindegaard, D.V. Møller, S.J. Shah, M.B. Treppendahl, S. Verma, W. Abhayaratna, F.Z. Ahmed, V. Chopra, J. Ezekowitz, M. Fu, H. Ito, M. Lelonek, V. Melenovsky, B. Merkely, J. Núñez, E. Perna, M. Schou, M. Senni, K. Sharma, P. Van der Meer, D. von Lewinski, D. Wolf, and M.C Petrie, for the STEP-HFpEF Trial Committees and Investigators*



Ciò che sappiamo è una goccia,
ciò che ignoriamo è un oceano.

Isaac Newton

THANK YOU!