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Beta-blockers and hypertension : unresolved question

The role of b-blockers, as initial therapy for hypertension, has been and remains unresolved .

Beta-blockers as First -line

ESH 2018-2023

YES/NO

ISH 2020

NO

WHO 2022

NO

ACC/AHA 2017

NO

NICE 2019

YES in young patients

CANADIAN 2020

YES

CHINES 2019

YES

JSH 2019

NO

JNC 8 2014

NO

Latin-Amer 2017

YES

The conflictual position of guidelines stems from the results of landmark studies which have shown a lower CV protection, comparing B-b with other antihypertensive agents.



- 1. Do B-b have an antihypertensive effect?**
- 2. Is this effect similar to that of other antihypertensive agents?**
- 3. Have B-b a CV protective effect in patients with hypertension?**
- 4. Is the CV protective effect of B-b different from that of other antihypertensive drugs?**
- 5. Is the CV protection of B -b different in young and old hypertensive patients?**

Included meta-analyses

Wisonge (2017)

Wright (2018)

Tomopoulus (2015-2020)

Wei (2020)

Kuyper (2014)

Khan (2006)

Law (2009)

Zhu (2022)

Turnbull (2008)

Bangalore (2008)

1. Do Beta-Blockers have an Antihypertensive Effect?

Recent meta-analyses have shown that B-b compared with placebo or no treatment

SBP/DBP

- 10.5/-7.0 mmHg

(n=18724 Pts)

Zanchetti A 2015

SBP/DBP

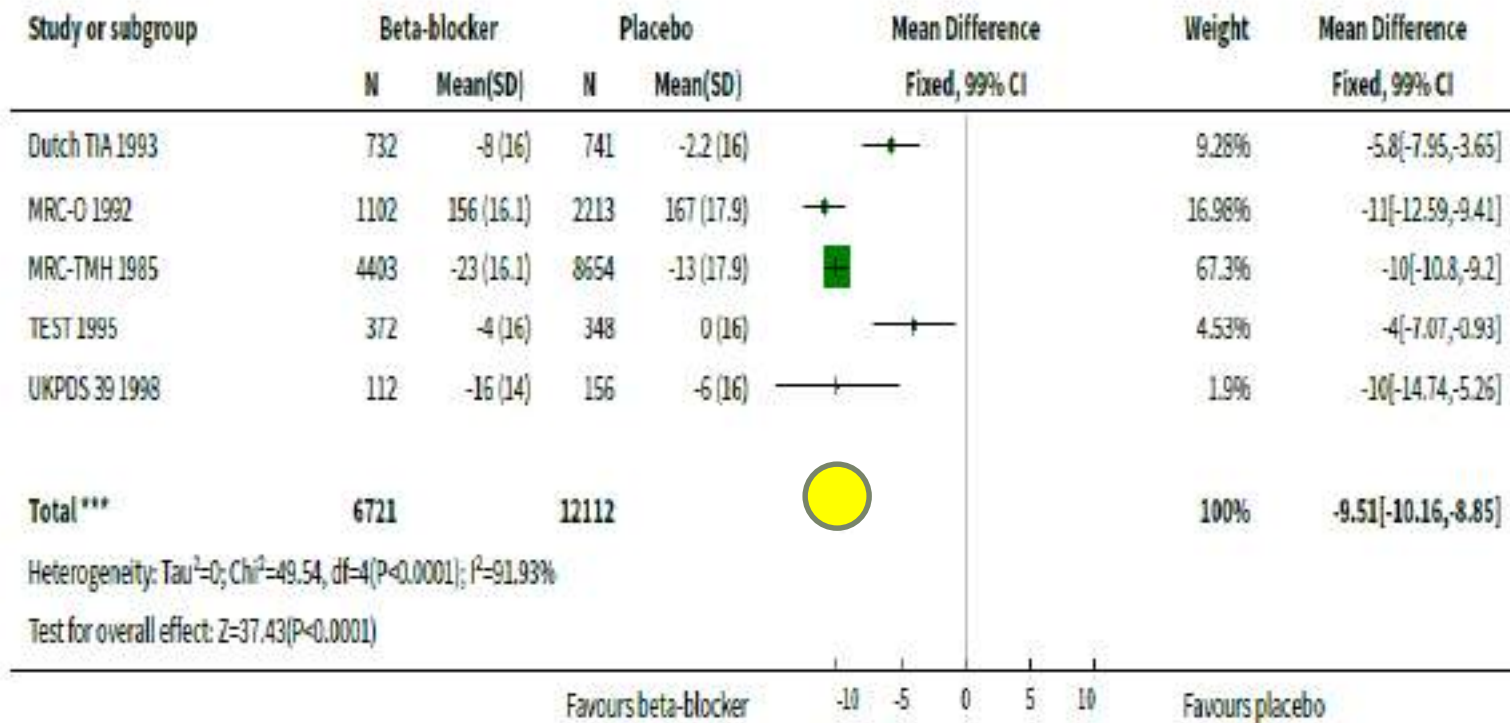
-9.6/-6.3 mmHg

(n= 22324 Pts)

Thomopoulos C 2020

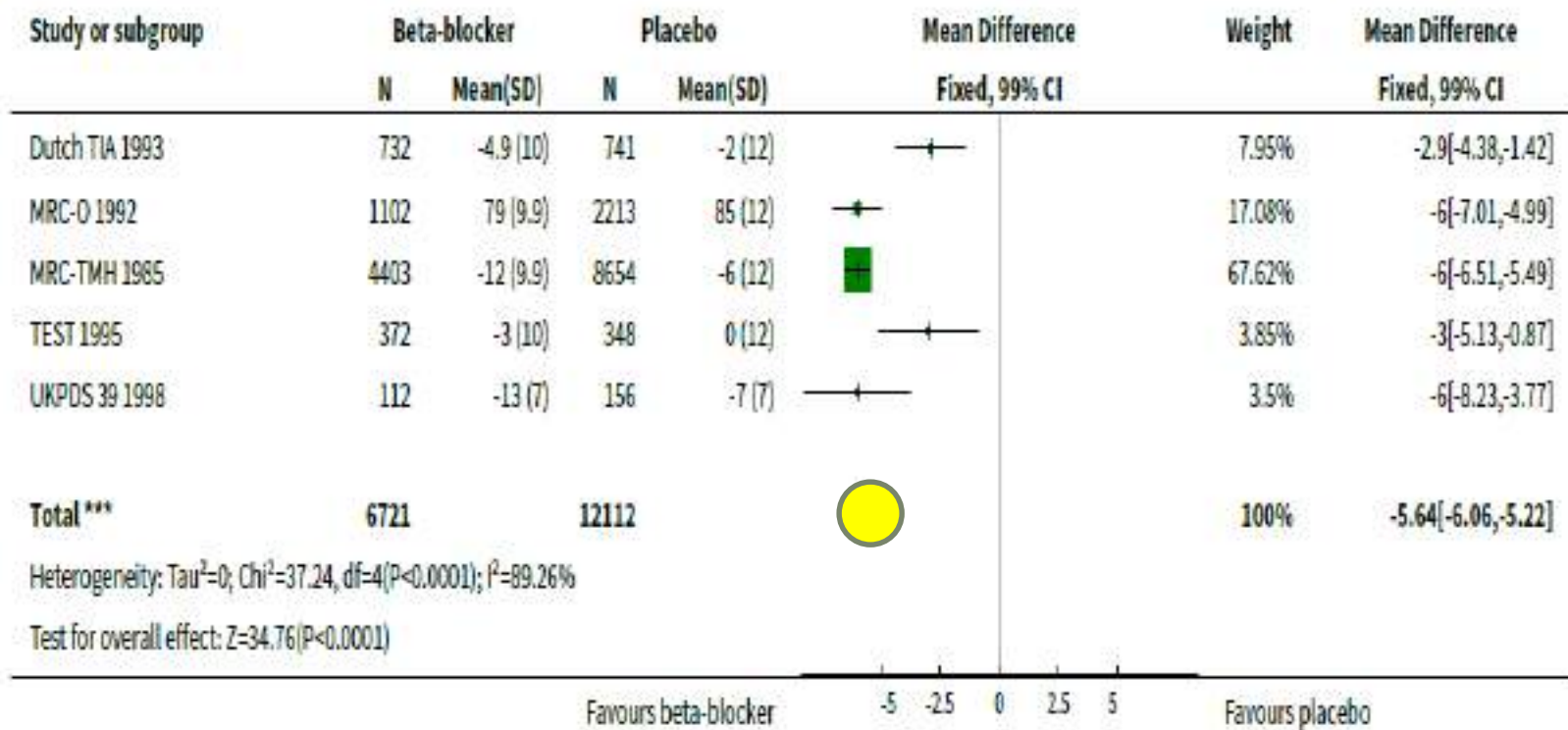
SBP

Analysis 2.6. Comparison 2 First-line beta-blocker vs placebo, Outcome 6 Systolic blood pressure.



DBP

Analysis 2.7. Comparison 2 First-line beta-blocker vs placebo, Outcome 7 Diastolic blood pressure.



Variable		Females
SBP	MD	-11.1 (95% CI, -14.5; -7.8)
	%	-7.9% (95% CI, -10.4; -5.4)
DBP	MD	-8.0 (95% CI, -10.6; -5.3)
	%	-9.4% (95% CI, -12.5; -6.2)
MAP	MD	-8.1 (95% CI, -11.7; -4.5)
	%	-7.5% (95% CI, -10.9; -4.2)
HR	MD	-10.8 (95% CI, -17.4; -4.2)
	%	-14.2% (95% CI, -22.8; -5.5)

BP Reduction according to gender

Males
-11.1 (95% CI, -14.0; -8.2)
-8.2% (95% CI, -10.4; -6.1)
-8.0 (95% CI, -10.1; -6.0)
-9.7% (95% CI, -12.2; -7.3)
-9.9 (95% CI, -17.0; -2.8)
-8.9% (95% CI, -10.9; -4.2)
-9.8 (95% CI, -11.1; -8.4)
-13.2% (95% CI, -15.1; -11.4)

Therefore, globally, there is evidence that B-b, significantly decrease BP in hypertensive patients, supporting the indication approved by FDA and EMA.

The antihypertensive effectiveness of b-blockers is particularly evident with b1-selective antagonist [Wong GWK et al 2016] and with vasodilating b-blockers [Van Bortel LM 2008], while it seems to be lower with non-selective, or with partial agonist activity [Wong GWK 2014].

**2. Is this Effect Similar to that of Other
Antihypertensive Agents?**

B-b vs other antihypertensive drugs

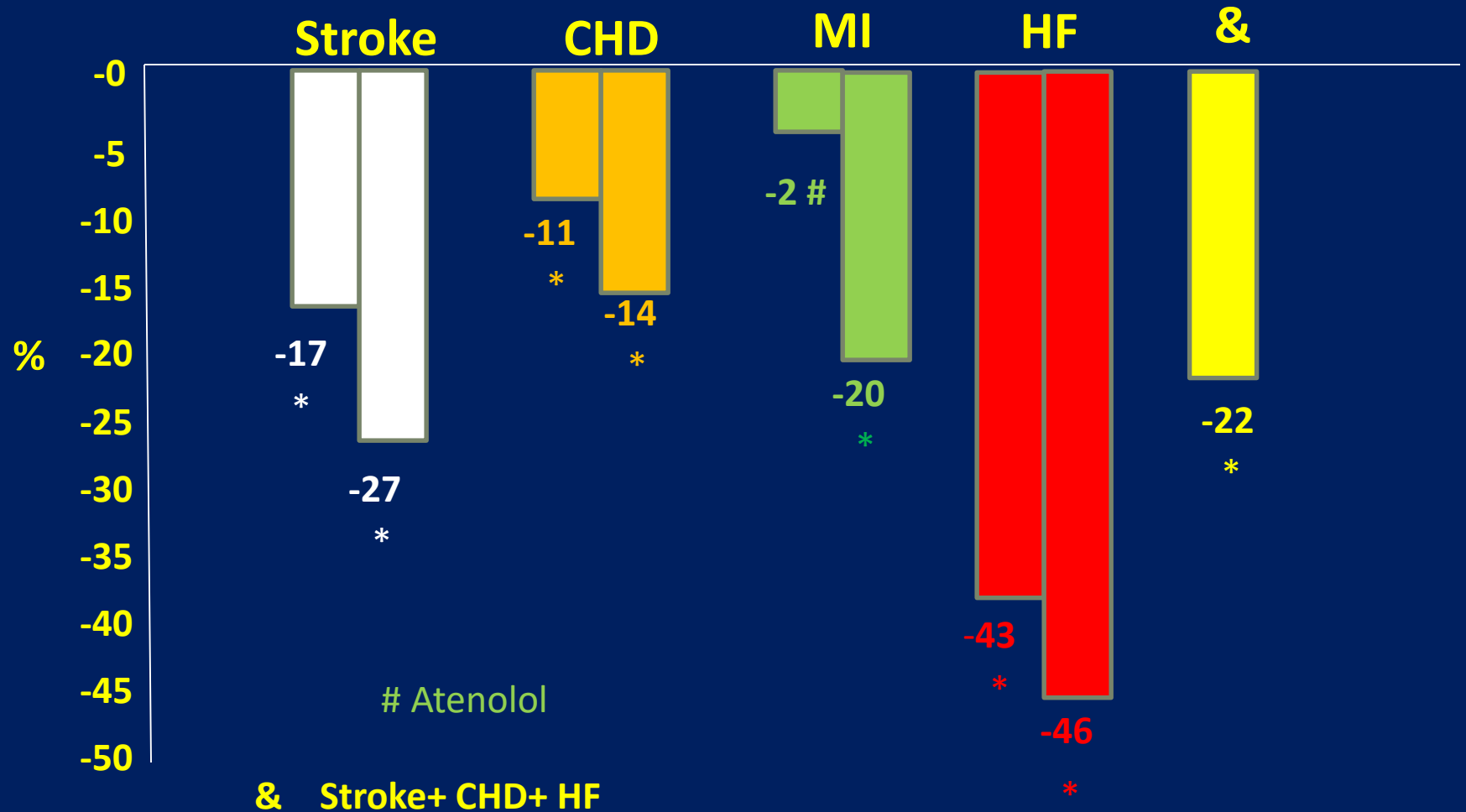
vs CCBs	+1.0 mmHg SBP	+0.7 mmHg DBP
vs RAASI	+0.8 mmHg SBP	- 0.5 mmHg DBP
vs Diuretics	+0.6 mmHg SBP	- 0.2 mmHg DBP

Globally : + 0.6, -1.4 mmHg SBP + 0.3, - 0.6 mmHg DBP

Globally, there is evidence that the antihypertensive effect of B-b is similar to that of other antihypertensive drugs

**3. Have β -B a Cardiovascular Protective Effect in
Patients with Hypertension?**

Comparison with placebo or no treatment (results of 9 meta-analyses) RRR



Except for some differences between the meta-analyses, B-b, lowered the risk of major CV outcomes, particularly stroke, which has been the major reason for change the position of these drugs from first-line treatment of hypertension

**4. Is the CV Protective Effect of B-b
different from that of other antihypertensive
drugs?**

PHOTO: MICHAEL BLOOM / SHUTTERSTOCK.COM



boeri

it's your head

Remember to ski and snowboard responsibly. www.boerisusa.com

B-b vs other antihypertensive drugs (7 meta-analyses)

	Stroke	CV Events	CHD	MI	HF
vs D	NS		NS		NS
vs CCBs	+23% +25% NS #	+18% NS	NS	NS	NS
vs RAASi	+25% +32% NS #	NS	NS	NS	NS
vs Others [°]	+18% +21% NS #			NS	

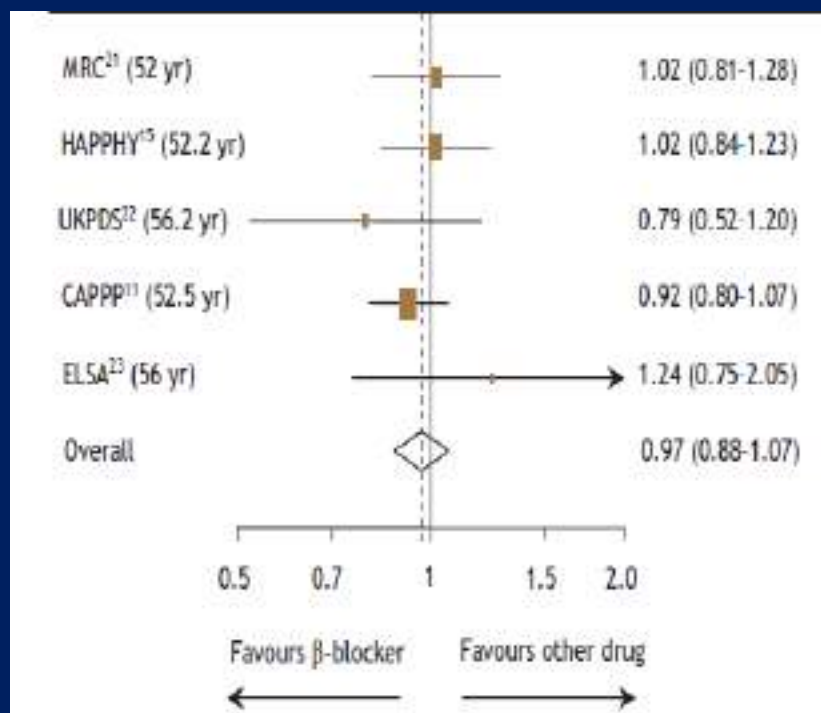
CV Mortality NS #

Zanchetti 2015

[°] Atenolol or non-Atenolol

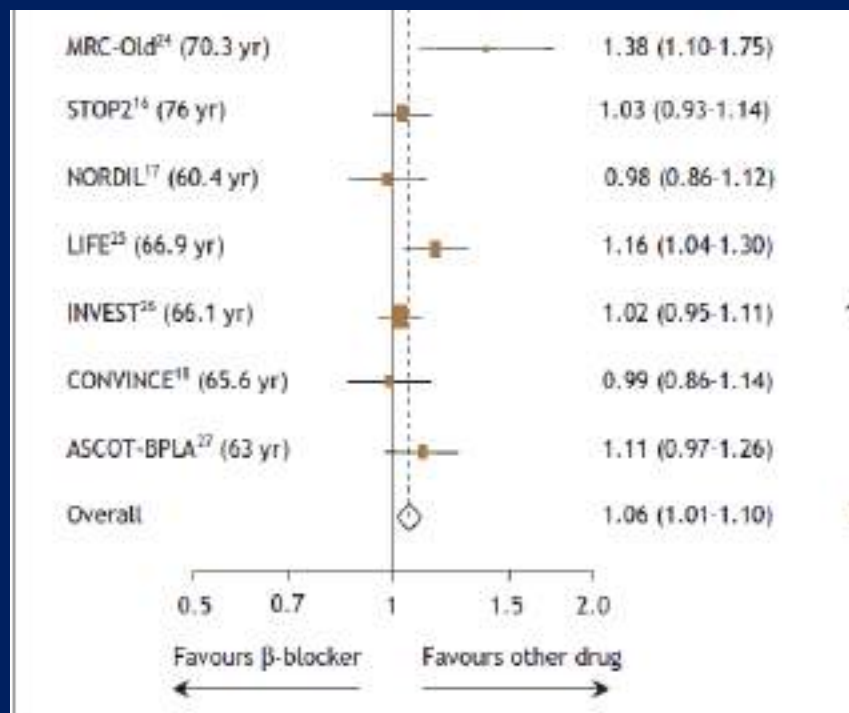
**Is the Cardiovascular Protection of B-b different in Young
and Old Hypertensive Patients?**

Risk ratios for the composite outcome (death, stroke or MI)



Younger patients

Older patients



Stroke

MI

CV events

	<60 yrs	>60 yrs		<60 yrs	>60 yrs		<60 yrs	>60 yrs
Atenolol vs others**	-22%	+17%		NS	NS		NS	NS
Non-atenolol vs others**	NS	NS		NS	NS		NS	NS

CONVINCE and INVEST NO Diff between Atenolol vs Verapamil

** Kuyper 2014

The cardiovascular protective effect of B-b, compared with other drug classes, shows a great variability, because studies have been performed :

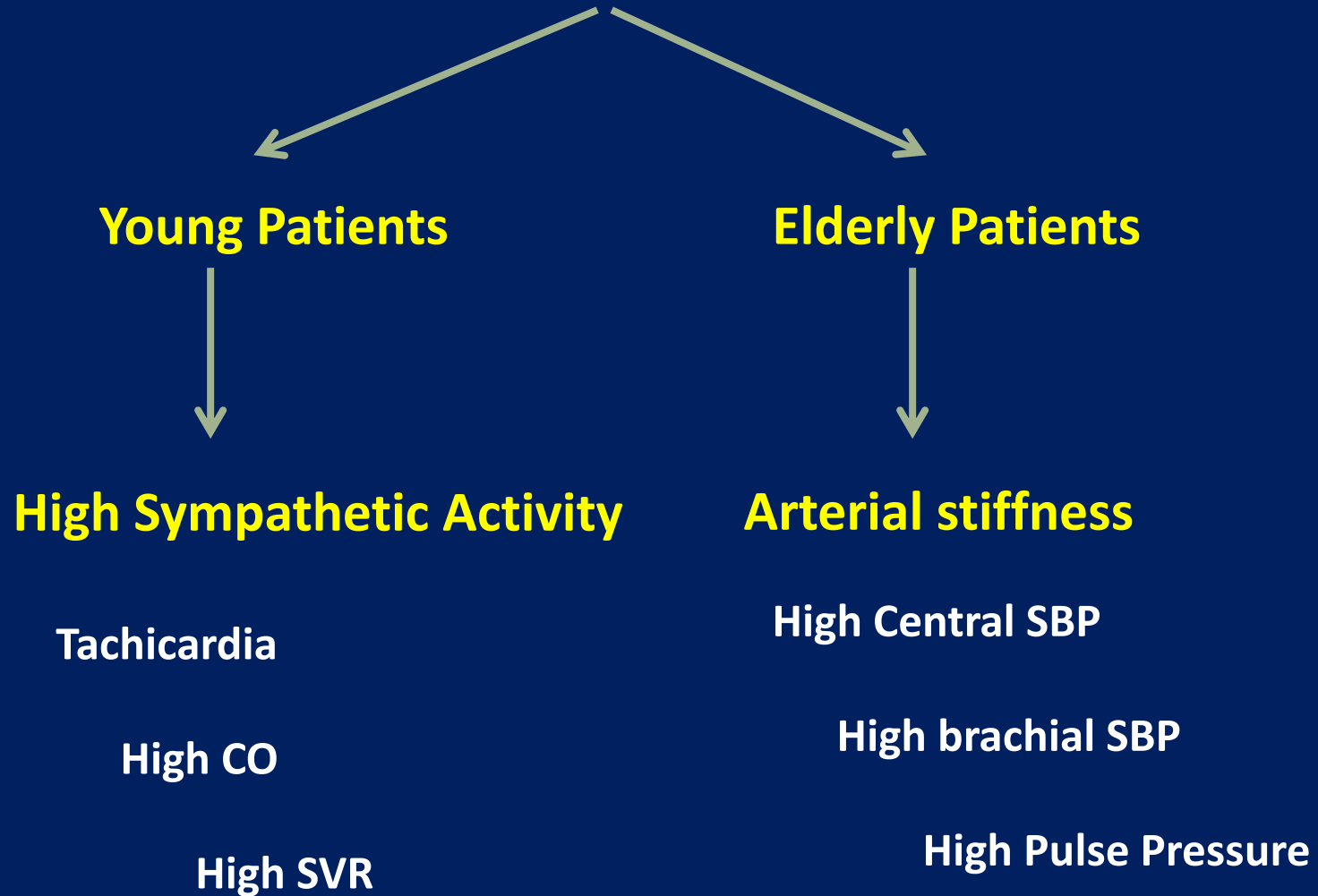
- different protocols**
- different statistical tests**
 - different follow-up**
 - different outcomes**
 - different age**
 - in a large part with atenolol**

Thus it is difficult to answer to the question as to whether one class of drugs is superior or not in protecting hypertensive patients from cardiovascular risk.

Rather than looking for differences in cardiovascular protective effect between B-b and other drug classes, we have to return to the:

- pathophysiology of hypertension**
- age of patients.**

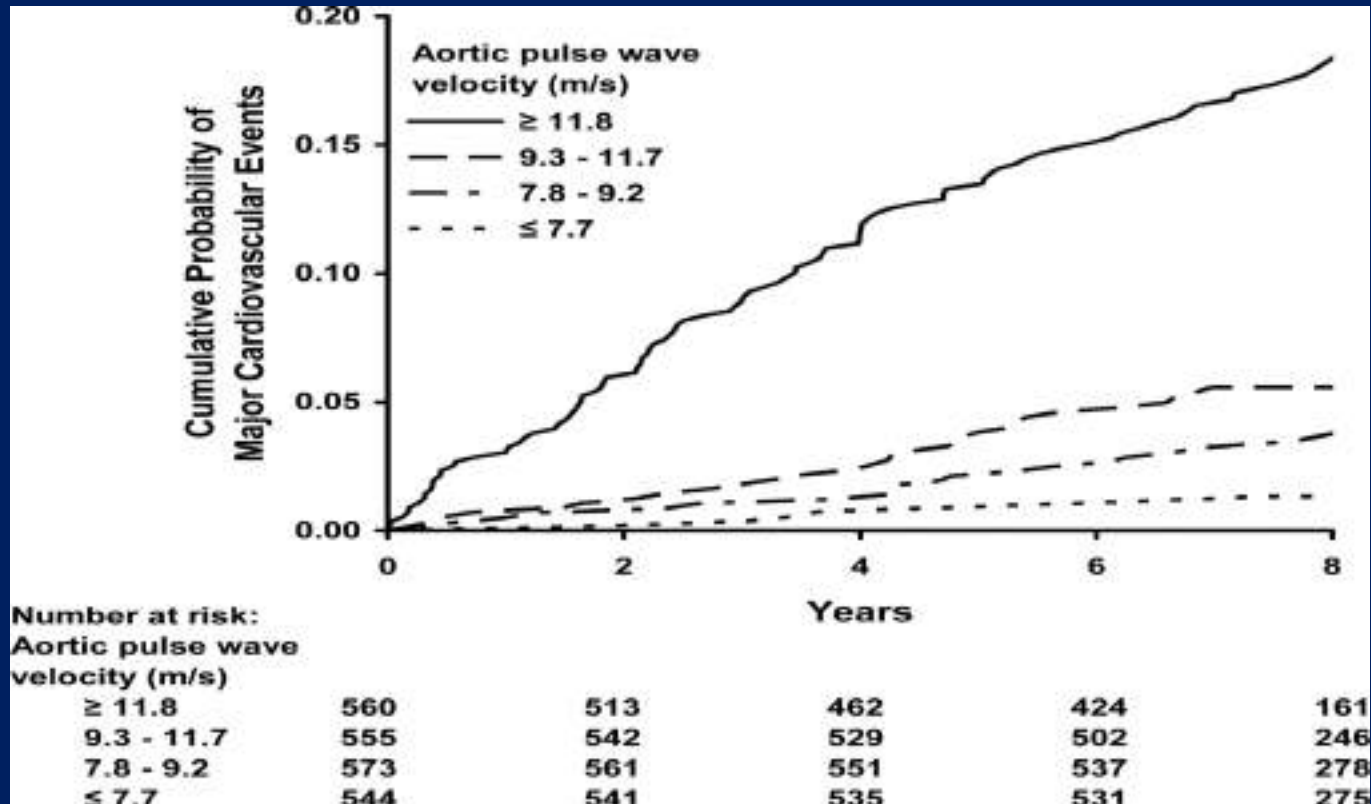
Pathophysiology of Hypertension

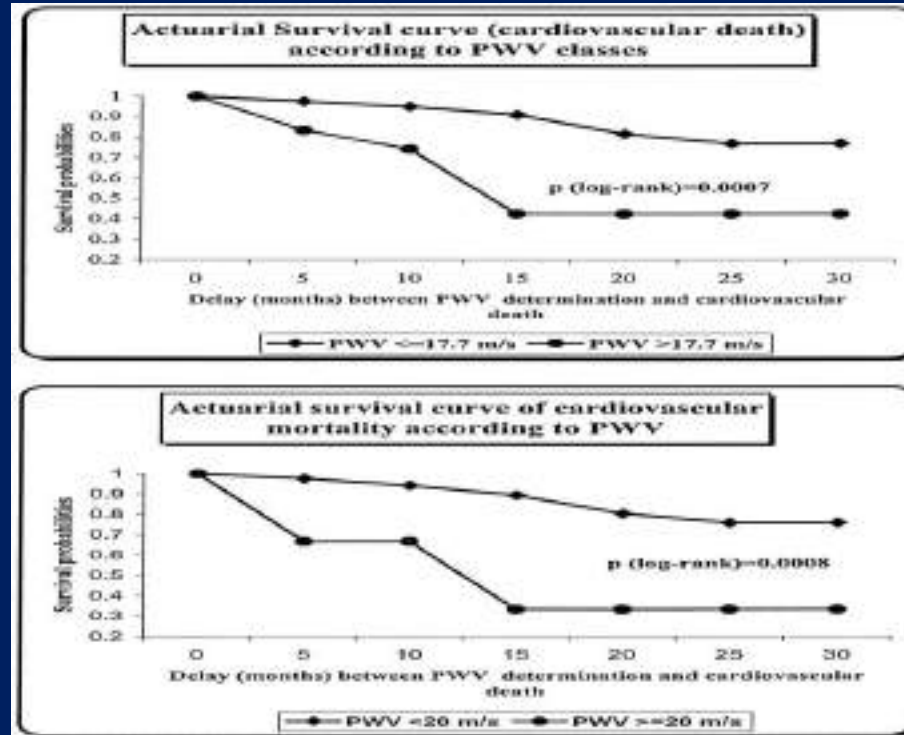


Arterial stiffness is a major risk factor for cardiovascular disease and is an important predictor of mortality in hypertensive patients

Increased arterial stiffness is linked to endothelial dysfunction and reduced nitric oxide (NO) plasma concentration

Correlation PWV and CV events





Suggested Therapeutic Approach

Young Patients

Selective B-b

HR ↓

CO ↓

Sympathetic Drive ↓

Renin secretion ↓

Elderly Patients

Vasodilating B-b

Central SBP ↓

PVR ↓

HR = ↓

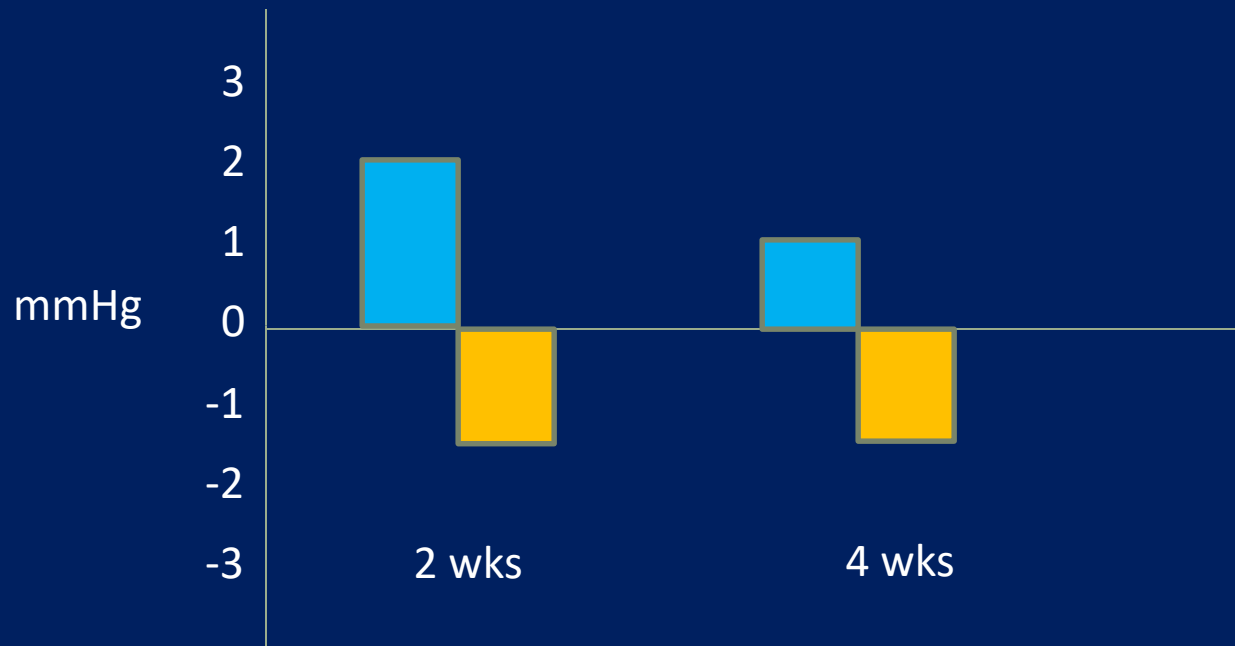
B-b with vasodilating effects, such as carvedilol and nebivolol reduces arterial stiffness. (Shah NK, 2011, Kim EJ 2014)

Nebivolol has a more significant impact on central BP than metoprolol. (Kampus P, 2011, Hayek SS 2015)

- Celiprolol , differently from Bisoprolol, lowered central BP in hypertensive subjects. ?? (Eguchi K, 2015)

Carvedilol and arterial stiffness

Augmentation Pressure

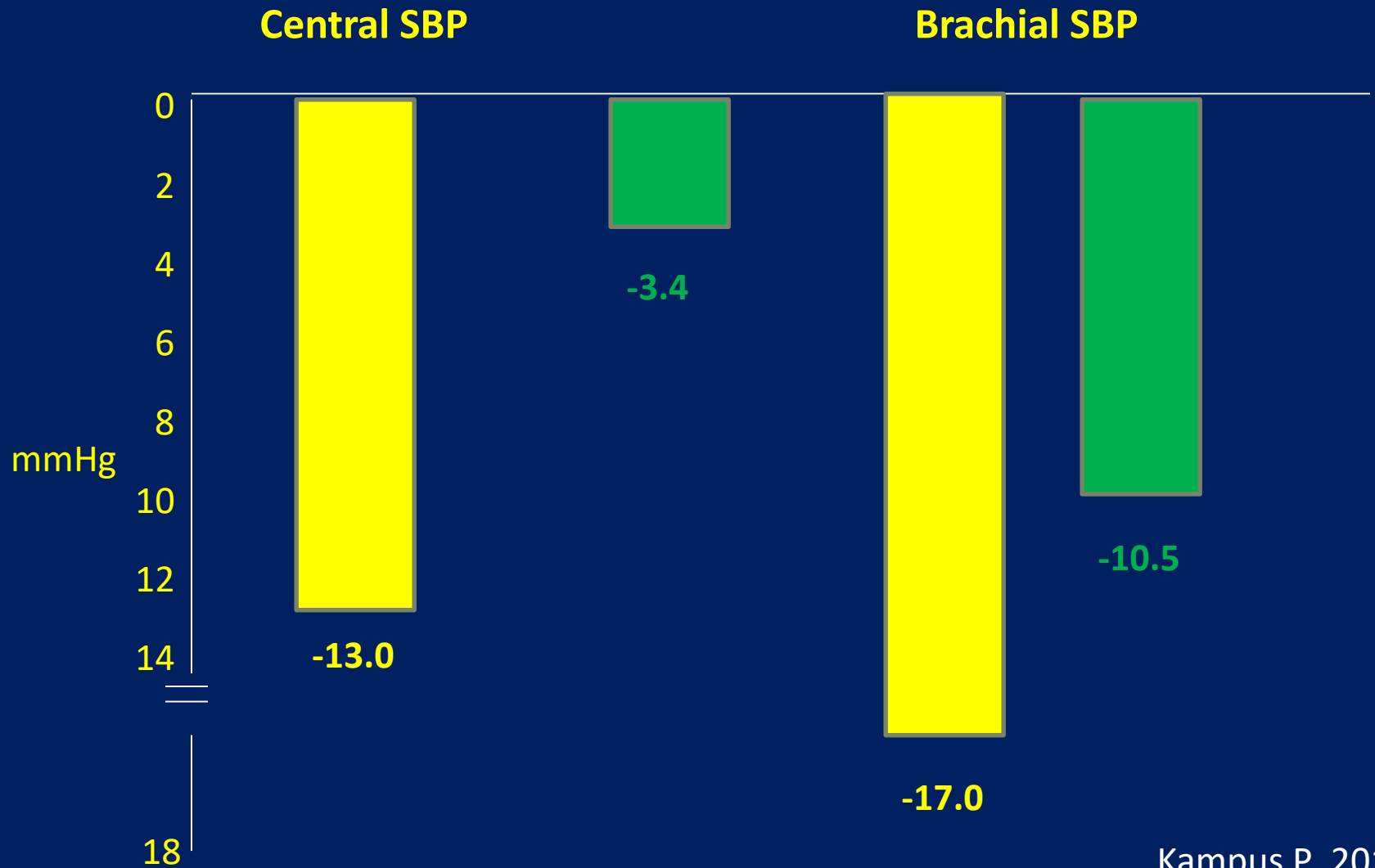


Atenolol

Carvedilol

Shah NK 2011

Nebivolol-Aortic SBP vs metoprolol



CONCLUSIONS I

1. **B-b have an antihypertensive activity**
2. **The antihypertensive effect is no different from that of other drugs**
3. **B-b have cardiovascular protective activity**
4. **The cardiovascular protective activity is , globally, no different from that of other drugs, but shows a large variability**
5. **Non-vasodilating, selective, B-b are particularly, indicated in young subjects**

CONCLUSIONS II

6. Vasodilating B-b, can be used in young (decrease SVR), but, particularly, in elderly because they decrease aortic SBP, associated with arterial stiffness

7. Among vasodilating B-b, nebivolol , differently from carvedilol, has the advantage : a) not causing orthostatic hypotension , b) to increase the bioavailability of nitric oxide (NO) , that is involved in cardiovascular protection

Thank You