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The New ESH Guidelines and the Role of Betablockers in Hypertension Management

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Disclosures

I have potential conflict of interest to report:

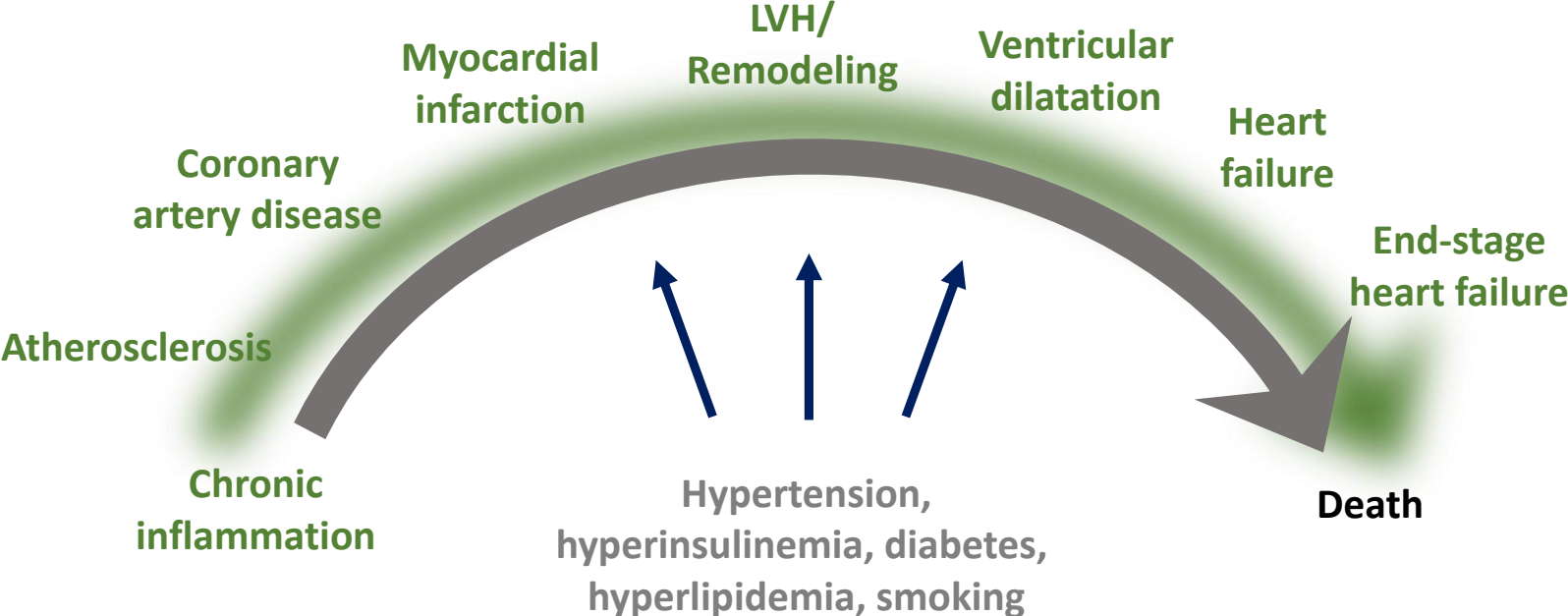
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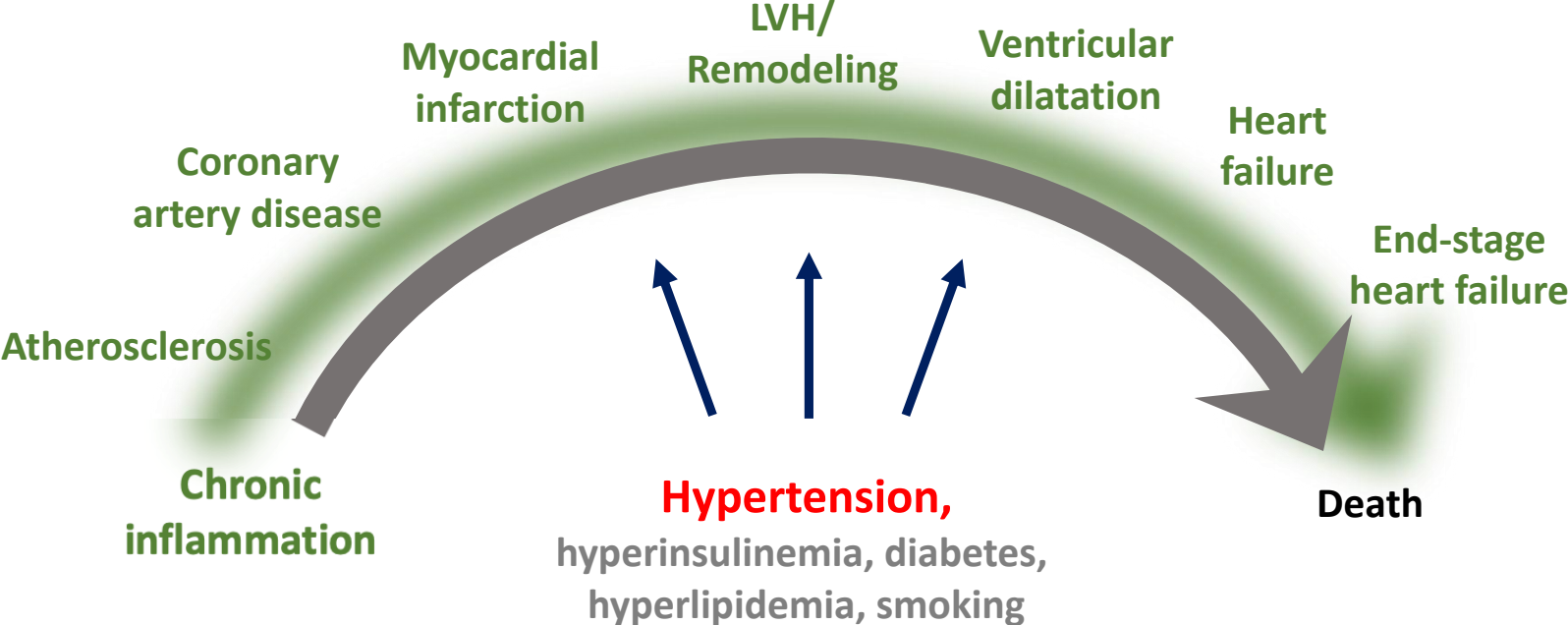
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Betablockers across the cardiovascular continuum



Betablockers across the cardiovascular continuum

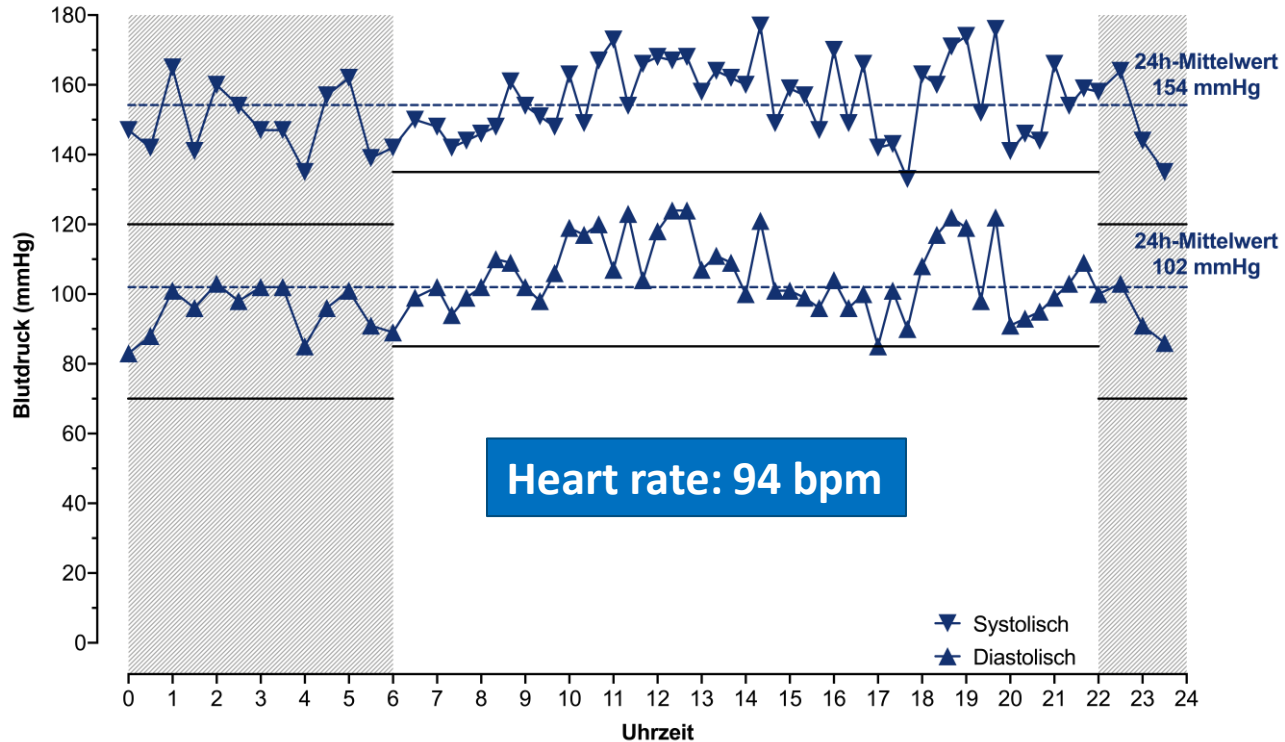


Case example



- Male, 44 years of age, stressfull live and job
- Complains of palpitations and angina
 - CAD ruled out by CT
- First diagnosis of hypertension
- Office BP 155/110 mmHg
- Heart rate 92 bpm
- Obstructive sleep apnea

Case example



Case example



Which treatment would you initiate?

- A) Calcium antagonist
- B) Beta blocker
- C) Angiotensin receptor blocker
- D) ACE-inhibitor
- E) Diuretic

Case example



Which treatment would you initiate?

A) Calcium antagonist






B) Beta blocker

C) Angiotensin receptor blocker

D) ACE-inhibitor

E) Diuretic

Mechanism of action of of antihypertensive drugs

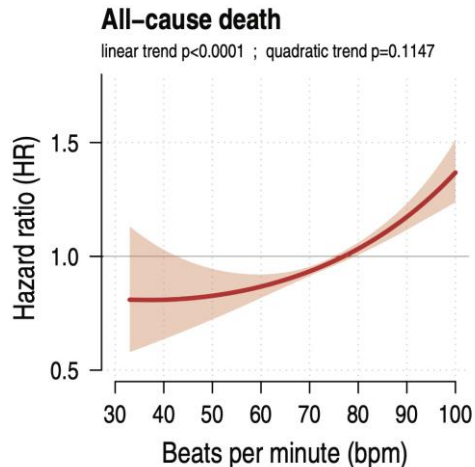
	BB	Diuretics	ARBs	ACEi	CCB
Target organ(s)					
Mechanism/s	<p>↓ heart rate by blocking β_1 receptors and reducing cardiac output</p> <p>↓ renin release and sympathetic activity</p>	<p>↑ excretion of sodium and water</p>	<p>Inhibits vasoconstriction, body fluid retention and sympathomimetic action</p>	<p>↓ renin angiotensin system and reduces blood pressure by suppressing tissue angiotensin</p>	<p>Blocks influx of calcium into vascular smooth muscle cells & reduces peripheral vascular resistance thereby decreases blood pressure</p>

BB: Beta blockers; ARB: Angiotensin Receptor Blockers; ACEi: Angiotensin Converting Enzyme Inhibitors; CCB: Calcium Channel Blockers

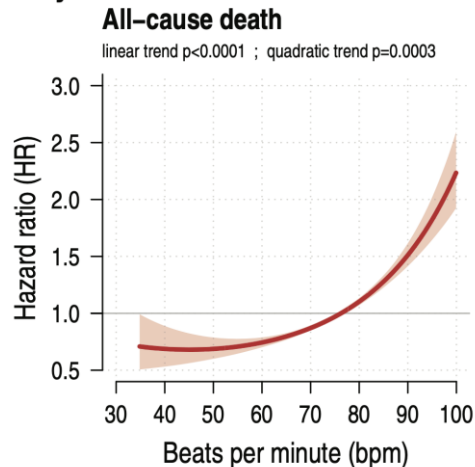
High heart rate associates with mortality in hypertension

ABPM recordings of 56,901 patients with complete 3,373,421 HR readings

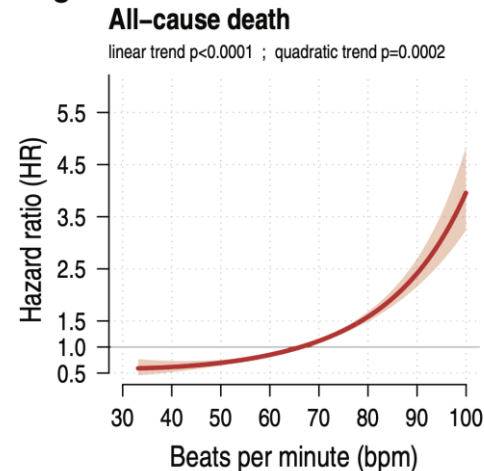
(a) Office



(c) Day

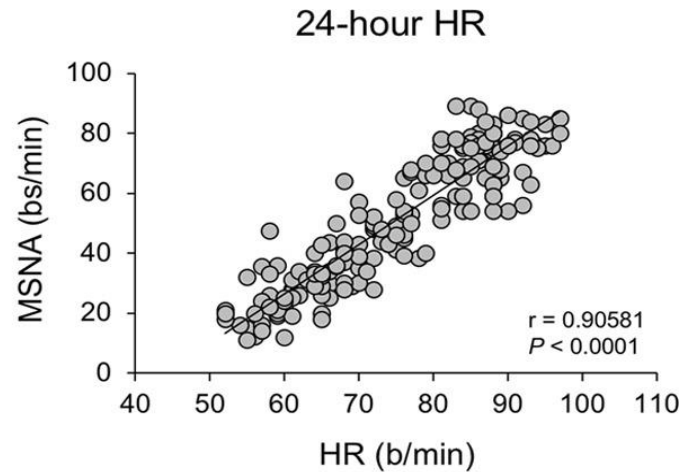
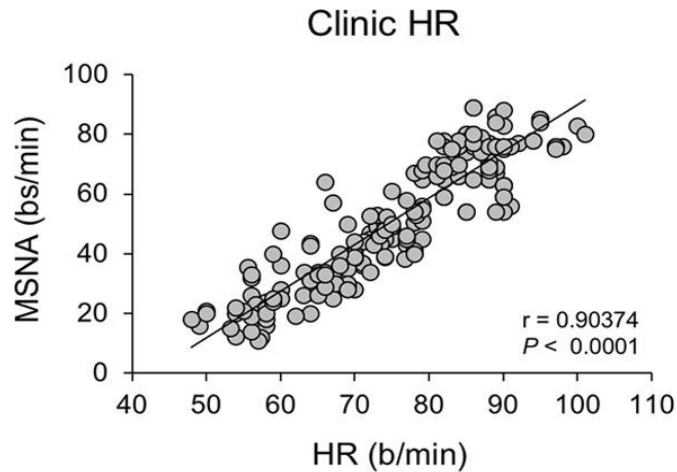


(d) Night



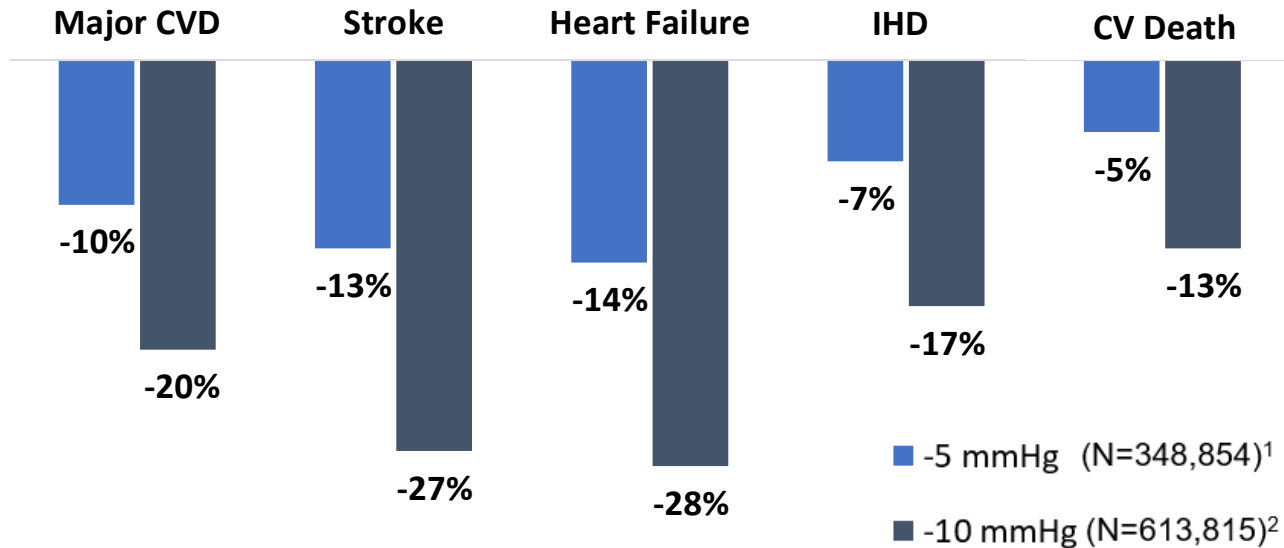
Direct continuous relationship between HR and increased sympathetic activity

Correlation between clinic and 24-hour heart rate and muscle sympathetic nerve traffic
193 untreated mild to moderate patients with hypertension (149 males and 44 females),
age 33-62 years



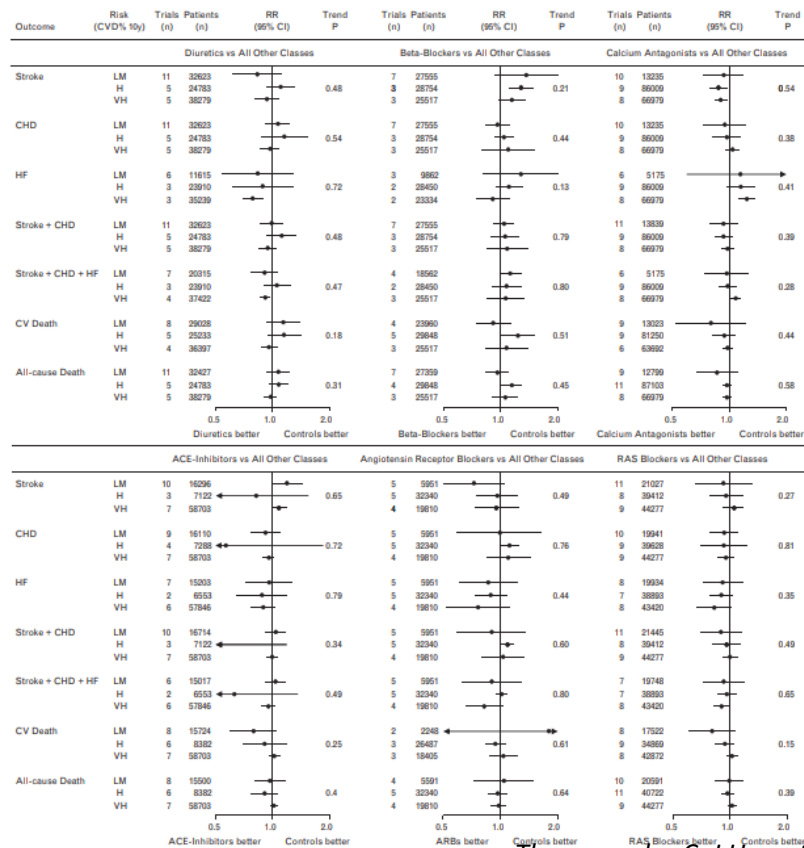
Risk reduction from 5 mmHg and 10 mmHg drop in OSBP

Relative Risk Reduction (%) in Two Large Meta-Analyses



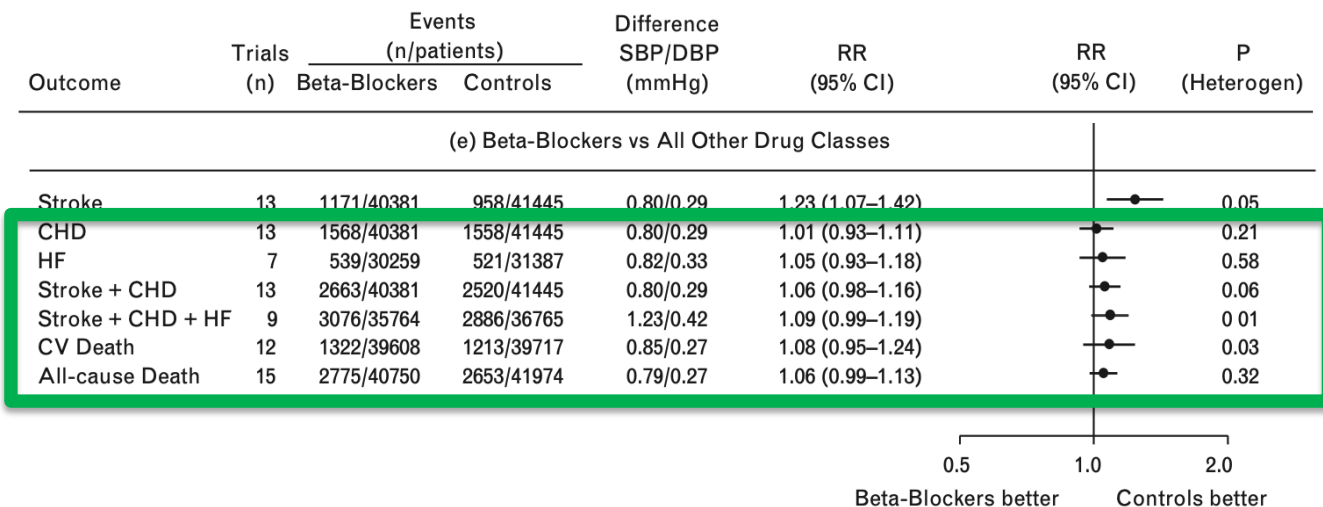
Head to head comparison of antihypertensive agents

50 RCTs for 58 drug comparisons published between 1966 and August 2014
247,006 patients (1,029,768 patient-years)



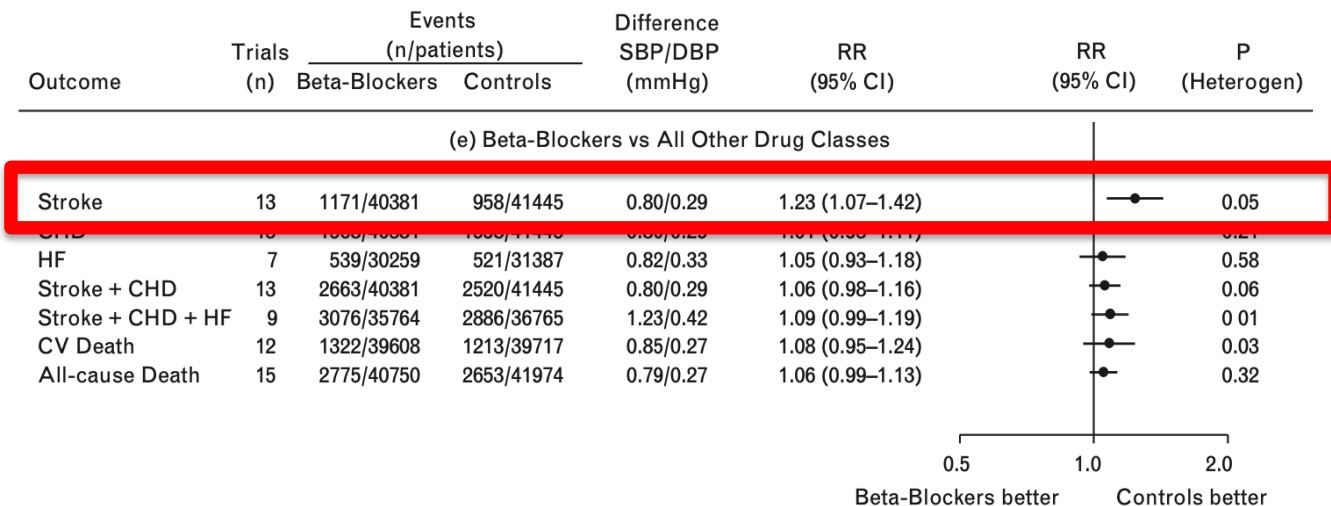
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Head to head comparison of antihypertensive agents

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Most recent meta-analysis on beta-blockers in hypertension

67 BP-lowering trials;
68,478 patients; mean follow-up 2.5 years; baseline SBP/ DBP, 136/82 mmHg;

Beta-blockers vs. placebo were associated with a lower incidence of

- major cardiovascular events (RR 0.85; 95% CI 0.78–0.92)
- all-cause death (RR 0.81; 95% CI 0.75– 0.86)

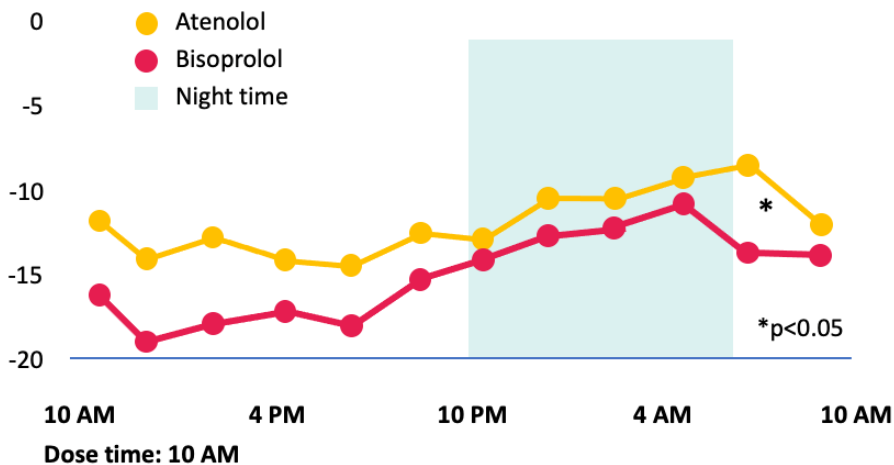
BP decrease with beta-blockers of 10.5/7.0 mmHg:

- reduction of major cardiovascular events by 22% (95% CI, 6-34)

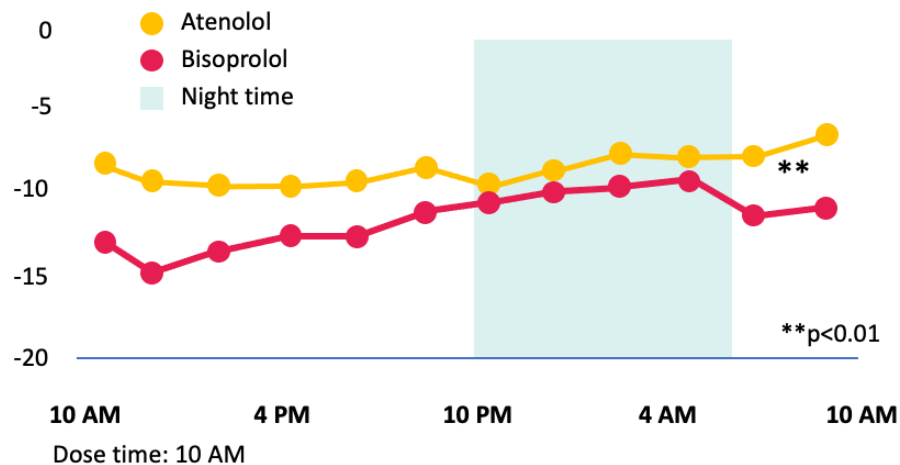
More effective 24-hour BP control with bisoprolol vs atenolol after once-daily dosing

RCT (bisoprolol 10 mg o.d., vs. atenolol 50 mg o.d.);
659 patients with mild-to-moderate hypertension (21-84 years);
ABPM after 8 weeks

Mean change in systolic BP (mmHg)



Mean change in diastolic BP (mmHg)



2018 ESC/ESH Guidelines for the management of arterial hypertension

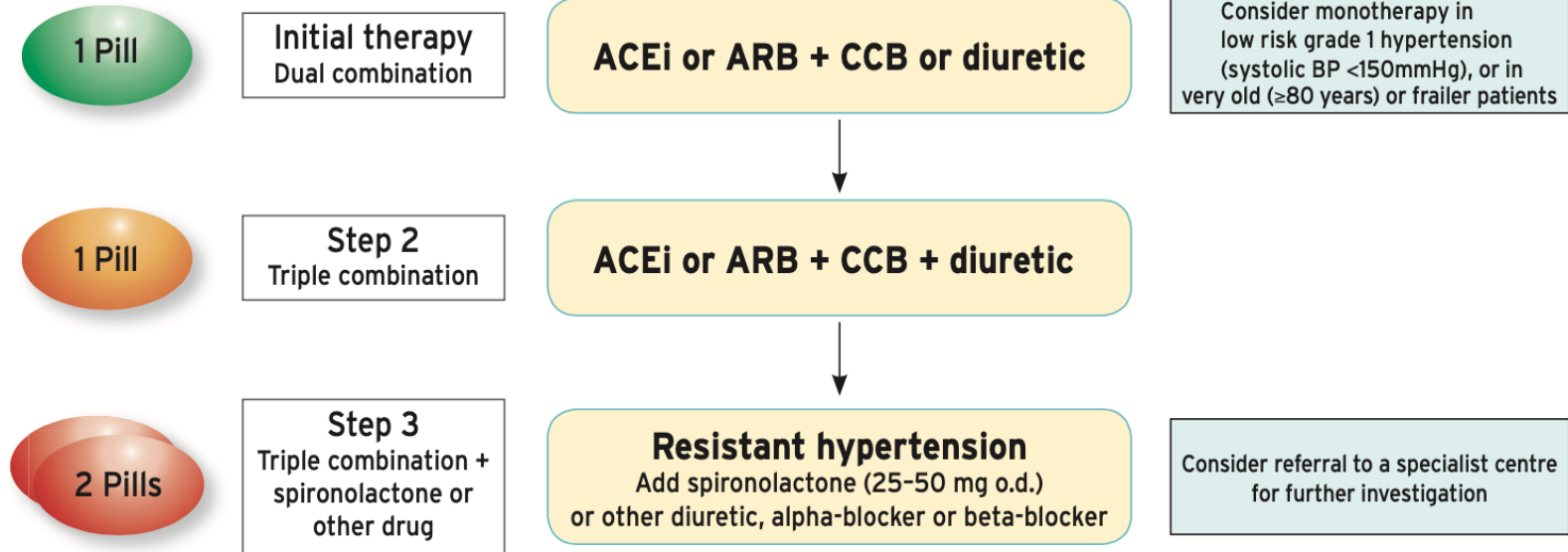
The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH)

Authors/Task Force Members: Bryan Williams* (ESC Chairperson) (UK), Giuseppe Mancia* (ESH Chairperson) (Italy), Wilko Spiering (The Netherlands), Enrico Agabiti Rosei (Italy), Michel Azizi (France), Michel Burnier (Switzerland), Denis L. Clement (Belgium), Antonio Coca (Spain), Giovanni de Simone (Italy), Anna Dominiczak (UK), Thomas Kahan (Sweden), Felix Mahfoud (Germany), Josep Redon (Spain), Luis Ruilope (Spain), Alberto Zanchetti[†] (Italy), Mary Kerins (Ireland), Sverre E. Kjeldsen (Norway), Reinhold Kreutz (Germany), Stephane Laurent (France), Gregory Y. H. Lip (UK), Richard McManus (UK), Krzysztof Narkiewicz (Poland), Frank Ruschitzka (Switzerland), Roland E. Schmieder (Germany), Evgeny Shlyakhto (Russia), Costas Tsioufis (Greece), Victor Aboyans (France), Ileana Desormais (France)

Choice of antihypertensive drugs

- The 2018 ESC/ESH guidelines state, that the following drug classes are all suitable for initiation and maintenance of antihypertensive treatment either as **monotherapy or in combination with each other** (IA)
 - Diuretics (thiazides/chlorthalidone/indapamide)
 - Calcium antagonists
 - ACE-inhibitors
 - Angiotensin receptor blockers
 - **Beta-blockers**

2018 ESC/ESH Guidelines on Hypertension



Beta-blockers

Consider beta-blockers at any treatment step, when there is a specific indication for their use, e.g. heart failure, angina, post-MI, atrial fibrillation, or younger women with, or planning, pregnancy

New European Guidelines on Hypertension 2023

2023 ESH Guidelines for the management of
arterial hypertension

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

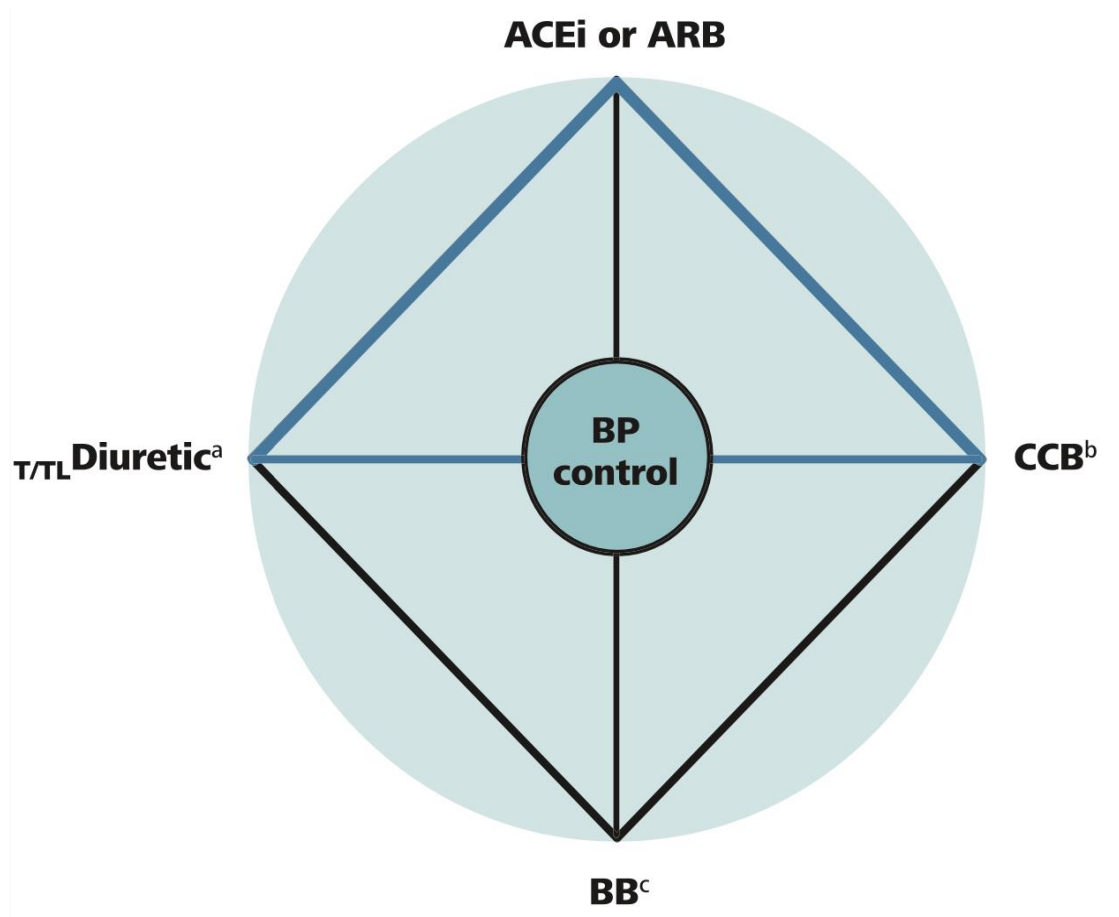
Endorsed by the European Renal Association (ERA)
and the International Society of Hypertension (ISH)

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Choice of antihypertensive drugs

- The 2023 ESH guidelines state, that the following drug classes are all suitable for initiation and maintenance of antihypertensive treatment either as **monotherapy or in combination with each other** (IA)
 - Diuretics (thiazides/chlorthalidone/indapamide)
 - Calcium antagonists
 - ACE-inhibitors
 - Angiotensin receptor blockers
 - **Beta-blockers**

Choice of antihypertensive drugs



New European Guidelines on Hypertension 2023

**Prefer SPCs
at any step**



Step 1

Dual combination

**Start with Dual Combination
Therapy in most patients**

Start with Monotherapy only in selected patients:

- Low risk hypertension and BP <150/95 mmHg
- or high-normal BP and very high CV risk
- or frail patients and/or advanced age

ACEi or ARB + CCB or T/TL Diuretic^a



Increase to full-dose if well tolerated

→ up to ~ 60% controlled^c

Step 2

Triple combination

ACEi or ARB + CCB + T/TL Diuretic



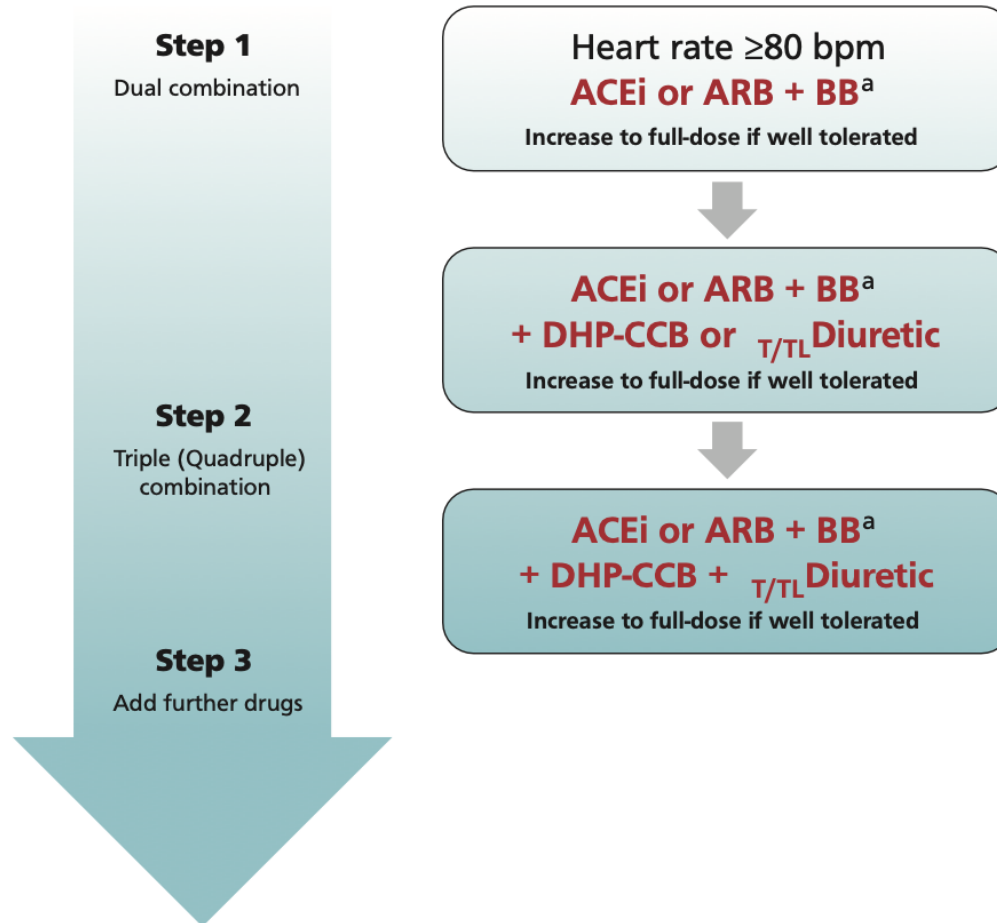
Increase to full-dose if well tolerated

→ up to ~ 90% controlled^c

BB^b

Can be used
as monotherapy
or at any step
of combination
therapy

New European Guidelines on Hypertension 2023



Conditions favoring beta blocker therapy: 2023 ESH Guidelines

Selected other conditions in which therapy with BBs can be favourable

Hypertension with elevated resting heart rate >80 bpm

Emergency, urgency and parenteral administration

Perioperative hypertension

Major noncardiac surgery

Excessive pressor response to exercise and stress

Hyperkinetic heart syndrome

Postural orthostatic tachycardia syndrome

Orthostatic hypertension

OSA

Peripheral arterial disease with claudication

COPD

Portal hypertension, cirrhosis-related esophageal varices and recurrent variceal bleeding

Glaucoma

Thyrotoxicosis, hyperthyroidism

Hyperparathyroidism in uremia

Migraine headache

Essential tremor

Performance anxiety and anxiety disorders

Psychiatric disorders (posttraumatic stress)

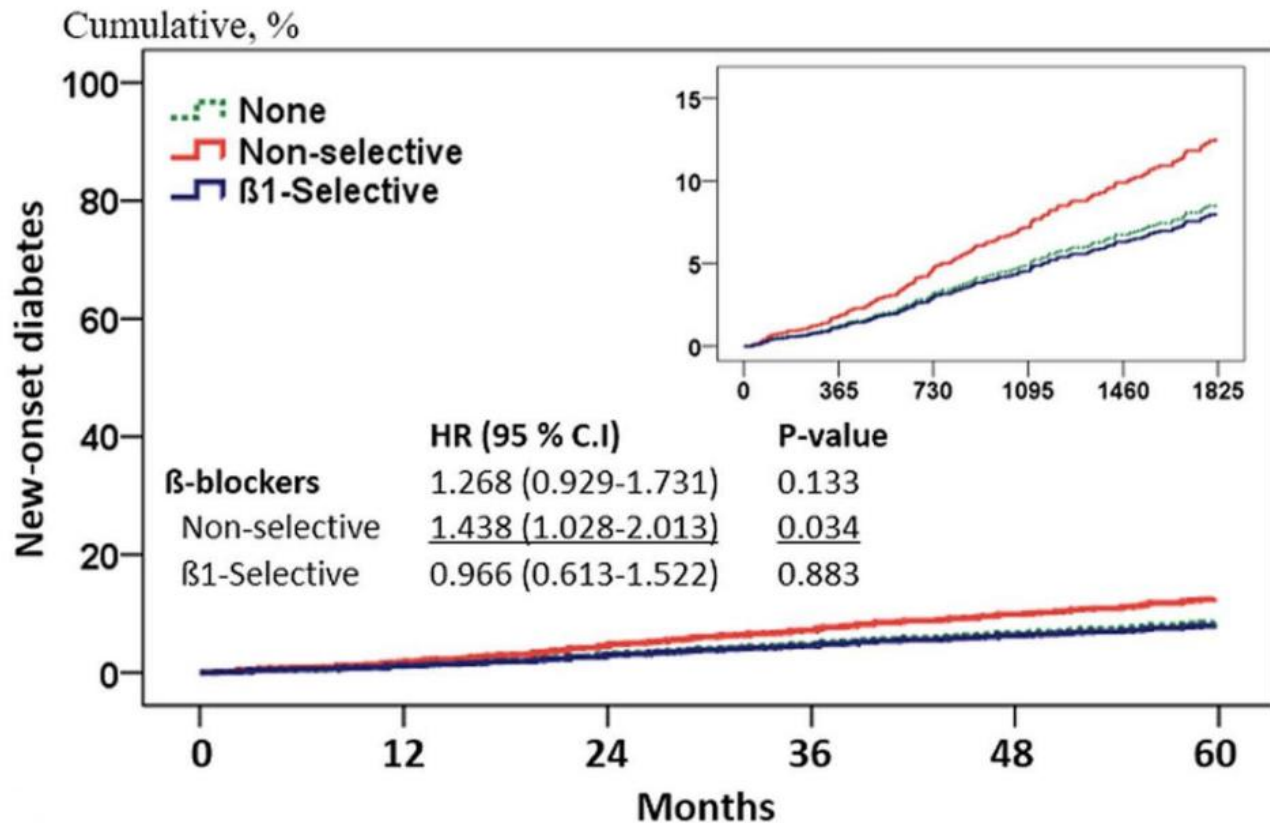
Contraindications or precautions to clinical use of β -blockers

	2023 ESH	2017 USA	2018–2019 China
Contraindications or precautions to clinical use of β -blockers	<ul style="list-style-type: none">• Severe asthma• Any high-grade sinoatrial or atrioventricular block• Bradycardia (e.g. heart rate <60 bpm)• Use with caution in any asthma, glucose intolerance, athletes or very physically active patients	<ul style="list-style-type: none">• Use a cardioselective agent for patients at risk of bronchospasm• Avoid β-blockers with ISA in ischaemic heart disease or HFrEF• Bradycardia• Risk of dysglycaemia with “traditional” β-blockers	<ul style="list-style-type: none">• Grade 2–3 AV block• Asthma• Caution in COPD, PVD, dysglycaemia, athletes• Avoid high doses of β-blocker in patients with non-ST-elevation ACS

Differences across beta-blockers

		β_1 receptor antagonist selectivity?	
		Yes	No
Intrinsic sympathomimetic activity?	No	Bisoprolol Metoprolol Atenolol Esmolol	Propranolol Sotalol Timolol Carvedilol ^a
	Yes	Xamoterol Acebutolol ^b Celiprolol ^{a,b} Nebivolol ^c	Pindolol ^b Oxprenolol Labetolol ^a Bucindolol ^a

Risk of new-onset diabetes during treatment with a b-blocker



65,686 hypertensive patients without DM from 2004 to 2014;

Endpoint: fasting blood glucose ≥ 126 mg/dL or HbA1c $\geq 6.5\%$

Mean follow-up: 30.9 ± 23.1 months

Beta-blockers and erectile dysfunction

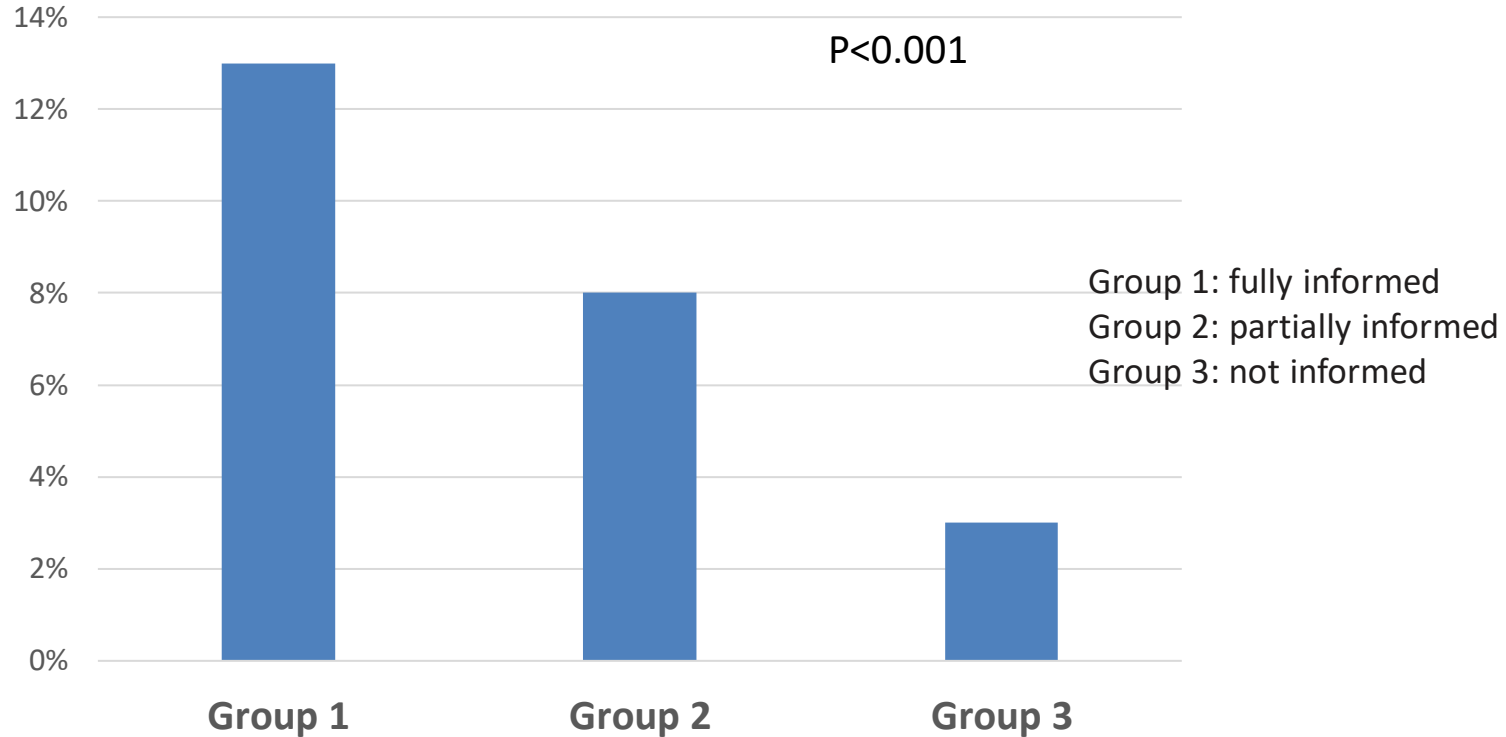
- 114 patients (age 57.8 ± 4.7 years) without ED but with newly diagnosed arterial hypertension
- 100 mg metoprolol/d
- Group 1: patients were fully informed (they knew that the drug was metoprolol and that it might induce ED)
- Group 2: patients were partially informed (they knew that the drug was metoprolol, but were not informed that it might induce ED).
- Group 3: patients were not informed either about the drug used or about the possible occurrence of ED.

Beta-blockers and erectile dysfunction

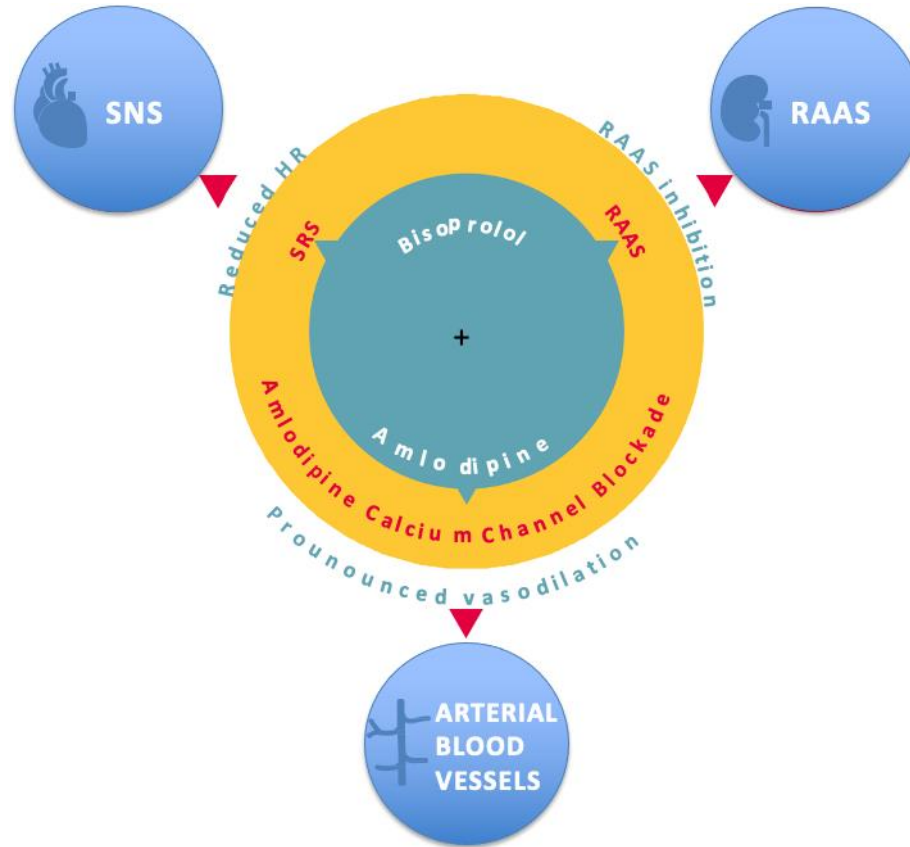
	Group 1 (n = 38)		Group 2 (n = 38)		Group 3 (n = 38)	
	before therapy	after therapy*	before therapy	after therapy*	before therapy	after therapy*
SBP, mm Hg	156 ± 5.8	149 ± 4.9	157 ± 5.9	149 ± 4.8	157 ± 5.8	149 ± 4.8
DBP, mm Hg	97 ± 3.5	89 ± 4.3	97 ± 4.1	88 ± 4.3	97 ± 4.0	88 ± 4.3
HR, beats/min	75 ± 5.4	63 ± 4.6	75 ± 5.4	63 ± 4.6	75 ± 5.6	62 ± 4.8

Beta-blockers and erectile dysfunction

Incidence of ED after 60 days

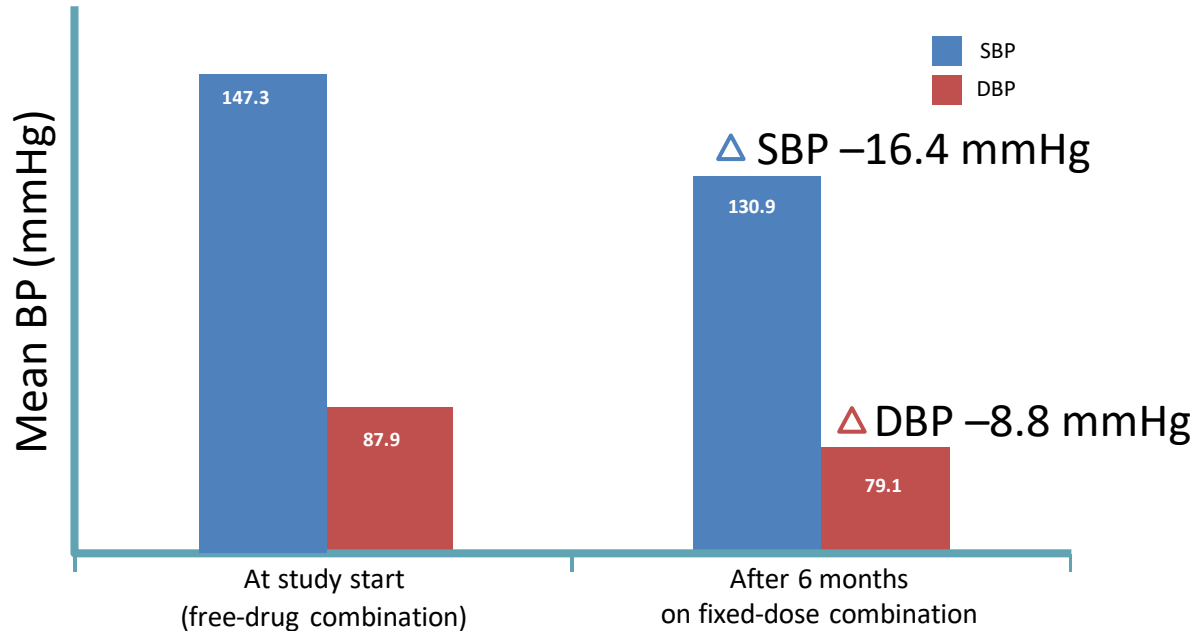


Beta-blocker and calcium channel blocker



Long-term improvement in BP control

10,532 patients (average age 59 years; 48% female)
Switched from monotherapy to FDC



Patient profiles



**Hypertensive patient with compelling indications
(angina, post MI, AF)**



**Hypertensive patient with sympathetic overactivity
(young and middle aged)**

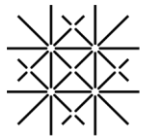


**Hypertensive patient with metabolic disturbances
(Diabetes, dyslipidemia, metabolic syndrome, obesity, insulin resistance)**



Hypertensive patient with CKD up to stage 3

Thank you



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