MANAGING CARDIOVASCULAR RISKS IN HYPERTENSIVE PATIENTS

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OUTLINE OF PRESENTATION

- Epidemiology of hypertension world wide and in Asia Pacific Region
- Hypertension, concurrent risk and disease burden
- Evidence Based Management of Concurrent CV risk in the hypertensive
- Conclusion

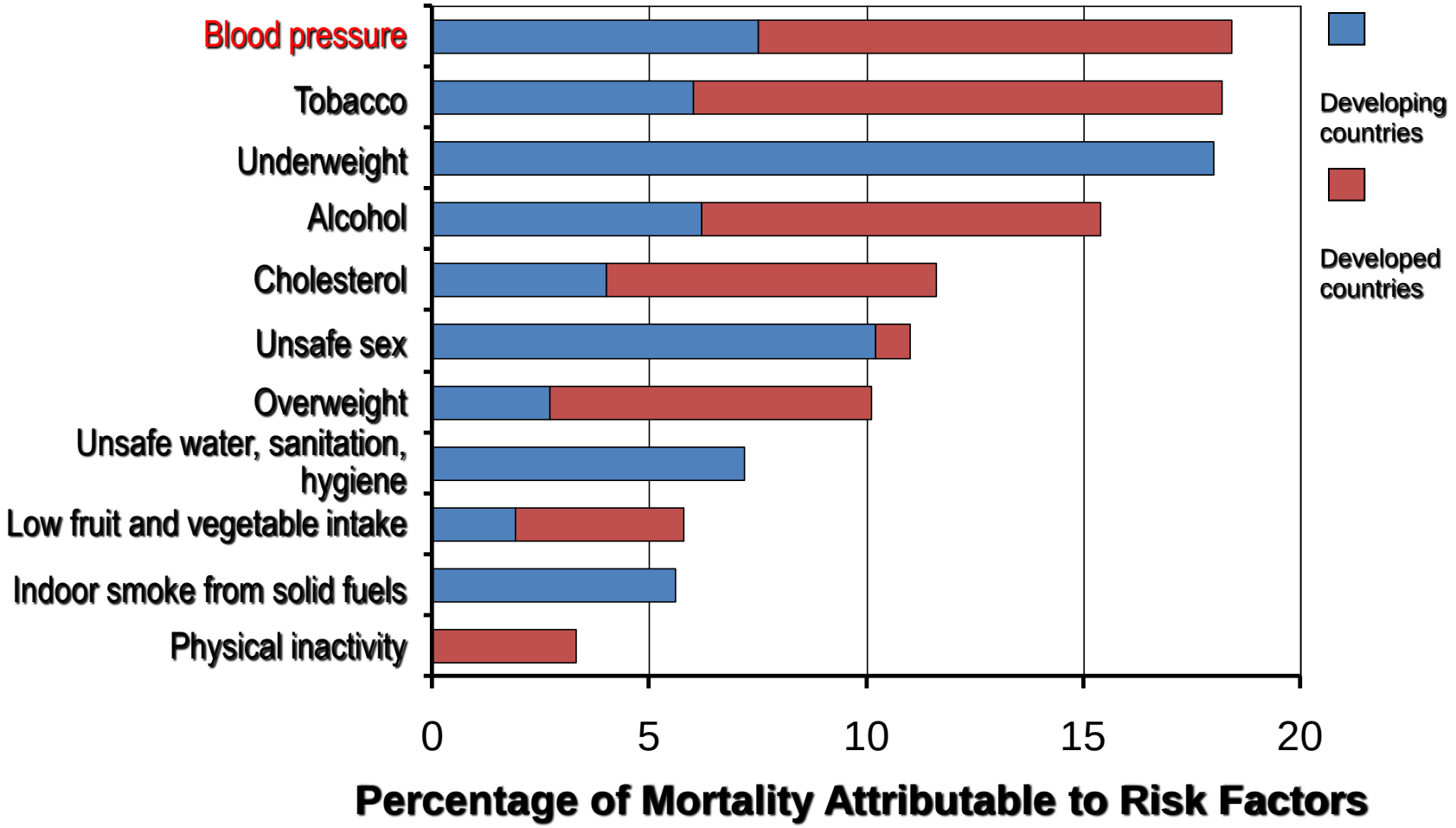
Current Status of Hypertension worldwide

- Most prevalent modifiable risk factor ; 1 billion individuals worldwide in 2000
- Results from periodic national surveys have shown a steady increase in its prevalence over time
- Estimated prevalence by 2025 will be 1.56 billion

Current Status of Hypertension worldwide

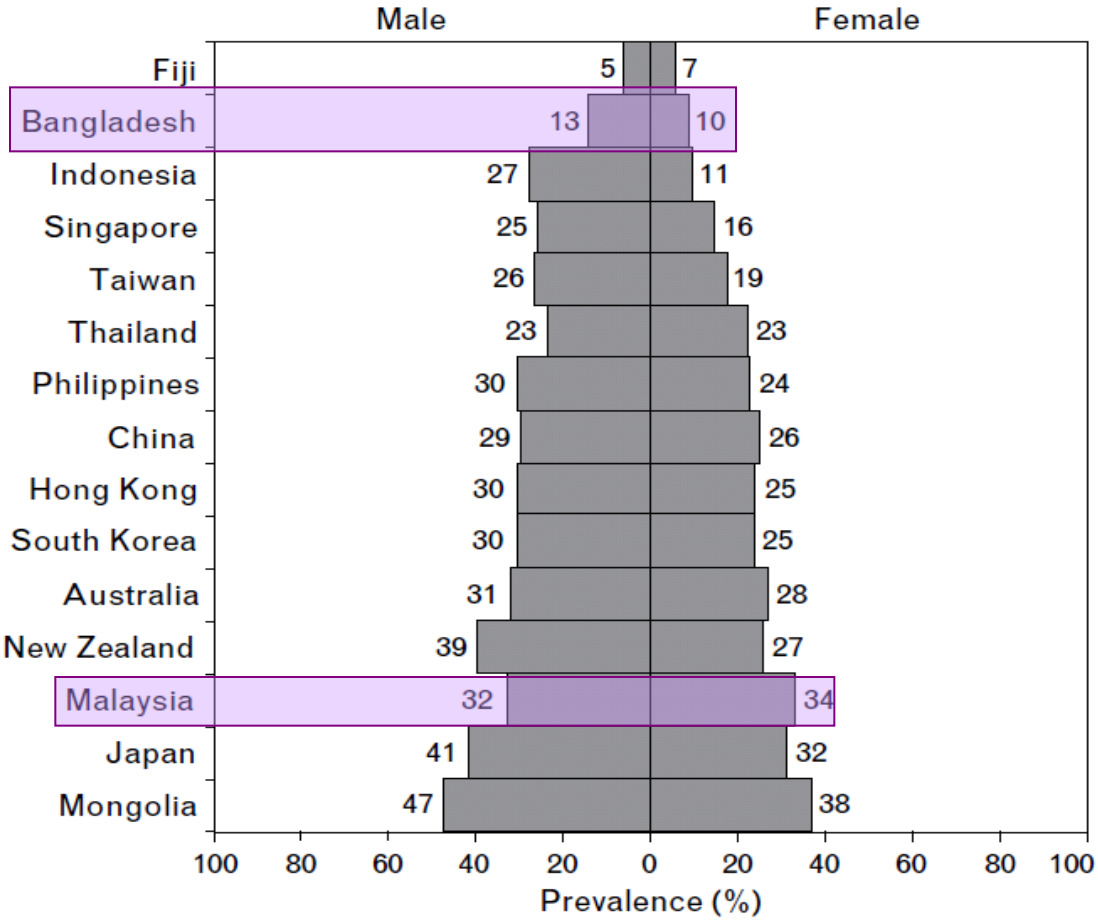
- A major health and financial burden globally
- The most important modifiable risk factor for morbidity and mortality worldwide
- Main contributor to cardiovascular disease worldwide

Contribution of Risk Factors to Burden of Disease Mortality*



*Based on The World Health Report 2003.
Yach et al. *JAMA*. 2004;291:2616-2622.

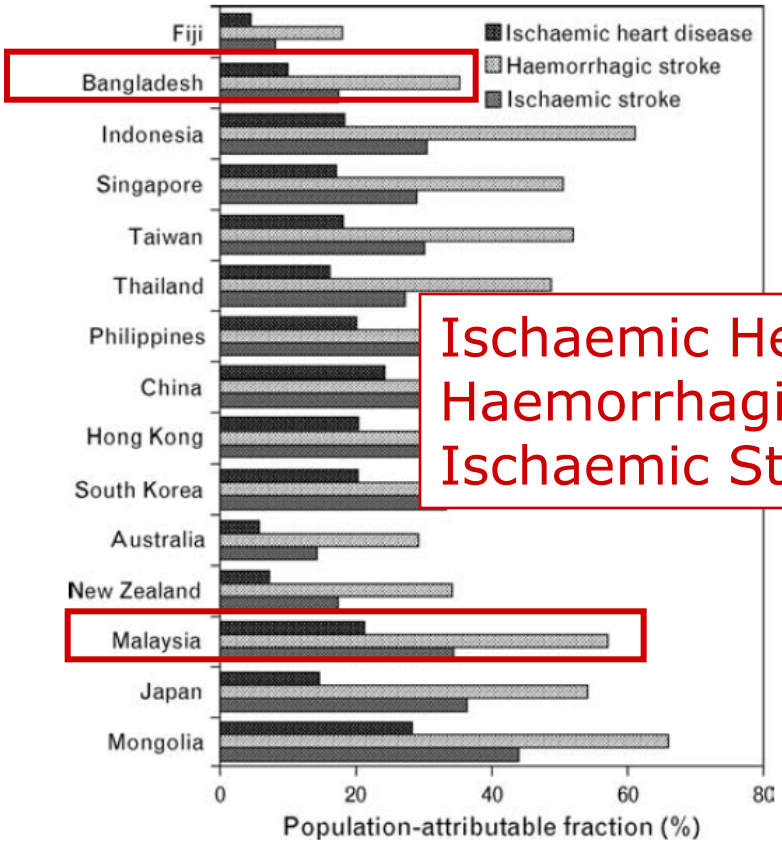
Prevalence of hypertension in the Asia-Pacific region

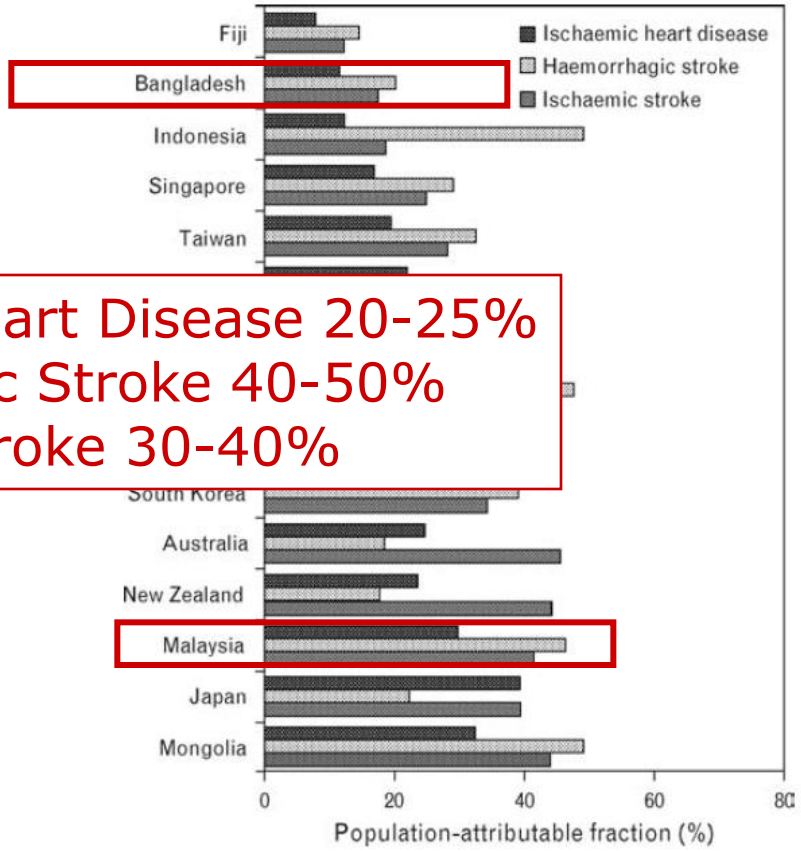


Crude prevalence of hypertension by sex – 1996-2004

Martiniuk ALC, for the Asia-Pacific Cohort Studies Collaboration, J Hypertens 2007; 25:73–79.

Population-attributable fractions for cardiovascular disease deaths due to hypertension in the Asia-Pacific region





Ischaemic Heart Disease 20-25%
Haemorrhagic Stroke 40-50%
Ischaemic Stroke 30-40%

Men **Women**

Martiniuk ALC, for the Asia-Pacific Cohort Studies Collaboration, J Hypertens 2007; 25:73–79.

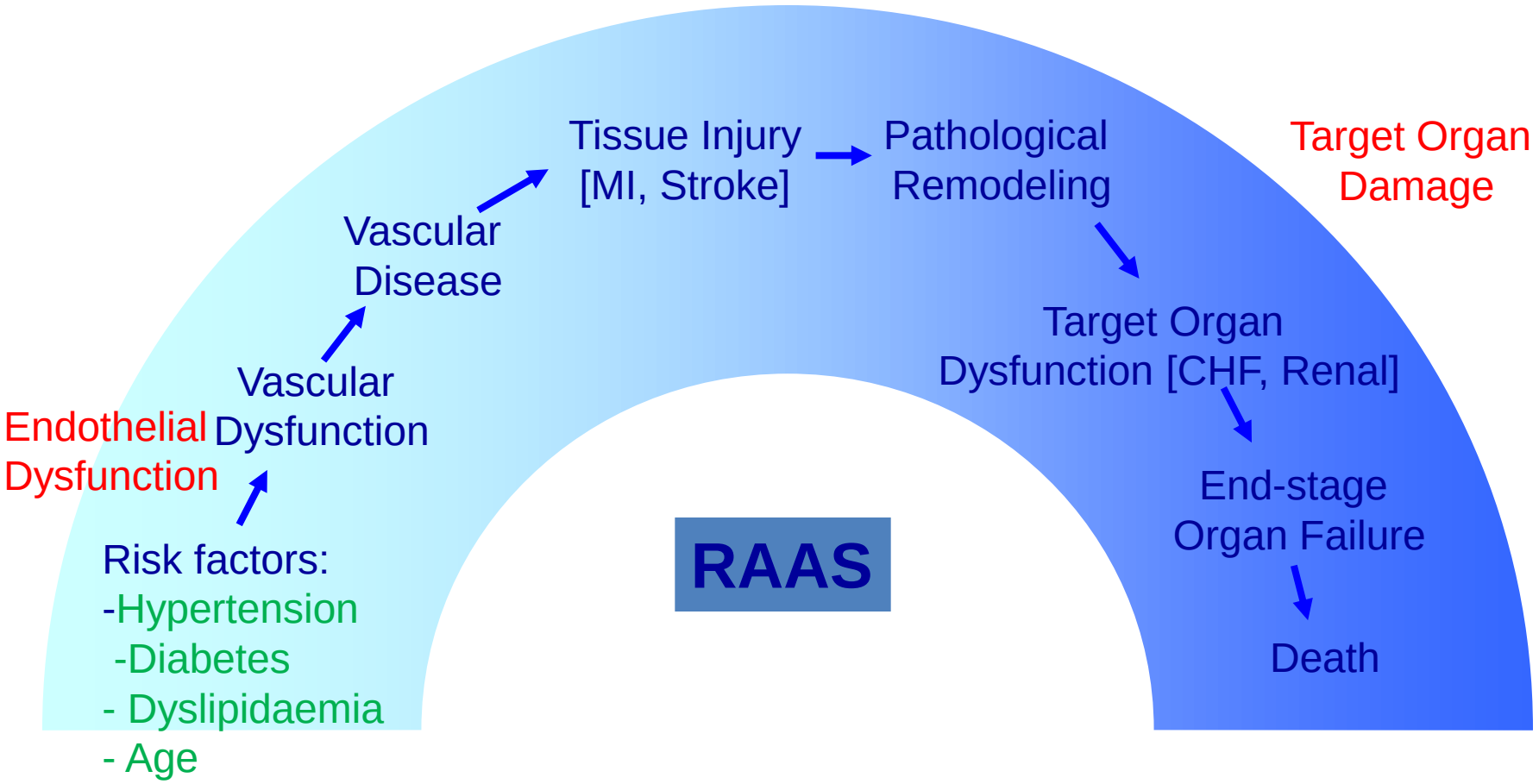
HYPERTENSION IN THE ASIA PACIFIC REGION AND CV RISK

- Contributes to two thirds (66%) of all cardiovascular events (compared to 46% worldwide)[1]

- Main cause of premature death in China[2]

1. Asia Pacific Cohort Studies Collaboration: Blood pressure and cardiovascular diseases in the Asia Pacific region. *J Hypertens 2003;21:707-716.*
2. He J , Gu D , Chen J et al Premature deaths attributable to blood pressure in China: a prospective cohort study. *Lancet 2009 Nov 21; 374 (9703):1765-72*

The Cardiovascular Continuum



Adapted from Dzau V, Braunwald E. Am Heart J. 1991 & Gibbons, 1999

Most Common Coexisting Risk

- Diabetes
- Dyslipidaemia
- Very elderly
- Prior CV events (CAD,CVA, HF, CKD,PVD)

What is the optimum way to manage these patients ?

- Follow the EVIDENCE

- EVIDENCE from primary outcome of major Randomise Control trials and nothing less !

The Diabetic Hypertension Trials

In order of priority

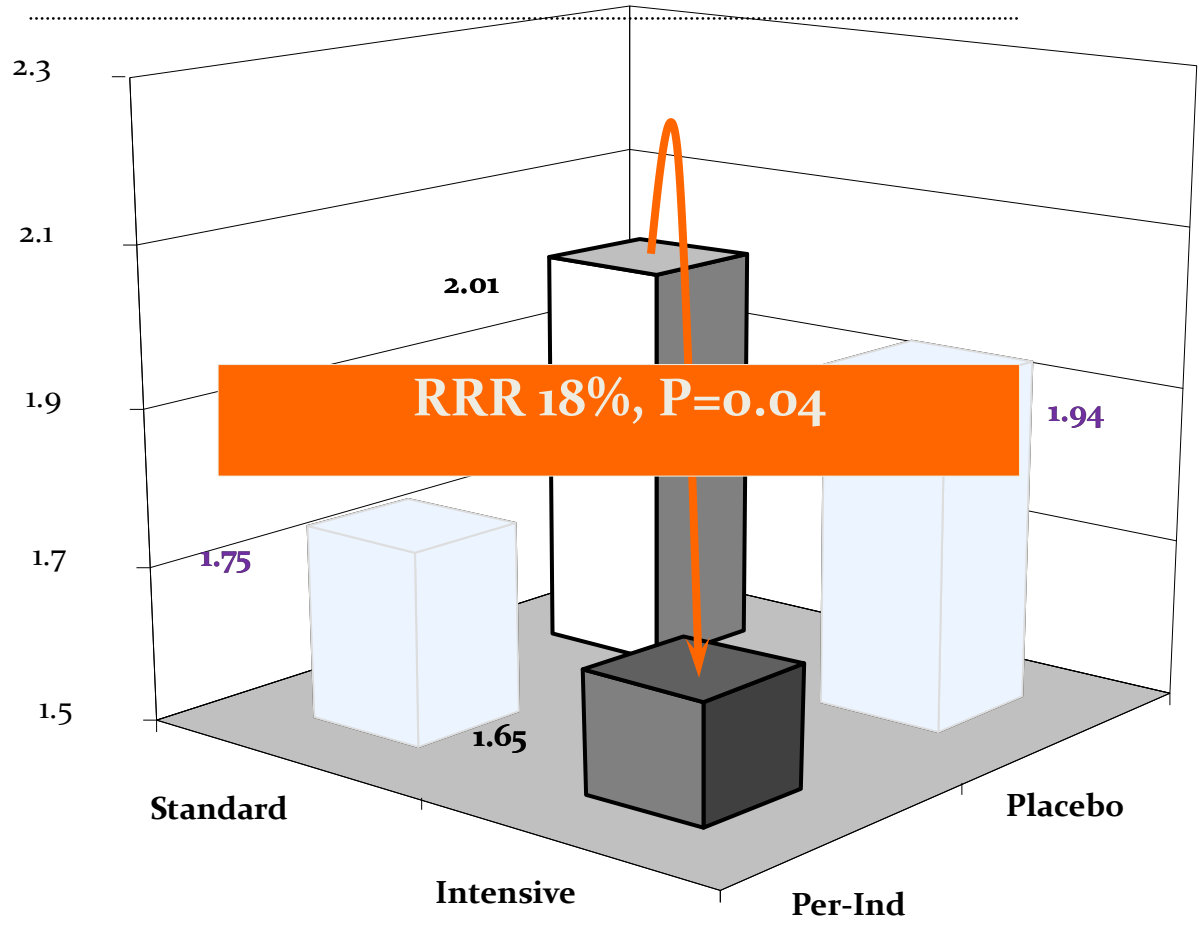
- ADVANCE (main study)
- ACCORD (main study)
- UKPDS (sub study)
- HOT (sub study)
- INVEST (sub analysis)

Dedicated Diabetic Hypertension Trial
(all patients studied were diabetics)

Trial	Year	BP difference	Outcome	Drugs
UKPDS	1998	154/ 88 vs 144/82	POSITIVE	Cap vs aten.
ADVANCE	2007	140/77 vs 135/75	POSITIVE	Coversyl Plus
ACCORD	2010	134/71 vs 119/ 64	NEGATIVE	All sorts

Importance of Holistic Approach ADVANCE (all cause mortality)

Annual event rate %



P for interaction=0.90

Dedicated Dyslipidaemic Hypertension Trials
(all patients were dyslipidaemic)

Trial	Year	Outcome	Drugs
ALLHAT	2002	NEGATIVE	Pravastatin (Lis vs Chlor vs amlo)
ASCOT	2005	POSITIVE	Atorvastatin (amlo ± per vs aten ± thia)

The CAD Pre - Hypertension Trials

- EUROPA
- ACTION

EVIDENCED BASED COMPELLING INDICATION IN PATIENTS WITH CAD

	Background Risk	Entry BP	Treatment	Achieved BP on treated arm	Primary outcome
EUROPA N = 12,218 (Lancet 2003)	24%/10y 27% HPT 12%DM	137/82 mmHg	Perindopril vs placebo	130/78 mmHg (5/2 v placebo)	20% RRR (p<0.003)
ACTION N= 7,655 (Lancet 2004)	~ 25%/10y 30%HPT 15%DM	137/80 mmHg	Nifedipine GITS vs placebo	130/76 mmHg (5/2 v placebo)	3% RRR (NS)

The CVA Hypertension Trials

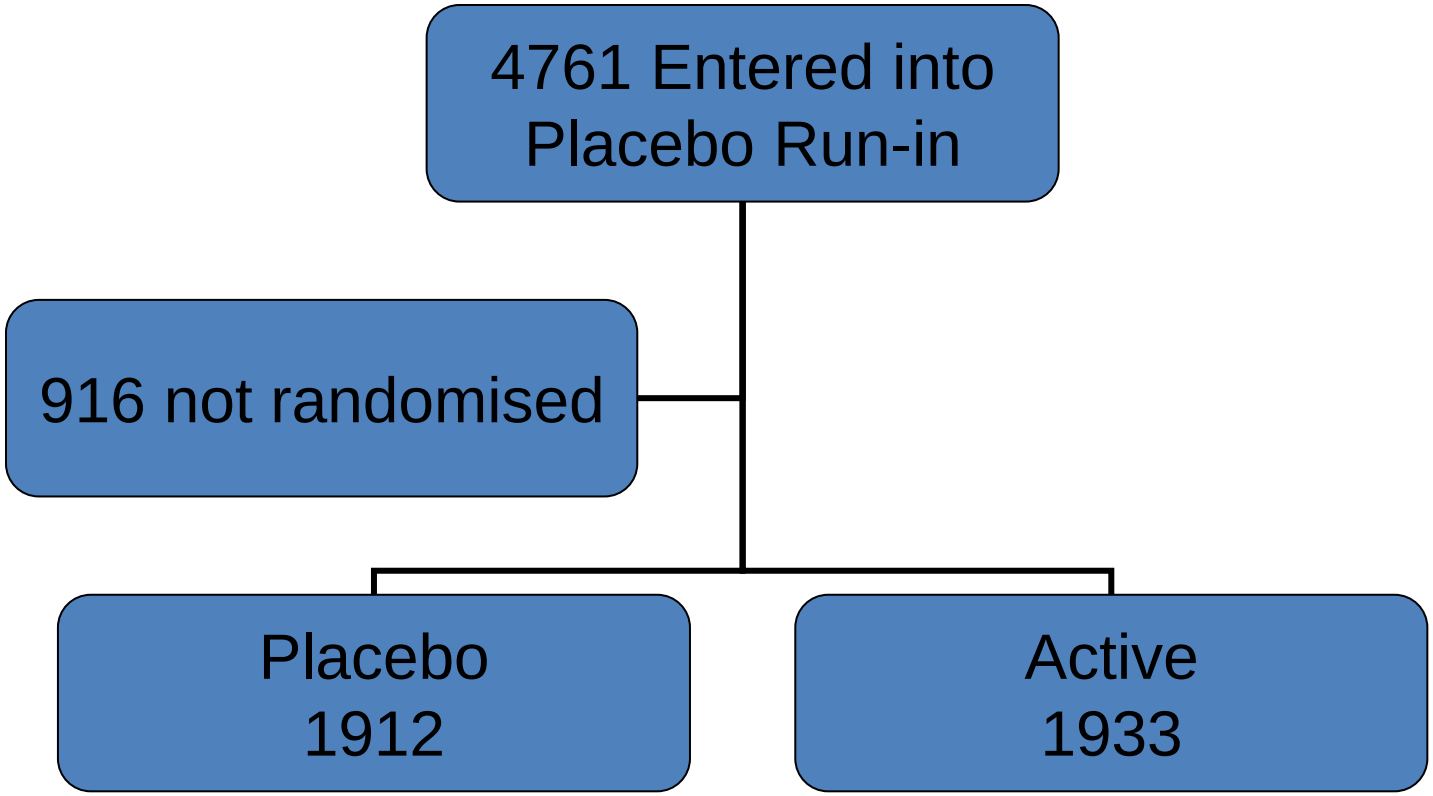
- PROGRESS
- PROFESS

EVIDENCED BASED COMPELLING INDICATION IN PATIENTS WITH PREVIOUS CVA

	Background CVA Risk	Entry BP	Treatment	Achieved BP on treated arm	Primary outcome
PROGRESS N = 6,105 (Lancet 2001)	35%/10y 50% HPT 13%DM	147/86 mmHg	Perindopril vs placebo	138/82 mmHg (9/4 v placebo)	28% RRR (p<0.0001)
PROFESS N= 20,332 (Lancet 2008)	37.5%/10y	144/84 mmHg	Telmisartan vs placebo	136/? mmHg (5.4/? v placebo)	5% RRR (NS)

The Very Elderly Hypertension Trials

- HYVET



- 3845 randomised; Western Europe (86) Eastern Europe (2144), China (1526), Australasia (19), Tunisia (70)

- At end of trial; 1882 still in double blind, 17 vital status not known, 220 in open follow-up

HYVET - Baseline data

	Placebo (n= 1912)	Active (n= 1933)
Age (years)	83.5	83.6
Female	60.3%	60.7%
Blood Pressure:		
Sitting SBP (mmHg)	173.0	173.0
Sitting DBP (mmHg)	90.8	90.8
Orthostatic Hypotension‡	8.8%	7.9%
Isolated Systolic Hypertension	32.6%	32.3%

‡ Fall in SBP ≥ 20mmHg and/or fall in DBP ≥ 10mmHg

HYVET Conclusions

- Antihypertensive treatment based on indapamide (SR) 1.5mg (± perindopril) reduced stroke mortality and total mortality in a very elderly cohort.
- NNT (2 years) = 94 for stroke and 40 for mortality
- Large and significant benefit in reduction of heart failure events and for combined endpoint of cardiovascular events
- Benefits seen early
- Treatment regime employed was safe

The CKD Hypertension Trial

Non Diabetic

- REIN using ramipril

Diabetic

- MICRO HOPE using ramipril
- RENAAL using losartan
- IDNT using irbesartan

The HF Hypertension Trial

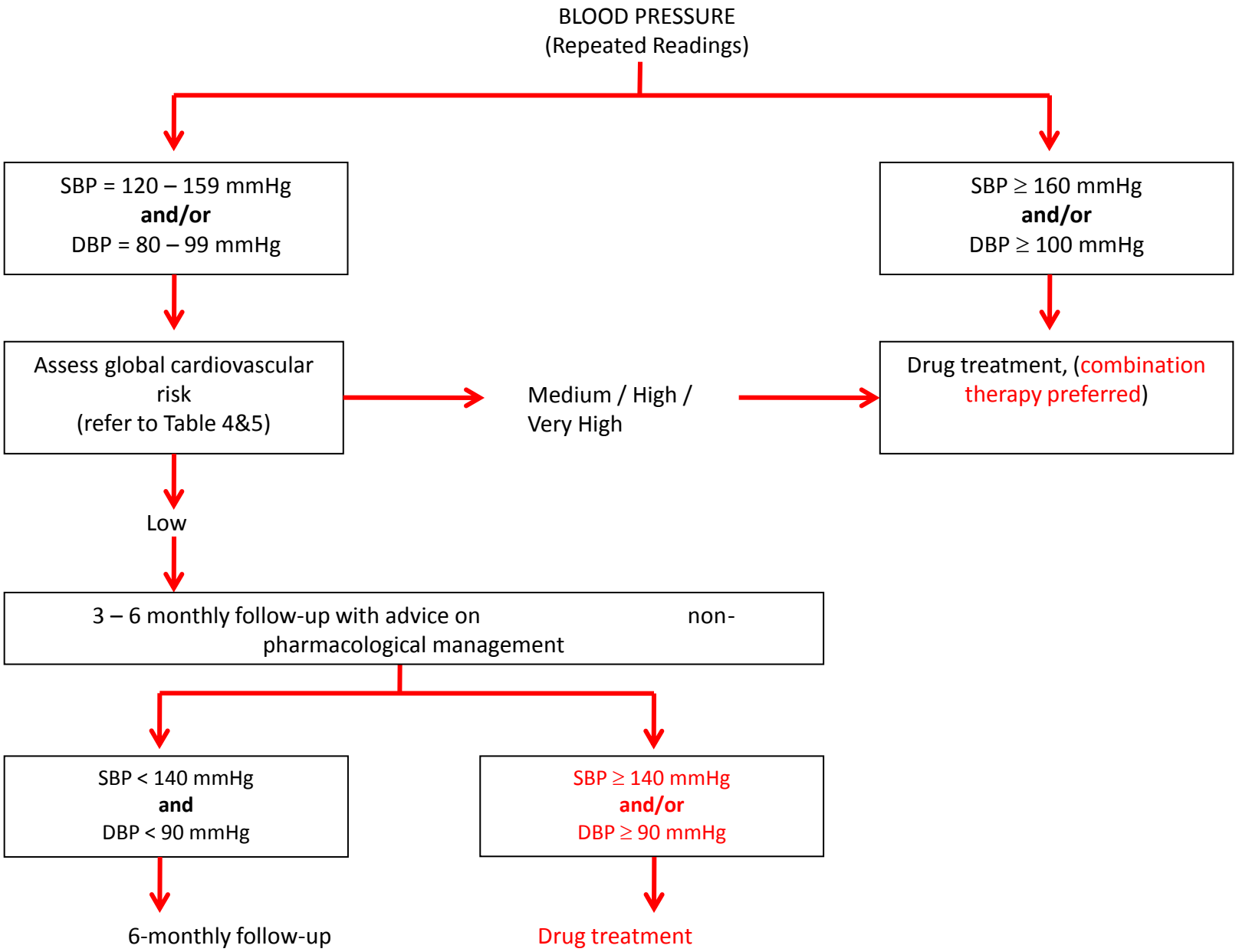
Post MI

- GISSI 3, ISIS 4, SAVE,SOLVD, AIRE, SMILE, TRACE, PREAMI using ACEI
- OPTIMAAL, VALIANT using ARB vs ACEI

Chronic HF

- CONSENSUS, CHEF PEP using ACE I
- ELITE,VALIANT using ARB vs ACEI
- CHARM using ARB

Algorithm for the Management of Hypertension



Risk Stratification

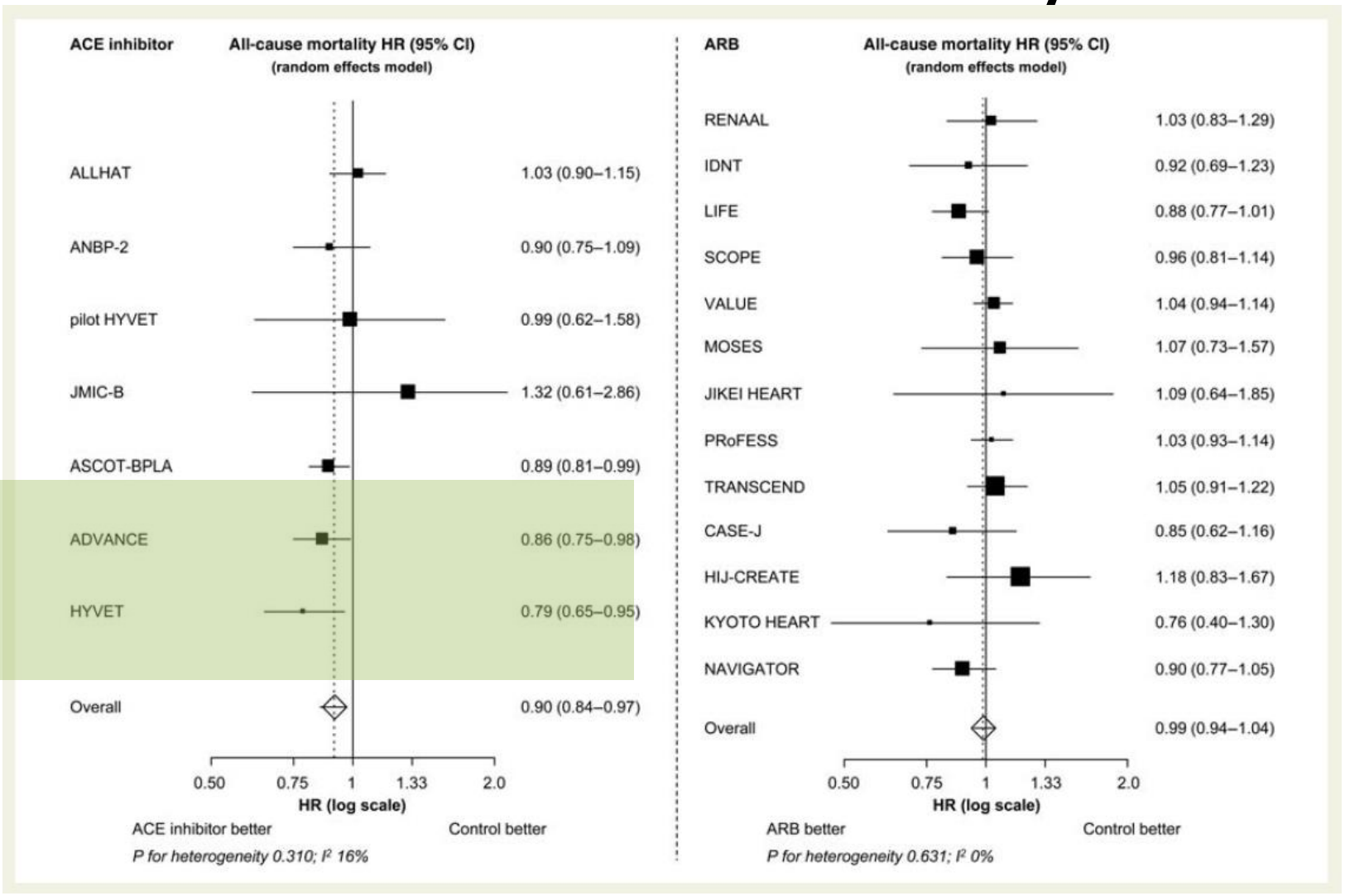
Co-existing Condition BP Levels (mmHg)	No RF No TOD No TOC	TOD or RF (1 – 2) No TOC	TOC or RF (≥ 3) or Clinical atherosclerosis	Previous MI or Previous stroke or Diabetes
SBP 130 – 139 and/or DBP 80 – 89	Low	Medium	High	Very high
SBP 140 – 159 and/or DBP 90 – 99	Low	Medium	High	Very high
SBP 160 – 179 and/or DBP 100 – 109	Medium	High	Very high	Very high
SBP ≥180 and/or DBP ≥110	High	Very high	Very high	Very high

Choice of anti-hypertensive drugs with concomitant conditions

Concomitant Condition	Diuretics	β-blockers	ACEIs	CCBs	Peripheral α-blockers	ARBs
Diabetes mellitus (without nephropathy)	+	+/-	+++	+	+/-	++
Diabetes mellitus (with nephropathy)	++	+/-	+++	++*	+/-	+++
Dyslipidaemia	+/-	+/-	+	+	+	+
Coronary heart disease	+	+++	+++	++	+	+++
Heart failure	+++	+++	+++	+@	+	+++
Peripheral vascular disease	+	+/-	+	+	+	+
Non-diabetic renal impairment	++	+	+++	+*	+	++
Elderly with no co-morbid conditions	+++	+	+	+++	+/-	+
Very elderly (>80yrs) with no co-morbidity	+++	+	+++	++	+/-	++

In hypertensive patients, only perindopril significantly

reduced mortality



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

CONCLUSION

- Hypertension will remain a major global health burden for years to come
- Patients must mere comprehensively risk stratified before management plan is instituted
- Results from major outcome trials and not theoretical consideration should guide our management plan
- ACEI based treatment has the best tract record on a wide spectrum of risk profile
- Perindopril based treatment is the only strategy to have shown consistent reduction with all cause mortality