

Hypertension

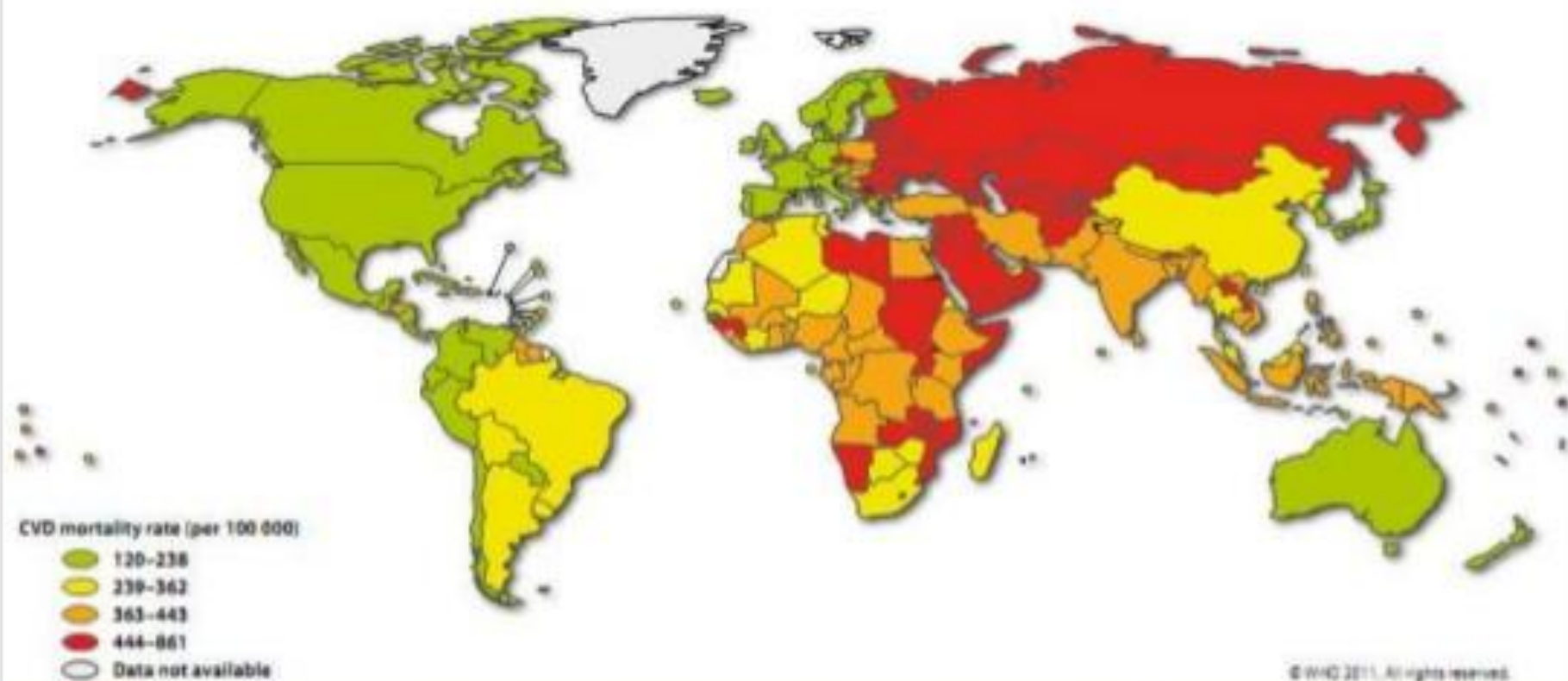
Current Challenges

Hypertension global burden

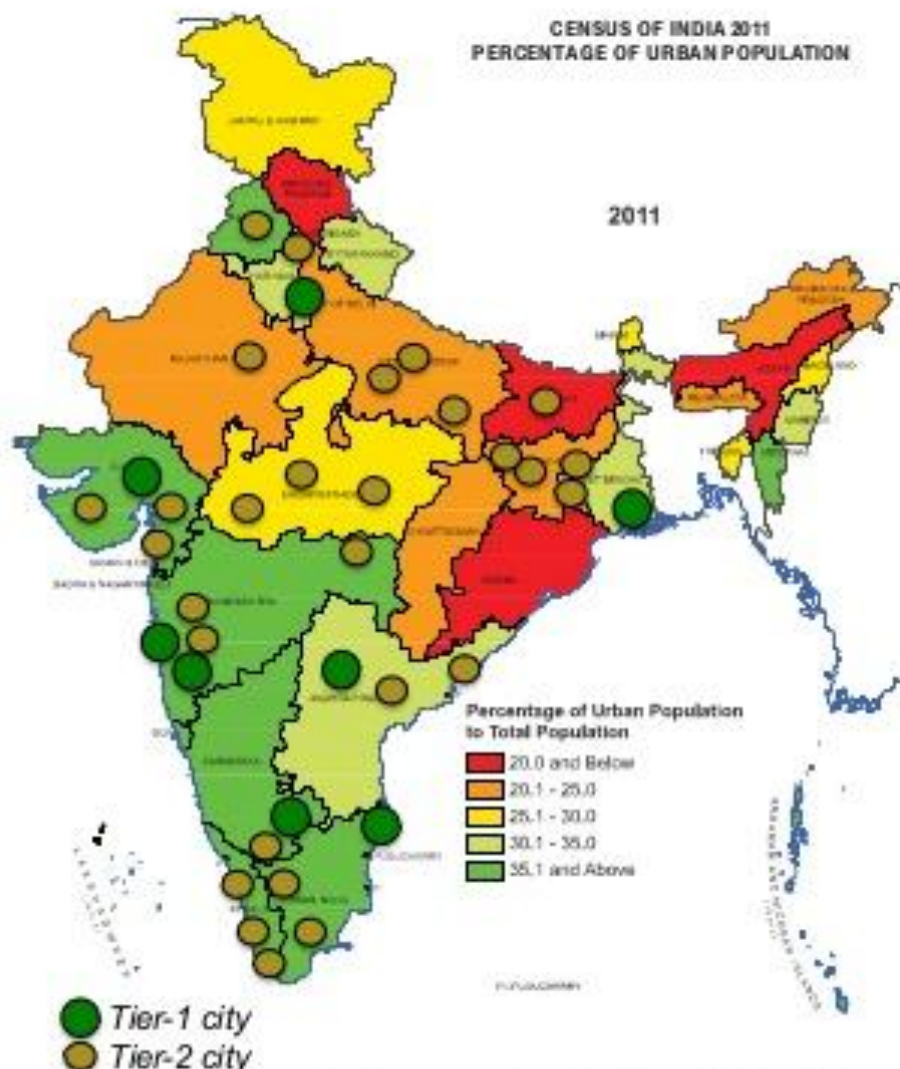
- Globally, the overall prevalence of hypertension or raised blood pressure in adults aged 25 and above was around 40% in 2008.
- Worldwide, hypertension is estimated to cause 7.5 million deaths, about 12.8% of the total deaths.
- Hypertension accounts for 57 million disability adjusted life years (DALYS) or 3.7% of total DALYS
- WHO has estimated that globally about 62% of cerebrovascular diseases and 49% of ischemic heart diseases are attributable to suboptimal blood pressure (systolic > 115 mmHg)
- One in three adults worldwide has high blood pressure.

World Map Showing The Global Distribution of CVD Mortality Rates in Males (Age Standardized, per 100.000)

Figure 6 World map showing the global distribution of CVD mortality rates in males (age standardized, per 100 000) (7).



India – a quick overview



People

- Population: 1.21 Billion
- Urban and Rural population share at 31% and 69%, respectively
- Top 20 cities account for ~5.3% of its total population
- 28 states & 7 Union Territories

Key, Select Economic Indicators

- GDP, *Purchasing Power Parity basis*
 - Total: US\$ 5.3 Trillion
 - Per Capita: US\$ 4,209
- In 2008, Urban GDP (~30% popln.) accounted for 58% of India's GDP (*share to go up to 70% by 2030*)
- Top 5 states (viz., Maharashtra, Gujarat, Andhra Pradesh, Tamil Nadu & Delhi) have highest share of GDP to total

Notes: UT is Union Territory – an administrative division that is under the direct rule of the central (federal) government

Sources: GDP estimates from The International Monetary Fund (2013); McKinsey Global Institute (2010 Report)

Hypertension in India

- About 33% urban and 25% rural Indians are hypertensive.
- Of these, 25% rural and 42% urban Indians are aware of their hypertensive status.
- Only 25% rural and 38% of urban Indians are being treated for hypertension.
- One-tenth of rural and one-fifth of urban Indian hypertensive population have their BP under control.

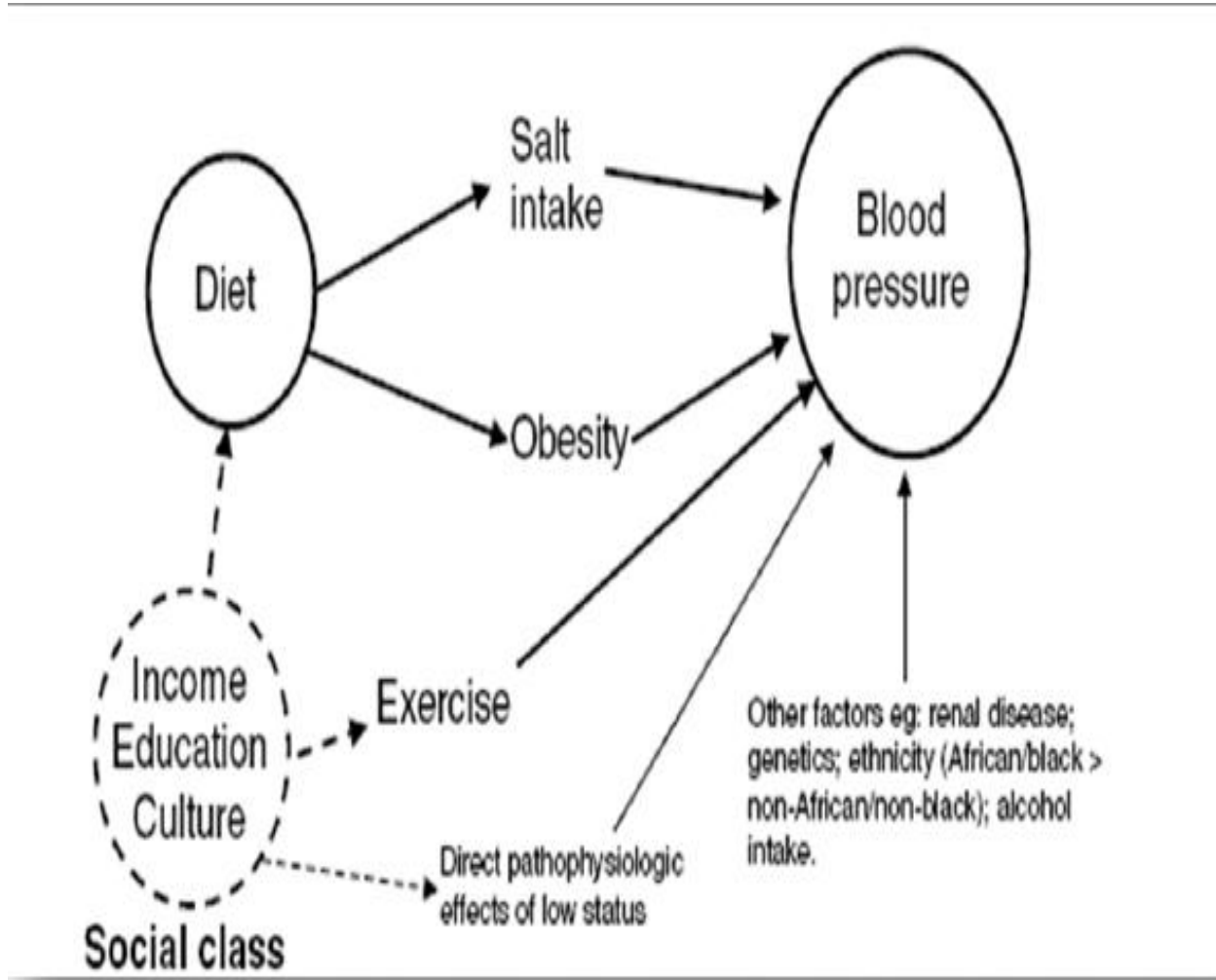
Risk Factors

Challenges in Hypertension

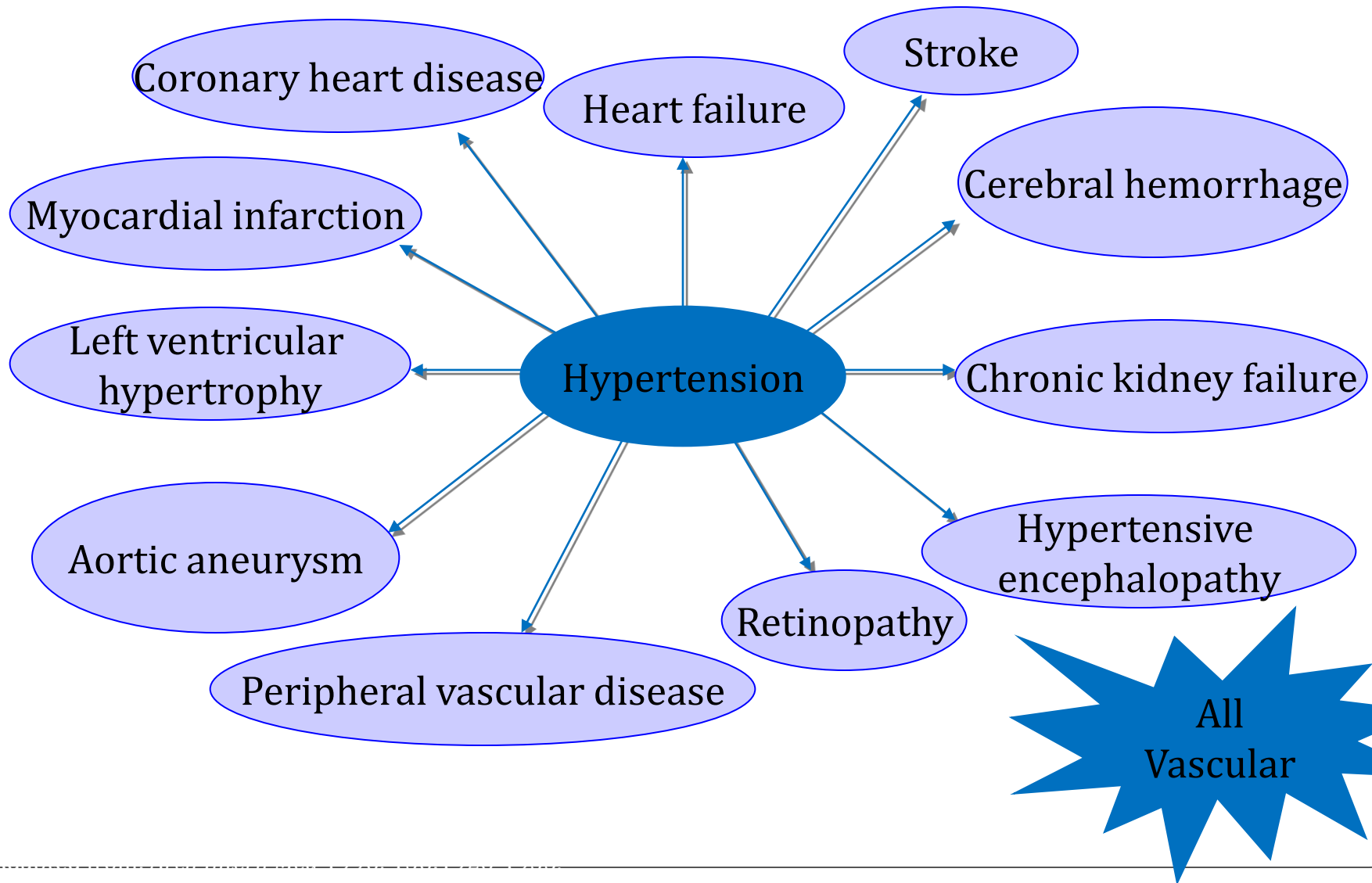
Hypertension-the problem statement

- Affects 20–60% of patients with diabetes.
- Substantially increases the risk of both macro vascular and micro vascular complications.
- Increases mortality by 7 folds.
- In diabetic nephropathy increases mortality by 37 folds.
- 85% of nephropathy patients have hypertension.

Influence of risk factors on BP

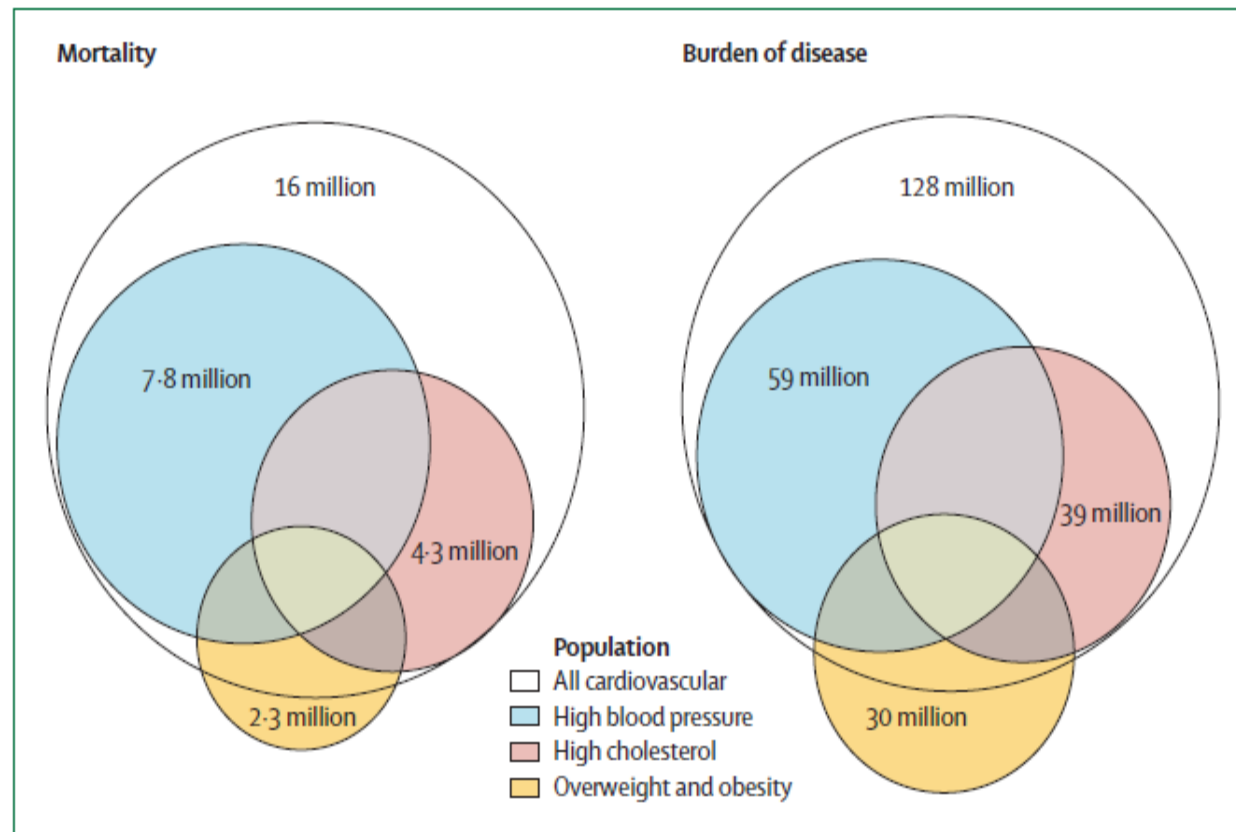


Diseases Attributable to Hypertension



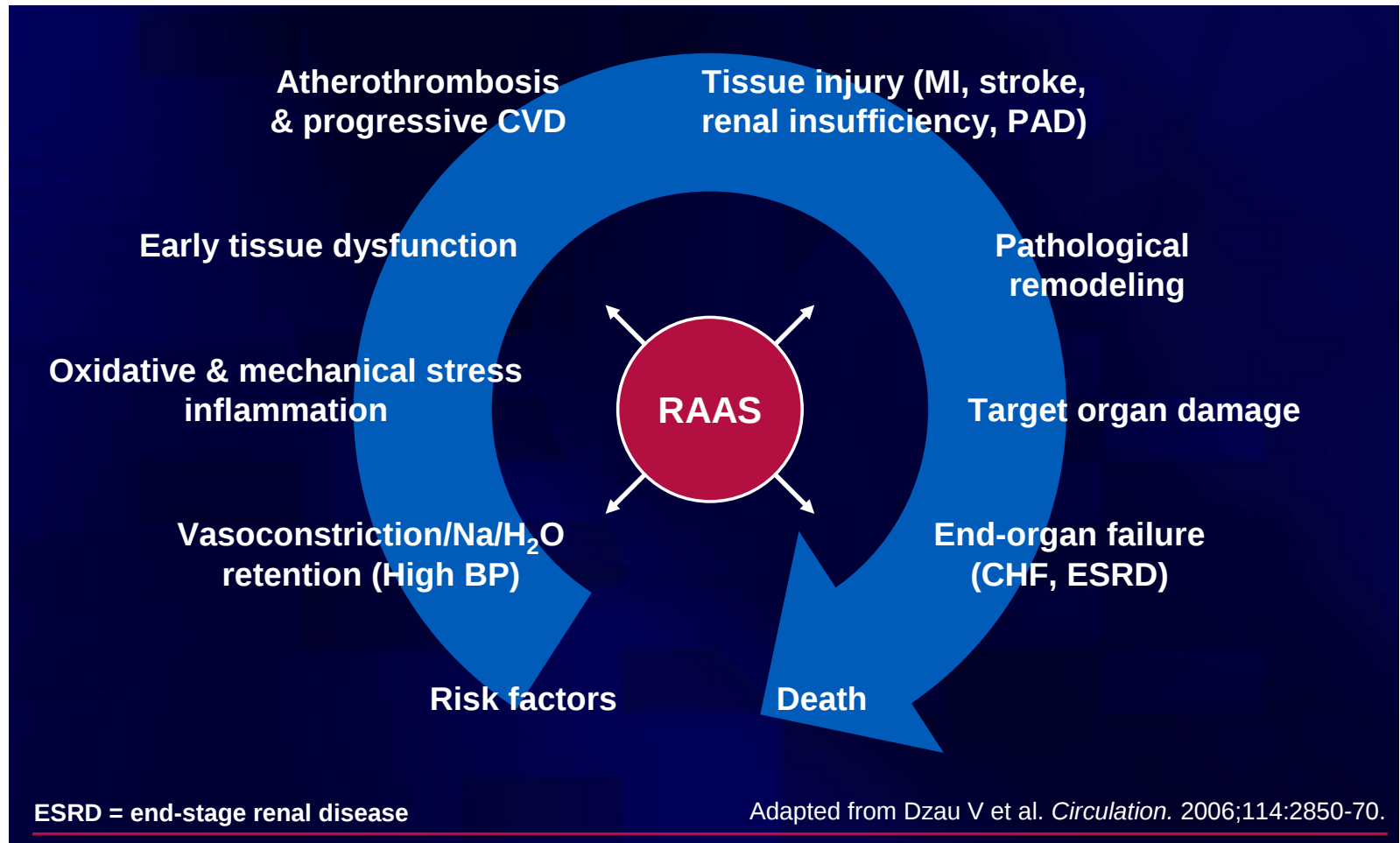
Hypertension often coexists with various conditions

58% of patients with hypertension suffer from unrecognized abnormalities of glucose metabolism i.e. either diabetes or impaired glucose tolerance



Global mortality and burden of cardiovascular disease and major risk factors for people aged 30 years

The Cardio-Renal Continuum



Challenges in Antihypertensive Therapy

How valid are office BP measurements?

- Clinicians generally agree home BP measurement should be implemented in clinical practice together with the use of ambulatory BP monitoring, both of which improve the assessment of 'real' BP levels of patients with hypertension.
- Both methods avoid the white-coat effect, in which patients experience elevated blood pressure in a clinical setting but not in other situations, and also allow the diagnosis of masked hypertension.

How valid are office BP measurements?

- In summary, threshold and in particular goal BP are enormously important for adequate control of BP, and the use of home or ambulatory BP estimations can help estimating the exact situation of the patient and improve the information obtained through office BP measurements.

Therapeutic (Clinical) Inertia?

Causes:

The failure of health care providers to initiate or intensify therapy when indicated

- ✓ Satisfaction with current BP level
- ✓ Elevated SBP more acceptable
- ✓ Use of “soft” reasons to avoid intensifying therapy
- ✓ Time constraints (15 min visits)
- ✓ Reluctance to use combination therapies
- ✓ Competing priorities

Threshold and target BPs

Questions Guiding the Evidence Review

Questions Guiding the Evidence Review

1. In adults with hypertension, does initiating antihypertensive pharmacologic therapy at specific BP thresholds improve health outcomes? **Goals**
2. In adults with hypertension, does treatment with antihypertensive pharmacologic therapy to a specified BP goal lead to improvement in health outcomes? **Targets**
3. In adults with hypertension, do various antihypertensive drugs or drug classes differ in comparative benefits and harms on specific health outcomes? **Impact of drugs**

From: 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

JAMA. 2013;(). doi:10.1001/jama.2013.284427

Table 1. Comparison of Current Recommendations With JNC 7 Guidelines

Topic	JNC 7	2014 Hypertension Guideline
Methodology	Nonsystematic literature review by expert committee including a range of study designs Recommendations based on consensus	Critical questions and review criteria defined by expert panel with input from methodology team Initial systematic review by methodologists restricted to RCT evidence Subsequent review of RCT evidence and recommendations by the panel according to a standardized protocol
Definitions	Defined hypertension and prehypertension	Definitions of hypertension and prehypertension not addressed, but thresholds for pharmacologic treatment were defined
Treatment goals	Separate treatment goals defined for “uncomplicated” hypertension and for subsets with various comorbid conditions (diabetes and CKD)	Similar treatment goals defined for all hypertensive populations except when evidence review supports different goals for a particular subpopulation
Lifestyle recommendations	Recommended lifestyle modifications based on literature review and expert opinion	Lifestyle modifications recommended by endorsing the evidence-based Recommendations of the Lifestyle Work Group
Drug therapy	Recommended 5 classes to be considered as initial therapy but recommended thiazide-type diuretics as initial therapy for most patients without compelling indication for another class Specified particular antihypertensive medication classes for patients with compelling indications, ie, diabetes, CKD, heart failure, myocardial infarction, stroke, and high CVD risk Included a comprehensive table of oral antihypertensive drugs including names and usual dose ranges	Recommended selection among 4 specific medication classes (ACEI or ARB, CCB or diuretics) and doses based on RCT evidence Recommended specific medication classes based on evidence review for racial, CKD, and diabetic subgroups Panel created a table of drugs and doses used in the outcome trials
Scope of topics	Addressed multiple issues (blood pressure measurement methods, patient evaluation components, secondary hypertension, adherence to regimens, resistant hypertension, and hypertension in special populations) based on literature review and expert opinion	Evidence review of RCTs addressed a limited number of questions, those judged by the panel to be of highest priority.
Review process prior to publication	Reviewed by the National High Blood Pressure Education Program Coordinating Committee, a coalition of 39 major professional, public, and voluntary organizations and 7 federal agencies	Reviewed by experts including those affiliated with professional and public organizations and federal agencies; no official sponsorship by any organization should be inferred

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; CKD, chronic

kidney disease; CVD, cardiovascular disease; JNC, Joint National Committee; RCT, randomized controlled trial

Comparison of Current Recommendations With JNC 7 Guidelines

Date of download: 12/21/2013

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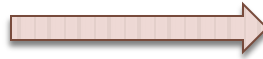
Concerning thresholds and goals!

Recommendations 1 -5

Recommendation 1

- **General population aged 60 years or older**

Initiate Treatment at :



**SBP ≥ 150 mmHg
Or
DBP ≥ 90 mmHg**

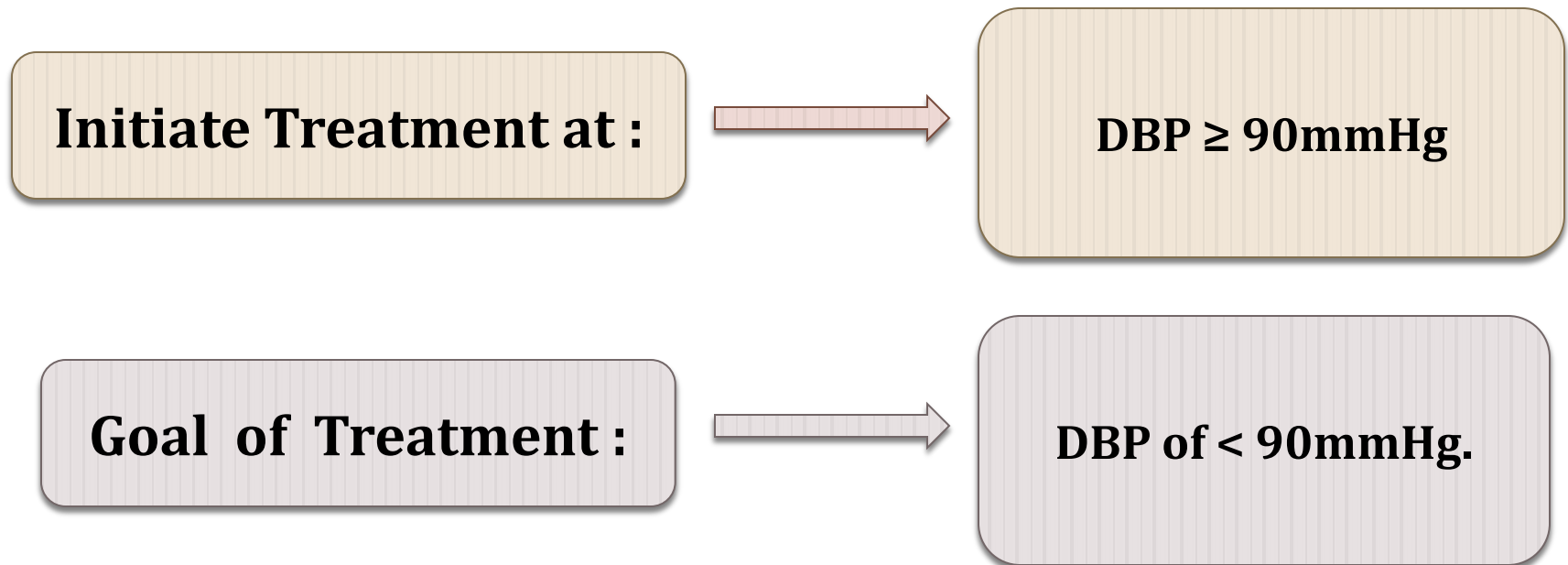
Goal of Treatment :



**SBP < 150 mmHg
OR
DBP of < 90 mmHg.**

Recommendation 2

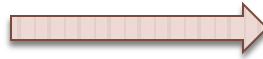
- **General population < 60 years**



Recommendation 3

- **General population < 60 years**

Initiate Treatment at :



SBP $\geq$ 140 mmHg

Goal of Treatment :

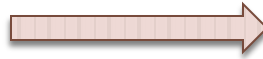


SBP of < 140 mmHg.

Recommendation 4

- **Population aged 18 years or older with CKD**

Initiate Treatment at:



**SBP $\geq$ 140 mmHg
Or
DBP $\geq$ 90 mmHg**

Goal of Treatment :

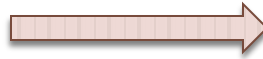


**SBP $<$ 140 mmHg
Or
DBP $<$ 90 mmHg**

Recommendation 5

- **Population aged 18 years or older with diabetes**

Initiate Treatment at:



**SBP $\geq$ 140 mmHg
Or
DBP $\geq$ 90 mmHg**

Goal of Treatment :



**SBP $<$ 140 mmHg
Or
DBP $<$ 90 mmHg**

Concerning selection of antihypertensive drugs.

Recommendations 6, 7, 8

Recommendation 6

- In General nonblack population, including those with diabetes
- Initial antihypertensive treatment should include any of the following:
 - A thiazide-type diuretic
 - Calcium channel blocker (CCB)
 - Angiotensin-converting enzyme inhibitor (ACEI) or
 - Angiotensin receptor blocker (ARB).

Recommendation 7

- In general population, including those with diabetes:
- Initial antihypertensive treatment should include :
 - Thiazide-type diuretic
 - CCB.

Recommendation 8

- Population aged 18 years or older with CKD and hypertension
- Initial (or add-on) antihypertensive treatment should include an ACEI or ARB to improve kidney outcomes.
- This applies to all CKD patients with hypertension regardless of race or diabetes status.

Recommendation 9

- The main objective of hypertension treatment is to attain and maintain goal BP.
- If goal BP is not reached within a month of treatment:
 - increase the dose of the initial drug **OR**
 - Add a second drug from one of the classes in recommendation 6 (thiazide-type diuretic, CCB, ACEI, or ARB).
- The clinician should continue to assess BP and adjust the treatment regimen until goal BP is reached.

Opinion for Starting & Adding Drugs

Recommendation 9

Recommendation 9

- If goal BP cannot be reached with 2 drugs:
 - Add and titrate a third drug from the list provided.
- Do not use an ACEI and an ARB together in the same patient.
- If goal BP cannot be reached using the drugs in recommendation 6 because of a contraindication or the need to use more than 3 drugs to reach goal BP: antihypertensive drugs from other classes can be used.



From: **2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)**

JAMA. 2013;():. doi:10.1001/jama.2013.284427

Table 5. Strategies to Dose Antihypertensive Drugs

Strategy	Description	Details
A	Start one drug, titrate to maximum dose, and then add a second drug	If goal BP is not achieved with the initial drug, titrate the dose of the initial drug up to the maximum recommended dose to achieve goal BP If goal BP is not achieved with the use of one drug despite titration to the maximum recommended dose, add a second drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB) and titrate up to the maximum recommended dose of the second drug to achieve goal BP If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose to achieve goal BP
B	Start one drug and then add a second drug before achieving maximum dose of the initial drug	Start with one drug then add a second drug before achieving the maximum recommended dose of the initial drug, then titrate both drugs up to the maximum recommended doses of both to achieve goal BP If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose to achieve goal BP
C	Begin with 2 drugs at the same time, either as 2 separate pills or as a single pill combination	Initiate therapy with 2 drugs simultaneously, either as 2 separate drugs or as a single pill combination. Some committee members recommend starting therapy with ≥ 2 drugs when SBP is >160 mm Hg and/or DBP is >100 mm Hg, or if SBP is >20 mm Hg above goal and/or DBP is >10 mm Hg above goal. If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose.

Abbreviations: ACEI, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; CCB, calcium channel blocker; DBP, diastolic blood pressure; SBP, systolic blood pressure.

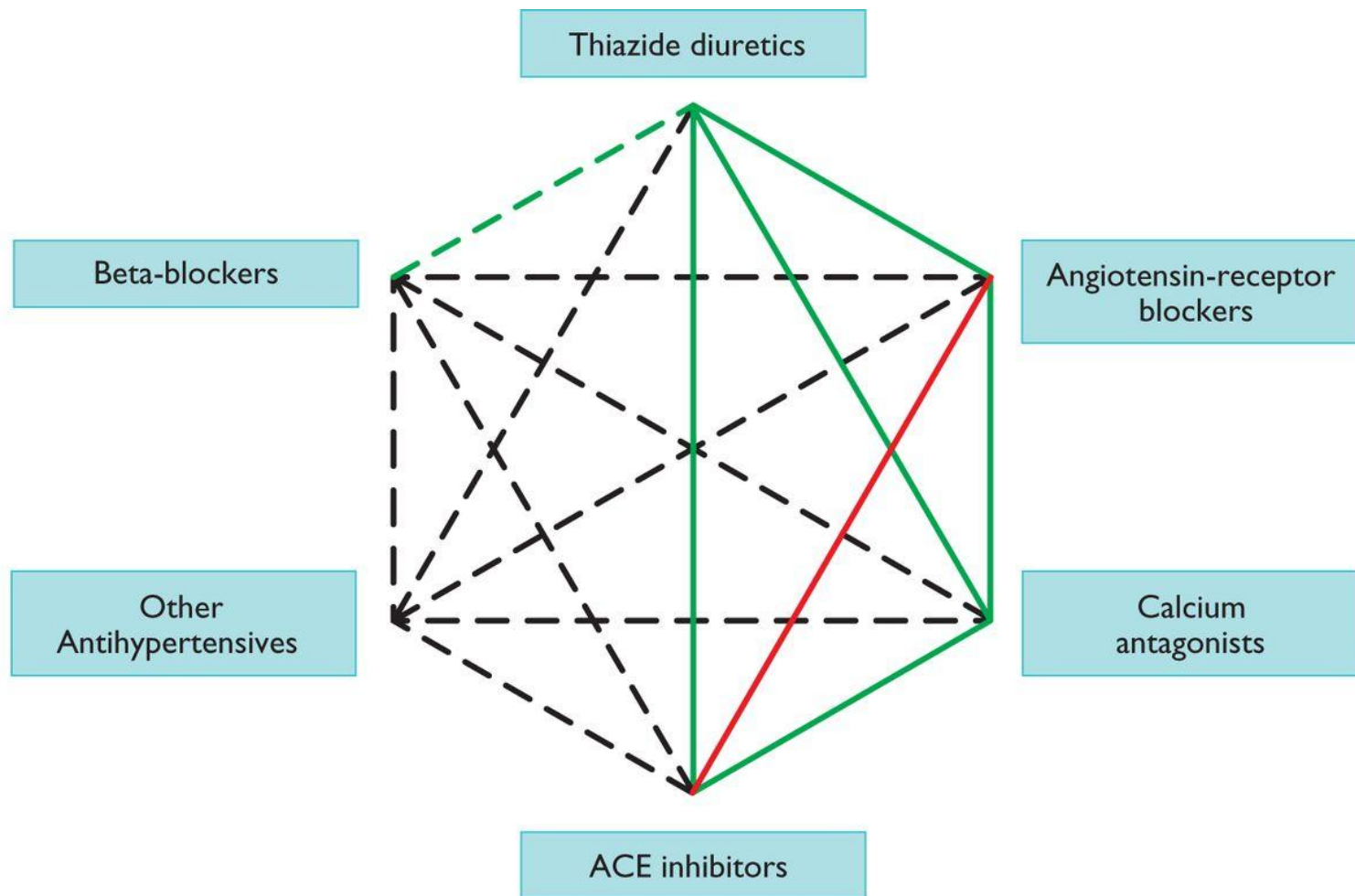
Recommendation 9

- For patients in whom goal BP cannot be attained using the above strategy OR
- The management of complicated patients for whom additional clinical consultation is needed.
- Referral to a hypertension specialist may be indicated

	JNC-8	ASH/ISH	AHA/ACC
Published on	18 th Dec 2013	19 th Dec 2013	21 st Nov 2013
Target goal For general patients including DM/CKD	<140/90	<140/90	<140/90 Lower targets may be appropriate for LVD, LVH, DM, CKD
For Elderly people	150/90(≥60 yrs)	150/90(≥80 yrs)	Lower targets for the Elderly
Treatment preference			
General <60 yrs	Initiate Thiazide-type Diuretic or ACEI or ARB or CCB For uptitration, any possible combination from above (avoid ACEI+ARB)	Stage 1 HT: ACEI or ARB (If needed, add CCB or Thiazide-type Diuretic)	Stage 1 HT: Thiazide for most patients or ACEI, ARB, CCB, (or combination, if uncontrolled)
		Stage 2 HT: ACEI or ARB + CCB or Thiazide-type Diuretic	Stage 2 HT: Thiazide with ACEI / ARB/ CCB, or ACEI with CCB
General ≥60 yrs	Same as above	Stage 1: CCB or Thiazide (If needed, add ACEI or ARB)	Same as Above
Hypertension with Diabetes	Same as above	ACEI or ARB If needed add CCB or thiazide-type diuretic	ACEI or ARB, thiazide, BB, calcium channel blocker
Hypertension with CKD	ACEI or ARB alone Or in combination with other	ACEI or ARB If needed add CCB or thiazide-type diuretic	ACEI or ARB

Comparison..(cont.)

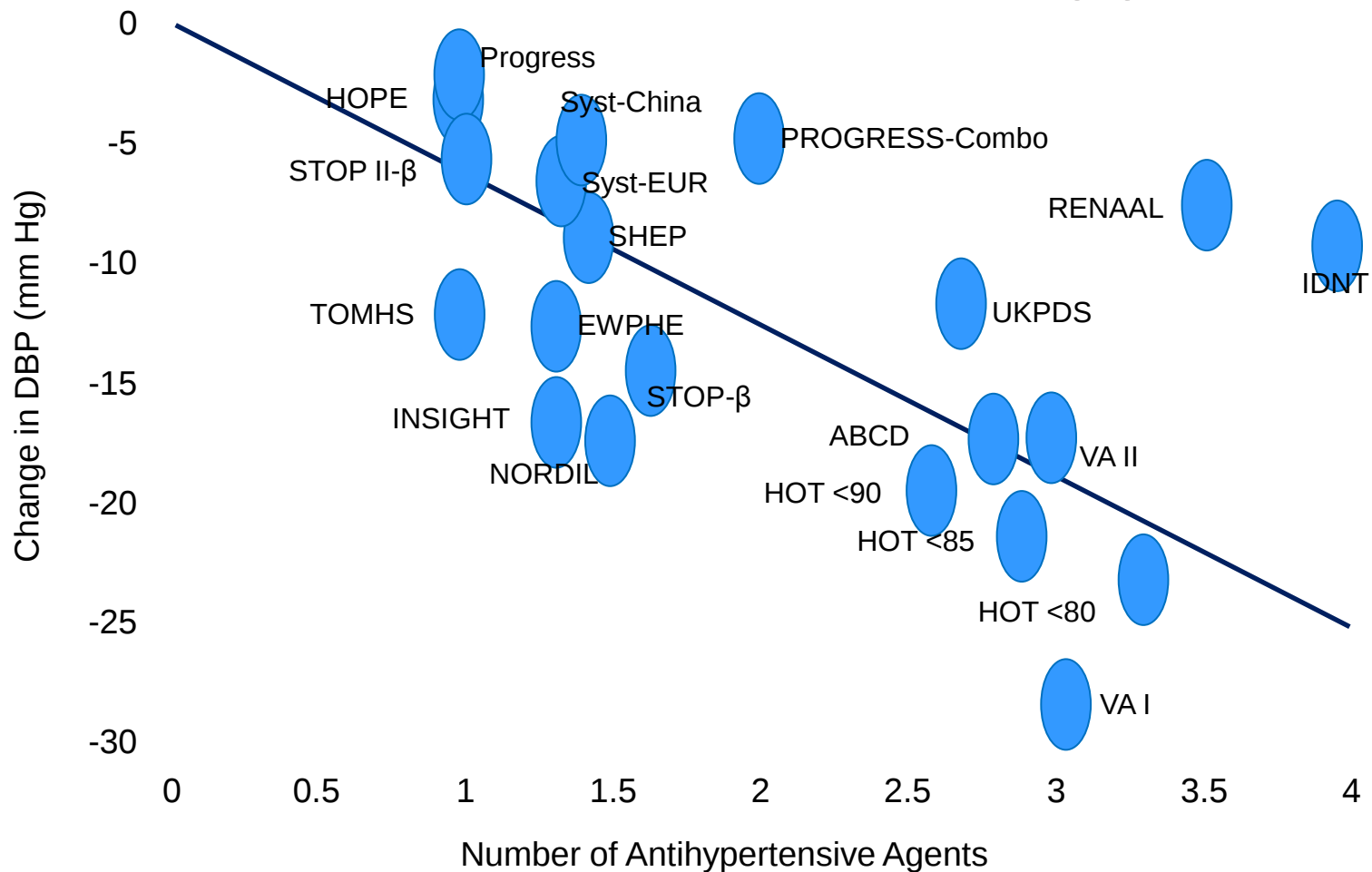
Hypertension with CAD	---	β -Blocker plus ARB or ACE inhibitor If needed add CCB or thiazide-type diuretic	β -Blocker, ACEI
Hypertension with stroke	---	ACE inhibitor or ARB If needed add CCB or thiazide-type diuretic	Thiazide, ACEI.
Hypertension with HF	---	ARB or ACE inhibitor+ β - blocker+ diuretic+ spironolactone regardless of blood pressure	ACEI or angiotensin-receptor blocker (ARB), BB, aldosterone antagonist, thiazide;



ACE = angiotensin-converting enzyme.

Green continuous lines: preferred combinations;
Green dashed line: useful combination (with some limitations);
Black dashed lines: possible but less well-tested combinations;
Red continuous line: not recommended combination.

Need for Combination Therapy



Patient Compliance

Challenges in Hypertension Management

How to improve adherence to antihypertensive treatment

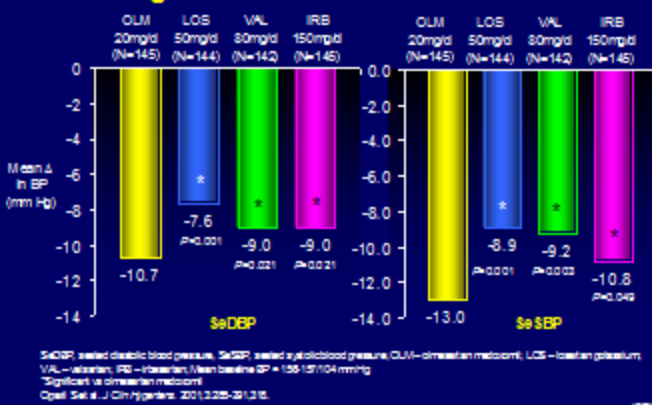
- Inform the patient about the risk of hypertension and the benefit of effective treatment
- Provide the patient with clear written and oral instructions about treatment
- Tailor the treatment regimen to the patient's lifestyle needs
- Simplify treatment by reducing, if possible, the number of daily medications

How to improve adherence to antihypertensive treatment

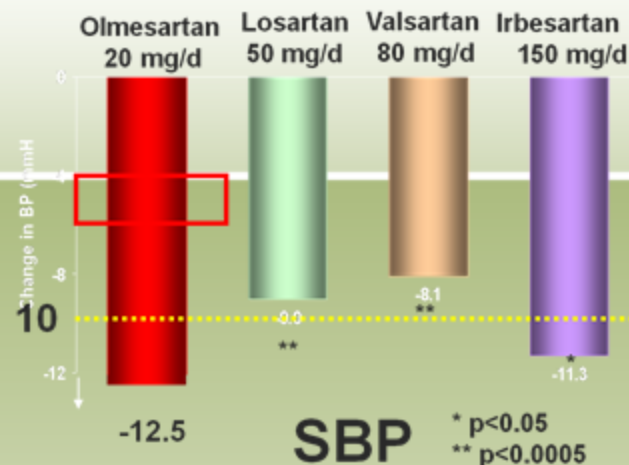
- Involve the patient's partner or family in information on disease and treatment plans
- Make use of self measurement of blood pressure at home and of behavioral strategies, such as reminder systems
- Pay great attention to adverse effects (even if subtle) and be prepared to change drug doses or drug types, if needed
- Engage in a dialog with the patient regarding adherence, and be informed of his or her problems
- Provide a reliable patient-support system at affordable prices

Olmesartan

Early Onset of Effect Change in Cuff DBP and SBP at Week 2



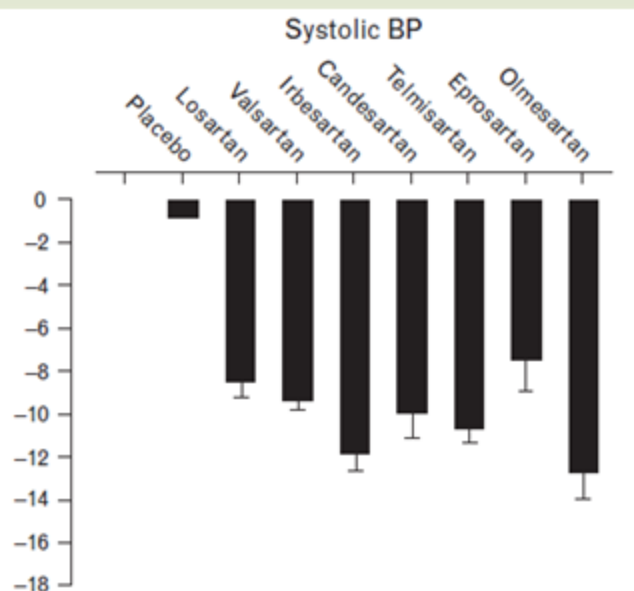
Strong BP lowering



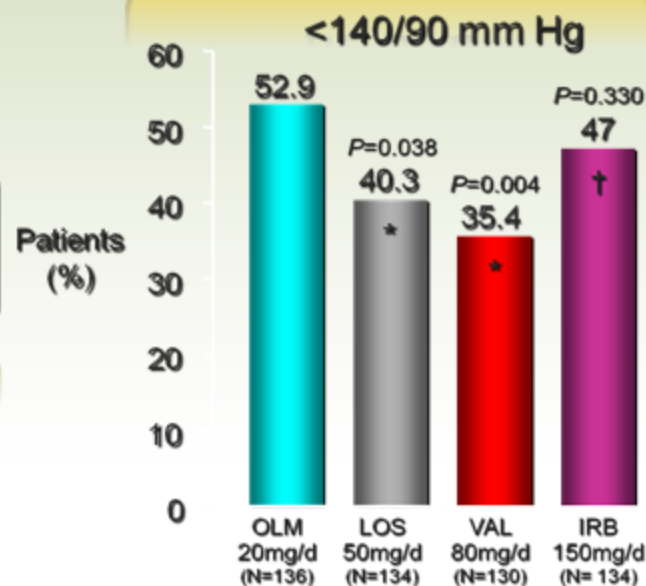
Faster Onset

**Superior
BP Control**

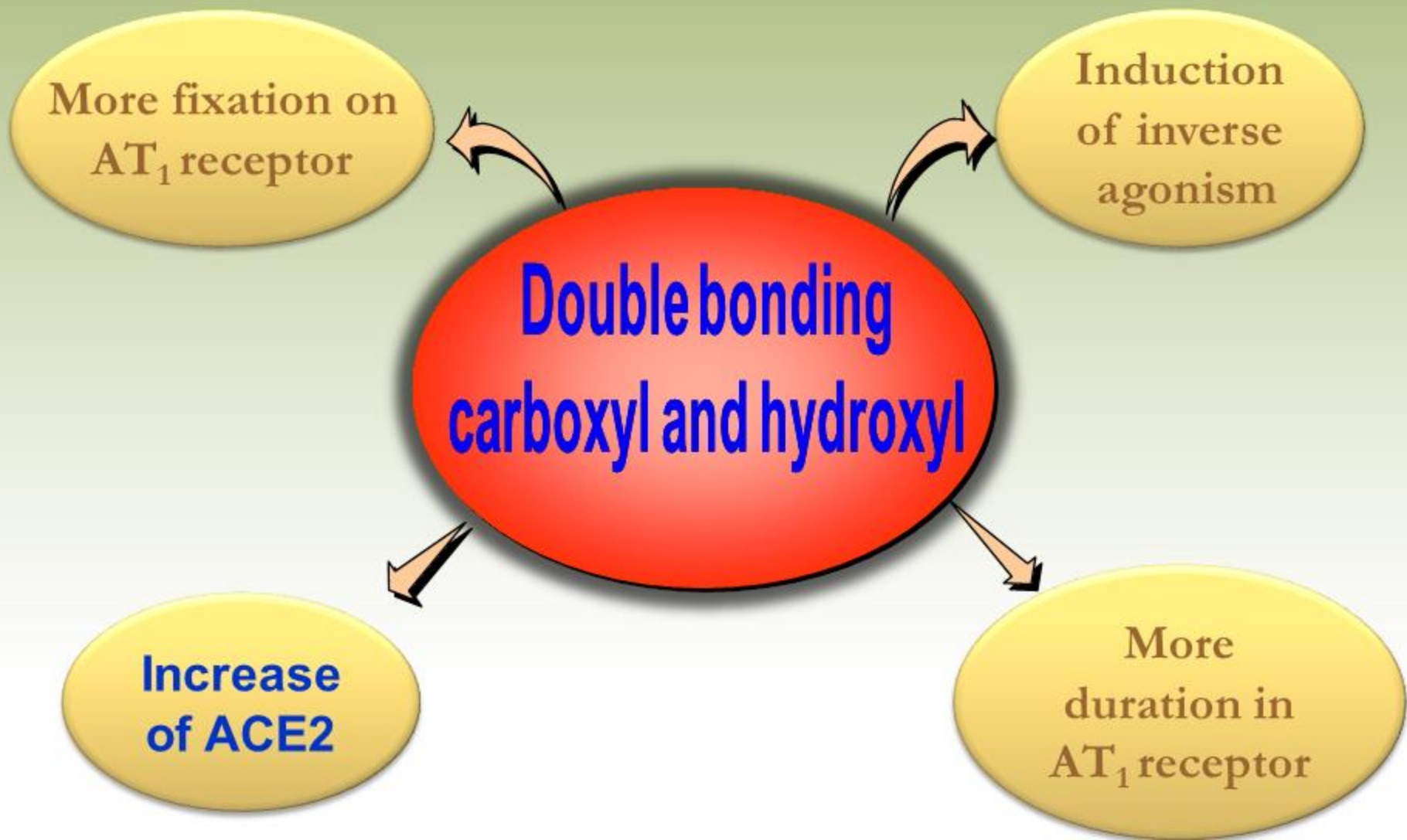
**More Pts achieving
BP Goal**



24 Hrs BP control

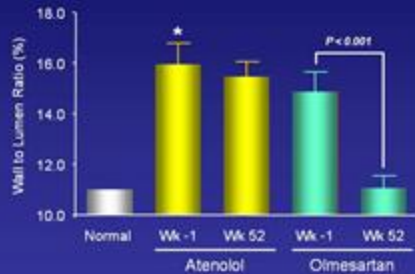


Unique Characteristic of Olmesartan



VIOS

Oltmesartan Medoximil But Not Atenolol Reverses Vascular Hypertrophy

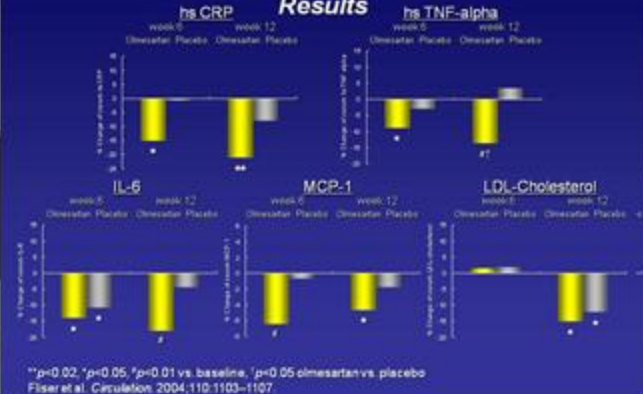


Journal of The American Society of Hypertension (2) 3: 165-172, 2008
Journal of The American Society of Hypertension (2) 3: 165-172, 2008

Anti-inflammatory

EUTOPIA

Results



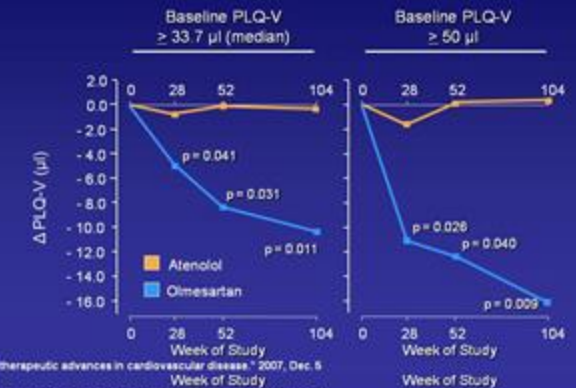
Vascular Hypertrophy

Vascular Protection

Anti-Atherosclerosis

MORE

Mean changes (Δ) in plaque volume (PLQ-V) from baseline at 28-, 52- and 104-week follow-up



Atheroma Regression

Changes in IVUS Parameters

Table 6

Changes in IVUS Parameters From Baseline to Follow-Up

	Control (n = 121)	Oltmesartan (n = 126)	p Value
Nominal change			
Atheroma volume (mm ³)	7.1 (1.8-12.4)*	-2.6 (-7.9-2.8)	0.011
Lumen volume (mm ³)	0.3 (-8.7-9.3)	0.4 (-7.6-8.3)	0.989
Vessel volume (mm ³)	7.8 (2.5-10.5)	-2.1 (-8.5-2.5)	0.178
PAV (%)	1.1 (0.1-2.1)†	-0.1 (-0.9-0.8)	0.085
Change in total atheroma volume and PAV			
Total atheroma volume (%)	5.4 (2.4-8.5)	0.6 (-1.9-3.1)	0.016
PAV (%)	3.1 (0.7-5.6)	-0.7 (-3.4-2.0)	0.038

Value within parentheses indicates 95% confidence interval. *p = 0.009; †p = 0.039 between baseline and follow-up.

Abbreviations as in Table 5.

Conclusion

- Key to the successful clinical management of hypertension is attaining the best BP control among patients with hypertension after having adequately established that BP is elevated and whether other cardiovascular risk factors exist.
- The long-term benefits of an adequate management of hypertension in a given patient are determined by the stage of cardiovascular and renal disease when treatment is initiated and on the basis of the adequacy of the simultaneous control of other coexisting cardiovascular risk factors.