Updated Guidelines in Hypertension Managements

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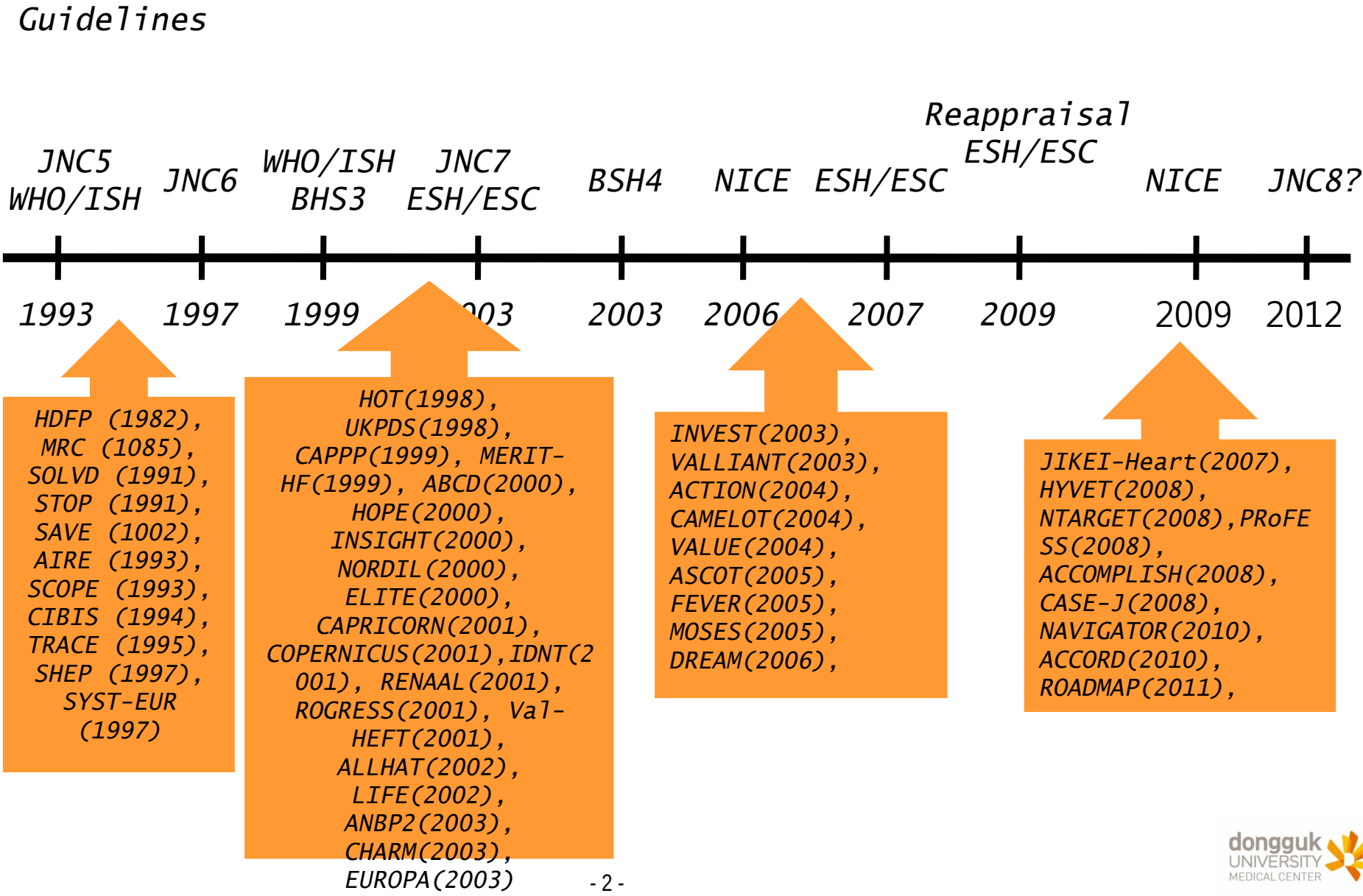
Guidelines and Clinical trials



Updates (? Changes)

- Classification of severity of hypertension
- Goal of blood pressure management: target BP
- Diagnosis of hypertension
- When to initiate drug treatment
- Choice of antihypertensive drugs: first line drug?

Blood Pressure Classification Systolic BP/Diastolic BP

	WHO/ISH	ESH-ESC	JCN 7	WHO/ISH	ESH-ESC	JCN 7
	SBP			DBP		
Optimal	< 120	< 120		< 80	< 80	
Normal	< 130	120-129	< 120	< 85	80-84	< 80
High-Normal	130-139	130-139		85-89	85-89	
Grade 1 Hypertension (mild)	140-159	140-159		90-99	90-99	
Subgroup: Borderline	140-149			90-94		
Grade2 Hypertension (moderate)	160-179	160-179		100-109	100-109	
Grade 3 Hypertension (severe)	≥ 180	≥ 180		≥ 110	≥ 110	
Isolated Systolic Hypertension	≥ 140	≥ 140		< 90	< 90	
Subgroup: Borderline	140-149			< 90		
Pre-Hypertension			120-139			80-89
Stage 1			140-159			90-99
Stage 2			≥ 160			≥ 100

Assessment of frequency of progression to hypertension in non-hypertensive participants in the Framingham Heart Study

	Age 35–64 years	Age 65–94 years
Baseline BP category		
*% hypertension at 1 year (95% CI)**		
Optimum BP	1·3 (1·1–1·6)	4·3 (3·1–5·7)
Normal BP	4·7 (4·0–5·5)	7·1 (5·5–9·0)
High normal BP	11·0 (9·6–12·6)	15·7 (13·0–18·8)
*% hypertension at 2 years (95% CI)**		
Optimum BP	2·7 (2·2–3·2)	8·3 (6·2–11·1)
Normal BP	9·2 (7·9–10·7)	13·7 (10·8–17·2)
High normal BP	20·8 (18·3–23·5)	28·9 (24·2–34·0)
*% hypertension at 3 years (95% CI)**		
Optimum BP	4·0 (3·3–4·8)	12·2 (9·2–16·1)
Normal BP	13·5 (11·6–15·7)	19·8 (15·7–24·6)
High normal BP	29·6 (26·2–33·1)	40·1 (34·0–46·4)

*Rates are per 100, and are adjusted for sex, age, body-mass index, baseline examinations, and baseline systolic and diastolic BP.

Table 4: **Incidence rates of hypertension at 1, 2, and 3 years**

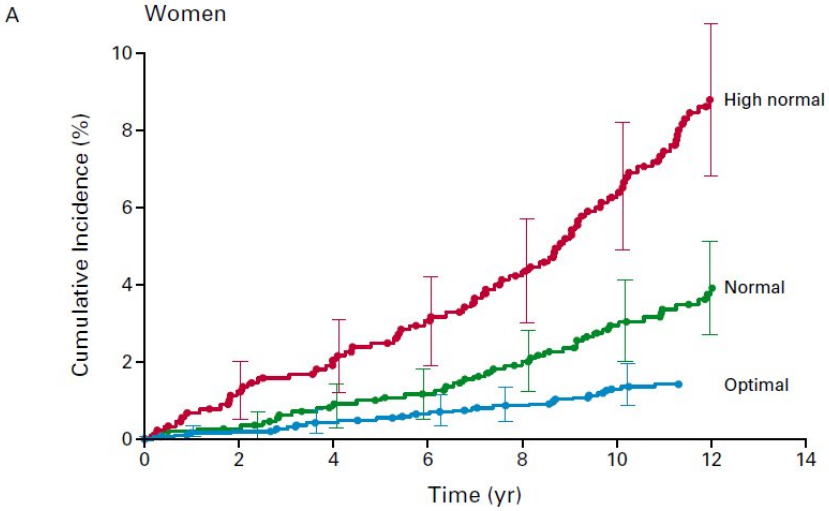
	Odds ratio (95% CI)	
	Age 35–64 years	Age 65–94 years
Variable		
Optimum BP	Referent	Referent
Normal BP	4·1 (3·4–4·9)*	2·0 (1·4–2·7)*
High normal BP	11·6 (9·6–14·0)*	5·5 (4·0–7·4)*
Age‡	1·6 (1·5–1·8)*	1·2 (0·95–1·5)†
Body-mass index‡	1·1 (1·1–1·2)*	1·0 (0·98–1·1)†
Weight gain‡	1·3 (1·2–1·4)*	1·2 (1·1–1·3)*

*p<0·0001; †p>0·10. ‡Odds ratios are for 10-year age difference, a difference in body-mass index of 2 kg/m^2, and for a 5% weight gain on follow-up. All models adjust for sex and baseline examination.

Table 5: **Odds ratios for multivariable logistic regression**

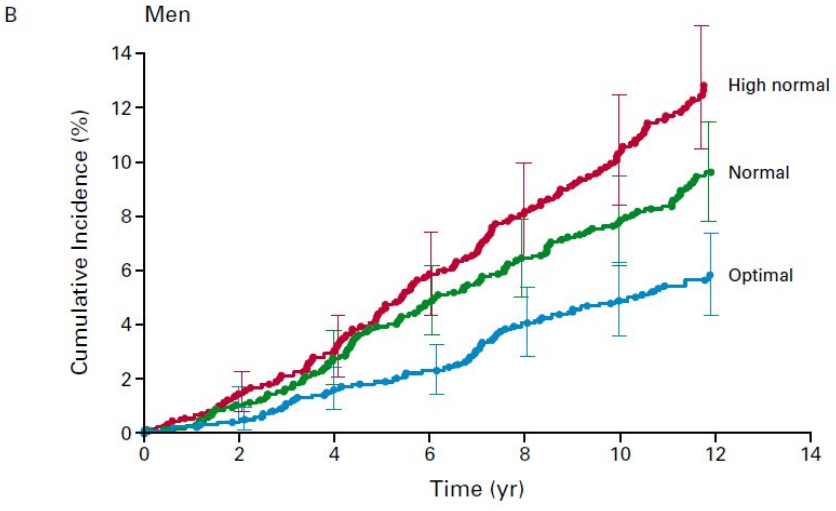
Lancet 2001; 358: 1682–86

Impact of high-normal blood pressure on the risk of car diovascular disease



No. at Risk

Optimal	1875	1867	1851	1839	1821	1734	887
Normal	1126	1115	1097	1084	1061	974	649
High normal	891	874	859	840	812	722	520



No. at Risk

Optimal	1005	995	973	962	934	892	454
Normal	1059	1039	1012	982	952	892	520
High normal	903	879	857	819	795	726	441

Optimal BP < 120/80 mm Hg
Normal BP 120 – 129/80 - 84 mm Hg
High-normal BP 130 – 139/85 - 89 mm Hg

Type of Model and Blood-Pressure Category*	Hazard Ratio (95% Confidence Interval)	
	Women (n=3892)	Men (n=2967)
Models with blood pressure defined at base line†		
Optimal (2880 subjects)	1.0	1.0
Normal (2185 subjects)	1.5 (0.9–2.5)‡	1.3 (1.0–1.9)§
High normal (1794 subjects)	2.5 (1.6–4.1)¶	1.6 (1.1–2.2)‖
P for trend across categories	<0.001	0.01
Models with blood-pressure category and covariates defined as time-dependent variables**		
Optimal	1.0	1.0
Normal	1.1 (0.6–2.0)‡	1.3 (0.8–1.9)‡
High normal	1.8 (1.0–3.1)§	1.6 (1.1–2.3)‖
Hypertension	2.9 (1.7–5.2)¶	2.0 (1.3–2.9)¶
P for trend across categories	<0.001	<0.001

N Engl J Med 2001;345:1291–1297

ESH/ESC 2007 announcement for “prehypertension”

1. even in the Framingham study the risk of developing hypertension was definitely higher in subjects with high normal (130–139/85–89mmHg) than in those with normal blood pressure (120–129/80–84mmHg) and therefore there is little reason to join the two groups together
2. given the ominous significance of the word hypertension for the layman, the term “prehypertension” may create anxiety and request for unnecessary medical visits and examinations in many subjects
3. most importantly, although lifestyle changes recommended by the 2003 JNC 7 Guidelines for all prehypertensive individuals may be a valuable population strategy, in practice this category is a highly differentiated one, with the extremes consisting of subjects in no need of any intervention (e.g. an elderly individual with a blood pressure of 120/80mmHg) as well as of those with a very high or high risk profile (e.g. after stroke or with diabetes) in whom drug treatment is required.

Updates (? Changes)

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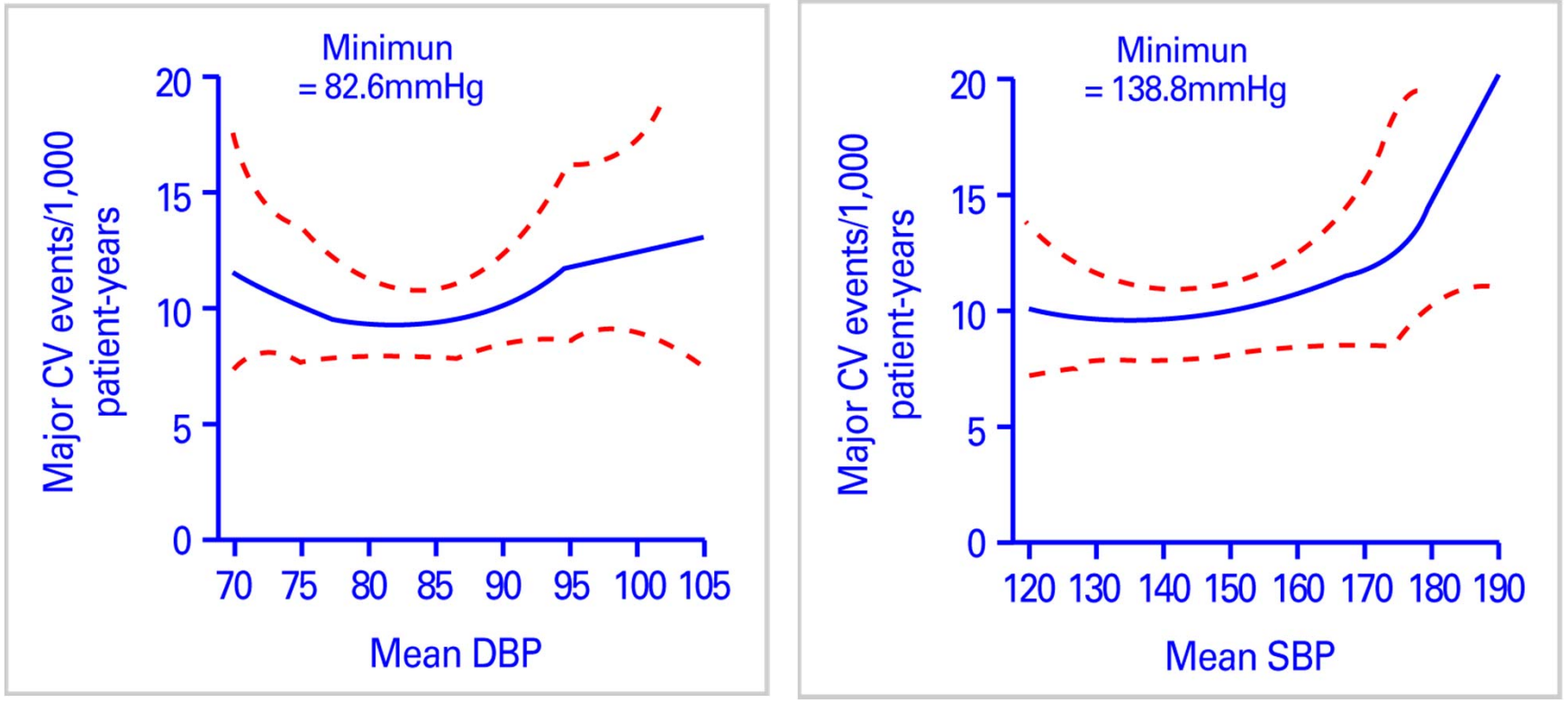
BP Goals of Treatment: HOT, estimated incidence of major CV events

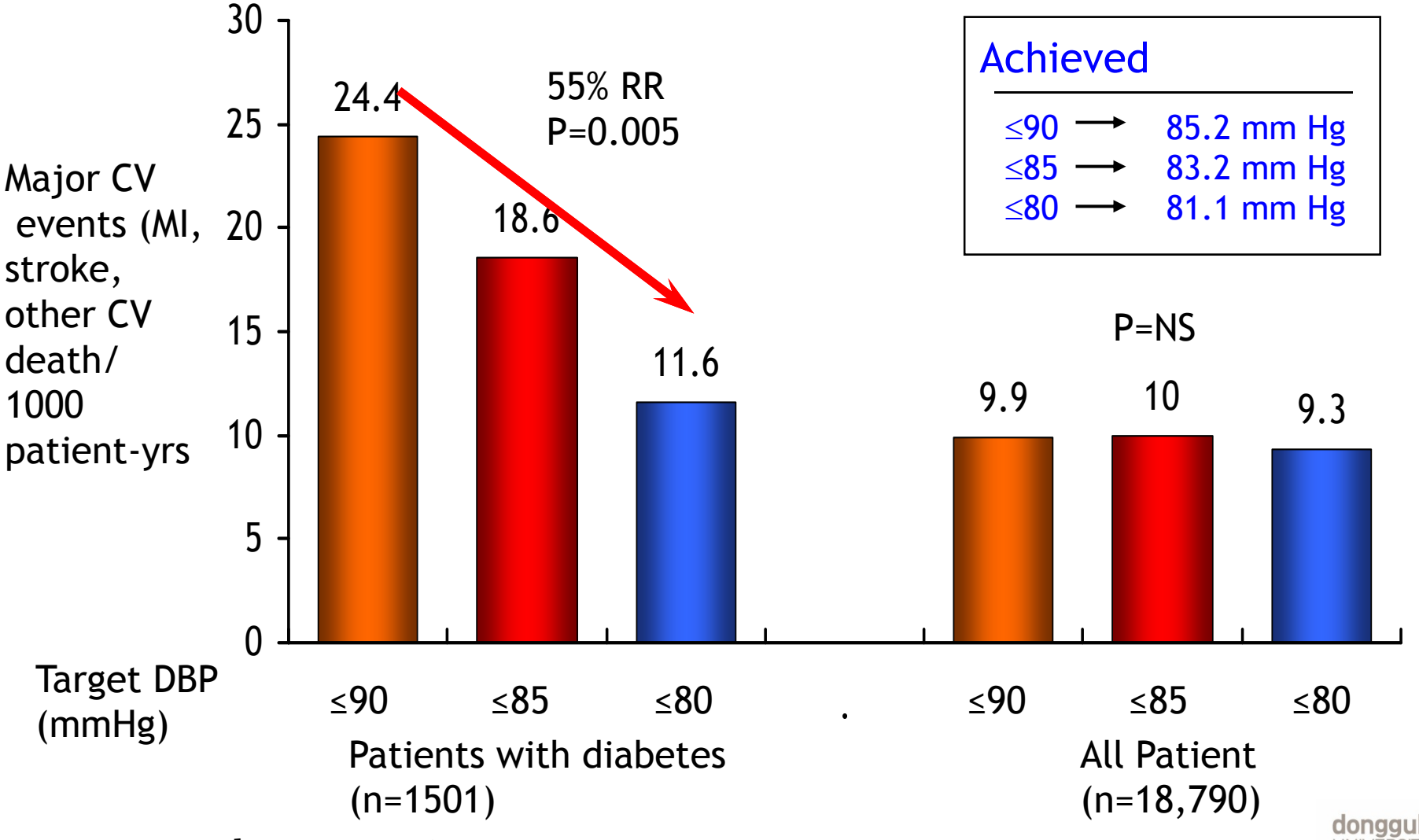


Benefits shown for lowering SBP to 140 mmHg and DBP to ≤85 mmHg but additional lowering SBP to 120 mmHg, and DBP to 70 mmHg appears to give little further benefit, although does not cause any significant additional risk

Hansson et al. Lancet 1998;351:1755–62

BP Goals of Treatment in High Risk Patients

HOT trial: Effect of target DBP on CV event over 4 yrs in patients with Diabetes



Hansson L. et al. Lancet 1998;351:1755-62

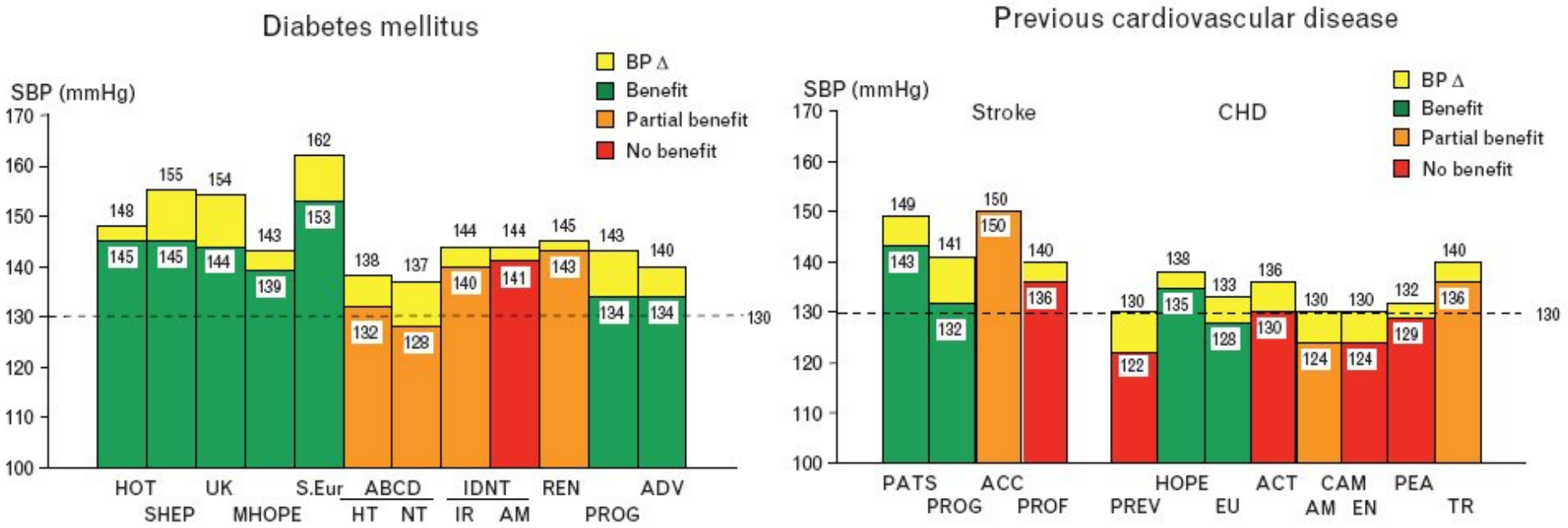
Goals of Therapy: JNC7

- Reduce CVD and renal morbidity and mortality.
- Treat to BP <140/90 mmHg or BP <130/80 mmHg in patients with diabetes or chronic kidney disease.
- Achieve SBP goal especially in persons > 50 years of age.

Goals of Therapy: ESH/ESC2007

- Maximum decrease in long-term total CV risk
- Treatment of
  - All reversible risk factors
  - Associated conditions
  - Raised BP per se
- Target BP
  - At least < 140/90 mmHg in all HTs
  - Definitely lower values, if tolerated
  - < 130/80 mmHg in diabetics and in high or very high risk patients, such as those with associated clinical conditions (stroke, myocardial infarction, renal dysfunction, proteinuria).
- SBP < 140 mmHg difficult to achieve, particularly in elderly
- In order to more easily achieve goal BP, antihypertensive treatment should be initiated before significant cardiovascular damage develops

Achieved SBP in patients randomized to a more active (filled rectangles) or less active (open rectangles) treatment in trials



Reappraisal of European guidelines on hypertension Management. J Hypertens 2009;27

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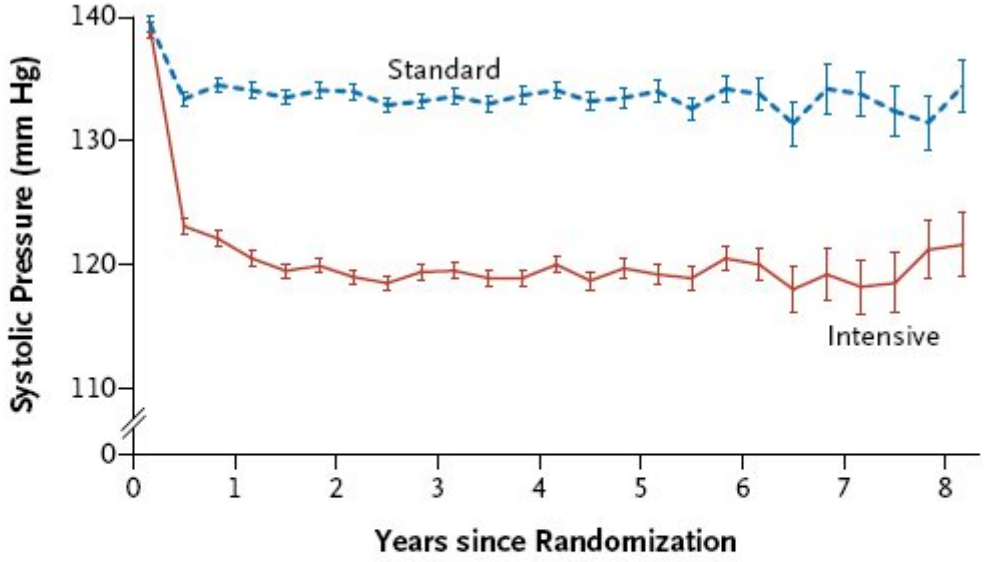
Effects of Intensive BP Control in Type 2 DM

N = 4733 with type 2 DM (high normal BP and hypertension ≥ 130 mmHg)

Intensive therapy < 120 mmHg (SBP)
Standard therapy <140 mmHg (SBP)

Primary composite outcome: nonfatal MI, nonfatal stroke, death from CV cause



Mean No. of Medications Prescribed								
Intensive	3.2	3.4	3.4	3.5	3.5	3.5	3.4	3.4
Standard	1.9	2.1	2.1	2.2	2.2	2.3	2.3	2.3
No. of Patients								
Intensive	2174	2071	1973	1792	1150	445	156	156
Standard	2208	2136	2077	1860	1241	504	203	201

ACCORD Study Group. N Engl J Med. 2010;362:1575-85.

Effects of Intensive BP Control in Type 2 DM: primary and secondary outcomes

Outcome	Intensive Therapy (N=2363)		Standard Therapy (N=2371)		Hazard Ratio (95% CI)	P Value
	no. of events	*%/yr*	*no. of events*	*%/yr*		
Primary outcome*	208	1.87	237	2.09	0.88 (0.73–1.06)	0.20
Prespecified secondary outcomes						
Nonfatal myocardial infarction	126	1.13	146	1.28	0.87 (0.68–1.10)	0.25
Stroke						
Any	36	0.32	62	0.53	0.59 (0.39–0.89)	0.01
Nonfatal	34	0.30	55	0.47	0.63 (0.41–0.96)	0.03
Death						
From any cause	150	1.28	144	1.19	1.07 (0.85–1.35)	0.55
From cardiovascular cause	60	0.52	58	0.49	1.06 (0.74–1.52)	0.74
Primary outcome plus revascularization or nonfatal heart failure	521	5.10	551	5.31	0.95 (0.84–1.07)	0.40
Major coronary disease event†	253	2.31	270	2.41	0.94 (0.79–1.12)	0.50
Fatal or nonfatal heart failure	83	0.73	90	0.78	0.94 (0.70–1.26)	0.67

No of stroke difference = 26

ACCORD Study Group. N Engl J Med. 2010;362:1575-85.

Effects of Intensive BP Control in Type 2 DM: SEA and AE

Variable	Intensive Therapy (N=2362)	Standard Therapy (N=2371)	P Value
Serious adverse events — no. (%)†			
Event attributed to blood-pressure medications	77 (3.3)	30 (1.27)	<0.001
Hypotension	17 (0.7)	1 (0.04)	<0.001
Syncope	12 (0.5)	5 (0.21)	0.10
Bradycardia or arrhythmia	12 (0.5)	3 (0.13)	0.02
Hyperkalemia	9 (0.4)	1 (0.04)	0.01
Angioedema	6 (0.3)	4 (0.17)	0.55
Renal failure	5 (0.2)	1 (0.04)	0.12
End-stage renal disease or need for dialysis	59 (2.5)	58 (2.4)	0.93
Adverse laboratory measures — no. (%)			
Potassium <3.2 mmol/liter	49 (2.1)	27 (1.1)	0.01
Potassium >5.9 mmol/liter	73 (3.1)	72 (3.0)	0.93
Elevation in serum creatinine			
>1.5 mg/dl in men	304 (12.9)	199 (8.4)	<0.001
>1.3 mg/dl in women	257 (10.9)	168 (7.1)	<0.001
Estimated GFR <30 ml/min/1.73 m²	99 (4.2)	52 (2.2)	<0.001

No of SEA difference = 47

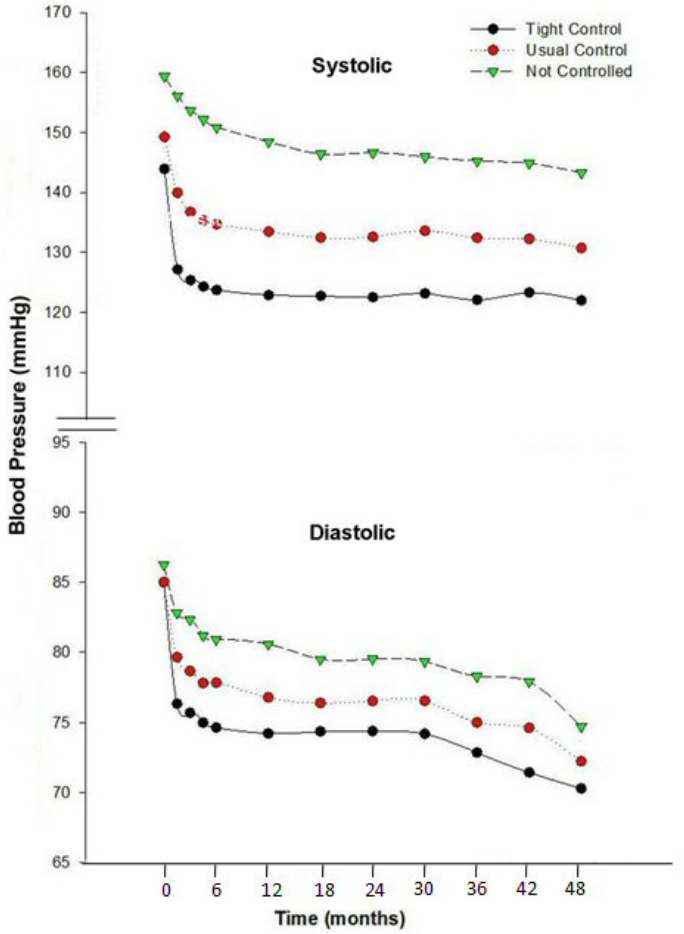
ACCORD Study Group. N Engl J Med. 2010;362:1575-85.

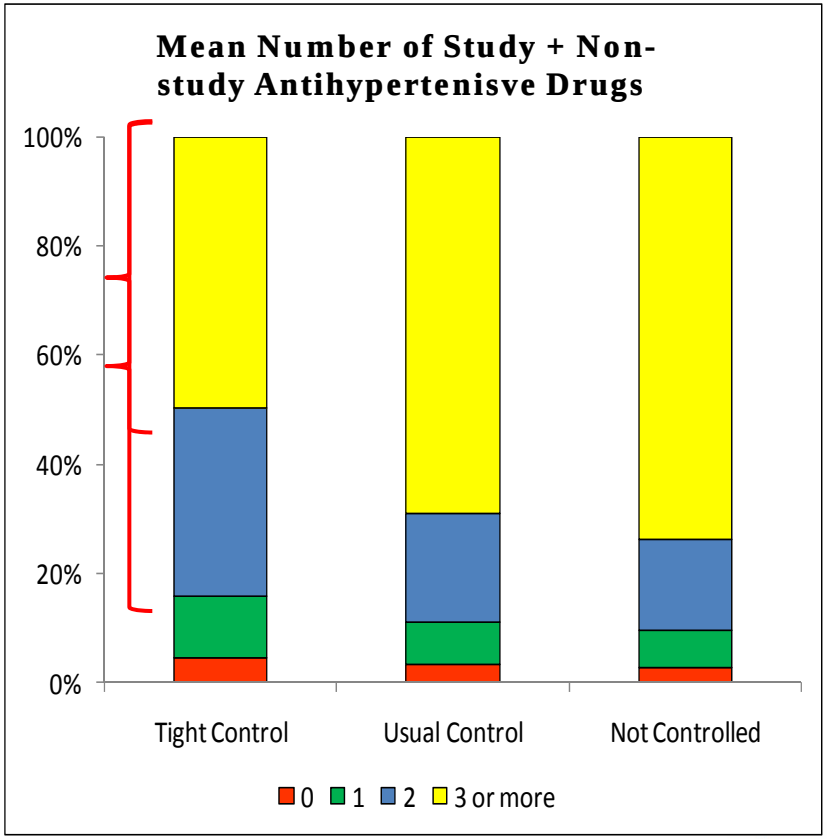
INVEST Results – BP Reduction

Patient with CAD and hypertension

Patients with diabetes at baseline grouped according to mean on-treatment SBP

Tight Control	• <130 mm Hg
Usual Control	• ≥130-<140 mm Hg
Not Controlled	• ≥140 mm Hg



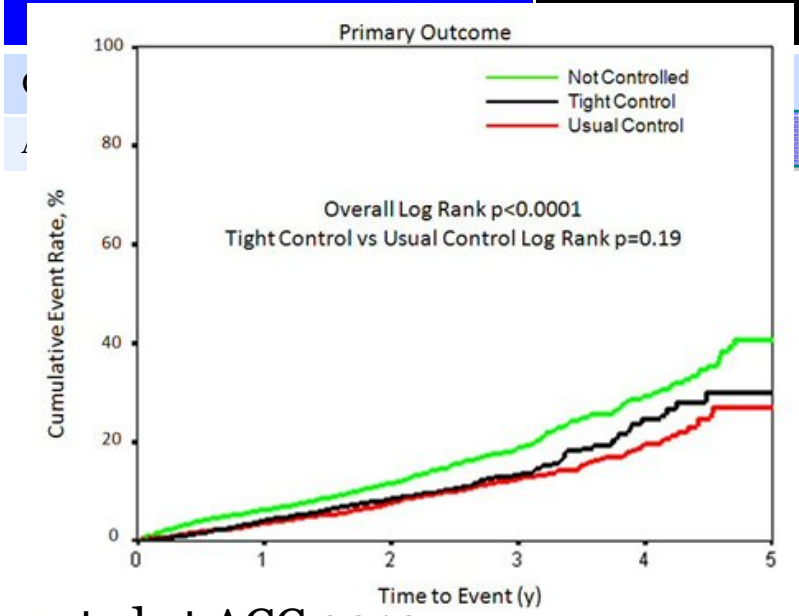


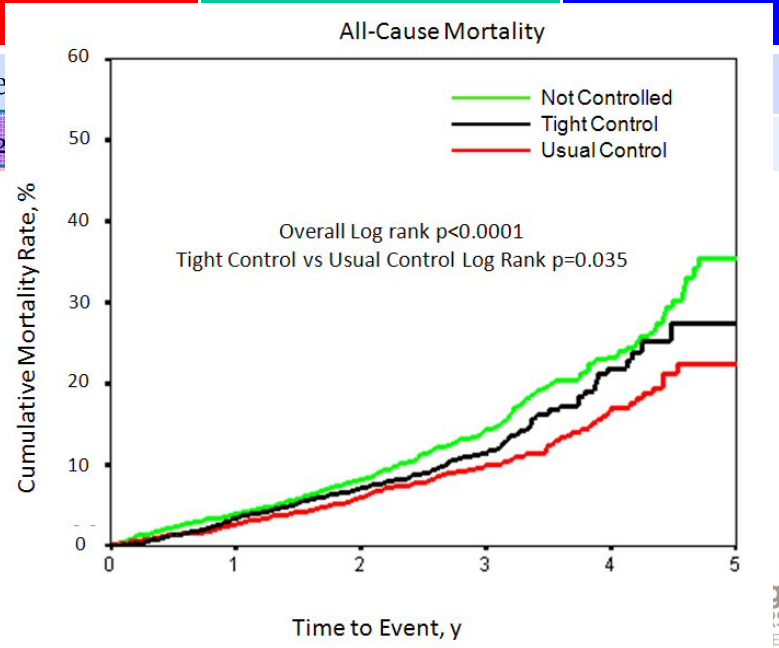
Presented at ACC 2010

Results of INVEST: Outcome Rates

INVEST Follow Up n=6400	Tight Control n=2,255	Usual Control n=1,970	Not Controlled n=2,175	p value
Outcome	# of Events (Event Rate %)			
Primary Outcome	286 (12.7)	249 (12.6)	431 (19.8)	< 0.0001
Nonfatal MI	29 (1.3)	33 (1.7)	67 (3.1)	0.008
Nonfatal Stroke	22 (1.0)	26 (1.3)	52 (2.4)	0.001
Total MI	108 (4.8)	100 (5.0)	185 (8.5)	< 0.0001
Total Stroke	34 (1.5)	33 (1.7)	70 (3.2)	0.0001
All Cause Mortality	248 (11.0)	201 (10.2)	334 (15.4)	< 0.0001

Extended Follow Up n=4370	Tight Control n=1,389	Usual Control n=1,423	Not Controlled n=1,558	p value





Presented at ACC 2010

2009 ESH/ESC Blood Pressure Goals of Treatment

Box 4. Blood pressure goals of treatment

(1) On the whole, there is sufficient evidence to recommend that SBP be lowered below 140 mmHg (and DBP below 90 mmHg) in all hypertensive patients, both those at low moderate risk and those at high risk. Evidence is only missing in the elderly hypertensive patients, in whom the benefit of lowering SBP below 140 mmHg has never been tested in randomized trials.

(2) The recommendation of previous guidelines to aim at a lower goal SBP (<130 mmHg) in diabetic patients and in patients at very high cardiovascular risk (previous cardiovascular events) may be wise, but it is not consistently supported by trial evidence. In no randomized trial in diabetic patients has SBP been brought down to below 130 mmHg with proven benefits, and trials in which SBP was lowered to below 130 mmHg in patients with previous cardiovascular events have given controversial results.

(3) Despite their obvious limitations and a lower strength of evidence, *post hoc* analyses of trial data indicate a progressive reduction of cardiovascular events incidence with progressive lowering of SBP down to about 120 mmHg and DBP down to about 75 mmHg, although the additional benefit at low BP values becomes rather small. A J-curve phenomenon is unlikely to occur until lower values are reached, except perhaps in patients with advanced atherosclerotic artery diseases.

(4) On the basis of current data, it may be prudent to recommend lowering SBP/DBP to values within the range 130–139/80–85 mmHg, and possibly close to lower values in this range, in all hypertensive patients. More critical evidence from specific randomized trials is desirable, however.

Reappraisal of European guidelines on hypertension Management.
J Hypertens 2009;27

The 2011 Canadian Hypertension Education Program

- The SBP treatment goal is a pressure level of <140mmHg (Grade C). The DBP treatment goal is a pressure level of <90 mm Hg (Grade A).
- For patients with nondiabetic chronic kidney disease, target BP is <130/80 mm Hg (Grade C).
- Persons with diabetes mellitus should be treated to attain SBPs of <130 mm Hg (Grade C) and DBPs of <80 mm Hg (Grade A)

Updates (? Changes)

- Classification of severity of hypertension
- Goal of blood pressure management: target BP
  - Elderly
- Diagnosis of hypertension
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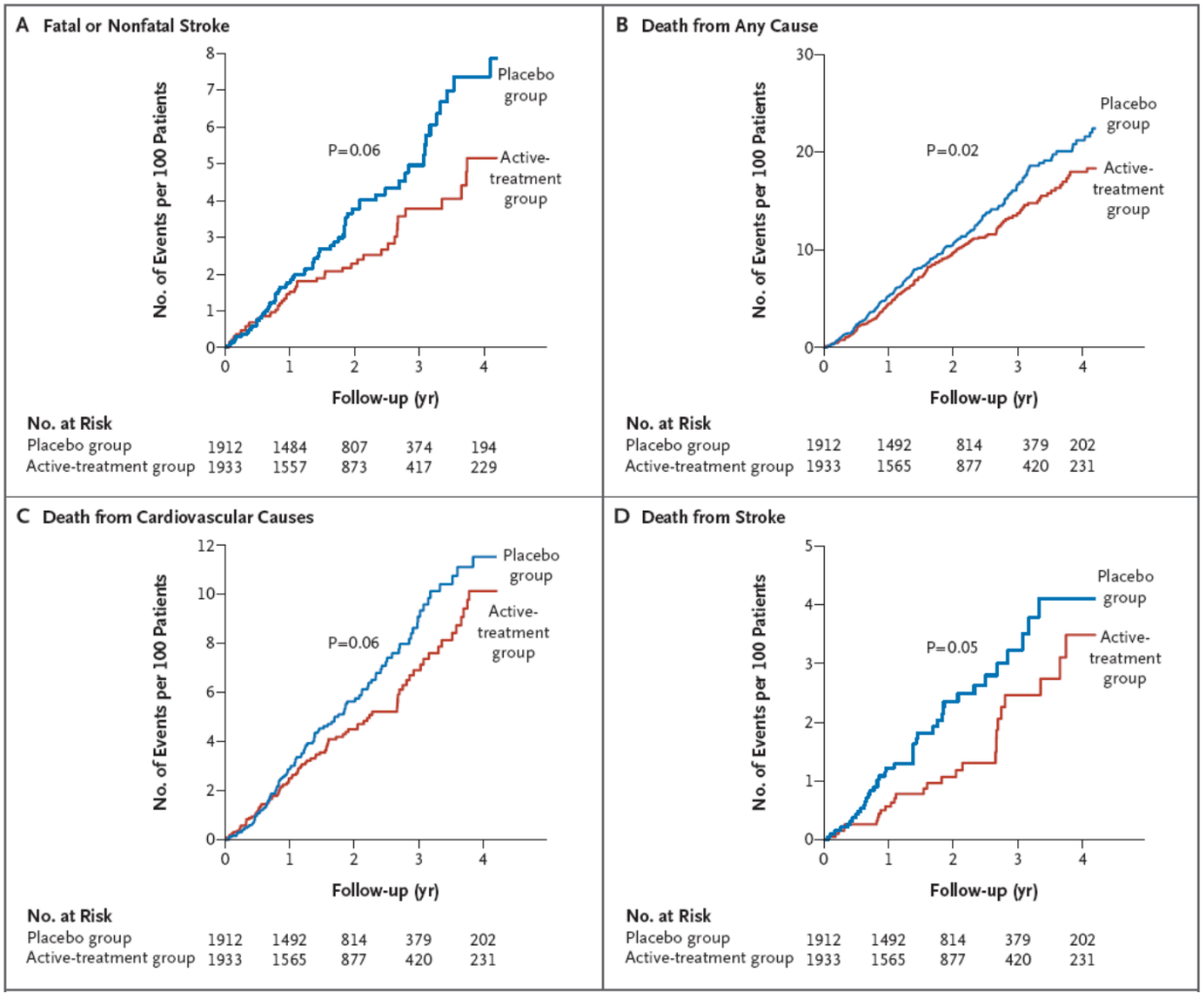
HYVET study;
benefit of hypertension treatment in > 80 years



Beckett, et al, N Engl J Med. 2008;358:1887-98

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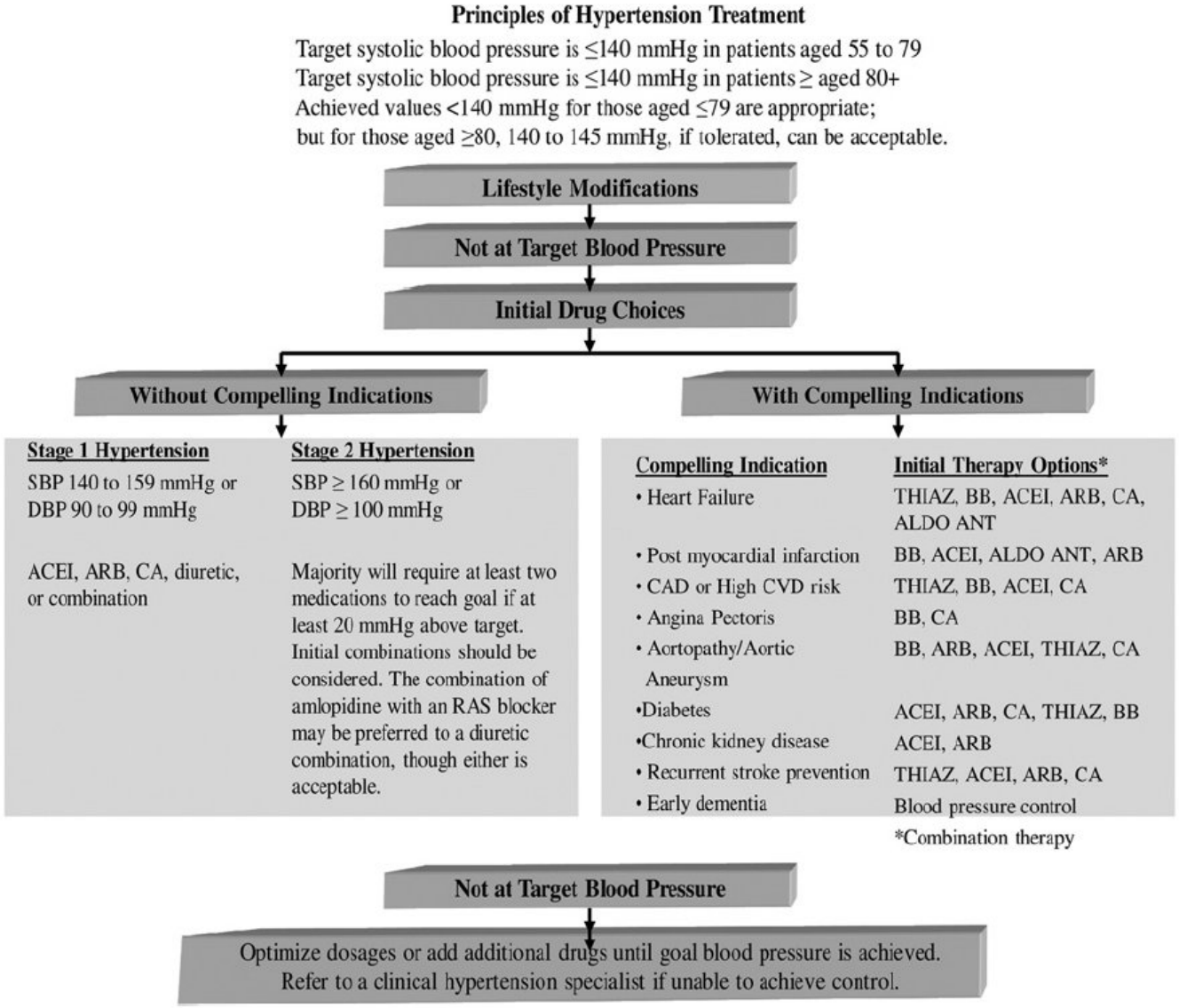
Hypertension treatment in the elderly patients - Now!!

- Our population is aging, and as hypertension affects most elderly people (65 years of age), these individuals are more likely to have organ damage or clinical cardiovascular disease (CVD). They represent management dilemmas because most hypertension trials had upper age limits or did not present age-specific results. However, because the Hypertension in the Very Elderly Trial (HYVET) documented antihypertensive therapy benefits in persons 80 years of age, it is timely to place into perspective issues relevant to hypertension management in elderly patients. *(ACCF/AHA 2011 expert Consensus Document on Hypertension in the Elderly)*

AACF/AHA 2011 Expert Consensus Document. J Am Coll Cardiol 2011;57:2037-2114

Treatment algorithm in the elderly hypertension



AACF/AHA 2011 Expert Consensus Document. J Am Coll Cardiol 2011;57:2037-2114

Management of Hypertension with antihypertensive agentrs in the Elderly: AACF/AHA 2011 Expert Consensus Document

- Should be treated
  - Patient > 80 yrs of age
    - Target SBP < 140~145 mmHg
  - Patient 65 ~ 79 yrs of age
    - Target SBP < 140 mmHg

- Start with single drug at the lowest dose, followed by gradual increasing the dose or a second drug if needed based on the BP response
  - The absorption and distribution of all type of antihypertensive medication is unpredictable in the elderly (half life↑)
  - Needs searching for inadequate BP control: noncompliance, volume overload, drug interaction, other medical condition, white-coat effect
  - Low dose thiazide, CCBs, RAAS blockers
  - Life style modifications: DASH diet, weight reduction, low salt diet, increasing physical activity, moderating alcohol consumption

AACF/AHA 2011 Expert Consensus Document. J Am Coll Cardiol 2011;57:2037-2114

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Diagnosis of hypertension: ABPM, SBPM

TABLE 5. Clinical Situations in Which Ambulatory Blood Pressure Monitoring May Be Helpful

Suspected white-coat hypertension in patients with hypertension and no target organ damage
Apparent drug resistance (office resistance)
Hypotensive symptoms with antihypertensive medication
Episodic hypertension
Autonomic dysfunction

JNC7, 2003

Box 3 Position statement: Ambulatory and home BP measurements

Ambulatory BP

- Although office BP should be used as reference, ambulatory BP may improve prediction of cardiovascular risk in untreated and treated patients
- Normal values are different for office and ambulatory BP (Table 5)
- 24-h ambulatory BP monitoring should be considered, in particular, when
  - considerable variability of office BP is found over the same or different visits
  - high office BP is measured in subjects otherwise at low total cardiovascular risk
  - there is a marked discrepancy between BP values measured in the office and at home
  - resistance to drug treatment is suspected
  - hypotensive episodes are suspected, particularly in elderly and diabetic patients
  - office BP is elevated in pregnant women and pre-eclampsia is suspected

ESH/ESC, 2007

Table 5 Blood pressure thresholds (mmHg) for definition of hypertension with different types of measurement

	SBP	DBP
Office or clinic	140	90
24-hour	125–130	80
Day	130–135	85
Night	120	70
Home	130–135	85

Diagnosis of hypertension: Benefits of ABPM

Clinical Features of 8295 Patients With Resistant Hypertension Classified on the Basis of Ambulatory Blood Pressure Monitoring

Alejandro de la Sierra, Julián Segura, José R. Banegas, Manuel Gorostidi, Juan J. de la Cruz, Pedro Armario, Anna Oliveras, Luis M. Ruilope

See Editorial Commentary, pp 889–890

Abstract—We aimed to estimate the prevalence of resistant hypertension through both office and ambulatory blood pressure monitoring in a large cohort of treated hypertensive patients from the Spanish Ambulatory Blood Pressure Monitoring Registry. In addition, we also compared clinical features of patients with true or white-coat–resistant hypertension. In December 2009, we identified 68 045 treated patients with complete information for this analysis. Among them, 8295 (12.2% of the database) had resistant hypertension (office blood pressure ≥140 and/or 90 mm Hg while being treated with ≥3 antihypertensive drugs, 1 of them being a diuretic). After ambulatory blood pressure monitoring, 62.5% of patients were classified as true resistant hypertensives, the remaining 37.5% having white-coat resistance. The former group was younger, more frequently men, with a longer duration of hypertension and a worse cardiovascular risk profile. The group included larger proportions of smokers, diabetics, target organ damage (including left ventricular hypertrophy, impaired renal function, and microalbuminuria), and documented cardiovascular disease. Moreover, true resistant hypertensives exhibited in a greater proportion a riser pattern (22% versus 18%; $P<0.001$). In conclusion, this study first reports the prevalence of resistant hypertension in a large cohort of patients in usual daily practice. Resistant hypertension is present in 12% of the treated hypertensive population, but among them more than one third have normal ambulatory blood pressure. A worse risk profile is associated with true resistant hypertension, but this association is weak, thus making it necessary to assess ambulatory blood pressure monitoring for a correct diagnosis and management. (*Hypertension*. 2011;57:898-902.) ● Online Data Supplement

Key Words: resistant hypertension ■ ambulatory blood pressure monitoring ■ circadian pattern ■ cardiovascular risk

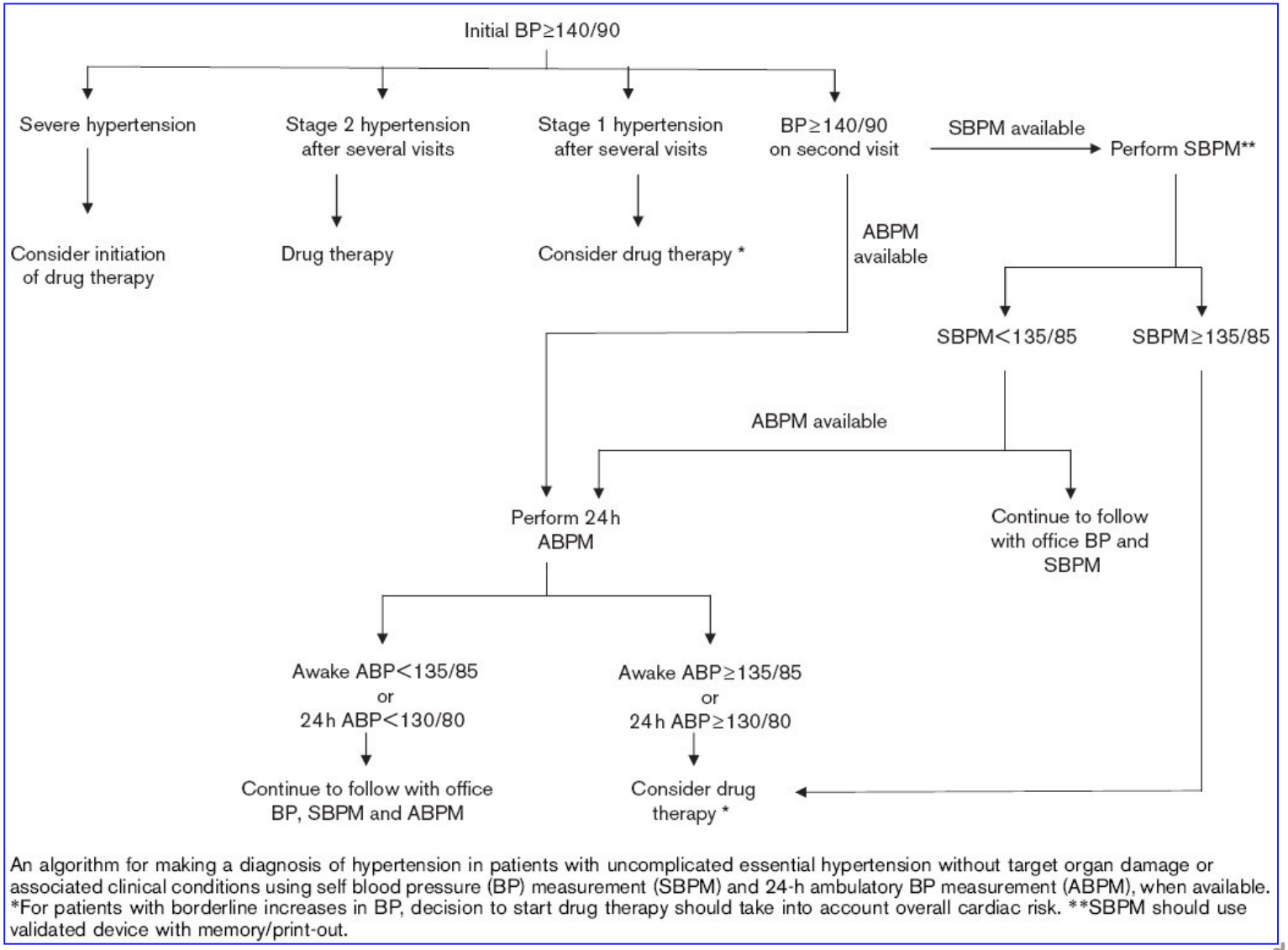
Table 2. Differences in Office, Daytime, and Nighttime BP, as Well as Circadian Pattern Distribution, Between RH Patients With Normal or Elevated 24-Hour BP

Parameter	True RH (N=5182)	White-Coat RH (N=3113)	*P*
Office SBP	164±18	157±15	<0.001
Office DBP	90±13	87±12	<0.001
Daytime SBP	145±13	122±8	<0.001
Daytime DBP	81±12	70±8	<0.001
Nighttime SBP	136±17	113±10	<0.001
Nighttime DBP	72±11	61±8	<0.001
Circadian SBP pattern distribution			<0.001
Extreme dippers, %	5.3	6.3	
Dippers, %	29.9	32.7	
Nondippers, %	42.5	43.3	
Risers, %	22.3	17.7	
Circadian DBP pattern distribution			<0.001
Extreme dippers, %	16.1	20.4	
Dippers, %	39.3	43.1	
Nondippers, %	32.5	26.8	
Risers, %	12.1	9.6	

Values are in millimeters of mercury. RH indicates resistant hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure.

de la Sierra A. Hypertension. 2011;57(5):898-902

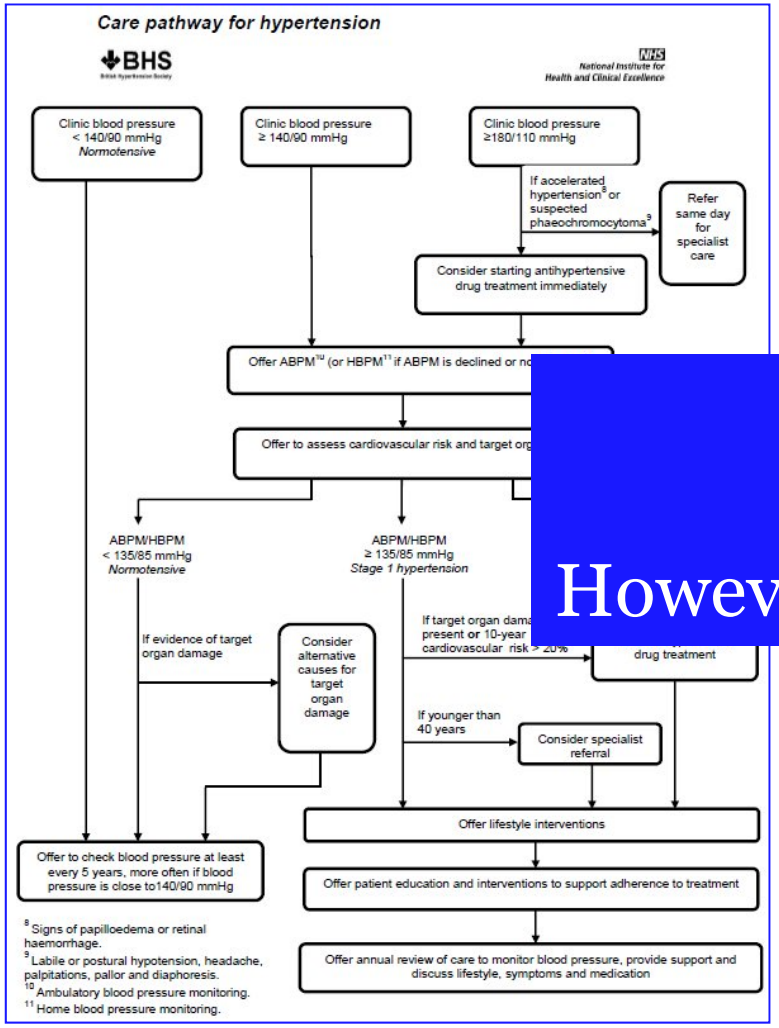
Suggested Algorithm for diagnosis hypertension: ABPM and HBPM

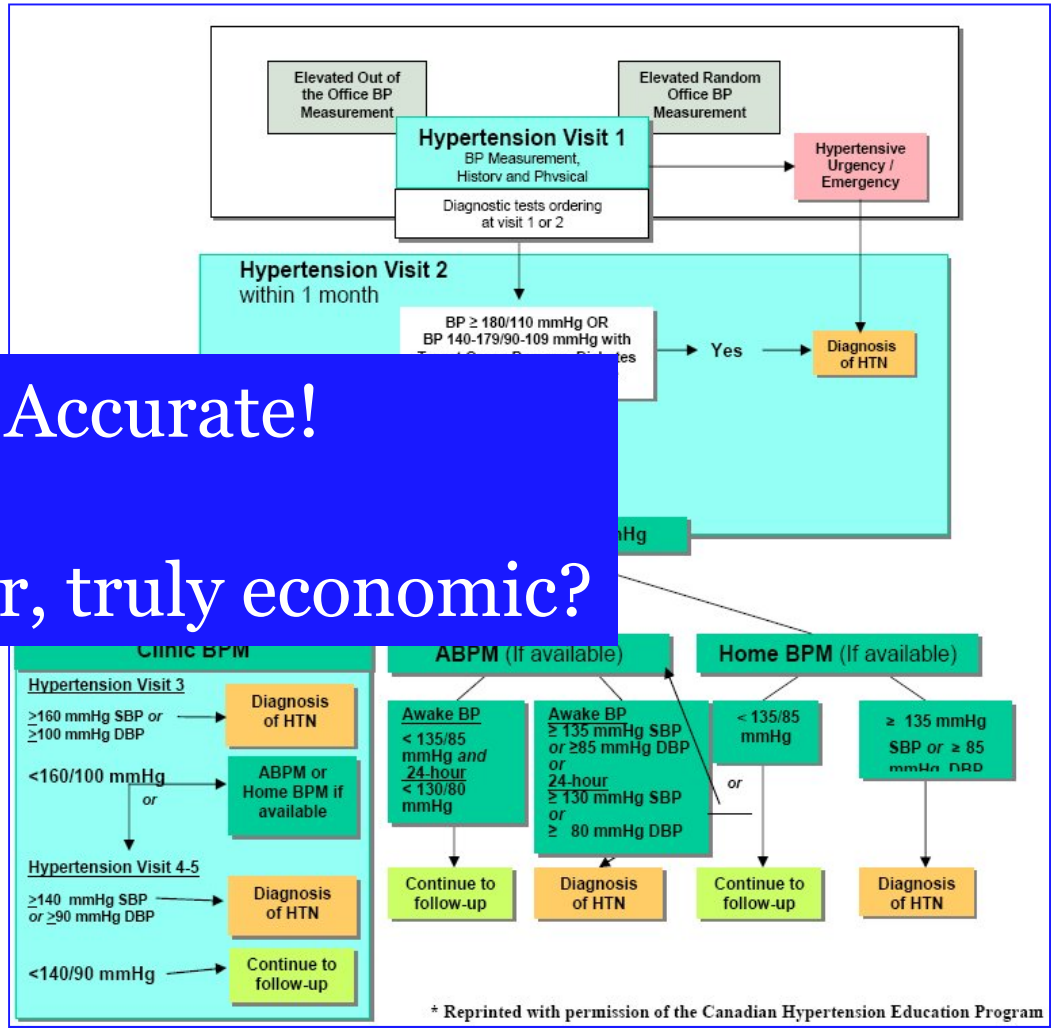


An algorithm for making a diagnosis of hypertension in patients with uncomplicated essential hypertension without target organ damage or associated clinical conditions using self blood pressure (BP) measurement (SBPM) and 24-h ambulatory BP measurement (ABPM), when available. *For patients with borderline increases in BP, decision to start drug therapy should take into account overall cardiac risk. **SBPM should use validated device with memory/print-out.

Myers MG. Blood Pressure Monitoring 2004, 9:283–286

Diagnosis of hypertension: ABPM, SBPM





Accurate!

However, truly economic?

NICE 2011

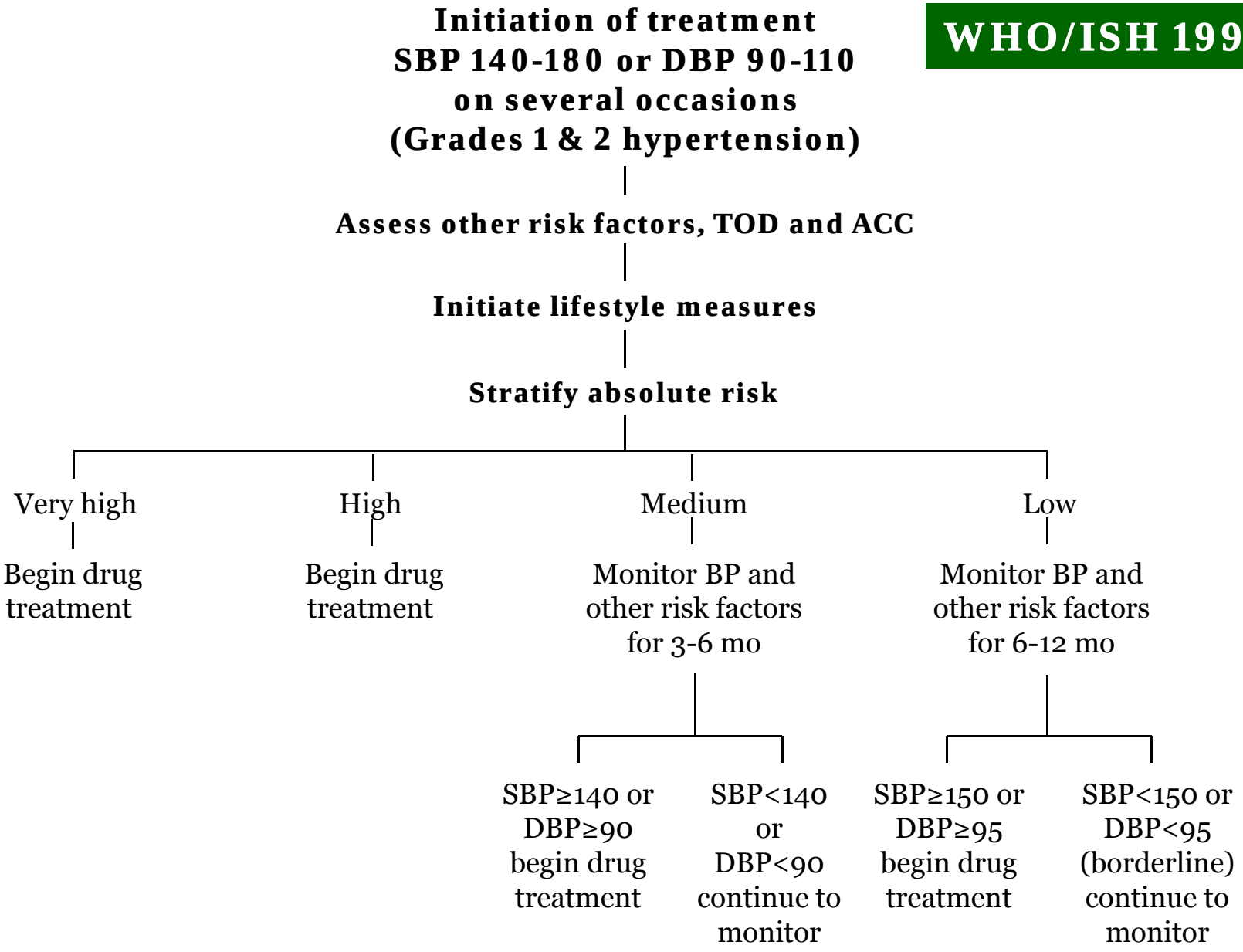
Canadian Hypertension Education Program 2011

dongguk UNIVERSITY MEDICAL CENTER

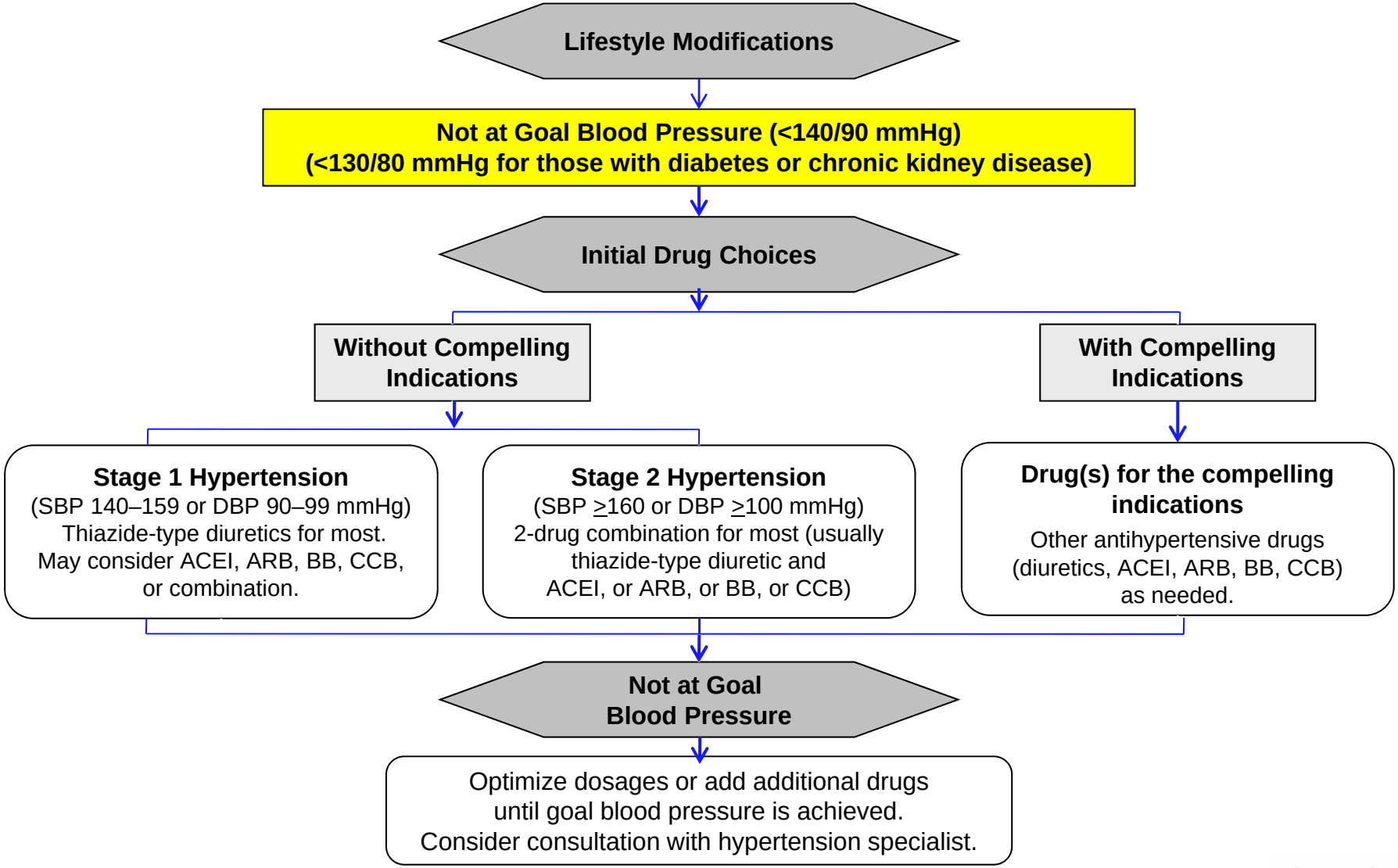
Updates (? Changes)

- Classification of severity of hypertension
- Goal of blood pressure management: target BP
- Diagnosis of hypertension
- When to initiate drug treatment
- Choice of antihypertensive drugs: first line drug?

WHO/ISH 1999



Algorithm for Treatment of Hypertension: JNC7



Initiation of antihypertensive treatment: ESH/ECS 2007

Other risk factors, OD or disease	Normal SBP 120-129 or DBP 80-84	High normal SBP 130-139 or DBP 85-89	Grade 1 HT SBP 140-159 or DBP 90-99	Grade 2 HT SBP 160-179 or DBP 100-109	Grade 3 HT SBP ≥180 or DBP ≥110
No other risk factors	No BP intervention	No BP intervention	Lifestyle changes for several months then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes + immediate drug treatment
1-2 risk factors	Lifestyle changes	Lifestyle changes	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes + immediate drug treatment
3 or more risk factors, MS, OD or diabetes	Lifestyle changes	Lifestyle changes and consider drug treatment	Lifestyle changes + drug treatment	Lifestyle changes + drug treatment	Lifestyle changes + immediate drug treatment
Diabetes	Lifestyle changes	Lifestyle changes + drug treatment			
Established CV or renal disease	Lifestyle changes + immediate drug treatment	Lifestyle changes + immediate drug treatment	Lifestyle changes + immediate drug treatment	Lifestyle changes + immediate drug treatment	Lifestyle changes + immediate drug treatment

Updates (? Changes)

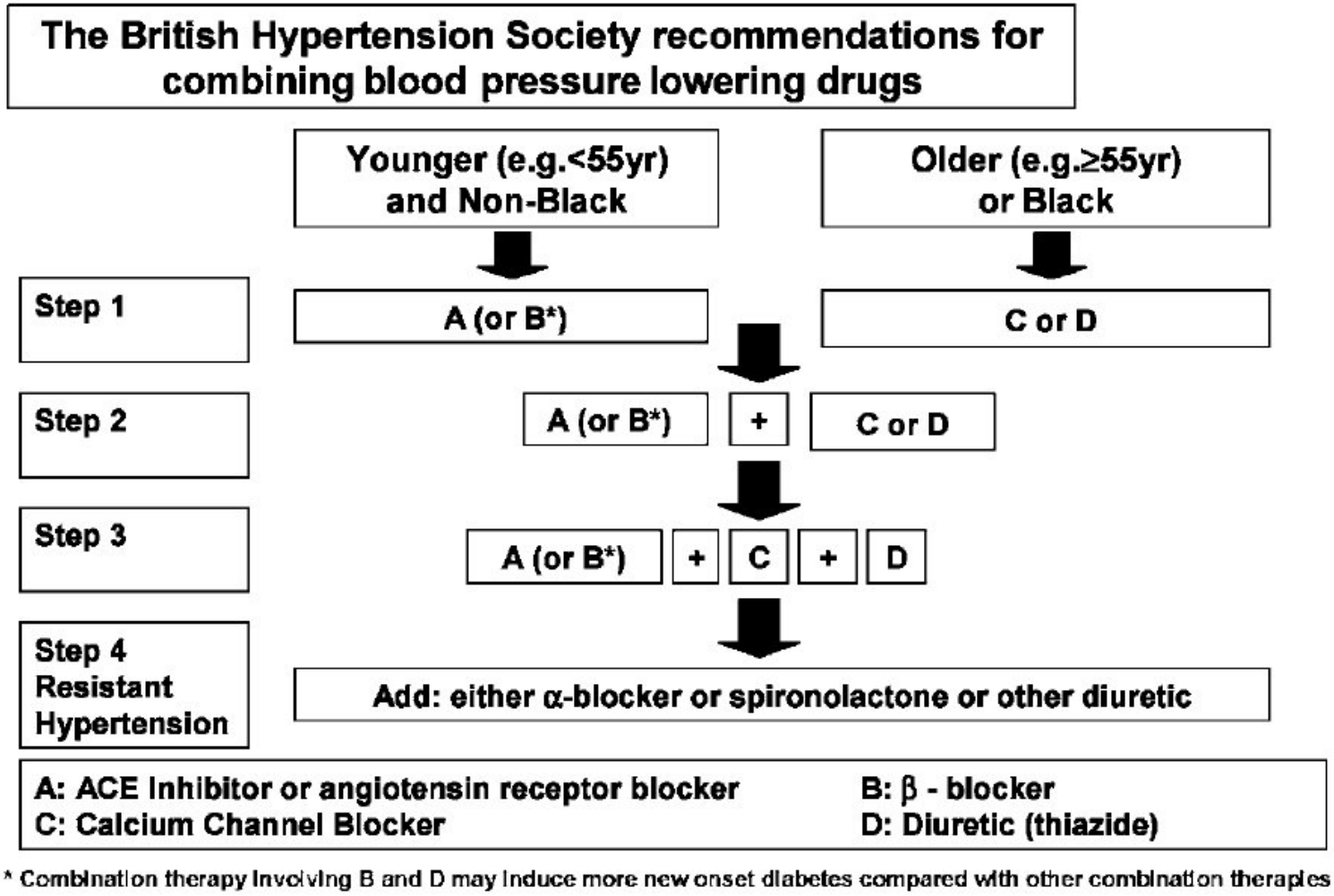
- Classification of severity of hypertension
- Goal of blood pressure management: target BP
- Diagnosis of hypertension
- When to initiate drug treatment
- Choice of antihypertensive drugs: first line drug?

Classification and Management of BP for adults: JNC7

BP classification	SBP* mmHg	DBP* mmHg	Lifestyle modification	Initial drug therapy	
				Without compelling indication	With compelling indications
Normal	<120	and <80	Encourage		
Prehypertension	120–139	or 80–89	Yes	No antihypertensive drug indicated.	Drug(s) for compelling indications. ‡
Stage 1 Hypertension	140–159	or 90–99	Yes	Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination.	Drug(s) for the compelling indications.‡ Other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed.
Stage 2 Hypertension	≥160	or ≥100	Yes	Two-drug combination for most† (usually thiazide-type diuretic and ACEI or ARB or BB or CCB).	

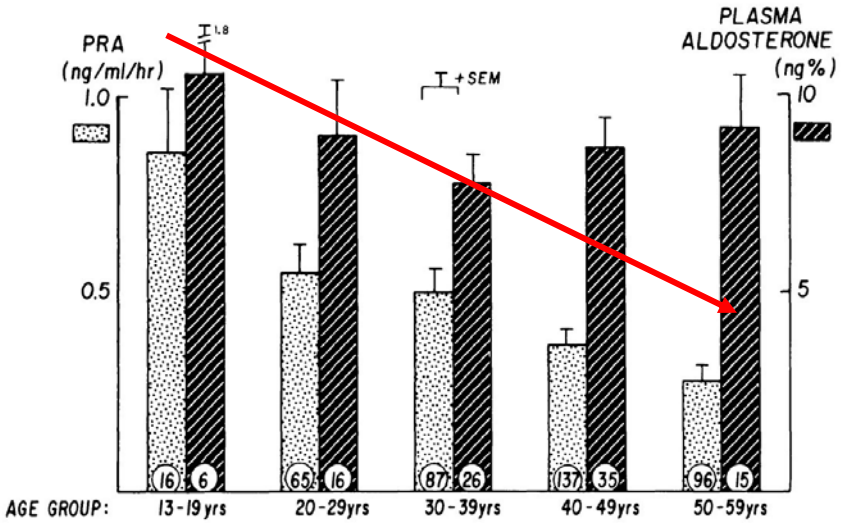
*Treatment determined by highest BP category.
†Initial combined therapy should be used cautiously in those at risk for orthostatic hypotension.
‡Treat patients with chronic kidney disease or diabetes to BP goal of <130/80 mmHg.

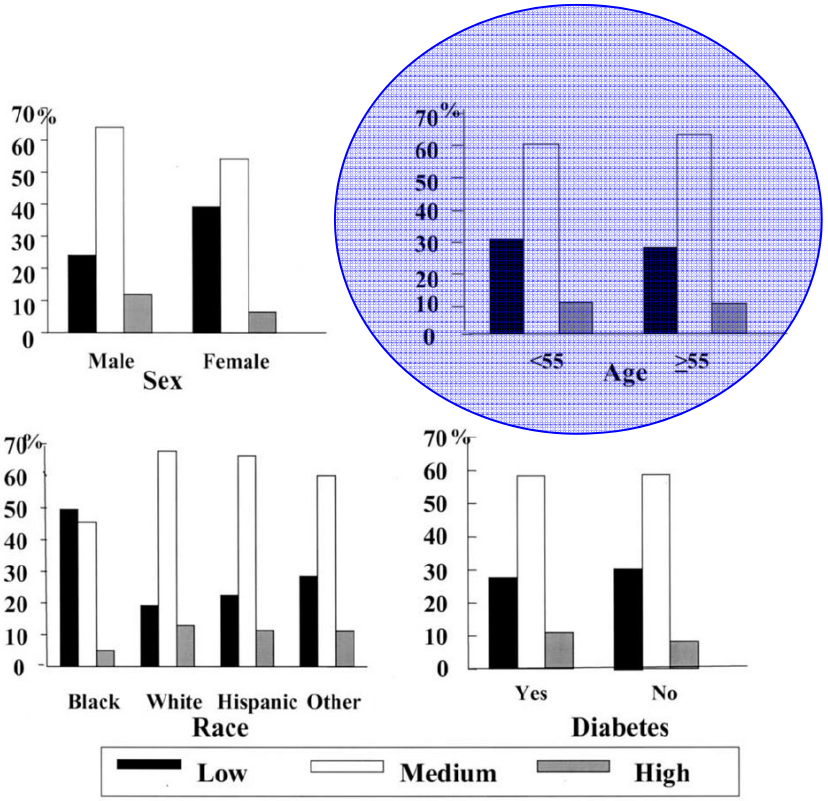
BHS recommendation for choice of antihypertensive agents



BHS Hypertension management guidelines. J Hum Hypertens 2004;18:139-185

Changes of renin activity by aging?



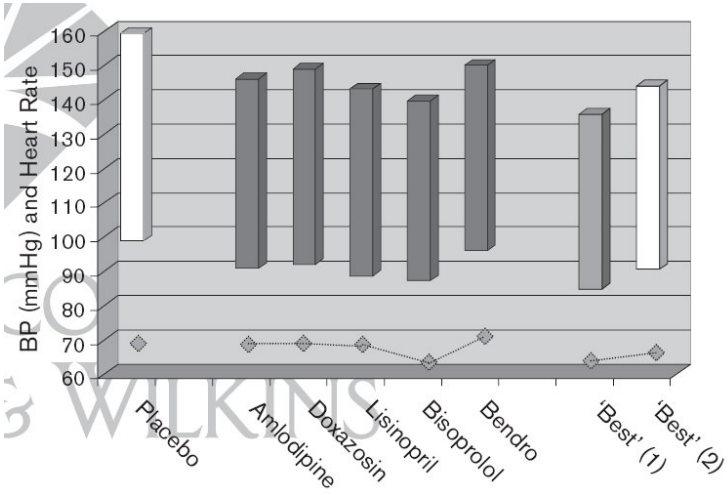


J Clin Endocrinol Metab. 1976;43:446-8
Am J Hypertens 2004;17:1-7

Different response of white and young hypertensives (< 55 years)

Table 1 **Clinic and 24-h blood pressures at baseline and on 'best' treatment**

			BP on placebo		BP on repeat	
Drug	*n*	Age	Clinic	24-h average	Clinic	24-h average
Amlodipine	5	49.0	162 ± 6/100 ± 6	161 ± 6/104 ± 5	154 ± 14/96 ± 4	144 ± 7/95 ± 4
Doxazosin	4	46.0	161 ± 13/100 ± 7	160 ± 9/102 ± 9	155 ± 4/100 ± 6	154 ± 6/102 ± 6
Lisinopril	10	46.5	159 ± 8/99 ± 7	160 ± 12/106 ± 9	137 ± 9/86 ± 6	136 ± 7/89 ± 5
Bisoprolol	13	42.5	160 ± 99/10 ± 6	155 ± 12/107 ± 6	140 ± 17/86 ± 8	135 ± 13/86 ± 7
Bendrofluazide	2	51.5	158 ± 14/95 ± 3	150 ± 19/103 ± 16	156 ± 2/99 ± 2	148 ± 14/99 ± 11



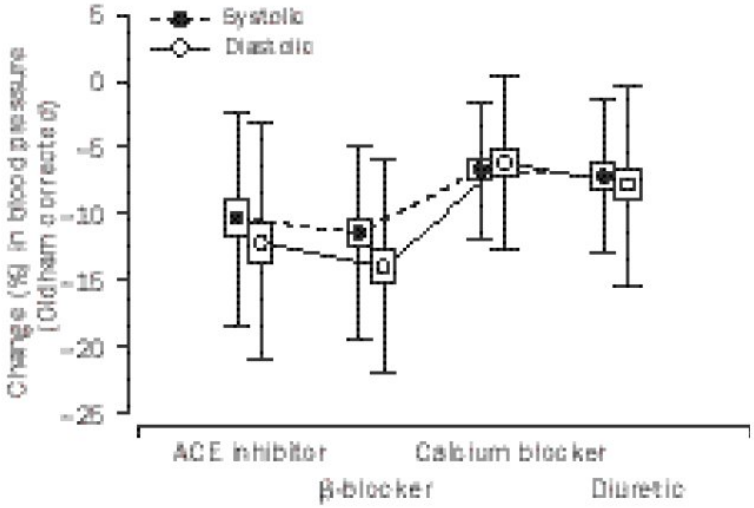
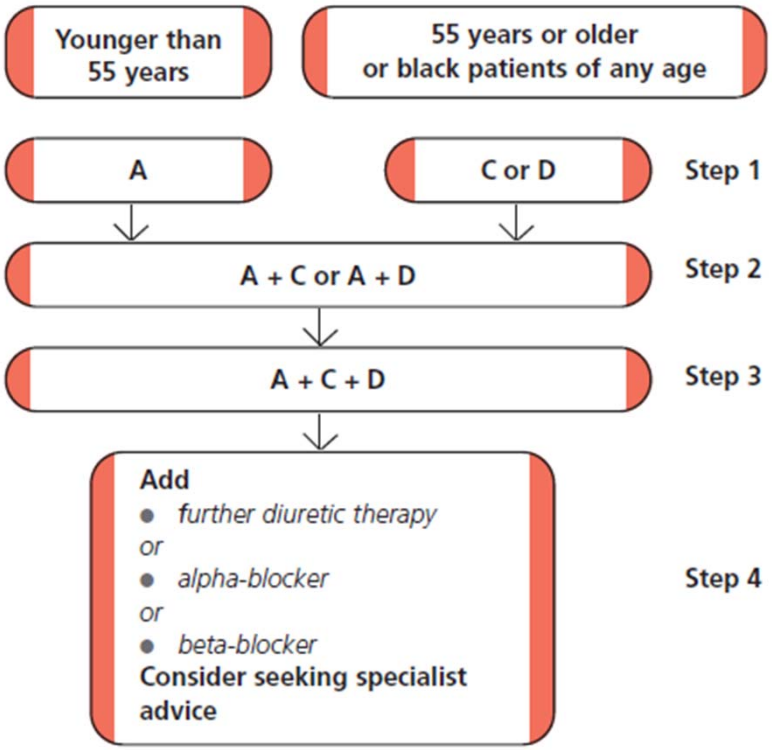


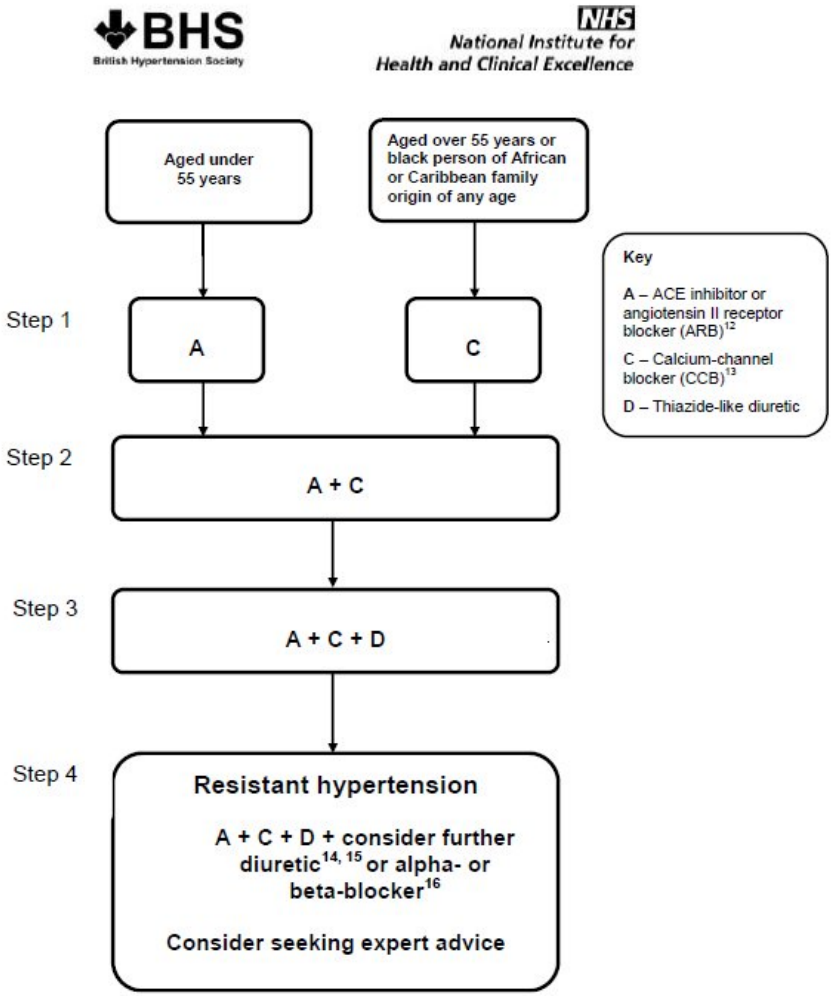
Figure 3: **Comparison of mean blood-pressure responses to four classes of antihypertensives in a Latin-square crossover study**
Values=mean, SD (bars), and SE (boxes) of the means, in 36 patients.

Lancet 1999;353:2008-2013
J Hypertens 2002;20:771-777, from UK

NICE/BHS recommendation of drug choice



2006년



2011년

Should β blockers remain first choice in the treatment of primary hypertension? A meta-analysis

Lars Hjalmar Lindholm, Bo Carlberg, Ola Samuelsson

Lancet 2005;366:1545-53

Summary

Background: β blockers have been used widely in the treatment of hypertension and are recommended as first-line drugs in hypertension guidelines. However, a preliminary analysis has shown that atenolol is not very effective in hypertension. We aim to substantially enlarge the data on atenolol and analyse the effect of different β blockers.

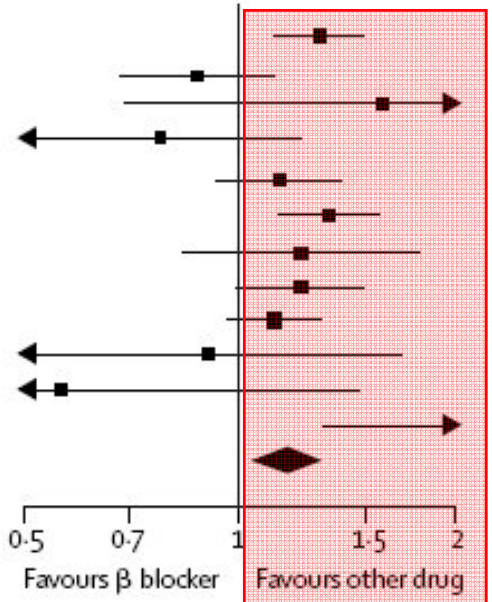
Methods: The Cochrane Library and PubMed were searched for β blocker treatment in patients with primary hypertension. Data were then entered into the Cochrane Collaboration Review Manager package and were summarised in meta-analyses. 13 randomised controlled trials (n=105 951) were included in a meta-analysis comparing treatment with β blockers with other antihypertensive drugs. Seven studies (n=27 433) were included in a comparison of β blockers and placebo or no treatment.

Findings: The relative risk of stroke was 16% higher for β blockers (95% CI 4–30%) than for other drugs. There was no difference for myocardial infarction. When the effect of β blockers was compared with that of placebo or no treatment, the relative risk of stroke was reduced by 19% for all β blockers (7–29%), about half that expected from previous hypertension trials. There was no difference for myocardial infarction or mortality.

Interpretation: In comparison with other antihypertensive drugs, the effect of β blockers is less than optimum, with a raised risk of stroke. Hence, we believe that β blockers should not remain first choice in the treatment of primary hypertension and should not be used as reference drugs in future randomised controlled trials of hypertension.

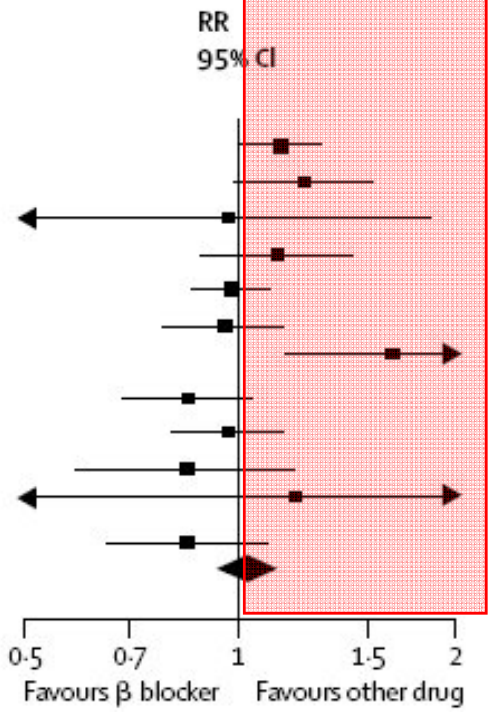
1A **Stroke**

	β blocker n/N	Other drug n/N	RR 95% CI	RR 95% CI
ASCOT-BPLA	422/9618	327/9639		1·29 (1·12–1·49)
CONVINCE	118/8297	133/8179		0·87 (0·68–1·12)
ELSA	14/1157	9/1177		1·58 (0·69–3·64)
HAPPHY	32/3297	41/3272		0·77 (0·49–1·23)
INVEST	201/11309	176/11267		1·14 (0·93–1·39)
LIFE	309/4588	232/4605		1·34 (1·13–1·58)
MRC Old	56/1102	45/1081		1·22 (0·83–1·79)
NORDIL	196/5471	159/5410		1·22 (0·99–1·50)
STOP-2	237/2213	422/4401		1·12 (0·96–1·30)
UKPDS	17/358	21/400		0·90 (0·48–1·69)
Yurenev	6/150	11/154		0·56 (0·21–1·48)
MRC	42/4403	18/4297		2·28 (1·31–3·95)
Total events	1650/51963	1594/53882		1·16 (1·04–1·30)
Test for heterogeneity: χ^2=22·39 (p=0·02)				

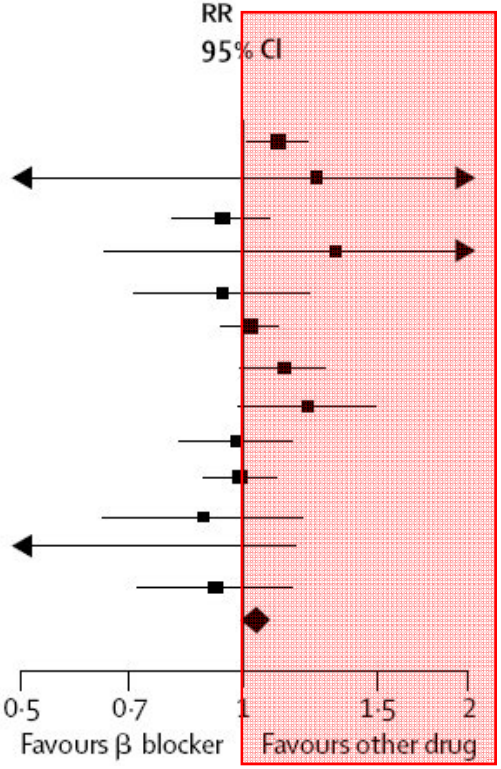


Myocardial infarction

	β blocker n/N	Other drug n/N	RR 95% CI	RR 95% CI
ASCOT-BPLA	444/9618	390/9639		1·14 (1·00–1·30)
CONVINCE	166/8297	133/8179		1·23 (0·98–1·54)
ELSA	17/1157	18/1177		0·96 (0·50–1·85)
HAPPHY	132/3297	116/3272		1·13 (0·88–1·44)
INVEST	441/11309	452/11267		0·97 (0·85–1·11)
LIFE	118/4588	198/1081		0·95 (0·78–1·16)
MRC Old	80/1102	48/4605		1·63 (1·15–2·32)
NORDIL	157/5471	183/5410		0·85 (0·69–1·05)
STOP-2	154/2213	318/4401		0·96 (0·80–1·16)
UKPDS	46/358	61/400		0·84 (0·59–1·20)
Yurenev	7/150	6/154		1·20 (0·41–3·48)
MRC	103/4403	119/4297		0·84 (0·65–1·10)
Total events	1935/51963	2042/53882		1·02 (0·93–1·12)
Test for heterogeneity: χ^2=20·67 (p=0·04)				



Mortality of all causes	β blocker n/N	Other drug n/N	RR 95% CI	RR 95% CI
ASCOT-BPLA	820/9618	738/9639		1·11 (1·01–1·22)
Berglund	5/53	4/53		1·25 (0·36–4·40)
CONVINCE	319/8297	337/8179		0·93 (0·80–1·08)
ELSA	17/1157	13/1177		1·33 (0·65–2·73)
HAPPHY	96/3297	101/3272		0·94 (0·72–1·24)
INVEST	893/11309	873/11267		1·02 (0·93–1·11)
LIFE	431/4588	383/1081		1·13 (0·99–1·29)
MRC Old	167/1102	134/1081		1·22 (0·99–1·51)
NORDIL	228/5471	231/5410		0·98 (0·82–1·17)
STOP-2	369/2213	742/4401		0·99 (0·88–1·11)
UKPDS	59/358	75/400		0·88 (0·64–1·20)
Yurenev	1/150	7/154		0·15 (0·02–1·18)
MRC	120/4403	128/4297		0·91 (0·72–1·17)
Total events	3525/52016	3766/53935		1·03 (0·99–1·08)
Test for heterogeneity: χ^2=15·73 (p=0·20)				



NICE Clinical Guideline, 2006

One class which caused particular debate was the beta-blockers. The GDG noted that in head-to-head trials, beta-blockers were usually less effective than the comparator drug at reducing major cardiovascular events, in particular stroke. Atenolol was the beta-blocker used in most of these studies and, in the absence of substantial data with other agents, it is unclear whether this conclusion applies to all beta-blockers. However, if atenolol studies are excluded, the total evidence on the use of beta-blockers for the treatment of hypertension is much less than for the other main d
indications fo
initial treatm

The widely used class of drug which is omitted from this regimen is the beta-blocker. The evidence overall suggests that clinical benefit is least likely (especially for stroke prevention) with these agents. However, given the relative lack of clinical outcome data from trials of treating hypertension with beta-blockers other than atenolol, concern about the generalisability of this conclusion, beyond atenolol, to all beta-blockers remains. The GDG felt that good studies with alternative beta-blockers in people with hypertension are required for this conclusion to be reversed. An additional concern is the increased risk of developing diabetes, particularly with the combination of a beta-blocker with a thiazide-type diuretic. Omitting beta-blockers from the routine treatment algorithm was therefore justified. Nevertheless, the GDG noted that there are certain compelling indications for beta-blockers which have been specified.

NICE Clinical Guideline, 2011

1.6.9 If diuretic treatment is to be initiated or changed, offer a thiazide-like diuretic, such as chlortalidone (12.5–25.0 mg once daily) or indapamide (1.5 mg modified-release once daily or 2.5 mg once daily) in preference to a conventional thiazide diuretic such as bendroflumethiazide or hydrochlorothiazide. **[new 2011]**

NOTE: in the previous NICE hypertension guidelines [425,436] a lot of the evidence for diuretics was on Chlorthiazide, which is no longer used in the UK and is why many of the studies have not been included in this review.

2007 ESH- ESC Guidelines for the management of hypertension

Box 10 Position statement: Choice of antihypertensive drugs

- The main benefits of antihypertensive therapy are due to lowering of BP *per se*.
- Five major classes of antihypertensive agents – thiazide diuretics, calcium antagonists, ACE inhibitors, angiotensin receptor antagonists and β-blockers – are suitable for the initiation and maintenance of antihypertensive treatment, alone or in combination. β-blockers, especially in combination with a thiazide diuretic, should not be used in patients with the metabolic syndrome or at high risk of incident diabetes.