Towards Holistic &
Comprehensive Cardiac Care

SPC ; strategy for better BP Control

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Outline of Presentation

- Current global and regional status of hypertension
- Shortfall in current management of hypertension
- Addressing the shortfall
- Conclusions

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The Burden of Hypertension

- Hypertension remains the leading cause of death
  - WHO estimates it kills 18 million per year
  - Hypertension shortens life by at least 5 years

Global Burden of Disease 2019

Gregory Roth et al .JAMA 2020 Dec, 76 (25) 2982–3021

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- Cardiovascular diseases (CVDs), principally ischemic heart disease (IHD) and stroke, are the leading cause of global mortality and a major contributor to disability.

- CVD burden continues its decades-long rise for almost all countries outside high-income countries, and alarmingly, the age-standardized rate of CVD has begun to rise in some locations where it was previously declining in high-income countries.

- Sustainable Development Goal 3 to achieve a 30% reduction in premature mortality due to non communicable diseases.

- Globally, the 6 leading modifiable CVD risk factors included **high systolic blood pressure**, diet, high low-density lipoprotein cholesterol, air pollution, high body mass index, and tobacco smoking.

THE Ongoing PANDEMIC

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- No 1 leading cause of death worldwide
- 17,900,000 deaths (31.0 % of all global death)
- 85% are due to myocardial infarction and CVA
- Over 75% are in low and middle – income countries
- Most are preventable by modification of risk factors

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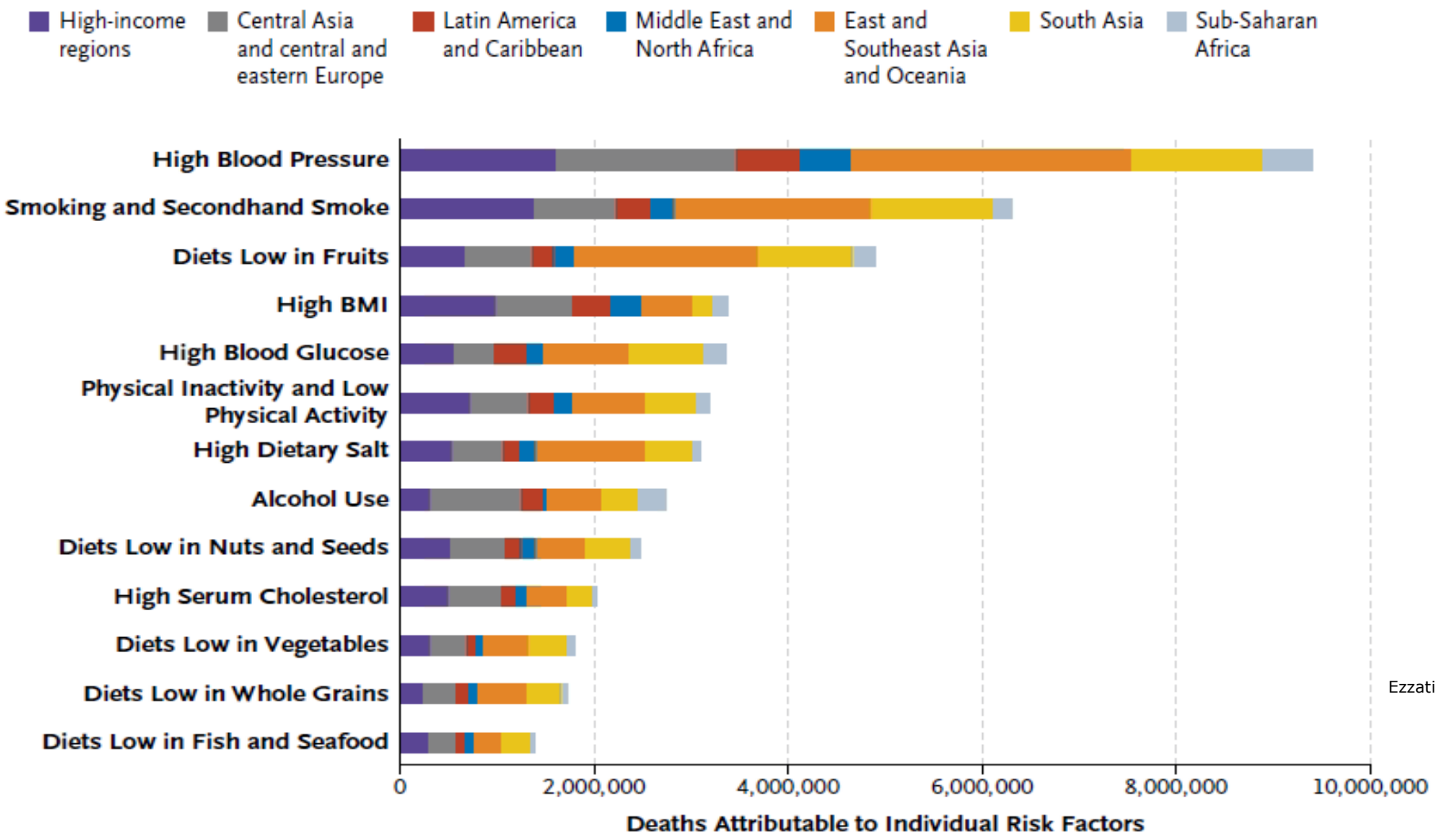

Ezzati et al. *N Engl J Med.* 2013;369:954-964.

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How are we doing ?-

(Nur Liana AB et al. Majid JHH, June 2018 and NHMS 2019)

(Htet AS et al BMC Public Health, October 2017)

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	2006 (Malaysia) 2004 (Yangon)	2015 (Malaysia) 2014 (Yangon)
Prevalence (>18 years) (25-74 years)	34.6% 26.7%	35.3% 34.6%
Aware	35.6% 19.4%	37.5% 27.8%
Treated	78.9% 43.1%	83.2% 40.1%
Control	27.5% 48.4%	37.4% 45.3%

American Journal of Cardiovascular Drugs (2024) 24:141–170
https://doi.org/10.1007/s40256-023-00625-1

REVIEW ARTICLE

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Management of Hypertension in the Asia-Pacific Region: A Structured Review

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Abstract

This article reviews available evidence regarding hypertension management in the Asia-Pacific region, focussing on five research questions that deal with specific aspects: blood pressure (BP) control, guideline recommendations, role of renin–angiotensin–aldosterone system (RAAS) inhibitors in clinical practice, pharmacological management and real-world adherence to guideline recommendations. A PubMed search identified 2537 articles, of which 94 were considered relevant. Compared with Europeans, Asians have higher systolic/diastolic/mean arterial BP, with a stronger association between BP and stroke. Calcium channel blockers are the most-commonly prescribed monotherapy in Asia, with significant variability between countries in the rates of angiotensin-converting enzyme inhibitors (ACEis)/angiotensin-receptor blockers (ARBs) and single-pill combination (SPC) use. In clinical practice, ARBs are used more commonly than ACEis, despite the absence of recommendation from guidelines and clinical evidence supporting the use of one class of drug over the other. Ideally, antihypertensive treatment should be tailored to the individual patient, but currently there are limited data on the characteristics of hypertension in Asia-Pacific individuals. Large outcome studies assessing RAAS inhibitor efficacy and safety in multi-national Asian populations are lacking. Among treated patients, BP control rates were ~ 35 to 40%; BP control in Asia-Pacific is suboptimal, and disproportionately so compared with Western nations. Strategies to improve the management of hypertension include wider access/availability of affordable treatments, particularly SPCs (which improve adherence), effective public health screening programs targeting patients to drive health-seeking behaviours, an increase in physician/patient awareness and early implementation of lifestyle changes. A unified Asia-Pacific guideline on hypertension management with pragmatic recommendations, particularly in resource-limited settings, is essential.

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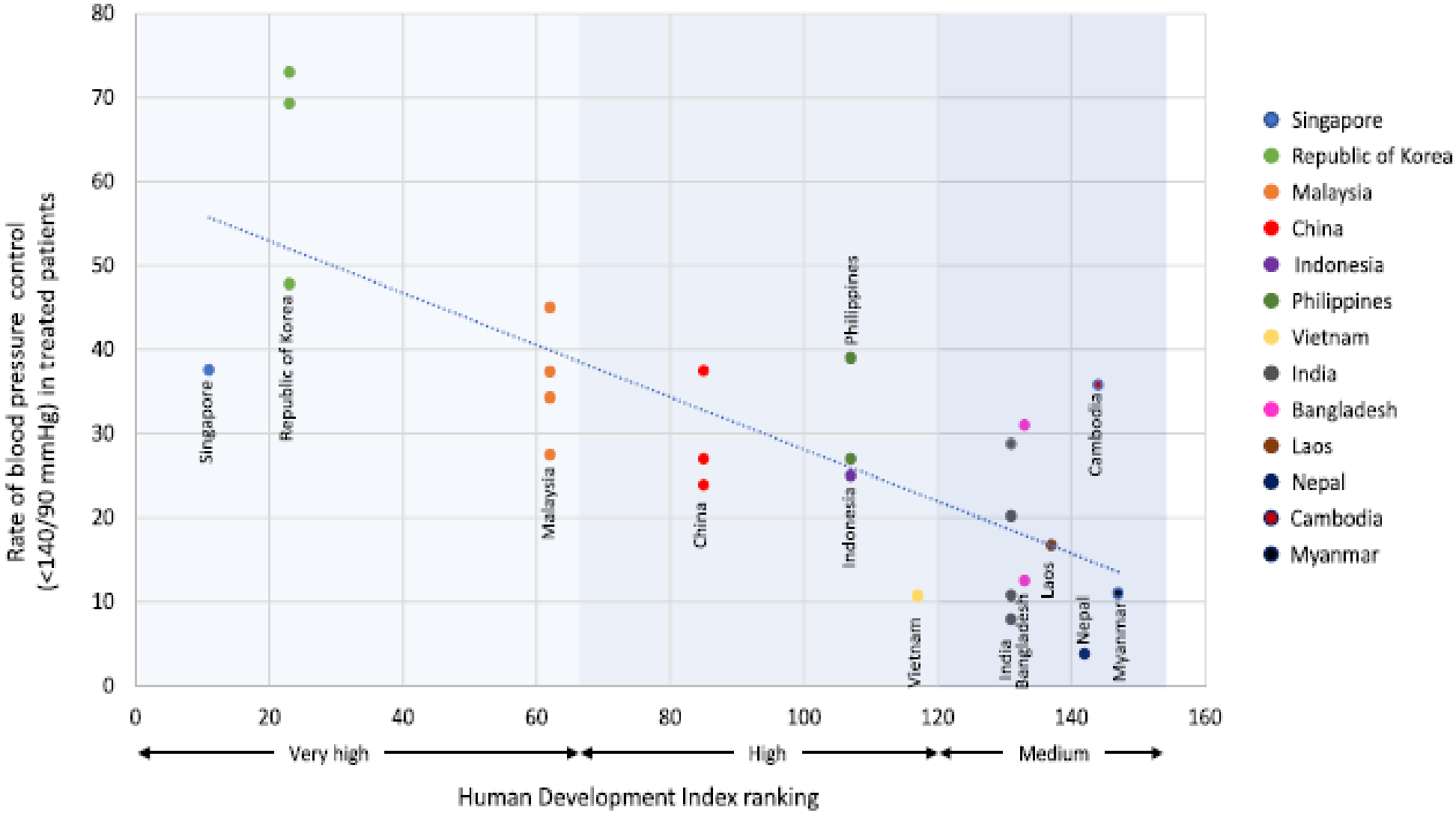
Blood pressure control in relation to development index



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Journal of Cardiology & Current Research

Mini Review

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Hypertension control: lessons from Malaysia, an upper-middle-income country

Summary

Hypertension is a major modifiable determinant of the increasing burden of cardiovascular diseases in Malaysia. When not controlled it increases the risk of heart disease, stroke, and renal disease. This paper, a contribution to development of an effective response to this challenge, reviews what is known about the prevalence, awareness, treatment and control of hypertension in Malaysia, identifying the factors contributing to inadequate levels of control and feasible measures to improve it. It reviews published data from Malaysia - with reference to other countries where relevant – to offer a comprehensive understanding of the problem. It is apparent that managing hypertension goes beyond the mere prescription of blood pressure (BP) lowering drugs. It involves a complex interplay of the healthcare delivery system, healthcare providers, and patients, recognising their differing educational, psychosocial, economic and residential status. Thus a one-size-fits-all approach will be patently inadequate to achieve good hypertension control. A paradigm shift towards a care for hypertension in Malaysia is needed.

Keywords: blood pressure, CVDs, non-communicable diseases, hypertension, heart disease, stroke

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Hypertension Control ; Lessons from Malaysia

(Yusoff K, Razak A, Rahman ARA et al., JCCR July 2021)

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	2006	2011	2015	2019	WHO 2021
Prevalence	34.6%	33.6%	35.3%	30.0%	18-27%
Awareness	35.6%	40.7%	37.5%	52.90%	54%
Treated	78.9 %	77.5%	83.2%	89.4%	42%
Control	27.5%	34.3%	37.4%	45.4%	21%

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VERY IMPORTANT !

" Substandard care is responsible for 84% of CV deaths, 81% of vaccine- preventable diseases and 61% of post-birth complication "

(*Muhammad Pate , Lancet Global Health Commision 2018*)

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Why the short fall ?

Difficult patients

Difficult disease

Difficult doctors

Difficult doctors

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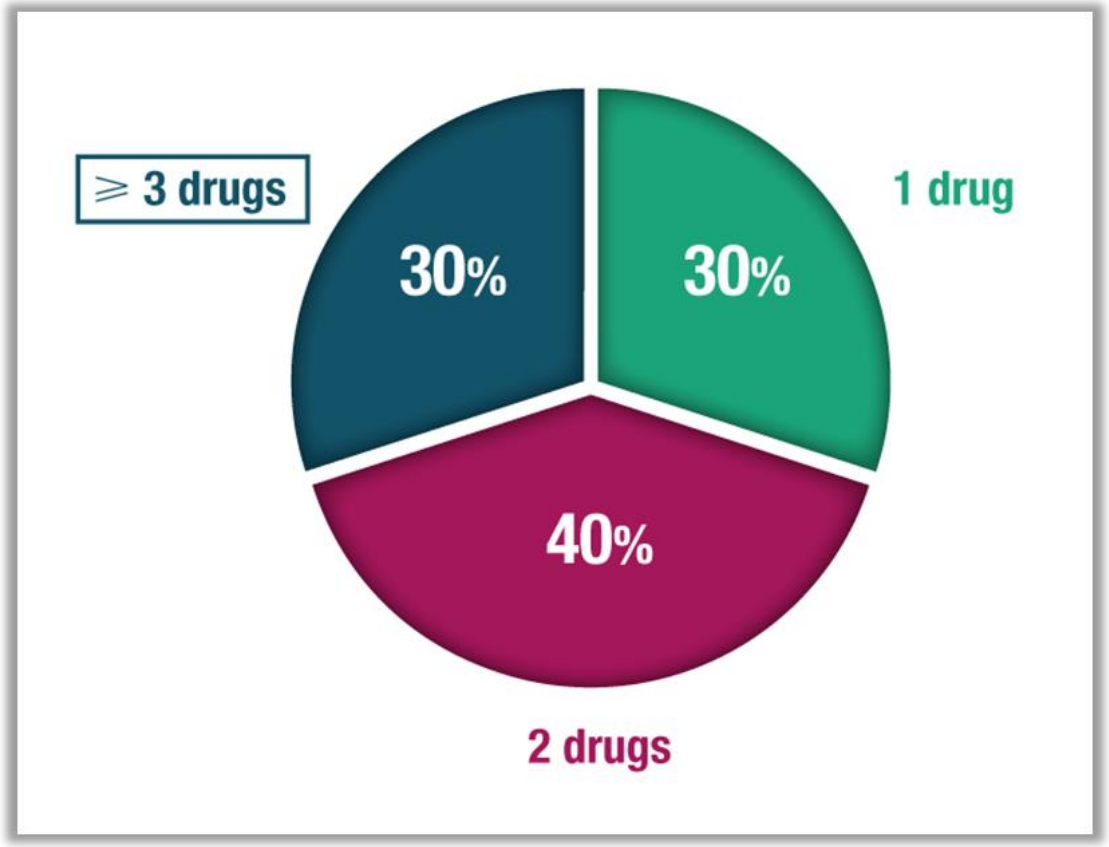
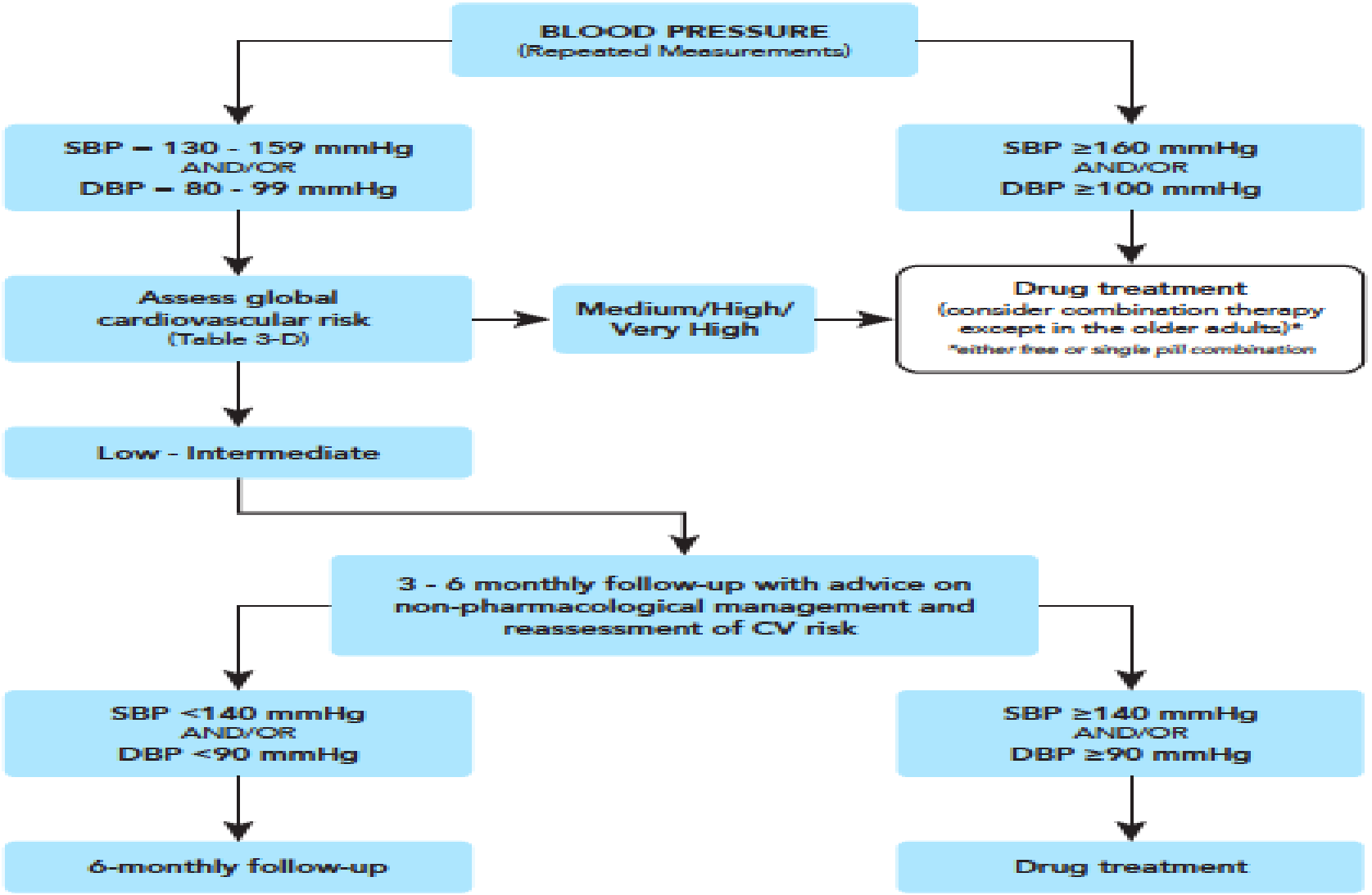
- Unclear of treatment targets
- Over reliance on monotherapy
- Treatment inertia

Over reliance monotherapy



18 652 patients
Northern Europe (Belgium, Germany, Sweden, Switzerland), **Southern Europe** (Greece, Italy, Spain, Turkey), **North America** (Canada), **Latin America** (Columbia, Mexico, Peru), **Middle East** (Kuwait, Lebanon, Qatar, Saudi Arabia, UAE), **Asia** (Hong Kong, Indonesia, Korea, Singapore, Taiwan, Thailand, Vietnam, Australia)

FIGURE 5-A Algorithm for the Management of Hypertension



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Latest Hypertension Guidelines

Guidelines	Year	Recommended first line
NICE	2019	Monotherapy as first line depending on age and ethnicity
ISH	2020	Ideally SPC or Step care Low dose combination then Full dose combination then triple combination
WHO	2021	SPC

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Latest Hypertension Guidelines

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Guidelines	Year	Recommended first line
ESH/ERA	2023	Dual combination therapy in most patients Preferred use of SPCs at any stage Monotherapy for • Low risk Grade 1 • High normal with high CV Risk

Latest Hypertension Guidelines

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Guidelines	Year	Recommended first line
ESC	2024	Monotherapy • Elevated BP (120-139/70-89mmHg) • Moderate to sever frailty • Symptomatic orthostatic hypertension Combination for the majority Low dose double combination

Why Single Pill Combination ?

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- The use of single-pill combination vs free combinations **reduce** the risk of **discontinuing treatment by 73%**[1]

- Single-pill combination **improves compliance rate by 24%** vs free combination[2]

1. Corrao G et al. *J of Hypertension.* 2010;28:1584-1590. *Cohort of 433 680 hypertensive patients*
2. Bangalore S et al. *Am J Med.* 2007;120:713-719. *Meta-analysis with 20 242 hypertensive patients*

Which Combination

Guidelines	Year	Recommended first line
ISH	2020	A+C+D A+C+D +D2
WHO	2021	Choose from A,C or D
ESH/ERA	2023	Dual combo ACEI or ARB + Diuretics (T/TL) ACEI or ARB + CCB Triple combo ACEI or ARB +CCB+DIU
ESC	2024	ACEI or ARB/ CCB/ DIU

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Using the Right Combination for the Right Patients

(Rahman AR et al Curr Med Res Opin 2015 March 26;1-10)

Study	Effective Combination	Comparator	Patient population studied	Outcome
HOT[35]	ß-blocker + CCB	No comparator	Patients aged 50–80 years with hypertension and diastolic BP ≥100 mmHg and ≤115 mmHg	Low rate of CV events with intensive BP lowering
PROGRESS[51]	ACEI + diuretic	Placebo	Post stroke or TIA	28% reduction in strokes (p<0.001)
HYVET[52]	ACEI + diuretic	Placebo	Very elderly (≥80 years) with hypertension	34% reduction in CV events (p<0.001)
ADVANCE[56]	ACEI + diuretic	Placebo	High-risk hypertension and diabetes	9% reduction in micro- and macrovascular complications (p=0.04)
LIFE[53]	ARB + diuretic	ß-blocker + diuretic	Hypertension with LVH	25% reduction in strokes (p<0.001)
VALUE[55]	CCB + diuretic	ARB + diuretics	High-risk hypertension	No significant difference in CV event rate between groups
ACCOMPLISH[58]	ACEI + CCB	ACEI + diuretic	High risk hypertension	21% reduction in CV events (p<0.001)
ASCOT[54]	ACEI + CCB	ß-blocker + diuretic	Medium-risk hypertension with no overt vascular disease	16% reduction in CV events (p<0.001)
INVEST[57]	ACEI + CCB	ß-blocker + diuretic	Hypertension + CAD	No significant difference in CV event rate between groups

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TABLE 5-A Effective Anti-Hypertensive Combinations Used in Outcome Trials

Effective combination	Patients studied
ACEI + thiazide-like diuretics	Post stroke[79], diabetes[83]
ARB + thiazide[82,112]	Hypertensive with Left Ventricular Hypertrophy. High risk hypertensives
CCB + ACEIs or ß-blocker + thiazide[80]	Patients with Coronary Artery Disease
CCB + thiazide[82]	High risk hypertensives
CCB + ACEI[110]	Medium risk hypertensives with no overt vascular diseases
ACEI + CCB[84]	High risk hypertensives
Thiazide-like diuretics + ACEI[113]	Very elderly (>80 years old)
CCB + thiazide or thiazide diuretics[114]	Medium risk hypertensives
CCB + ARB[114]	Medium risk hypertensives
CCB + ß- blocker[114]	Medium risk hypertensives

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TABLE 5-A Effective Anti-Hypertensive Combinations Used in Outcome Trials

Effective combination	Patients studied
ACEI + thiazide-like diuretics	Post stroke[79], diabetes[83]
ARB + thiazide[82,112]	Hypertensive with Left Ventricular
CCB +	
CCB +	
CCB +	
ACEI +	
Thiazid	
CCB +	
CCB + ARB[114]	Medium risk hypertensives
CCB + ß- blocker[114]	Medium risk hypertensives

Table 9.4-C: RAS Blockers Use in Co-Morbidities[36-48]

Condition	ACEIs	ARBs
Diabetes mellitus	Preferred	If ACEI intolerant
Diabetes mellitus (eGFR>60) + albuminuria/proteinuria	Either	Either
Diabetes mellitus type 1 (eGFR <60) +/-		If ACEI tolerant
		Either
		If ACEI tolerant
		If ACEI tolerant
		Either
		If ACEI tolerant
		referred

ACE-I is preferred over ARB in most hypertensive patients

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What Needs Improving ?

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More patients should be on treatment

More patients on treatment should be controlled

Combination therapy especially SPC should be given in the vast majority of patients

The essence of hypertension therapeutics

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The benefits of BP lowering are not a "class effect" and vary between the different drugs with each class . Hence the best approach for treatment tailored to individual patient needs should be evidenced – based specific drugs, rather than a drug class recommendation for achieving therapeutic targets

JG Wang April 2014

Evidence based free and 'add on' combination

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Effective combination	Patients studied
ACEI + thiazide like	Post stroke
ARB + thiazide	Hypertensive with Left Ventricular Hypertrophy
CCB + ACEIs or B-blocker + thiazide	Patients with Coronary Artery Disease
ARB + thiazide or CCB +thiazide	High risk hypertensive
CCB +ACEI	Medium risk hypertensive with no overt vascular diseases
Thiazide like + ACEI	Very elderly (>80 years old)

Evidence based SPC

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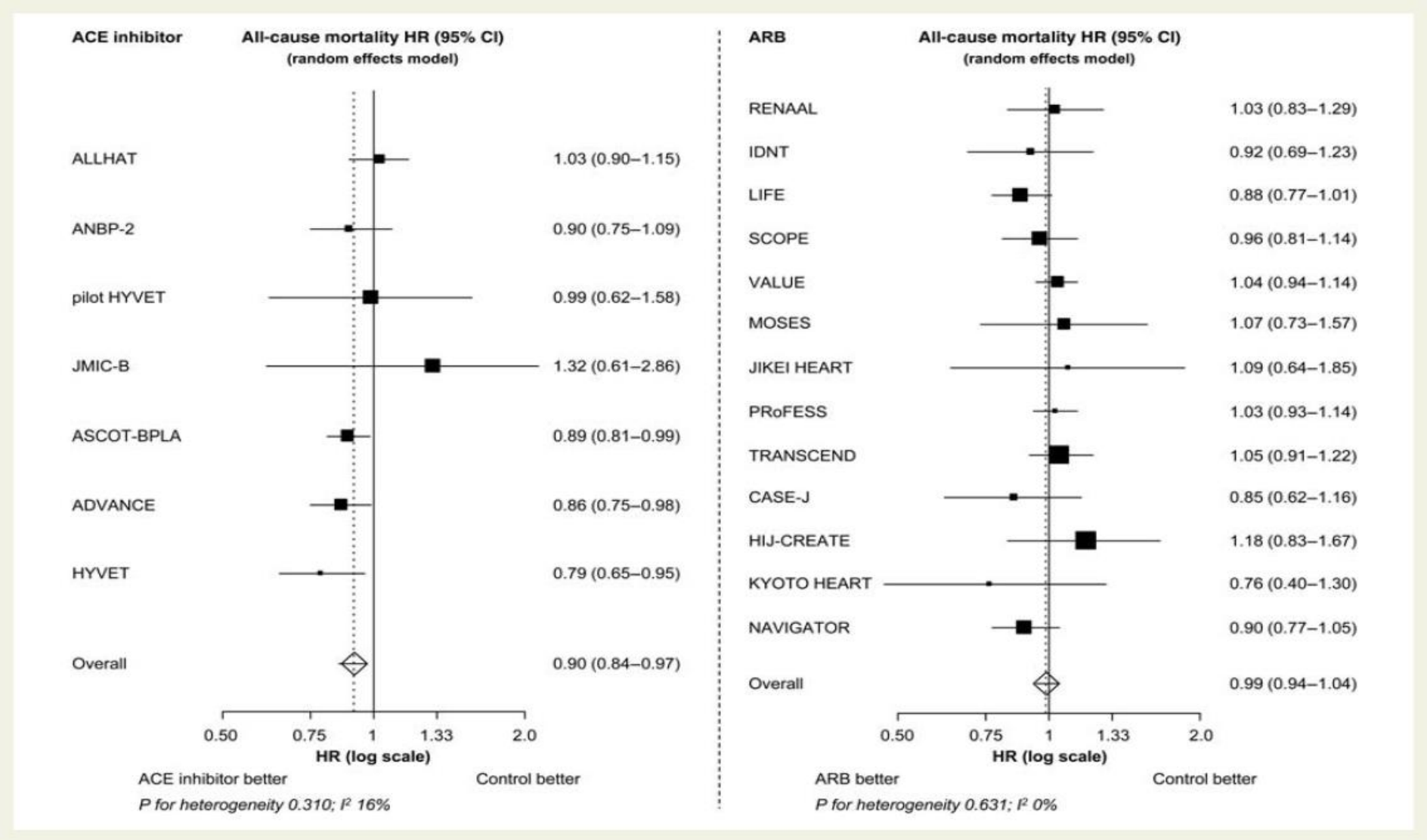
Effective combination	Patients studied
ACEI + Thiazide like Single Pill Combination	Diabetic with stage 1 hypertension
ACEI + CCB Single Pill Combination	High risk hypertensive with ISH

In hypertensive patients, only perindopril based treatment

reduced mortality



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van Vark LC et al. *Eur Heart J.* 2012;33(16):2088-2097.

All-cause mortality: effect of Perindopril

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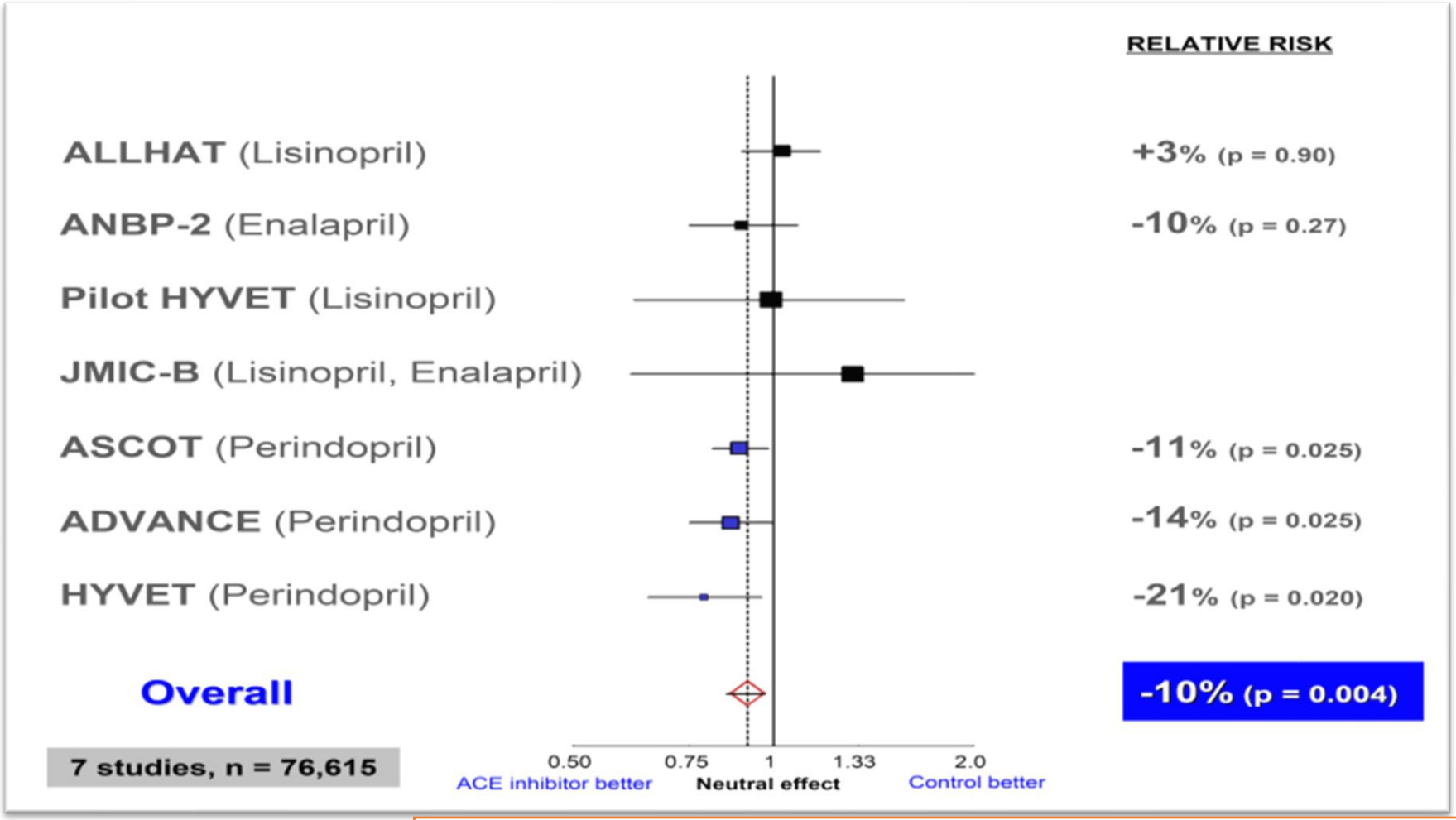

Reference: Van Vark LC, Bertrand M, Brugts J, Fox K, et al. Eur Heart J 2012; 33(16):2088-2097

Combination in Hypertension ; An Asia Pacific Consensus Viewpoint

Rahman AR et al Curr Med Res Opin 2015 March 26;1-10

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Monotherapy is recommended for first line treatment of patients with low risk stage 1 hypertension, with the preferred drug classes varying by indication

Patients with stage 2 hypertension and stage 1 with medium risk and beyond should receive combination therapy with two drugs, plus a third antihypertensive agent if necessary to achieve BP control

Recommended combinations vary according to indication and most include an ACEI

A diuretic is a mandatory component of a triple-combination regimen

Although hydrochlorothiazide was the most common diuretic in general use, the Asia-Pacific consensus workgroup favour indapamide

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CONCLUSIONS

1. Hypertension remains the main public health hazard worldwide
2. Hypertension control remains abysmal worldwide especially in the developing world
3. Optimum use of Single Pill Combination will significantly reduce the short fall of BP control
4. ACEI remain an integral and evidence based component of any combination therapy
5. Perindopril based combination therapy reduces morbidity and mortality including among Asia Pacific patients


THANK YOU

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