NEW DIMENSION IN MANAGING UNCONTROLLED HYPERTENSION

Bangladesh Society of Medicine

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OUTLINE OF PRESENTATION

- Current status of hypertension in the Asia
- Challenges of Managing Hypertension
- Managing Uncontrolled Hypertension
- Conclusion

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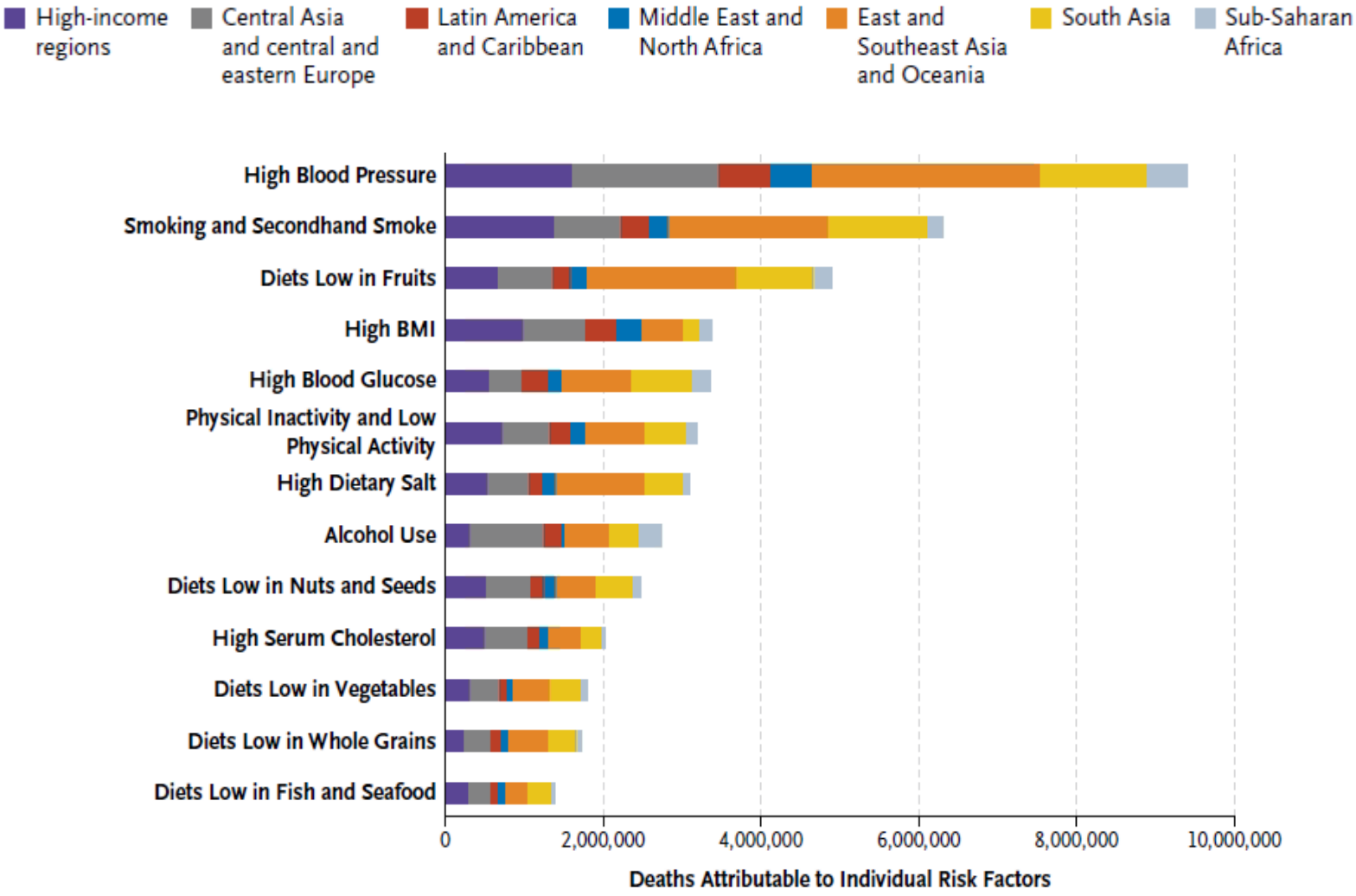
CURRENT STATUS OF HYPERTENSION WORLDWIDE

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

HIGH BLOOD PRESSURE IS STILL THE LEADING CAUSE OF DEATH WORLDWIDE



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

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HYPERTENSION AND HEALTH BURDEN IN THE REGION

- Contributes to two thirds (66%) of all cardiovascular events (compared to 46% worldwide)[1]
- Main cause of premature death in China[2]
- Treating all Hypertensives in China could cost-effectively prevent about 800,000 CVD events annually[3]

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*
3. *Gu D,He J et al.* The Cost-Effectiveness of low-cost essential antihypertensives medicines for hypertension control in China *.PLos Me 2015;12e1001850*

ASIA PACIFIC REGION CV MORTALITY

(SUH I, J HYPERTENS SEP 2016;34 SUPPL 1)

Decreasing	Increasing
South Korea	Philippines
Singapore	Pakistan
New Zealand	Myanmar
Australia	China

CHALLENGE 1

- Awareness of hypertension is low despite the clear relationship between high BP and CVD[1–3]

1. Sharma AK, *et al*. *Indian Heart J 2*006;58:21-7.
2. Sison J, *et al*. *Philipp J Cardiol* 2007;35:1-9
3. Rampal L, *et al*. *Public Heal*th 2008;122:11-18.

CHALLENGE 2

Low rates of awareness usually corresponded with suboptimal treatment rates, particularly in low-income Asian countries[4]

4. Perkovic V, *et al. Hypertension* 2007;50:991-7.

CHALLENGE 3

Despite being on treatment, control rates are still poor in the Asia Pacific Region

PREVALENCE, AWARENESS, TREATMENT AND CONTROL IN ASIA

Country	Patients (n)	Prevalence (%)	Awareness (%)	Treated (%)	Controlled (%)
China[1]	13,364	43.8	26.2	22.2	3.9
India[2] (>35years)	4,711	42.3	33.5	36.7	
Korea[3] (≥ 30 years)	8,485	24.9	63.5	54.8	38.0
Malaysia[4] (> 30 years)	18,809	43.3	38.8	79	35.0
Singapore[5]	5,022	41.5	51.8	84.4	27.1
Bangladesh [6] (>35 years)	7.876	24.4	50.1	41.2	31.4

1. Li H, *et al*. *J Hypertens* 2010;28:432-8. **2.** Sharma AK, *et al. Indian Heart J* 2006;58:21-7. **3.** Korean National Health and Nutrition Examination Survey (KNHANES) 2008 [Korean]. Available at: http://knhanes.cdc.go.kr. **4.** Institute of Public Health (IPH) 2008. The Third National Health and Morbidity Survey 2006 Vol. 2. Ministry of Health Malaysia pp 199-316 ISBN 978-983-3887-30-9. **5.** Wu Y, *et al. J Hypertens* 2009;27:190-7.**6**. Rahman MM et al. J Hypertens 2015;33(3) :465-72

WHY POOR CONTROL RATES

- Patient Factor
- Disease Factor
- Doctors factor

DOCTORS FACTOR

- Diagnostic Inertia
- Over reliance on monotherapy
- Treatment Inertia
- Clinical myopia

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COMBINATION THERAPY IN THE RECENT GUIDELINES

NICE UK 2011	ESC/ESH 2013	ASH/ISH 2013	JNC 8 2014	MSH/MOH 2014
Use as second line	First line in stage 2 and high risk	First line in stage 2	Optional first line in all groups	First line in stage 2 and high risk stage 1

WHY COMBINATION THERAPY

- Multiple mechanisms involved in the pathogenesis of hypertension
- Effectiveness of monotherapy limited by stimulation of counter-regulatory mechanisms
- Effective BP control seen in only 30% of patients on monotherapy
- Combination therapy results in a much higher responder rate (>80%)
- BP goals difficult to attain with monotherapy in patients with diabetes or target organ damage

WHICH COMBINATION ?

NICE UK 2011	ESC/ESH 2013	ASH/ISH 2013	JNC 8 2014	MSH/MOH 2014
Use as second line	First line in stage 2 and high risk	First line in stage 2	Optional first line in all groups	First line in stage 2 and high risk stage 1
RAAS + CCB	Various possible permutations with some preferred	RAAS + CCB or thiazide	Based on age and ethnicity	Evidence driven patient group

Drug Combinations in Hypertension: Recommendations

Preferred (based on outcome trials)
ACEI /thiazide or thiazide like
ARB/ thiazide
ACEI /CCB
B-Blocker /thiazide
Thiazide diuretics/K+ sparing diuretics
CCB / thiazide

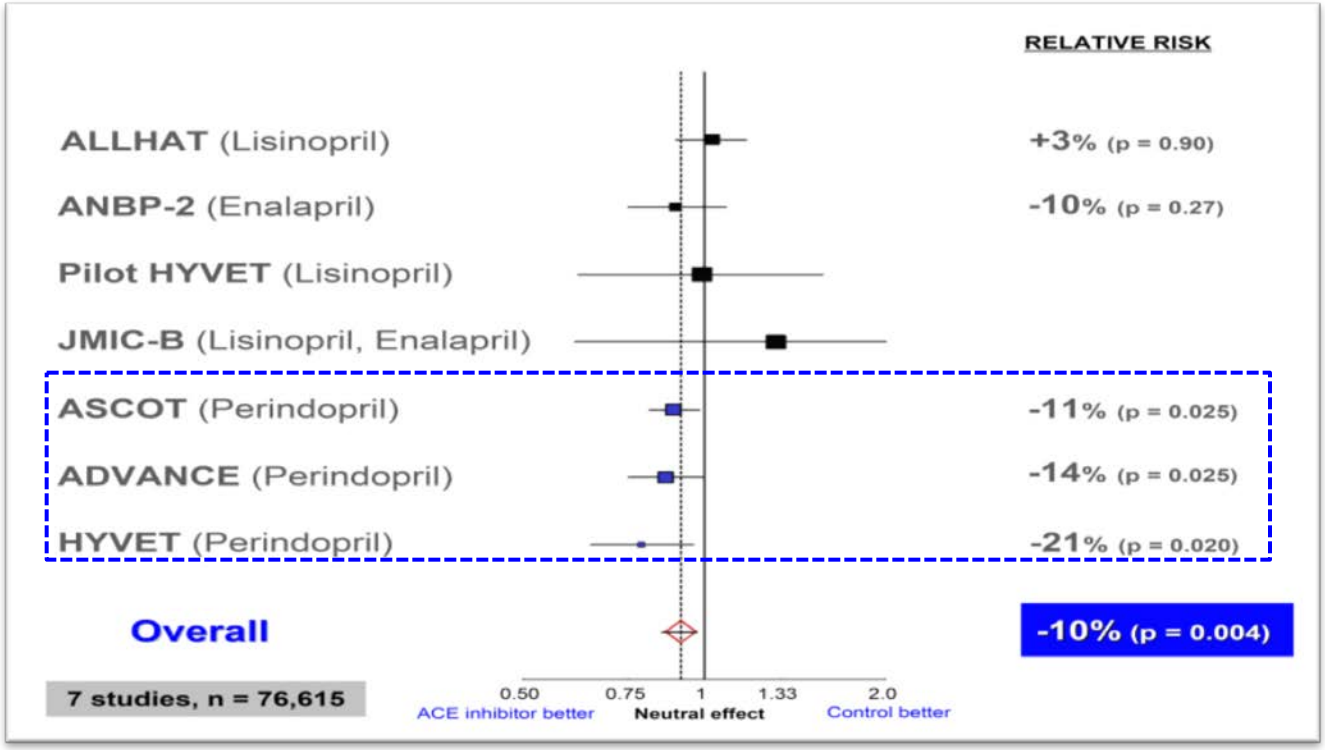
Acceptable (no outcome trial evidence yet)
ARB/CCB
B-Blocker/ thiazide like
DRI/diuretic

ARB = angiotensin receptor blocker
ACE = angiotensin-converting enzyme
CCB = calcium channel blocker
DRI = direct renin inhibitor

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	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	ACEI + diuretic	Placebo	Post stroke or TIA	28% reduction in strokes (p<0.001)
HYVET	ACEI + diuretic	Placebo	Very elderly (≥80 years) with hypertension	34% reduction in CV events (p<0.001)
ADVANCE	ACEI + diuretic	Placebo	High-risk hypertension and diabetes	9% reduction in micro- and macrovascular complications (p=0.04)
LIFE	ARB + diuretic	ß-blocker + diuretic	Hypertension with LVH	25% reduction in strokes (p<0.001)
VALUE	CCB + diuretic	ARB + diuretics	High-risk hypertension	No significant difference in CV event rate between groups
ACCOMPLISH	ACEI + CCB	ACEI + diuretic	High risk hypertension	21% reduction in CV events (p<0.001)
ASCOT	ACEI + CCB	ß-blocker + diuretic	Medium-risk hypertension with no overt vascular disease	16% reduction in CV events (p<0.001)
INVEST	ACEI + CCB	ß-blocker + diuretic	Hypertension + CAD	No significant difference in CV event rate between groups

All-cause mortality: effect of Perindopril



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

CLINICAL TRIALS VS REALITY

Bahl VK et al. *(Am J Cardiovasc Drugs 2009;9:135-42)*

- Efficacy and tolerability of combination of Perindopril and Amlodipine
- 1,250 hypertensive patients in India over 2 months.
- Blood pressure reduced by 41.9/23.2 mmHg with an excellent tolerability profile.

Abdelhady A et al. *(Clin Drug Investig. 2016 May;36(5):357-66)*

- Efficacy of the combination of Perindopril and Amlodipine in achieving target blood pressure.
- In 1996 hypertensive patients, 93% achieved target blood pressure over 3 months .

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CONCLUSION

- Hypertension is common in most Asian countries and is increasing in incidence with adoption of unhealthy lifestyle
- Hypertension and associated CVD are major public health challenges
- Low hypertension control rates will translate into CV events, mainly premature events
- Over reliance on monotherapy contributes to poor control rates
- Combination therapy chosen must be evidenced based and must be proven to reduced CV events including mortality
- ACEi based combination is the combination of choice *(Rahman et al CMRO March 2015)*
- Perindopril based combination has the best evidence base especially in combination with amlodipine and with indapamide