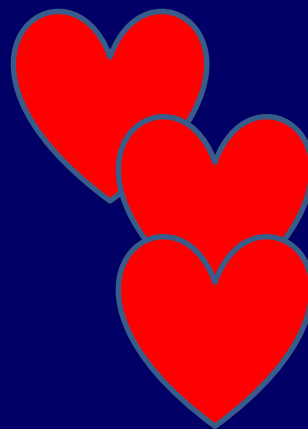
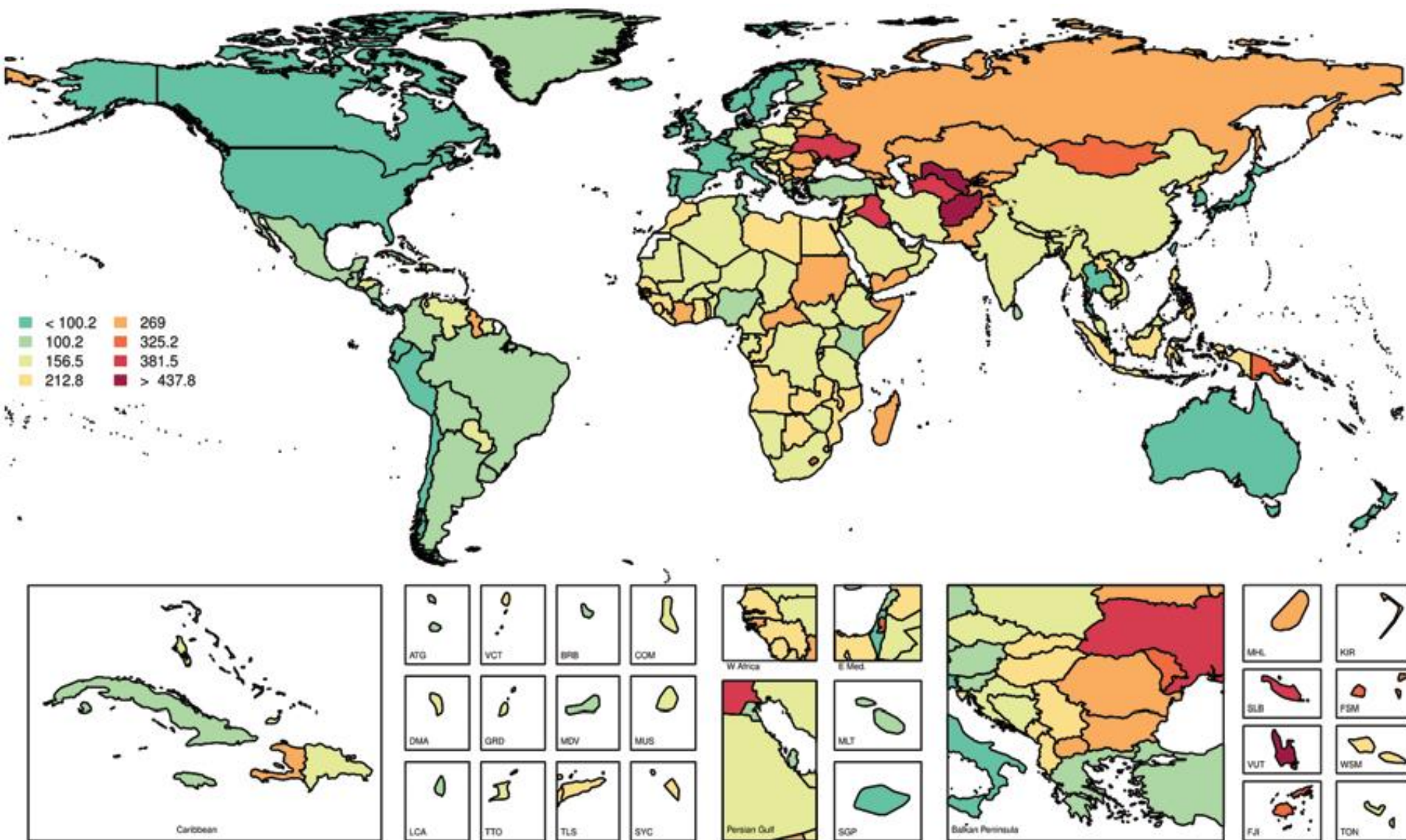


Κατευθυντήριες οδηγίες αντιμετώπισης αρτηριακής υπέρτασης



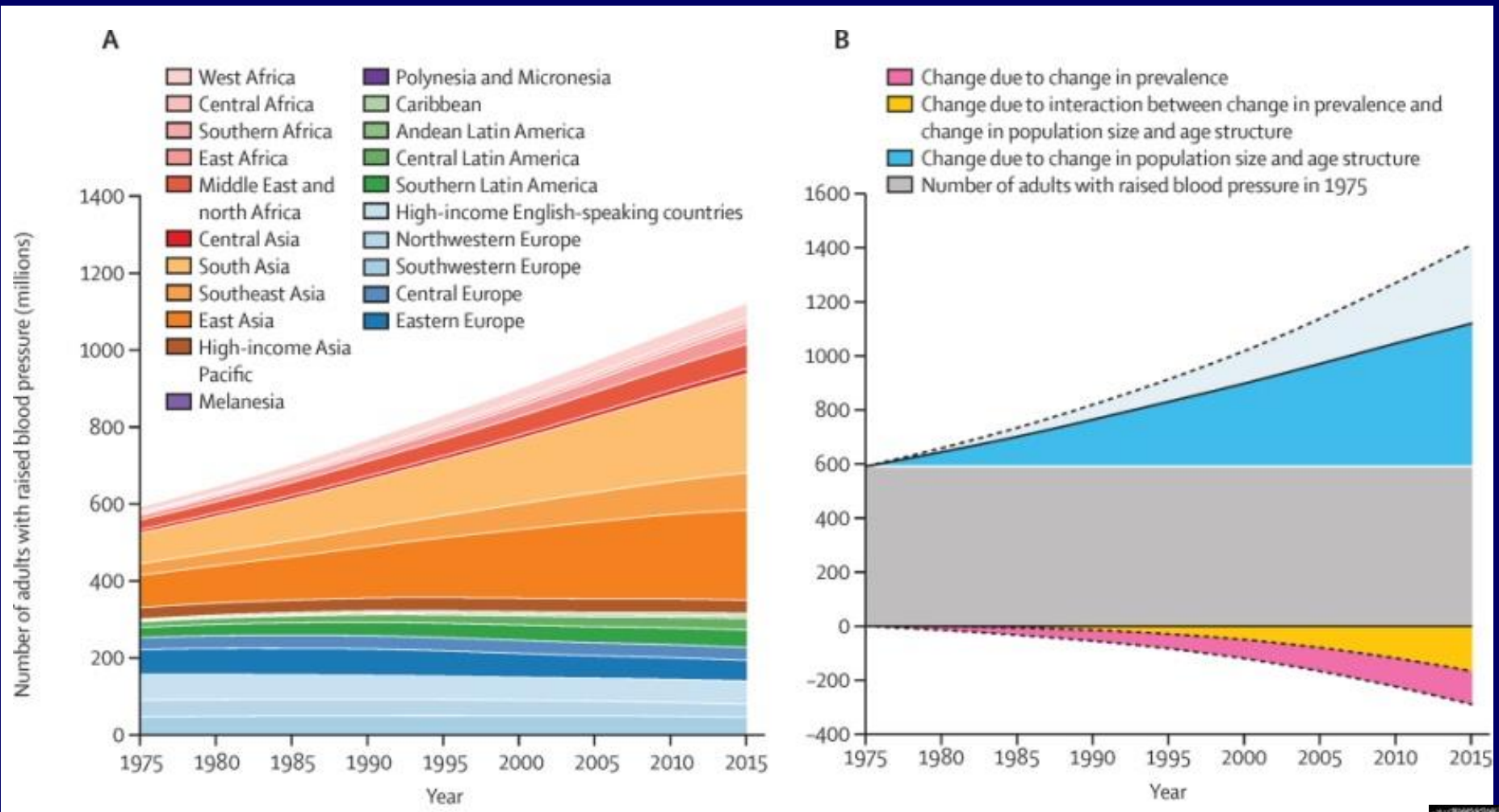
Μαρία Παπαβασιλείου
Καρδιολόγος FESC, EHS
Διευθύντρια Κέντρου Υπέρτασης-one day clinic
Metropolitan General Hospital Athens

Age-standardized global mortality rates attributable to high SBP per 100 000, both sexes, 2016.

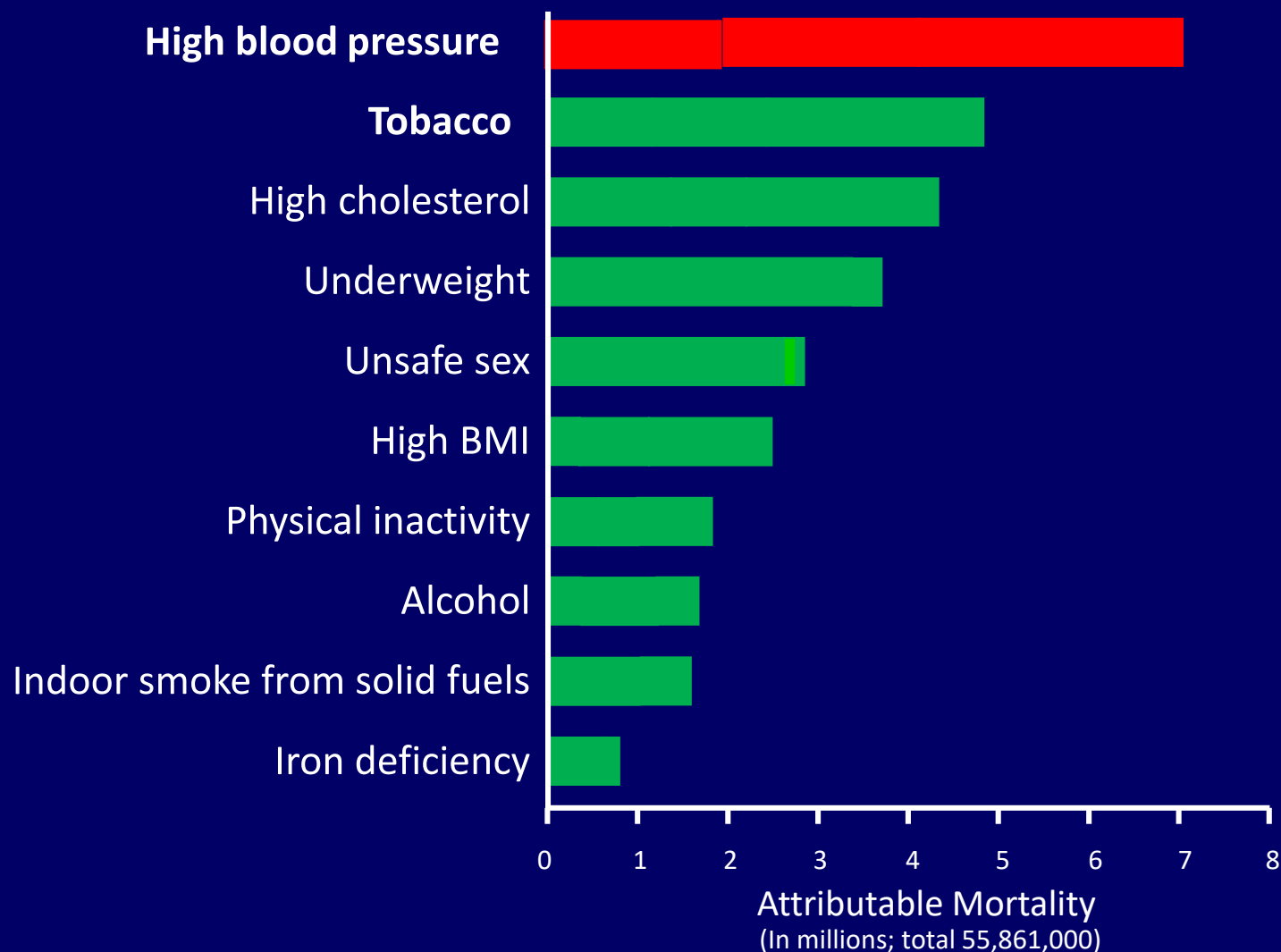


Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19·1 million participants

Trends in the number of adults aged 18 years and older with raised BP



Proportion of deaths attributable to leading risk factors worldwide (WHO 2000)



HTN GUIDELINES

VS

ESC/ESH 2018

ACC/AHA 2017

New concepts

- BP measurement (ABPm, HBPM)
- Less conservative treatment of BP in older and very old patients (biological age)
- A SPC treatment strategy to improve BP control
- New target ranges for BP in treated patients
(aim for 140/90, then proceed to 130/80, but no lower than 120/70)
- Detecting poor adherence to drug therapy
- A key role for nurses, pharmacists in the longer-term management of hypertension

Changes in the 2017 ACC/AHA Blood Pressure guidelines?

Selected highlights:

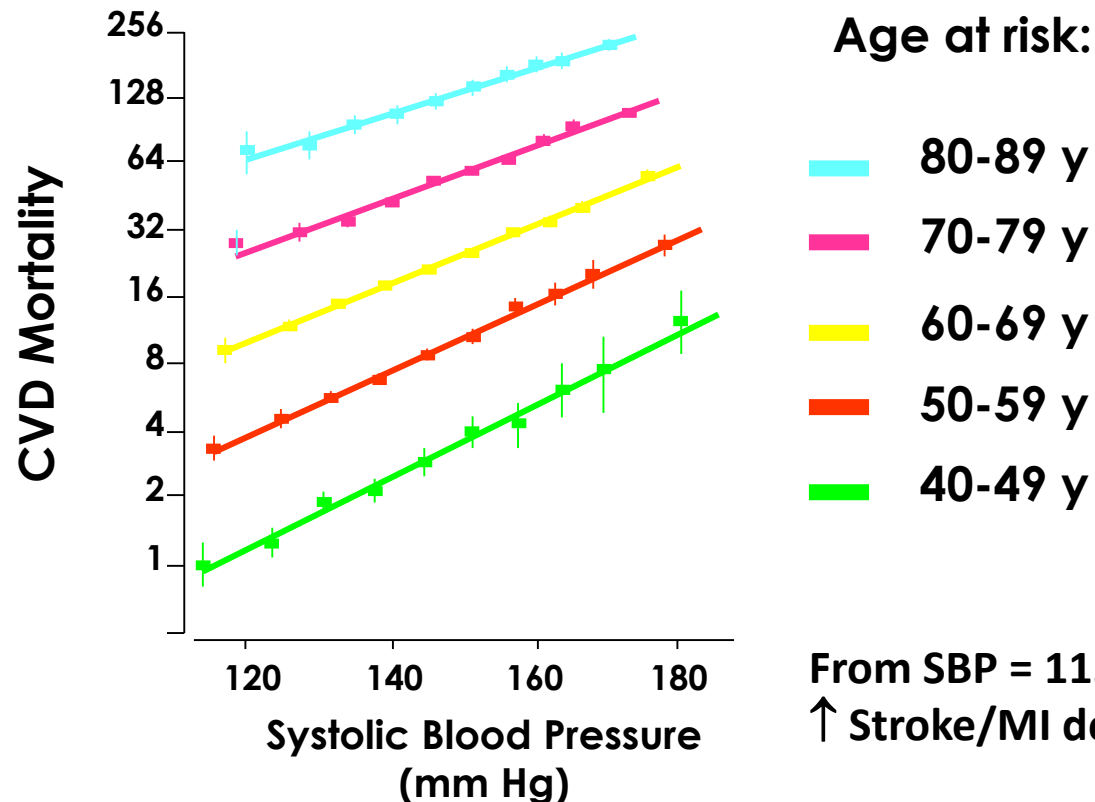
1. **New BP classification system**
2. **Use of BP levels *and* CVD risk to guide antihypertensive medication initiation**
3. **Lower targets for BP during treatment of hypertension**

Classification of BP



Rationale: Association of SBP and CV mortality by decade of age

Data from 61 prospective observational studies of blood pressure and mortality
n= 958,074



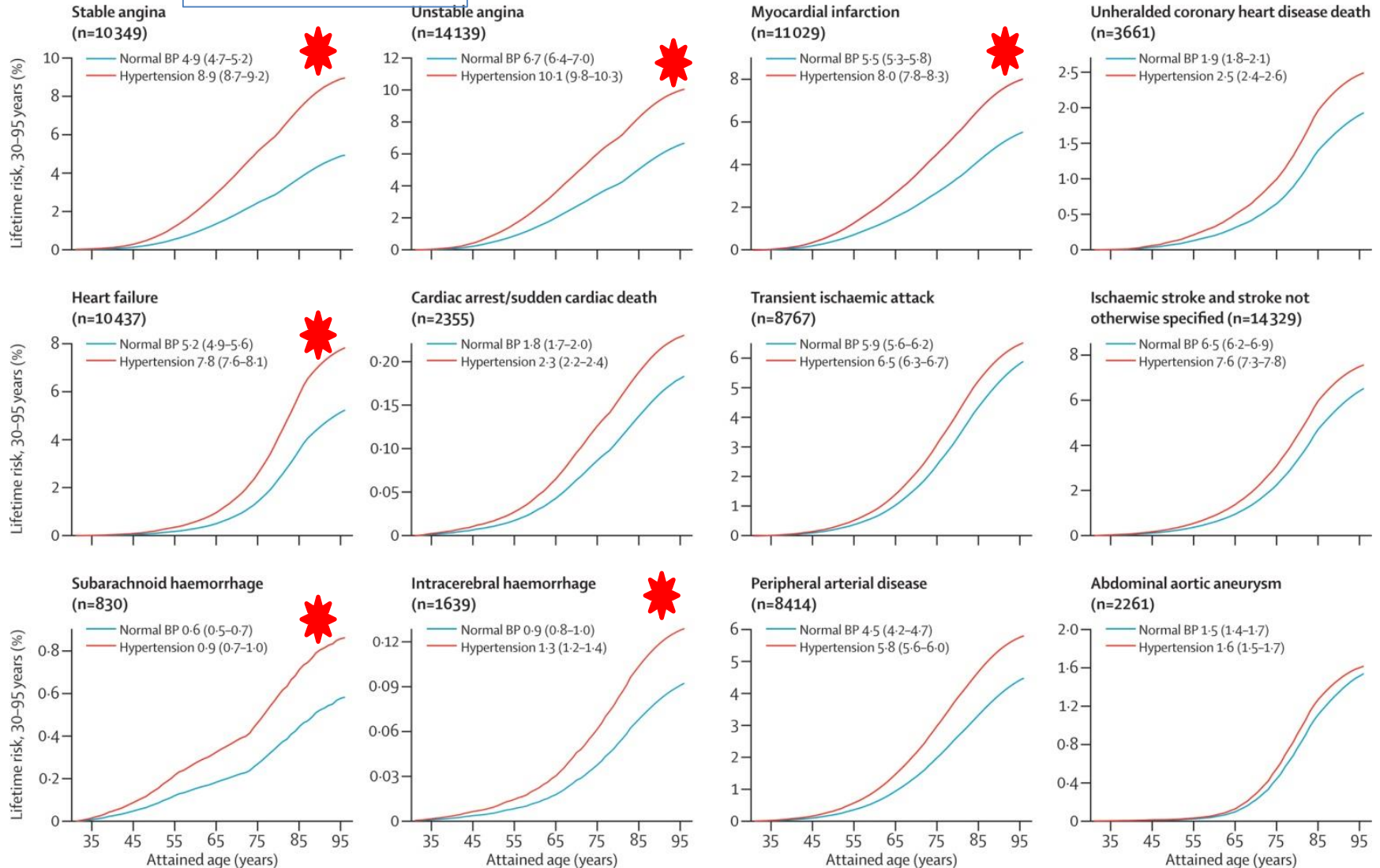
From SBP = 115: \uparrow SBP 2 mmHg \rightarrow
 \uparrow Stroke/MI death 10%/7%

Lewington. *Lancet*. 2002

BP and incidence of twelve CVDs: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people

Lifetime risk of 12 different CVD in people with HTN or normal BP from index age 30 years

5.2 y Follow-up

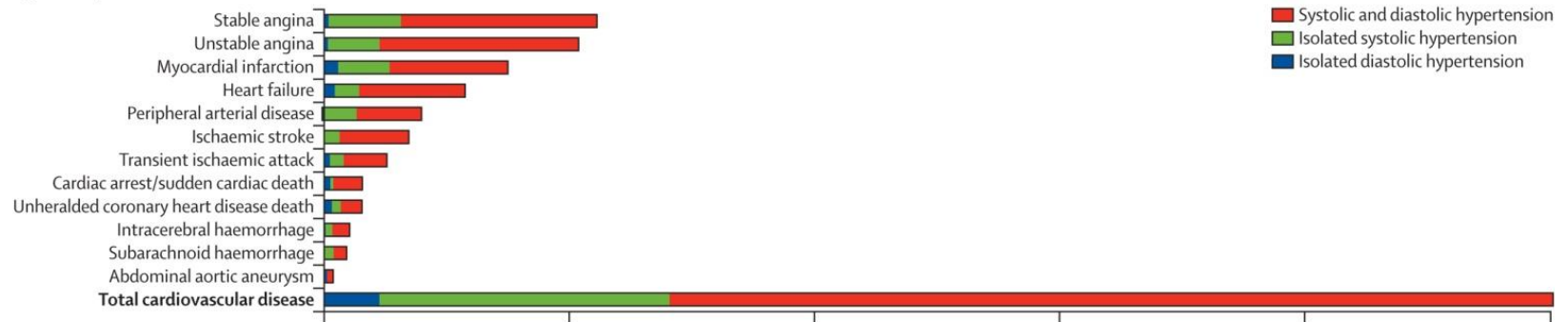


with no evidence of a J-shaped increased risk at lower BP

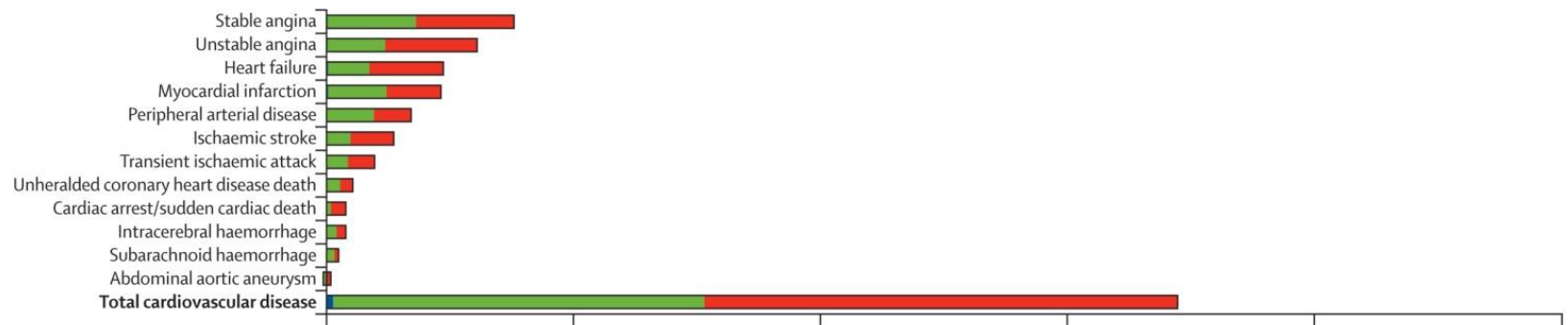
Rapsomaniki E et al The Lancet 2014

Years of life lost to CVD up to 95 years of age associated with HTN at index ages 30, 60 and 80 years

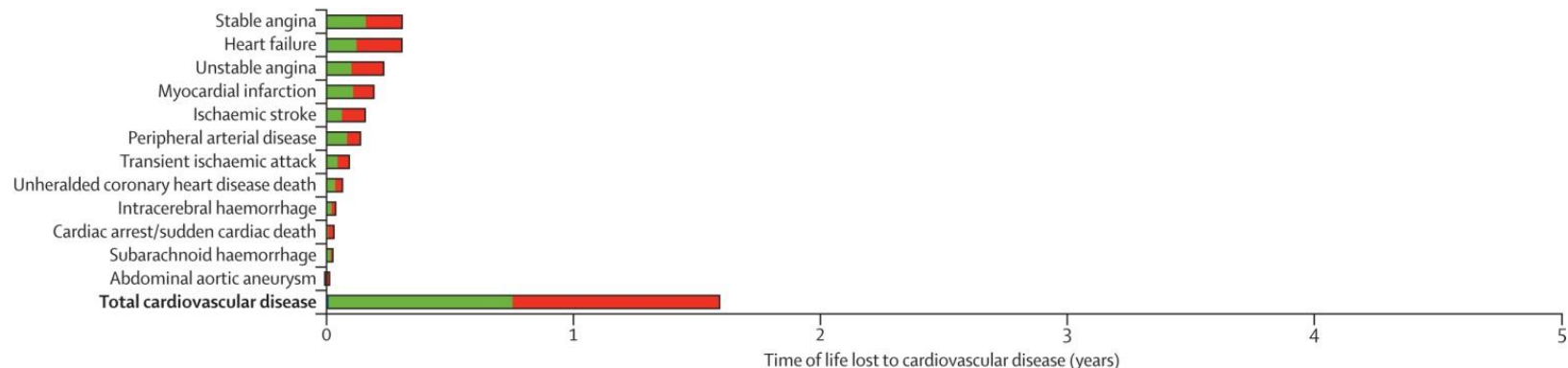
Age 30–95 years



Age 60–95 years



Age 80–95 years



Eleni Rapsomaniki et al The Lancet 2014

ESC/ESH vs. ACC/AHA Hypertension Guideline

| ESC/ESH 2018 (June) | | | | ACC/AHA 2017 (Nov) | | |
|---------------------|-----------------|--------|------------------|---------------------|-----------------|------------------|
| Category | Systolic (mmHg) | | Diastolic (mmHg) | Category | Systolic (mmHg) | Diastolic (mmHg) |
| Optimal | <120 | and | <80 | Normal | <120 | <80 |
| Normal | 120-129 | and | 80-84 | Elevated BP | 120-129 | <80 |
| High Normal | 130-139 | and/or | 85-89 | Stage 1 | 130-139 | 80-89 |
| Grade 1 | 140-159 | and/or | 90-99 | Stage 2 | ≥140 | ≥90 |
| Grade 2 | 160-179 | and/or | 100-109 | Hypertensive crisis | ≥180 | ≥120 |
| Grade 3 | ≥ 180 | and/or | ≥ 110 | | | |

Compiled by **plexus**md

Highlight #1: Changes in BP Categories from JNC7 to the New 2017 ACC/AHA BP Guideline

| SBP | | DBP | JNC7 | 2017 ACC/AHA |
|---------|-----|-------|----------------------|----------------------|
| <120 | and | <80 | Normal BP | Normal BP |
| 120–129 | and | <80 | Prehypertension | Elevated BP |
| 130–139 | or | 80–89 | Prehypertension | Stage 1 hypertension |
| 140–159 | or | 90–99 | Stage 1 hypertension | Stage 2 hypertension |
| ≥160 | or | ≥100 | Stage 2 hypertension | Stage 2 hypertension |



Classification of blood pressure

| Recommendation | Class | Level |
|--|----------|----------|
| It is recommended that BP be classified as optimal, normal, high-normal, or grades 1–3 hypertension, according to office BP. | I | C |

a Class of recommendation

b Level of evidence

| COR | LOE | Recommendation for Definition of High BP |
|----------|-------------|--|
| I | B-NR | BP should be categorized as normal, elevated, or stage 1 or 2 hypertension to prevent and treat high BP. |

Measurement of BP



Patients should be seated comfortably in a quiet environment for 5 min before beginning BP measurements.

Three BP measurements should be recorded, 1–2 min apart, and additional measurements only if the first two readings differ by > 10 mmHg.

BP is recorded as the average of the last two BP readings.

Additional measurements may have to be performed in patients with unstable BP values due to arrhythmias, such as in patients with AF, in whom manual auscultatory methods should be used as most automated devices have not been validated for BP measurement in patients with AF.

Use a standard bladder cuff (12–13 cm wide and 35 cm long) for most patients, but have larger and smaller cuffs available for larger (arm circumference > 32 cm) and thinner arms, respectively.

The cuff should be positioned at the level of the heart with the back and arm supported, to avoid muscle contraction and isometric-exercise dependent increases in BP.

When using auscultatory methods, use phase I and V (sudden reduction/disappearance) Korotkoff sounds to identify SBP and DBP, respectively.

Measure BP in both arms at the first visit to detect possible between-arm differences.

Use the arm with the higher value as the reference.

Measure BP 1 minute and 3 min after standing from seated position in all patients at the first measurement to exclude orthostatic hypotension.

Lying and standing BP measurements should also be considered in subsequent visits in older people, in people with diabetes, and in other conditions in which orthostatic hypotension may frequently occur.

Record heart rate and use pulse palpation to exclude arrhythmia.

Accurate Measurement of BP

Key Steps for Proper BP Measurements

Step 1: Properly prepare the patient.

Step 2: Use proper technique for BP measurements.

Step 3: Take the proper measurements needed for diagnosis and treatment of elevated BP/hypertension.

Step 4: Properly document accurate BP readings.

Step 5: Average the readings.

Step 6: Provide BP readings to patient.

Selection Criteria for BP Cuff Size for Measurement of BP in Adults

| Arm Circumference | Usual Cuff Size |
|-------------------|-----------------|
| 22–26 cm | Small adult |
| 27–34 cm | Adult |
| 35–44 cm | Large adult |
| 45–52 cm | Adult thigh |

Body Position and BP Measurement

SBP has been reported to be 3–10 mm Hg higher in the supine than the seated position.²⁰

DBP is \approx 1–5 mm Hg higher when measured supine vs seated.²⁰

In the supine position, if the arm is resting on the bed, it will be below heart level.

When BP measurements are taken in the supine position, the cuffed arm should be supported with a pillow.

In the seated position, the right atrium level is the midpoint of the sternum or the fourth intercostal space.

If a patient's back is not supported (eg, the patient is seated on an examination table), SBP and DBP may be increased by 5–15 and 6 mm Hg, respectively.²¹

Having legs that are crossed during BP measurement may raise SBP by 5–8 mm Hg and DBP by 3–5 mm Hg.²²

If the upper arm is below the level of the right atrium (eg, when the arm is hanging down while in the seated position), the readings will be too high.

The cuffed arm should be held up by the observer or resting on a table at heart level. If the arm is held up by the patient, BP will be raised.

BP indicates blood pressure; DBP, diastolic blood pressure; and SBP, systolic blood pressure.

Automated Office BP Measurement Preferred

- Automated office blood pressure (AOBP) is the preferred method of performing in-office BP measurement

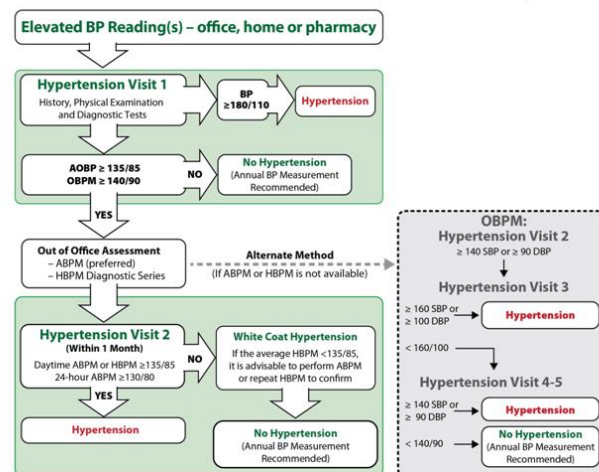


II. Criteria for the diagnosis of hypertension and recommendations for follow-up: overview

CHEP 2016 Guidelines

What's new?

- New thresholds and targets for high risk patients (SPRINT)
- Assessing** clinic blood pressures using automatic electronic (oscillometric) monitors
- Adopting** healthy behaviours is integral to the management of hypertension (focus on potassium supplementation)
- Updating** the recommendation for lipid screening in patients with hypertension (now can be completed non-fasting)
- Updating** the treatment of patients with hypertension with concurrent coronary artery disease
- New** recommendations on the diagnosis and management of hypertension in pediatric patients (*NOT the focus of this presentation*)





Comparisons of blood pressure readings obtained in clinical settings using different methods of blood pressure measurement

| | Mean blood pressure* (mmHg) | | |
|---------------------------------|---|---------------------------------|--------------------------|
| | Centre for Studies in Primary Care ₁ | ABPM referral unit ₂ | CAMBO trial ₃ |
| Routine manual office BP | 151/83 | 152/87 | 150/81 |
| Automated office BP | 140/80 | 132/75 | 135/77 |
| Awake ambulatory BP | 142/80 | 134/77 | 133/74 |

*The automated office blood pressure (BP) and awake ambulatory BP were similar, and both were lower than the routine manual BP obtained in community practice.

1. Beckett L et al, *BMC Cardiovasc. Disord.* 2005; 5: 18. 2. Myers MG et al, *J. Hypertens.* 2009; 27: 280. 3. Myers MG, et al. *BMJ* 2011; 342: d286.



Predictive value of AOBP

AOBP predicts end-organ damage

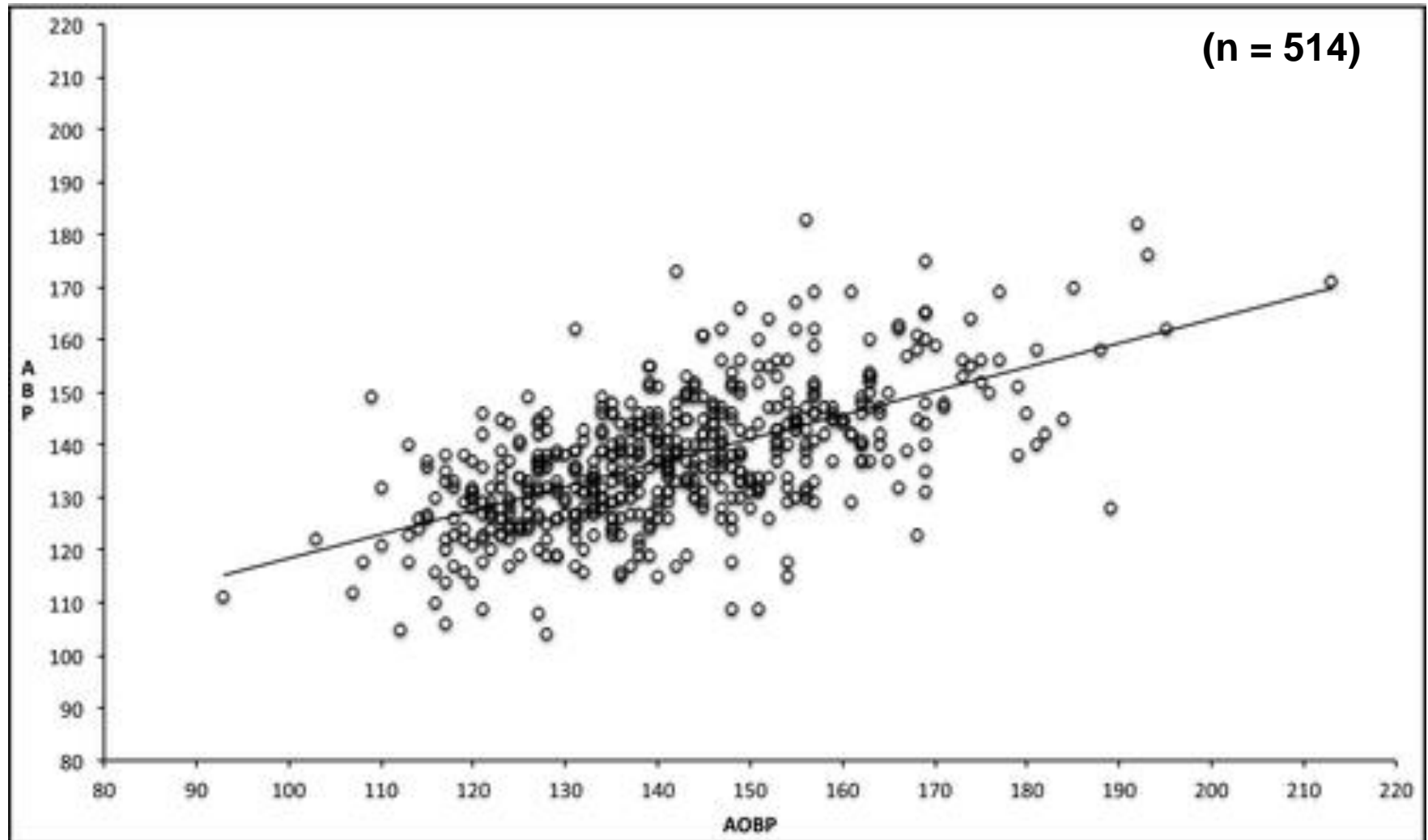
- Systolic AOBP correlates with **LVMI** similarly to awake ABPM
- AOBP and 24-h ABPM have similar predictive ability for **microalbuminuria**
- AOBP is more strongly associated with **cIMT** (compared to OBPM)

cIMT: Carotid Intima Media Thickness

LVMI: Left Ventricular Mass Index

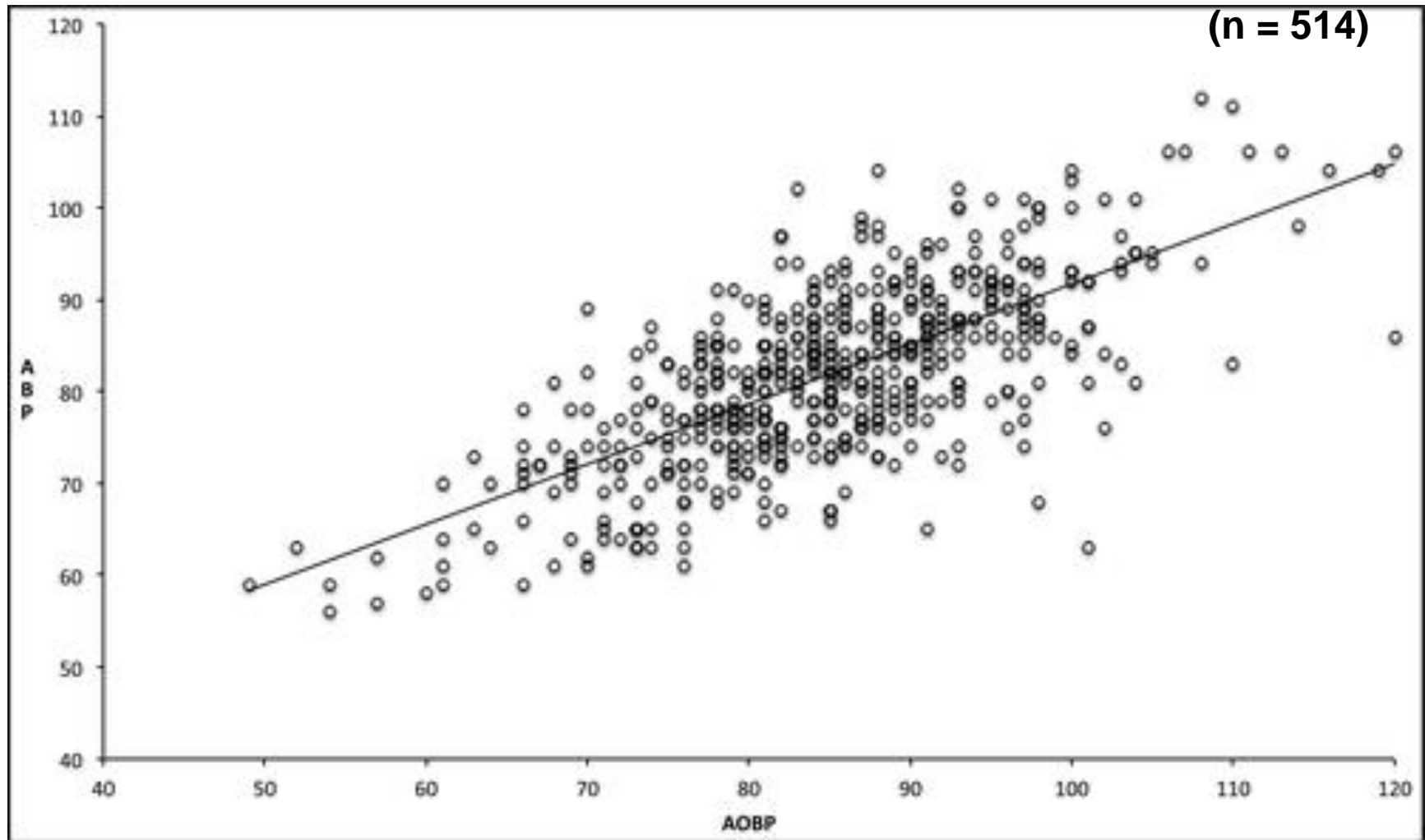
**Comparison of awake ambulatory BP and automated office BP using linear regression analysis in
untreated patients in routine clinical practice**

**Scatter plot and regression line for the association between awake ambulatory
(A)BP and automated office (AO)BP for SBP**



Comparison of awake ambulatory blood pressure and automated office blood pressure using linear regression analysis in untreated patients in routine clinical practice

Scatter plot and regression line for the association between awake ambulatory (A)BP and diastolic automated office (AO)BP for DBP



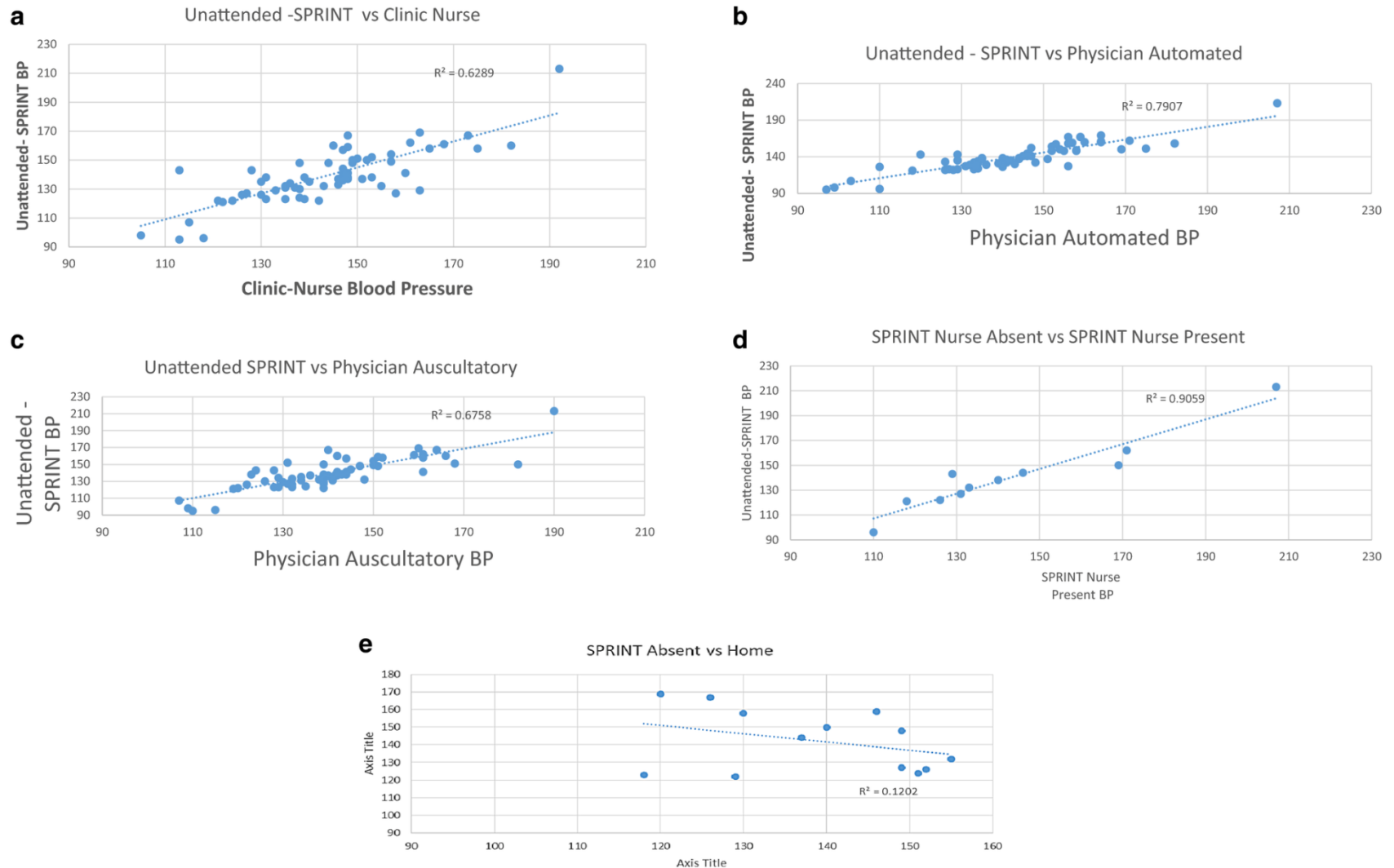
Studies Comparing AOBP With Awake Ambulatory

| Study | Participants, n | Population | Type of BP Measurement, mm Hg | |
|----------------------------------|-----------------|---------------------|-------------------------------|--------------------------|
| | | | Automated Office SBP/DBP | Awake Ambulatory SBP/DBP |
| Myers et al ⁴⁸ | 309 | ABPM unit | 132/75 | 134/77 |
| Beckett and Godwin ⁴⁹ | 481 | Family practice | 140/80 | 142/80 |
| Myers et al ⁴³ | 62 | Hypertension clinic | 140/77 | 141/77 |
| Myers et al ⁵⁰ | 200 | ABPM unit | 133/72 | 135/76 |
| | 200 | ABPM unit | 132/76 | 134/77 |
| Myers ⁵¹ | 254 | ABPM unit | 133/80 | 135/81 |
| Godwin et al ⁵² | 654 | Family practice | 139/80 | 141/80 |
| Myers et al ⁵³ | 139 | ABPM unit | 141/82 | 142/81 |
| Myers et al ⁴⁷ | 303 | Family practice | 135/77 | 133/74 |
| Andreadis et al ⁵⁴ | 90 | Hypertension clinic | 140/88 | 136/87 |
| Myers et al ⁵³ | 100 | ABPM unit | 137/79 | 139/80 |
| Padwal et al ⁵⁵ | 100 | Research unit | 136/79 | 136/80 |
| Armstrong et al ⁴² | 422 | ABPM unit | 141/83 | 139/81 |
| Ringrose et al ⁵⁶ | 96 | ABPM unit | 131/82 | 143/84 |
| Mean | | | 136.4/79.3 | 137.9/79.6 |

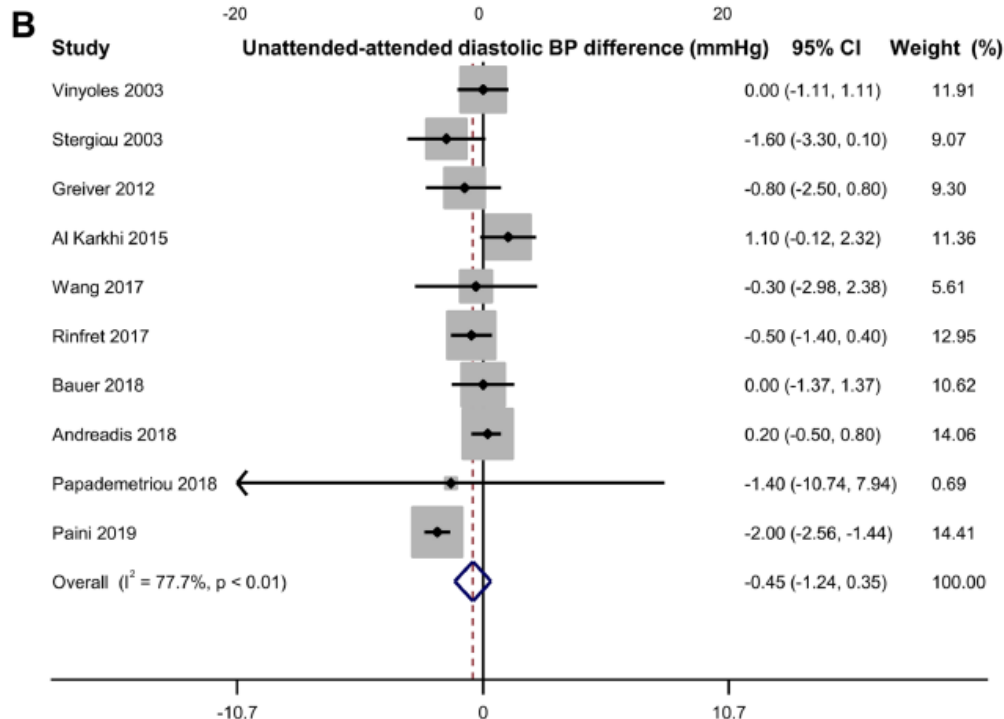
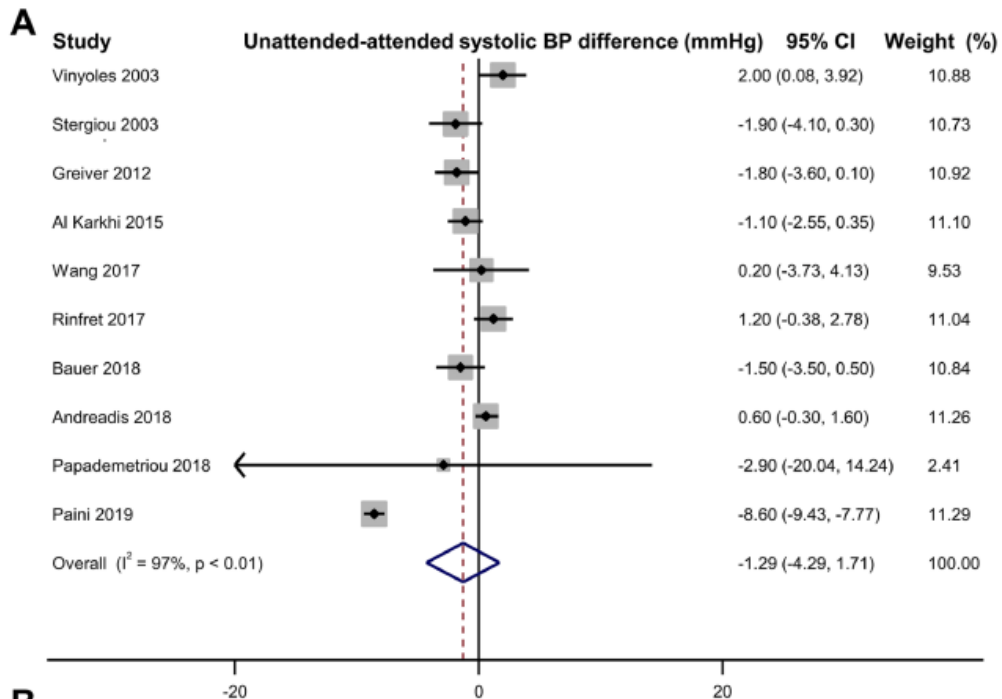
ABPM indicates ambulatory blood pressure monitoring; AOBP, automated office blood pressure; BP, blood pressure; DBP, diastolic blood pressure; and SBP, systolic blood pressure.



Unobserved automated office BP is similar to other clinic BP measurements: A prospective randomized study



Vasilios Papademetriou et al The Journal of Clinical Hypertension, 2018,



**Unattended versus
attended automated
office BP:
Systematic review and
meta-analysis of studies
using the same
methodology for both
methods**

Summary Points From the Scientific Statement on the Measurement of BP in Humans

BP components

Several BP components (SBP and DBP, pulse pressure, mean arterial pressure) are associated with CVD risk.

SBP and DBP levels are used to define hypertension in most guidelines, including the 2017 Hypertension Clinical Practice Guidelines.

BP measure in the office

The auscultatory BP method has been the traditional approach for measuring BP but is increasingly being replaced with the oscillometric method.

Aneroid sphygmomanometers require frequent calibration (every 2–4 wk for handheld devices and every 3–6 mo for wall-mounted devices).

AOBP devices, which can be used with or without staff present (attended and unattended AOBP, respectively), should be considered for use in measuring office BP.

Unattended AOBP has been associated with a lower prevalence of white-coat effect compared with office BP measured through auscultation and reduces the possibility of human error in BP measurement.

Office BP should be measured ≥ 2 times at each clinic visit.

Training of personnel is crucial for BP measurement, even when AOBP is being used.

24-h ABPM

ABPM is the preferred approach for assessing out-of-office BP.

The main indications for ABPM are to detect white-coat hypertension and masked hypertension.

White-coat hypertension may not be associated with an increased risk for CVD.

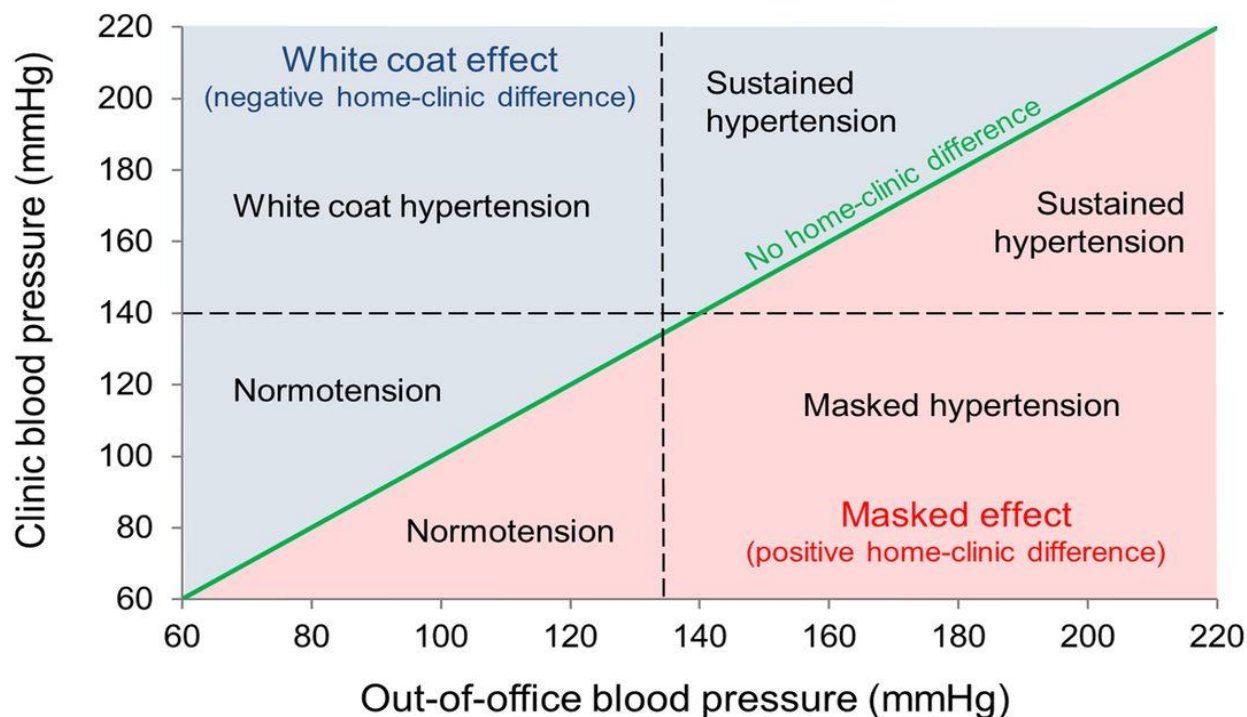
Masked hypertension is associated with a risk for CVD approaching that for individuals with sustained hypertension.

Nocturnal hypertension is common among blacks. ABPM is the preferred approach to assess for nocturnal hypertension.

ABPM / HBPM

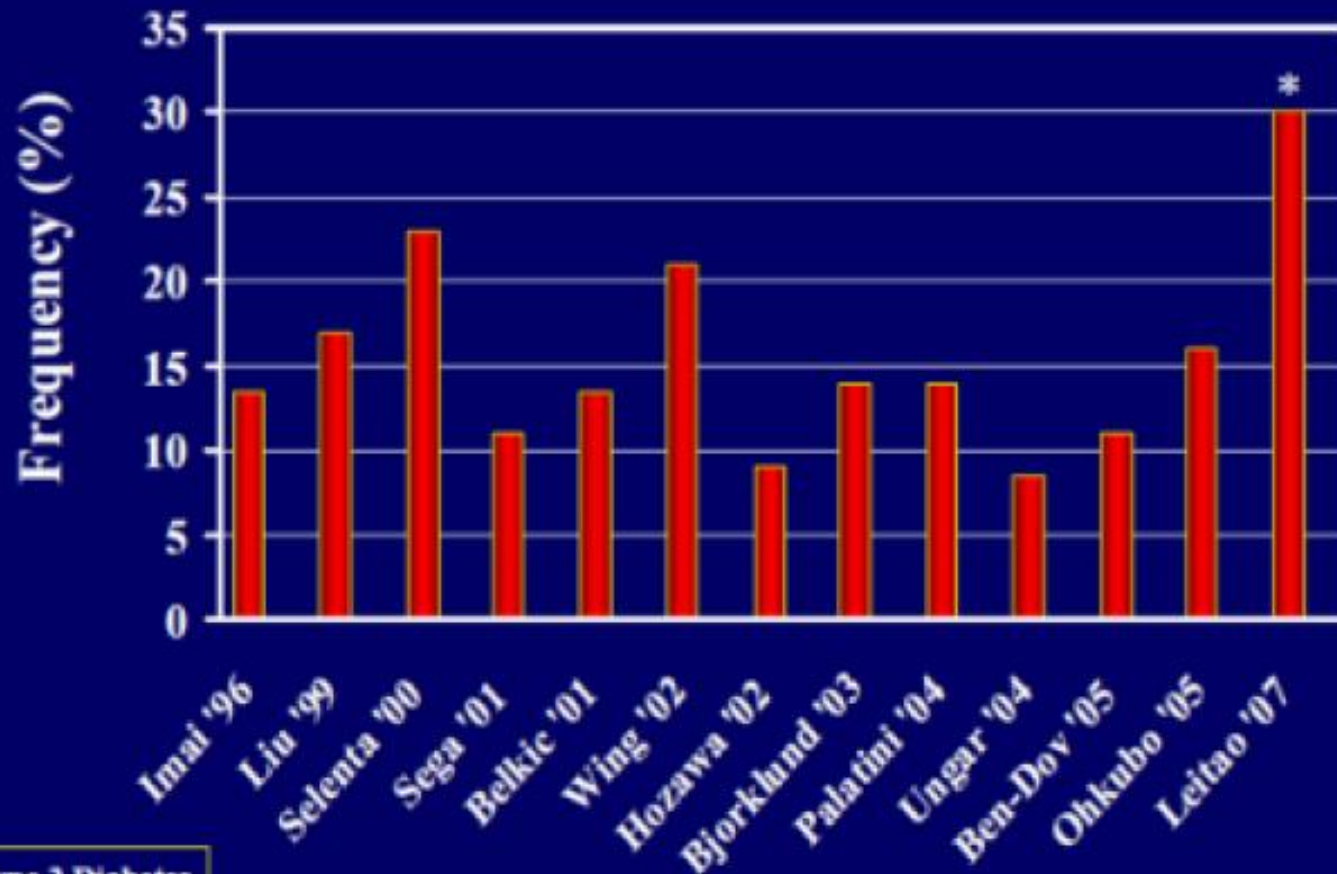


Definitions of normotension, HTN and the home-clinic BP difference

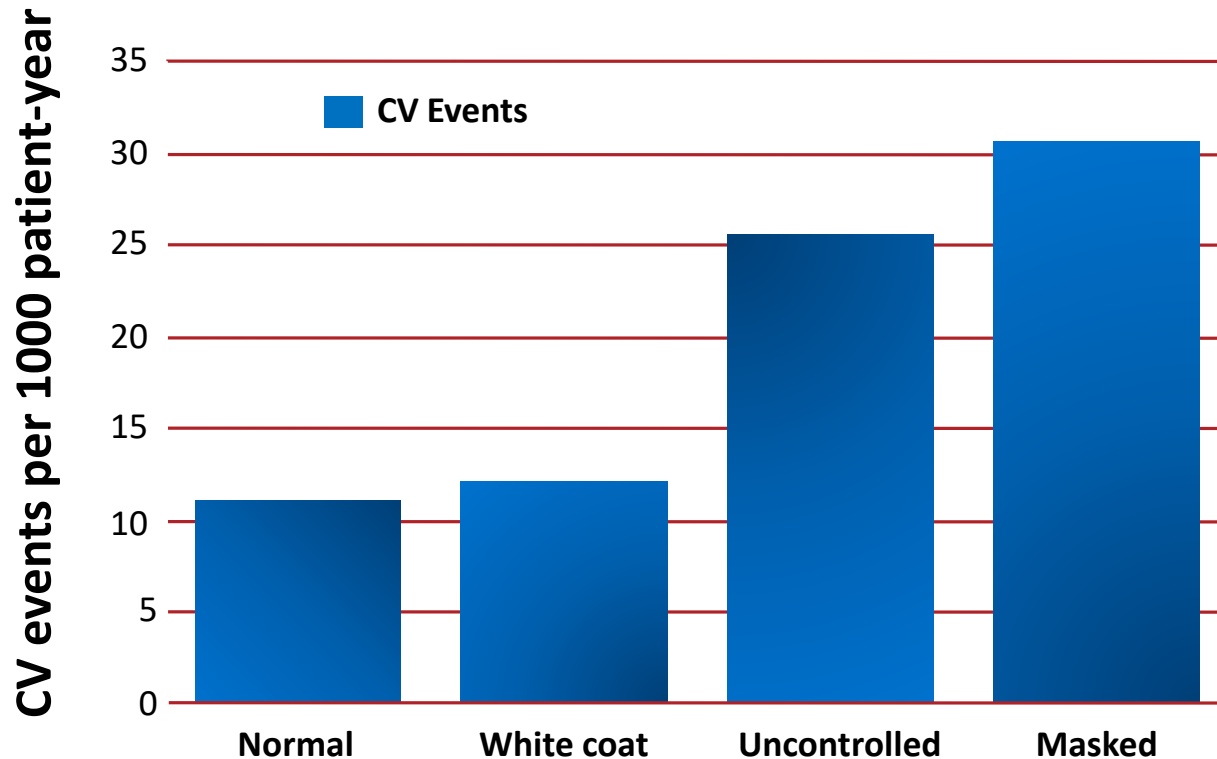


| Condition | Clinic blood pressure | Out-of-office blood pressure | Home-clinic blood pressure difference |
|-------------------------|-----------------------|------------------------------|---------------------------------------|
| Normotension | <140/90mmHg | <135/85mmHg | Positive or negative |
| Sustained hypertension | ≥140/90mmHg | ≥135/85mmHg | Positive or negative |
| White coat hypertension | ≥140/90mmHg | <135/85mmHg | Negative |
| Masked hypertension | <140/90mmHg | ≥135/85mmHg | Positive |
| White coat effect | > out-of-office BP | < clinic BP | Negative |
| Masked effect | < out-of-office BP | > clinic BP | Positive |

Prevalence of Masked Hypertension in Adults Identified with **ABPM**



The Prognosis of *White Coat* and *Masked* Hypertension

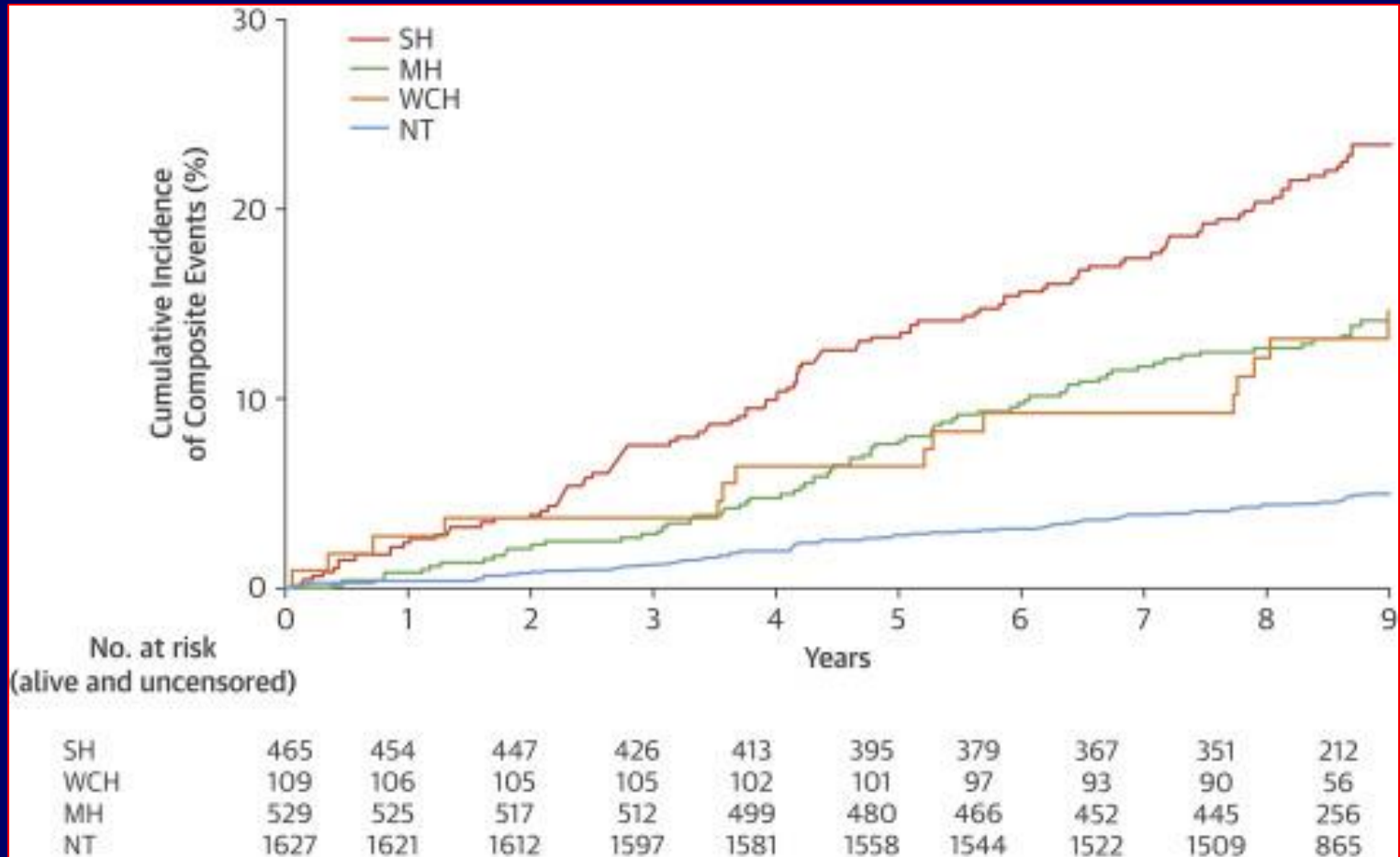


Prevalence of masked hypertension is approximately 10% in the general population (prevalence is higher in diabetic patients).

Prevalence is approximately 10% in hypertensive patients.

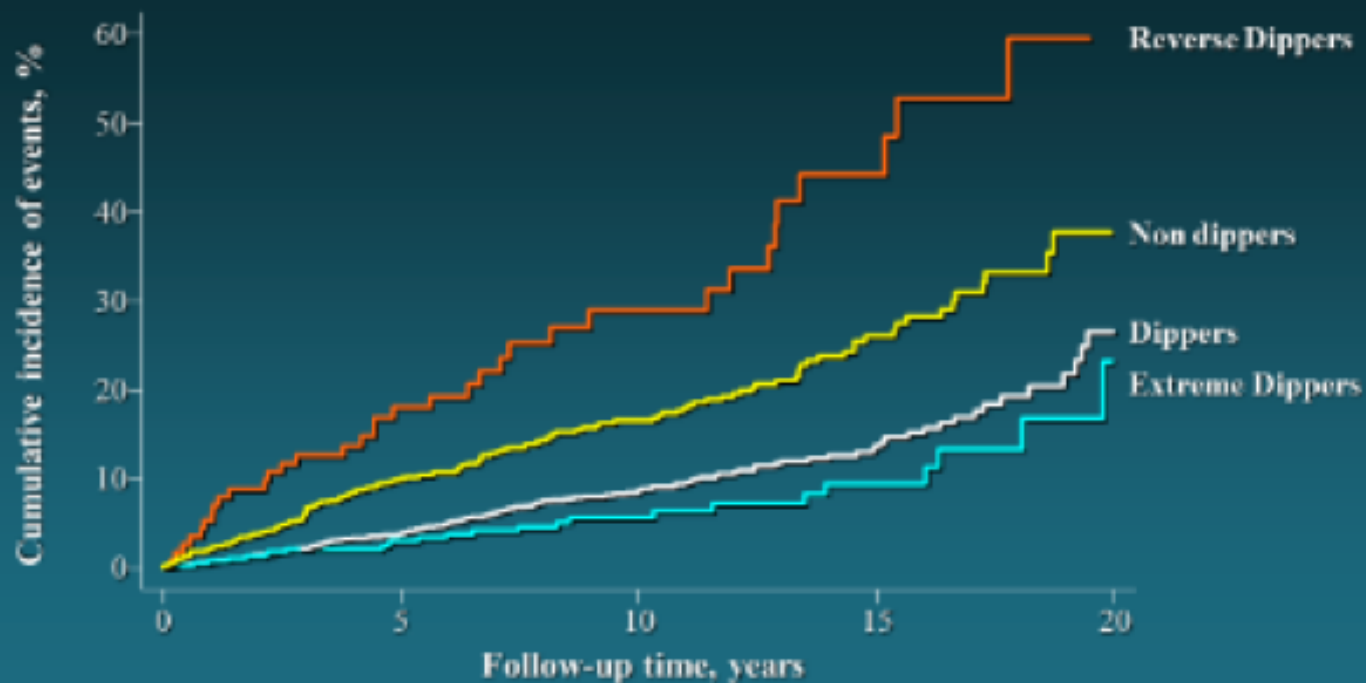
Okhubo T, et al. *J Am Coll Cardiol* 2005;46;508-15

Kaplan-Meier Curves for the Cumulative Incidence of Composite CV Events Among the Normotension, White-Coat HTN, Masked HTN and Sustained HTN Groups

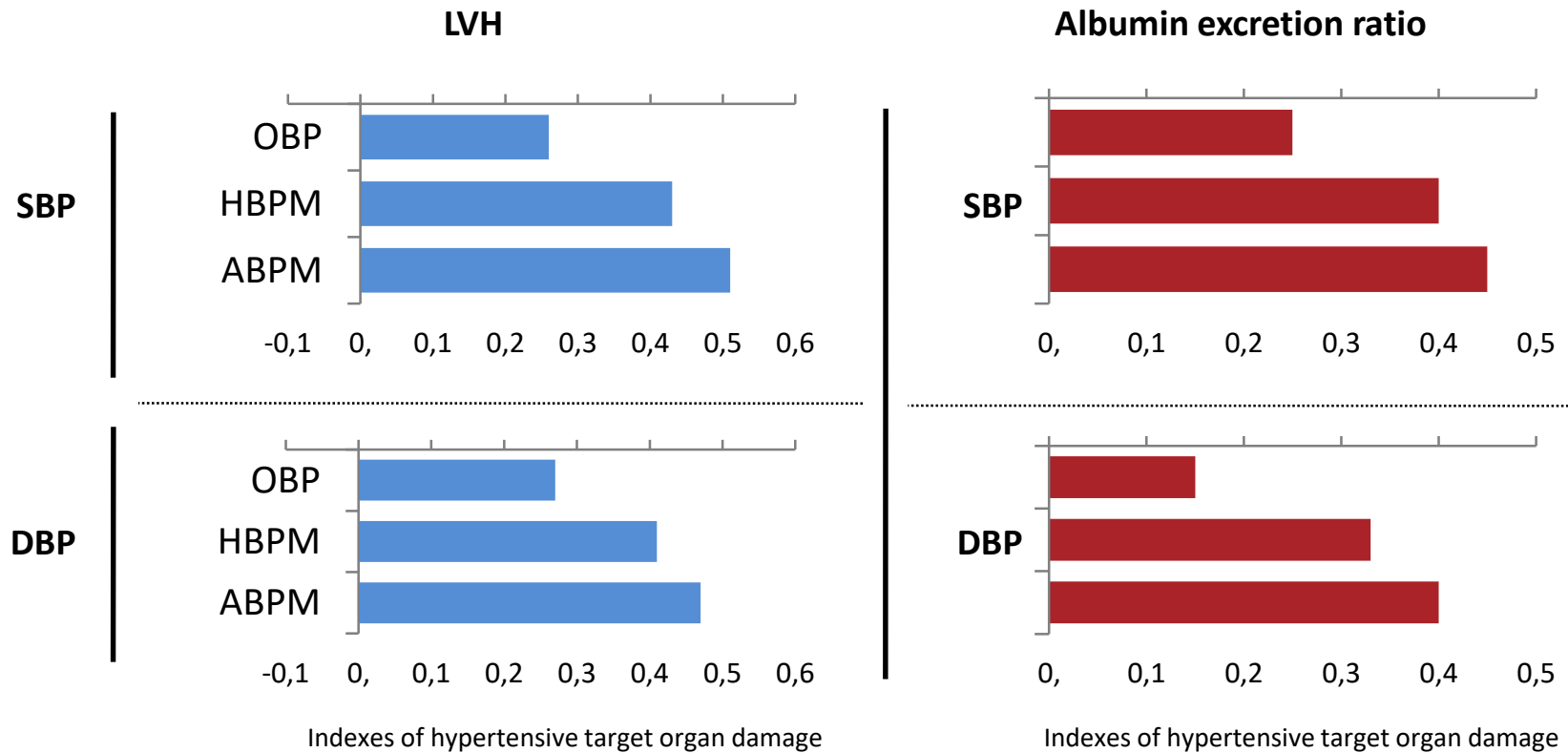


There was a significant difference among the 4 groups over a median follow-up period of 9.5 years.

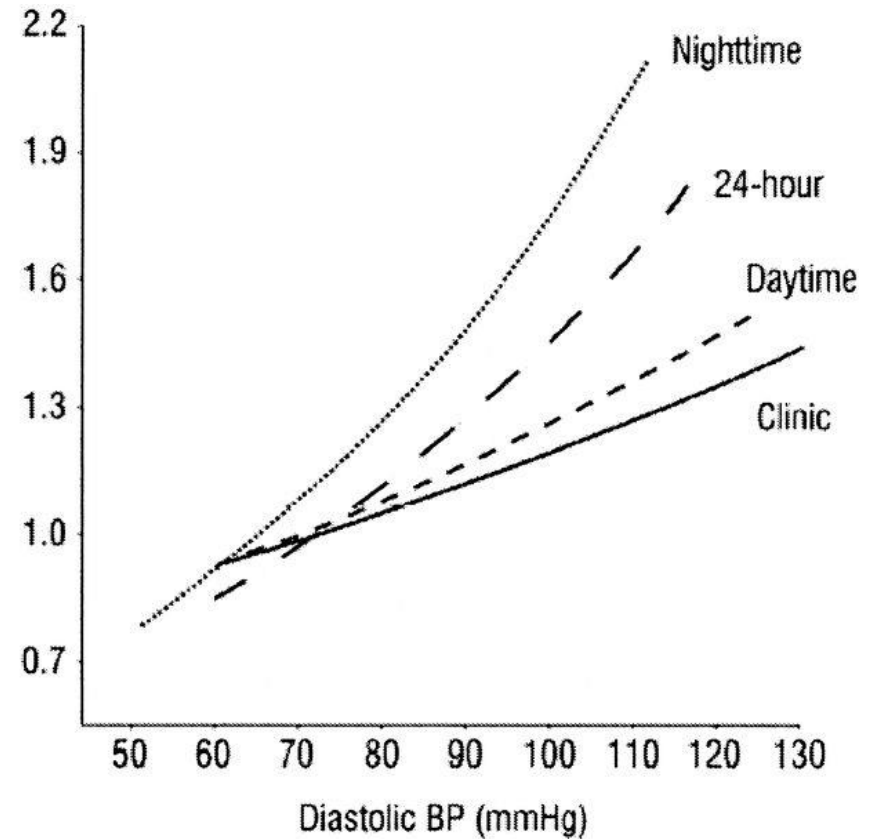
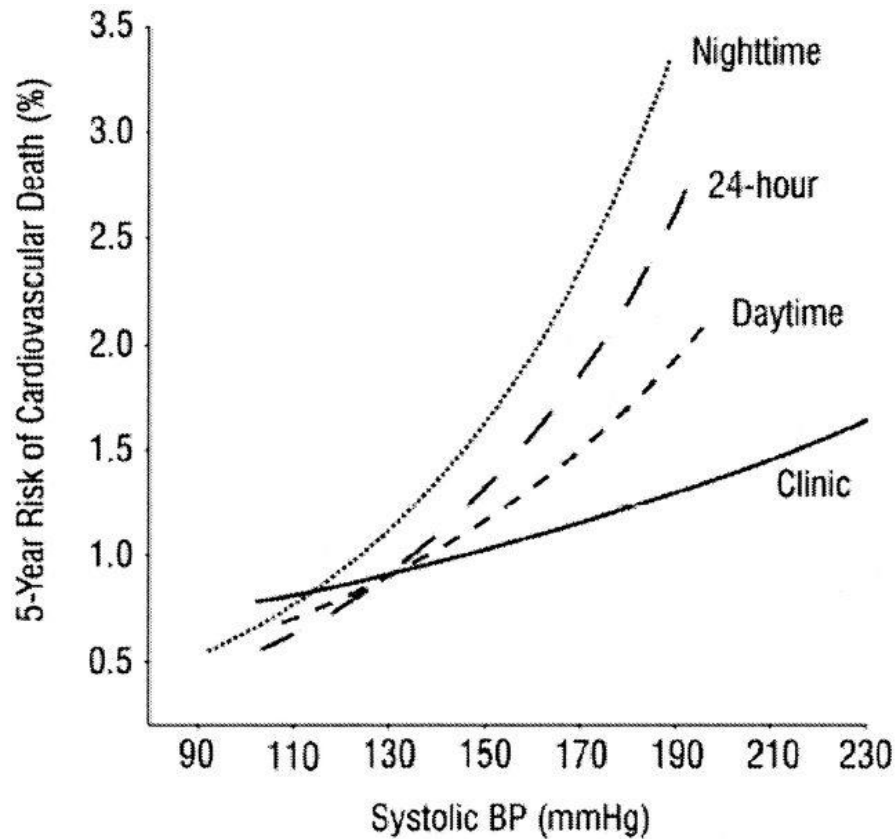
Cumulative Incidence of Cardiovascular Events in Dippers, Nondippers, Reverse Dippers, and Extreme Dippers



Out-of-Office BP Measurements are More Highly Correlated With BP-Related Risk



5-year risk of CV death in the study cohort of 5,292 patients for clinic BP and ambulatory BP monitoring

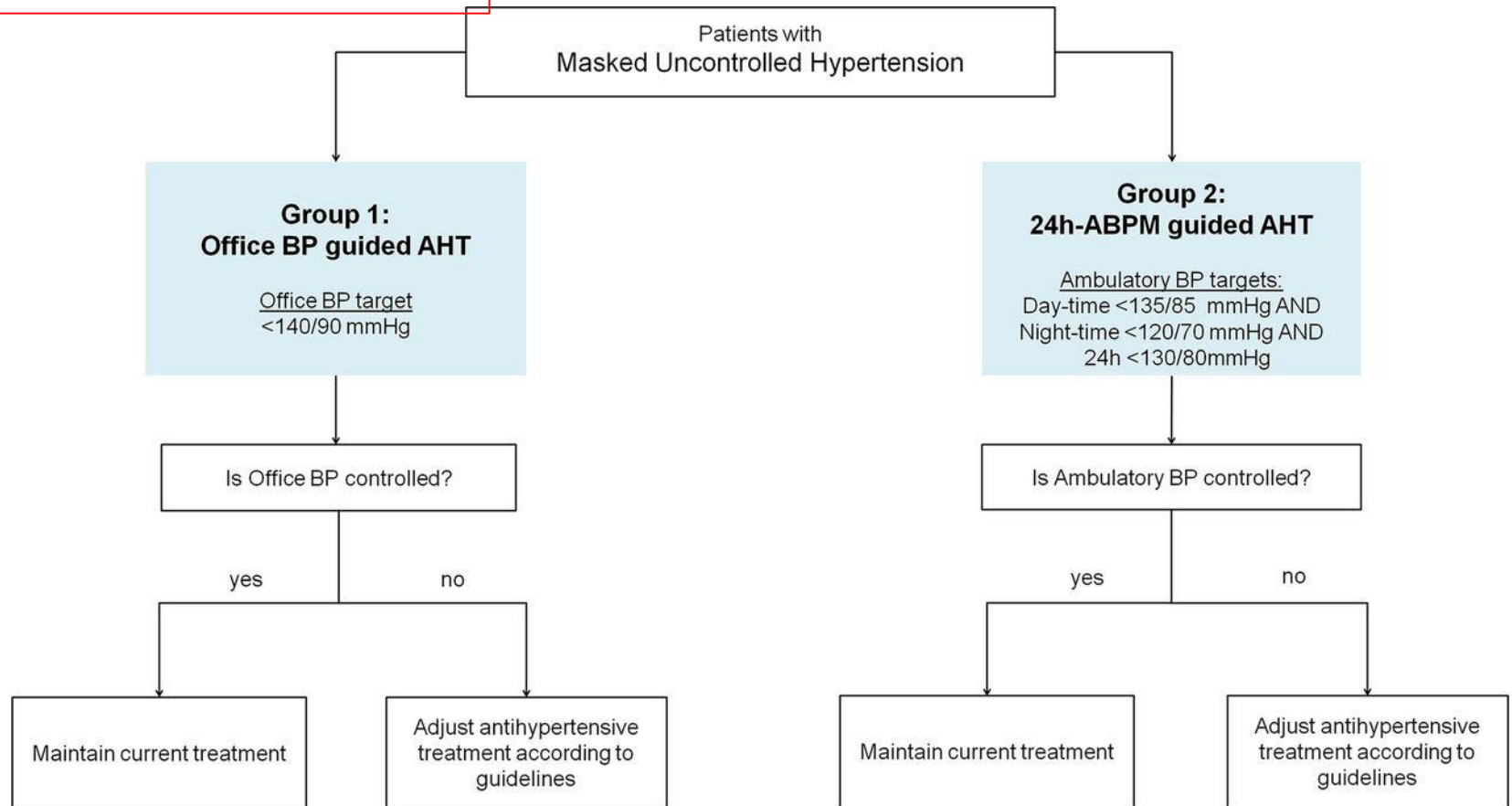


Bryan Williams JACC 2006;48:1698-1711

MASKed-unconTrolled hypERTension “MASTER” study

Randomisation groups and patient flow in the study

N= 1240 treated hypertensives



Gianfranco Parati et al.
BMJ Open 2018

The effects of MUCH management strategy based on ABPM or on OBPM on CV and renal intermediate outcomes (changing LV mass and microalbuminuria, coprimary outcomes) at 1 year and on CV events at 4 years and on changes in BP-related variables will be assessed

Comparison of ABPM and HBPM

| ABPM | HBPM |
|---|--|
| Advantages <ul style="list-style-type: none"> • Can identify white-coat and masked hypertension • Stronger prognostic evidence • Night-time readings • Measurement in real-life settings • Additional prognostic BP phenotypes • Abundant information from a single measurement session, including short-term BP variability | Advantages <ul style="list-style-type: none"> • Can identify white-coat and masked hypertension • Cheap and widely available • Measurement in a home setting, which may be more relaxed than the doctor's office • Patient engagement in BP measurement • Easily repeated and used over longer periods to assess day-to-day BP variability |
| Disadvantages <ul style="list-style-type: none"> • Expensive and sometimes limited availability • Can be uncomfortable | Disadvantages <ul style="list-style-type: none"> • Only static BP is available • Potential for measurement error • No nocturnal readings |

ABPM/HBPM

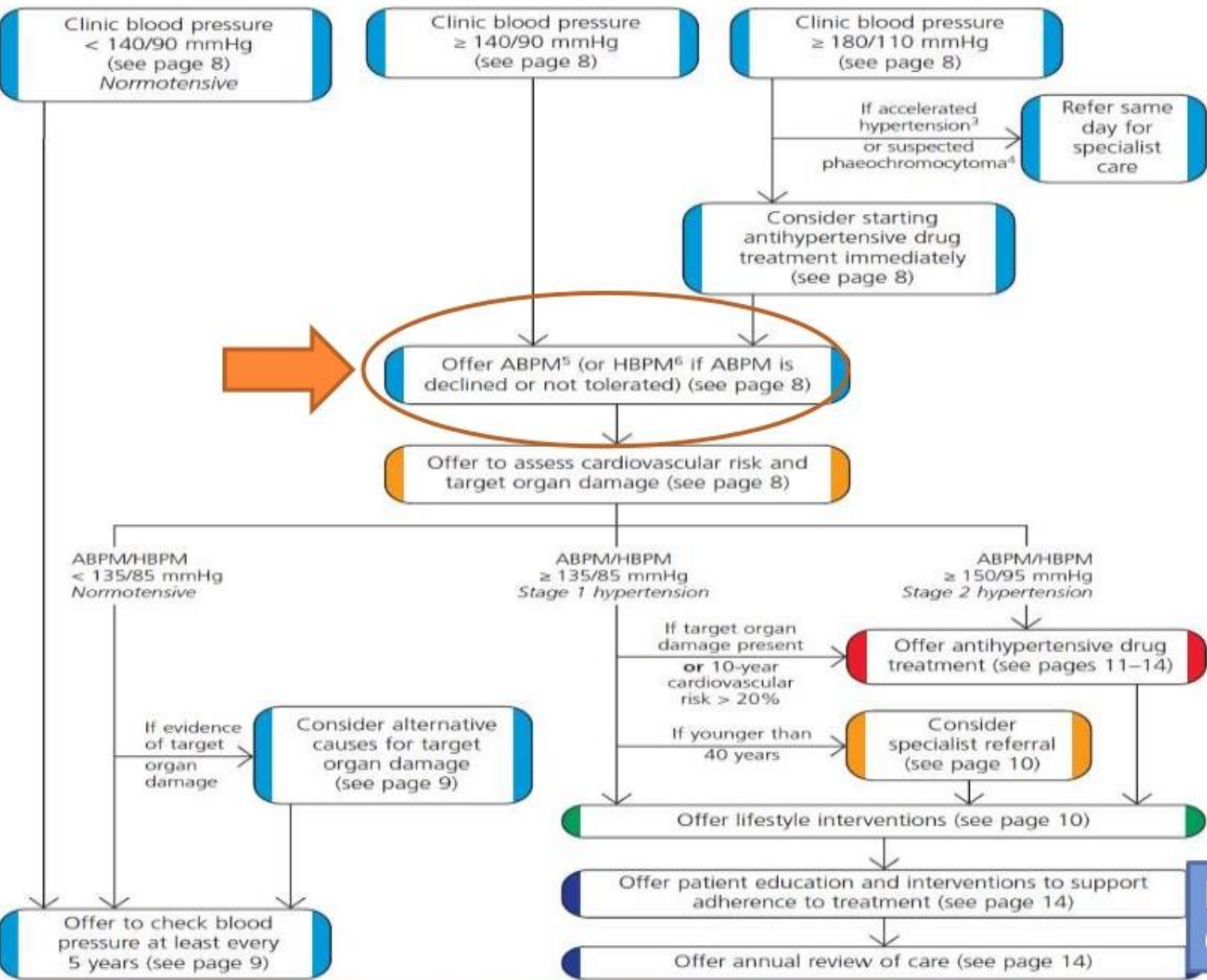
ESH /ESC 2018

| Recommendations | Class ^a | Level ^b |
|--|--------------------|--------------------|
| Out-of-office BP (i.e. ABPM or HBPM) is specifically recommended for a number of clinical indications, such as identifying white-coat and masked hypertension, quantifying the effects of treatment, and identifying possible causes of side effects ^{17,54,62,68,72} (e.g. symptomatic hypotension). | I | A |




| COR | LOE | Recommendation for Out-of-Office and Self-Monitoring of BP |
|-----|-----------------|--|
| I | A ^{SR} | Out-of-office BP measurements are recommended to confirm the diagnosis of hypertension and for titration of BP-lowering medication, in conjunction with telehealth counseling or clinical interventions. |

ACC/AHA 2017

Care pathway for hypertension



Definitions of HTN according to office, ambulatory, and home BP levels



| Category | SBP (mmHg) | | DBP (mmHg) |
|-----------------------------|---------------|--------|---------------|
| Office BP ^a | ≥140 | and/or | ≥90 |
| Ambulatory BP | | | |
| Daytime (or awake) mean | ≥135 | and/or | ≥85 |
| Night-time (or asleep) mean | ≥120 | and/or | ≥70 |
| 24 h mean | ≥130 | and/or | ≥80 |
| Home BP mean | ≥135 | and/or | ≥85 |

©ESC/ESH 2018

BP = blood pressure; DBP = diastolic blood pressure; SBP = systolic blood pressure.

^aRefers to conventional office BP rather than unattended office BP.

DEFINITIONS OF HIGH BP

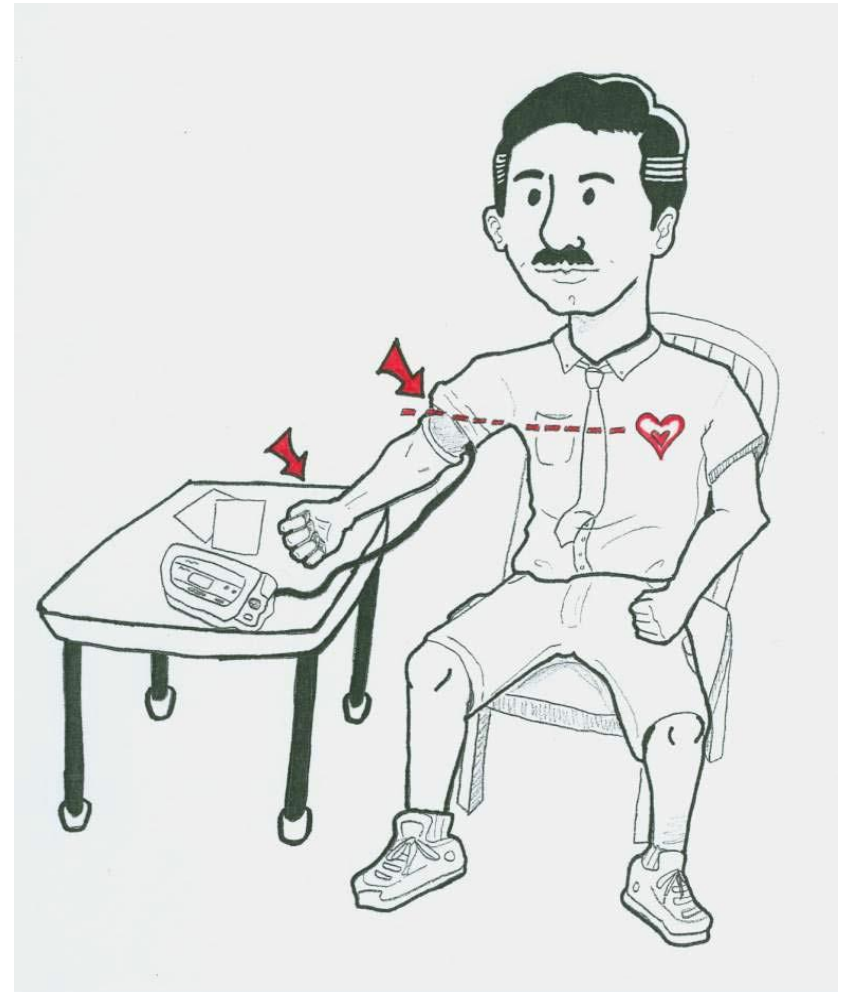
2017 ACC/AHA

| Definitions | Office-Based BP (mm Hg) | 24-Hour mean Ambulatory BP (mm Hg) | Self-Recorded BP (mm Hg) |
|----------------|----------------------------|--|-----------------------------|
| Normal | <120/80 | <115/75 | <120/80 |
| Elevated BP | 120-129/<80 | — | — |
| HTN, Stage 1 | 130-139/80-89 | ≥125/75 | ≥130/80 |
| HTN, Stage 2 | ≥140/90 | ≥130/80 | ≥135/85 |
| White Coat HTN | ≥130/80 | <125/75 | <130/80 |
| Masked HTN | <130/80 | ≥125/75 | ≥130/80 |

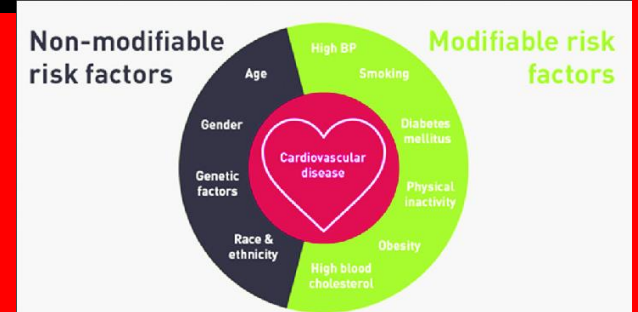
Resistant HTN: Rx 3 different categories including diuretic, not at target

Correct Technique for home BP readings

- Sit calmly with back support, feet flat on floor for 5 minutes before taking a reading.
- Upper arm should be bare.
- When taking a reading the arm with cuff should be supported on a firm surface at heart level.
- Caffeine, smoking, and exercise should be avoided for at least 30 minutes before the reading is taken.
- The cuff should fit snugly.

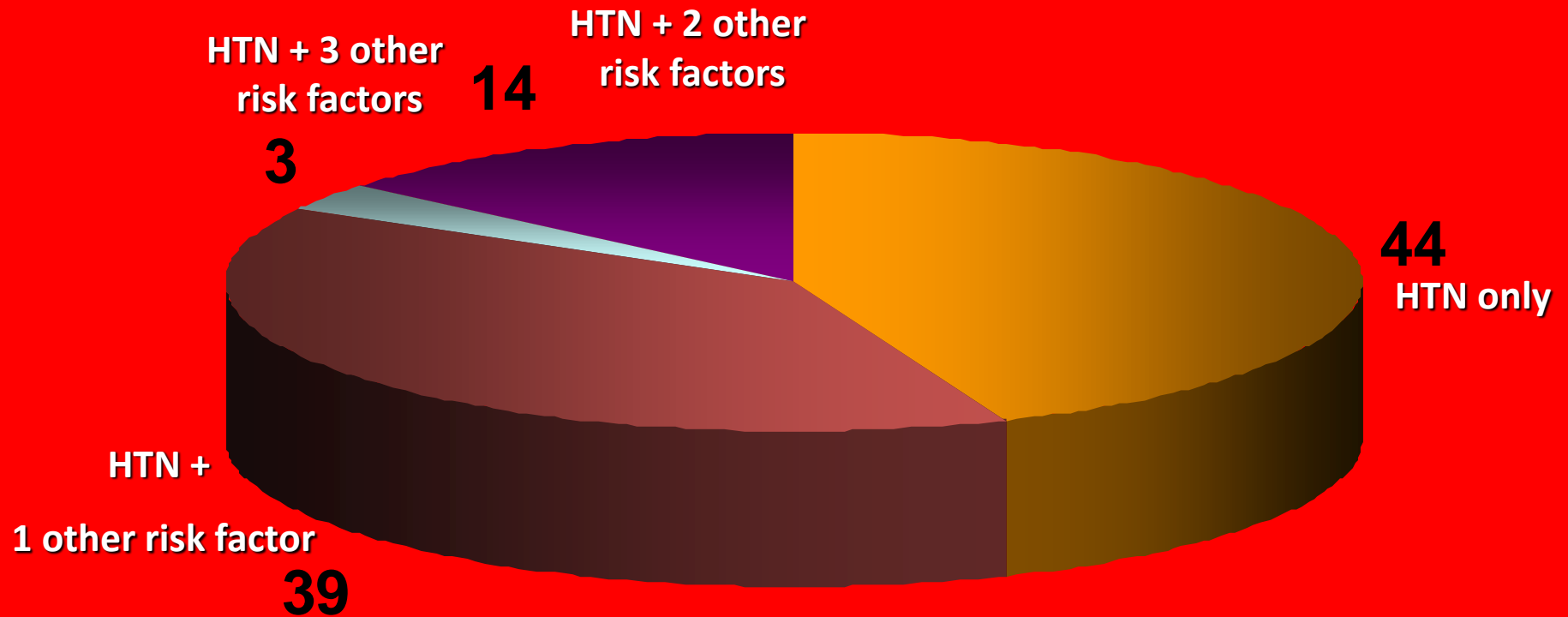


BP and CVD Risk



HTN Commonly Clusters with Other Risk Factors

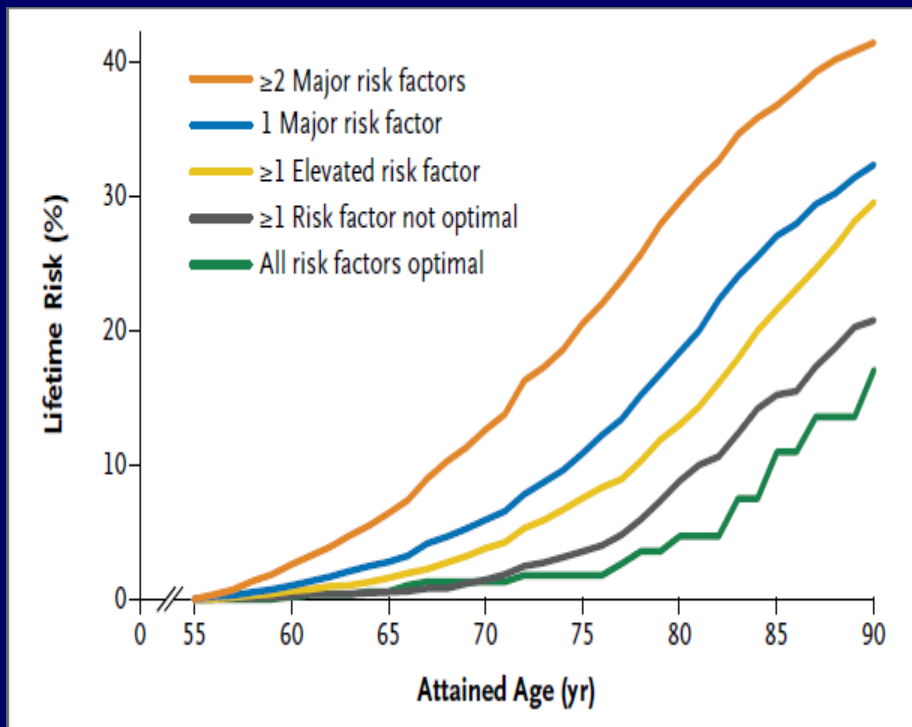
Kaiser Permanente Northwest database;
N=57,573 aged ≥ 35 years with HTN and no CVD



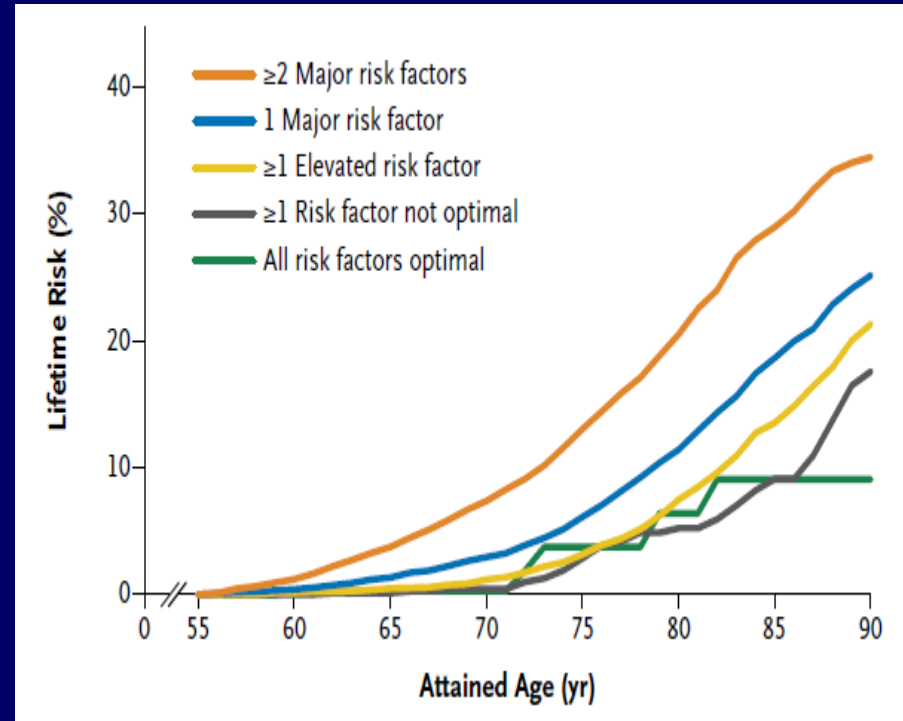
Other risk factors: obesity,* hyperlipidemia, and diabetes

*Body mass index ≥ 30 kg/m²

Lifetime Risks of Cardiovascular Disease Death by Number of Risk Factors and Attained Age



Men



Women

Optimal risk factors: total cholesterol <180 mg/dl, blood pressure <120/80, non-smoking, non-diabetic.

Major risk factors: current smoker, diabetes, treated cholesterol or untreated cholesterol ≥ 240 mg/dl, treated hypertension or untreated systolic BP ≥ 160 mmHg or diastolic BP ≥ 100 mmHg.

(Berry et al. , 2012)

Factors influencing CV risk in patients with hypertension - 1

| Demographic characteristics and laboratory parameters |
|---|
| Sex (men > women) |
| Age |
| Smoking – current or past history |
| Total cholesterol and HDL-C |
| Uric acid |
| Diabetes |
| Overweight or obesity |
| Family history of premature CVD (men aged < 55 years and women aged < 65 years) |
| Family or parental history of early onset hypertension |
| Early onset menopause |
| Sedentary lifestyle |
| Psychosocial and socioeconomic factors |
| Heart rate (resting values > 80 beats per min) |

Factors influencing CV risk in patients with hypertension - 2

| Asymptomatic HMOD |
|--|
| Arterial stiffening: Pulse pressure (in older people) ≥ 60 mmHg Carotid-femoral PWV > 10 m/s |
| ECG LVH |
| Echocardiographic LVH |
| Microalbuminuria or elevated albumin-creatinine ratio |
| Moderate CKD with eGFR 30–59 mL/min/1.73 m ² (BSA) |
| Ankle-brachial index < 0.9 |
| Advanced retinopathy: haemorrhages or exudates, papilloedema |

Factors influencing CV risk in patients with hypertension - 3

| Established CV or renal disease |
|--|
| Cerebrovascular disease: ischaemic stroke, cerebral haemorrhage, TIA |
| CAD: myocardial infarction, angina, myocardial revascularization |
| Presence of atheromatous plaque on imaging |
| Heart failure, including HFpEF |
| Peripheral artery disease |
| Atrial fibrillation |
| Severe CKD with eGFR < 30 mL/min/1.73 m ² |

10-year CV risk categories (SCORE system)

| | |
|-----------------------|---|
| Very high risk | <p>People with any of the following:</p> <p>Documented CVD, either clinical or unequivocal on imaging.</p> <ul style="list-style-type: none"> • Clinical CVD includes acute myocardial infarction, acute coronary syndrome, coronary or other arterial revascularization, stroke, TIA, aortic aneurysm and PAD. • Unequivocal documented CVD on imaging includes significant plaque (i.e. $\geq 50\%$ stenosis) on angiography or ultrasound. It does not include increase in carotid intima-media thickness. • Diabetes mellitus with target organ damage, e.g. proteinuria or a with a major risk factor such as grade 3 hypertension or hypercholesterolaemia • Severe CKD (eGFR < 30 mL/min/1.73 m²) • A calculated 10-year SCORE of $\geq 10\%$ |
| High risk | <p>People with any of the following:</p> <ul style="list-style-type: none"> • Marked elevation of a single risk factor, particularly cholesterol > 8 mmol/L (> 310 mg/dL) e.g. familial hypercholesterolaemia, grade 3 hypertension (BP $\geq 180/110$ mmHg) • Most other people with diabetes mellitus (except some young people with type 1 diabetes mellitus and without major risk factors, that may be moderate risk) • Hypertensive LVH • Moderate CKD (eGFR 30–59 mL/min/1.73 m²) • A calculated 10-year SCORE of 5–10% |
| Moderate risk | <p>People with:</p> <ul style="list-style-type: none"> • A calculated 10-year SCORE of 1% to $< 5\%$ • Grade 2 hypertension • Many middle-aged people belong to this category <div> <ul style="list-style-type: none"> ▪ family history of premature CAD ▪ abdominal obesity ▪ physical activity pattern ▪ HDL-C ▪ TG ▪ hsCRP ▪ social class </div> |
| Low risk | <p>People with:</p> <ul style="list-style-type: none"> • A calculated 10-year SCORE of $< 1\%$ |

Classification of HTN stages according to BP levels, presence of CV risk factors, HTN-mediated organ damage, or comorbidities

| Hypertension disease staging | Other risk factors, HMOD, or disease | BP (mmHg) grading | | | |
|-----------------------------------|--|---|-------------------------------------|---------------------------------------|--|
| | | High normal SBP 130-139 DBP 85-89 | Grade 1 SBP 140-159 DBP 90-99 | Grade 2 SBP 160-179 DBP 100-109 | Grade 3 SBP ≥ 180 or DBP ≥ 110 |
| Stage 1 (uncomplicated) | No other risk factors | Low risk | Low risk | Moderate risk | High risk |
| | 1 or 2 risk factors | Low risk | Moderate risk | Moderate to high risk | High risk |
| | ≥ 3 risk factors | Low to Moderate risk | Moderate to high risk | High Risk | High risk |
| Stage 2 (asymptomatic disease) | HMOD, CKD grade 3, or diabetes mellitus without organ damage | Moderate to high risk | High risk | High risk | High to very high risk |
| Stage 3 (established disease) | Established CVD, CKD grade ≥ 4 , or diabetes mellitus with organ damage | Very high risk | Very high risk | Very high risk | Very high risk |

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Risk modifiers increasing CV risk estimated by the SCORE system

| |
|--|
| Social deprivation – the origin of many causes of CVD |
| Obesity (measured by BMI) and central obesity (measured by waist circumference) |
| Physical inactivity |
| Psychosocial stress, including vital exhaustion |
| Family history of premature CVD (occurring at age < 55 years in men and < 60 years in women) |
| Autoimmune and other inflammatory disorders |
| Major psychiatric disorders |
| Treatment for infection with human immunodeficiency virus |
| Atrial fibrillation |
| Left ventricular hypertrophy |
| CKD |
| Obstructive sleep apnoea syndrome |

Correction factors for the SCORE CV risk estimates in first-generation immigrants to Europe

| Region of origin | Multiplication factor |
|--------------------|-----------------------|
| Southern Asia | 1.4 |
| Sub-Saharan Africa | 1.3 |
| Caribbean | 1.3 |
| Western Asia | 1.2 |
| Northern Africa | 0.9 |
| Eastern Asia | 0.7 |
| South America | 0.7 |

CVD Risk Factors Common in Patients With Hypertension

| Modifiable Risk Factors* | Relatively Fixed Risk Factors† |
|---|--|
| <ul style="list-style-type: none">• Current cigarette smoking, secondhand smoking• Diabetes mellitus• Dyslipidemia/hypercholesterolemia• Overweight/obesity• Physical inactivity/low fitness• Unhealthy diet | <ul style="list-style-type: none">• CKD• Family history• Increased age• Low socioeconomic/educational status• Male sex• Obstructive sleep apnea• Psychosocial stress |

*Factors that can be changed and, if changed, may reduce CVD risk.

†Factors that are difficult to change (CKD, low socioeconomic/educational status, obstructive sleep apnea, cannot be changed (family history, increased age, male sex), or, if changed through the use of current intervention techniques, may not reduce CVD risk (psychosocial stress).

CKD indicates chronic kidney disease; and CVD, cardiovascular disease.

Hypertension and CV risk assessment

| Recommendation | Class | Level |
|--|----------|----------|
| CV risk assessment with the SCORE system is recommended for hypertensive patients who are not already at high or very high risk due to established CVD, renal disease or diabetes, a markedly elevated single risk factor (e.g. cholesterol), or hypertensive LVH. | I | B |

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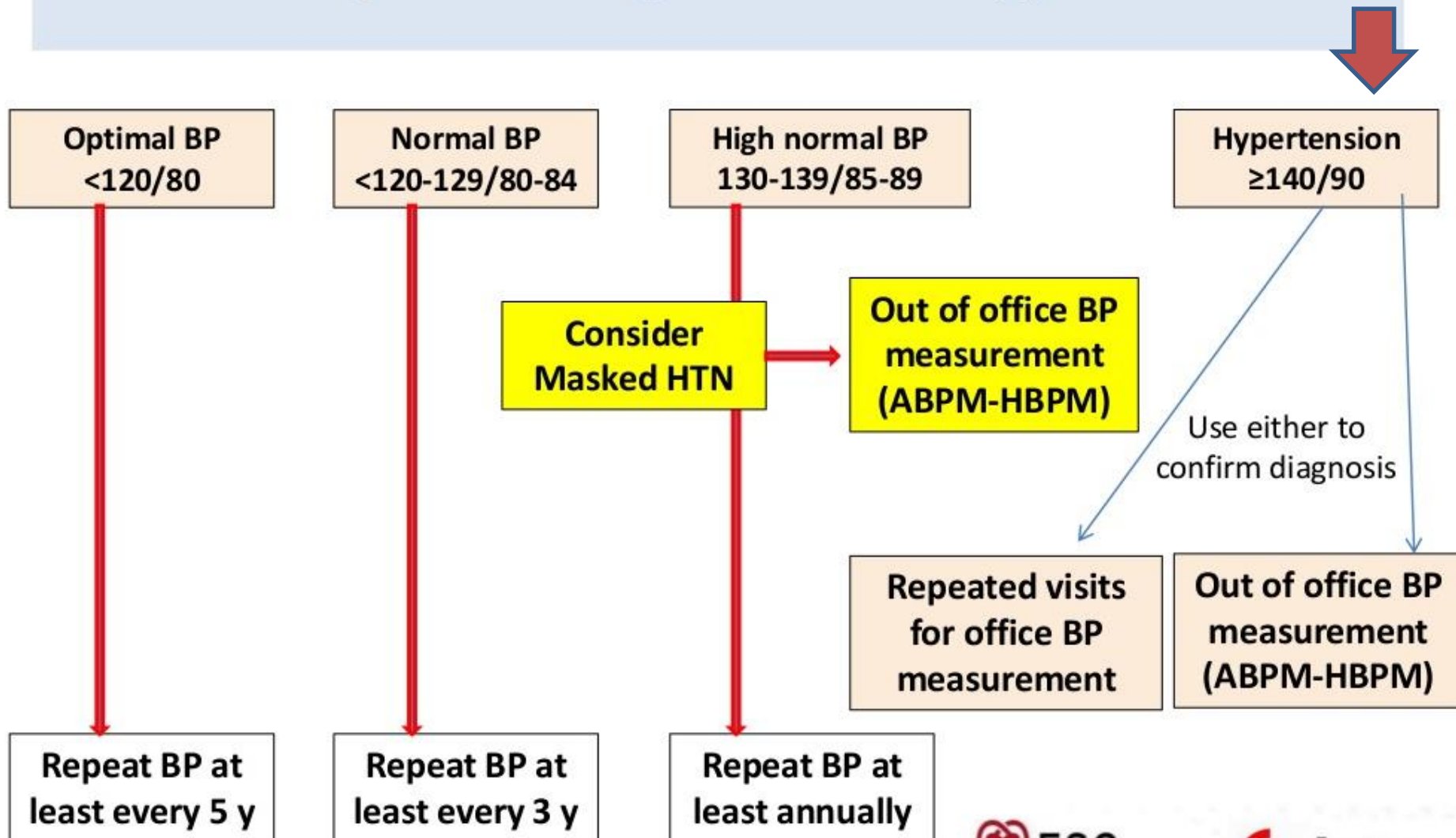
| COR | LOE | Recommendation for Coexistence of Hypertension and Related Chronic Conditions |
|----------|-------------|--|
| I | B-NR | Screening for and management of other modifiable CVD risk factors are recommended in adults with hypertension. |

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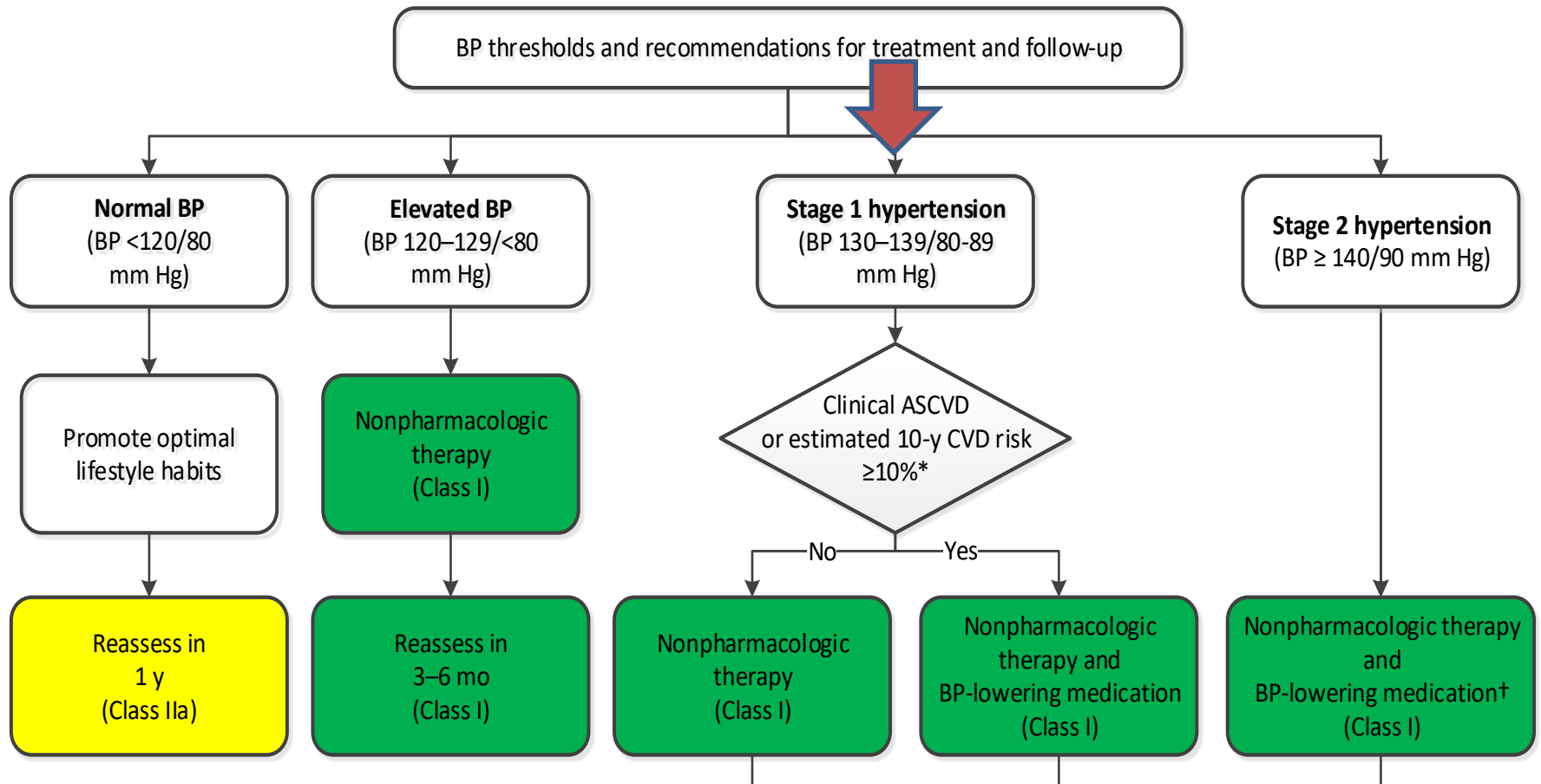
SCREENING DIAGNOSIS



Screening and Diagnosis of Hypertension



BP Thresholds and Recommendations for Treatment and Follow-Up



Patient Evaluation

Key steps in physical examination

| |
|---|
| Body habitus |
| Weight and height measured on a calibrated scale, with calculation of BMI |
| Waist circumference |
| Signs of HMOD |
| Neurological examination and cognitive status |
| Fundoscopy examination for hypertensive retinopathy |
| Palpation and auscultation of heart and carotid arteries |
| Palpation of peripheral arteries |
| Comparison of BP in both arms (at least once) |
| Secondary hypertension |
| Skin inspection: cafe-au-lait patches of neurofibromatosis (phaeochromocytoma) |
| Kidney palpation for signs of renal enlargement in polycystic kidney disease |
| Auscultation of heart and renal arteries for murmurs or bruits indicative of aortic coarctation, or renovascular hypertension |
| Comparison of radial with femoral pulse: to detect radio-femoral delay in aortic coarctation |
| Signs of Cushing's disease or acromegaly |
| Signs of thyroid disease |

Routine work-up for evaluation of hypertensive patients

| Routine laboratory tests |
|---|
| Haemoglobin and/or haematocrit |
| Fasting blood glucose and glycated HbA _{1c} |
| Blood lipids: total cholesterol, LDL cholesterol, HDL cholesterol |
| Blood triglycerides |
| Blood potassium and sodium |
| Blood uric acid |
| Blood creatinine and eGFR |
| Blood liver function tests |
| Urine analysis: microscopic examination; urinary protein by dipstick test or, ideally, albumin:creatinine ratio |
| 12-lead ECG |

Assessment of HMOD - 1

| Basic screening tests for HMOD | Indication and interpretation |
|--------------------------------|---|
| 12-lead ECG | Screen for LVH and other possible cardiac abnormalities and to document heart rate and cardiac rhythm |
| Urine albumin:creatinine ratio | To detect elevations in albumin excretion indicative of possible renal disease |
| Blood creatinine and eGFR | To detect possible renal disease |
| Fundoscopy | To detect hypertensive retinopathy, especially in patients with grade 2 or 3 hypertension |

HMOD: hypertension-mediated organ damage

Assessment of HMOD - 2

| More detailed screening for HMOD | Indication and interpretation |
|--|--|
| Echocardiography | To evaluate cardiac structure and function, when this information will influence treatment decisions |
| Carotid ultrasound | To determine the presence of carotid plaque or stenosis, particularly in patients with cerebrovascular disease or vascular disease elsewhere |
| Abdominal ultrasound and Doppler studies | To evaluate renal size and structure (e.g. scarring) and exclude renal tract obstruction as possible underlying causes of CKD and hypertension Evaluate abdominal aorta for evidence of aneurysmal dilatation and vascular disease. Examine adrenal glands for evidence of adenoma or phaeochromocytoma (CT or MRI preferred for detailed examination) Renal artery Doppler studies to screen for the presence of renovascular disease, especially in the presence of asymmetric renal size |
| PWV | An index of aortic stiffness and underlying arteriosclerosis |
| ABI | Screen for evidence of PAD |
| Cognitive function testing | To evaluate cognition in patients with symptoms suggestive of cognitive impairment |
| Brain imaging | To evaluate the presence of ischaemic or haemorrhagic brain injury, especially in patients with a history of cerebrovascular disease or cognitive decline |

Basic and Optional Laboratory Tests for Primary Hypertension

| | |
|-------------------------|-------------------------------------|
| Basic testing | Fasting blood glucose* |
| | Complete blood count |
| | Lipid profile |
| | Serum creatinine with eGFR* |
| | Serum sodium, potassium, calcium* |
| | Thyroid-stimulating hormone |
| | Urinalysis |
| | Electrocardiogram |
| Optional testing | Echocardiogram |
| | Uric acid |
| | Urinary albumin to creatinine ratio |

*May be included in a comprehensive metabolic panel.

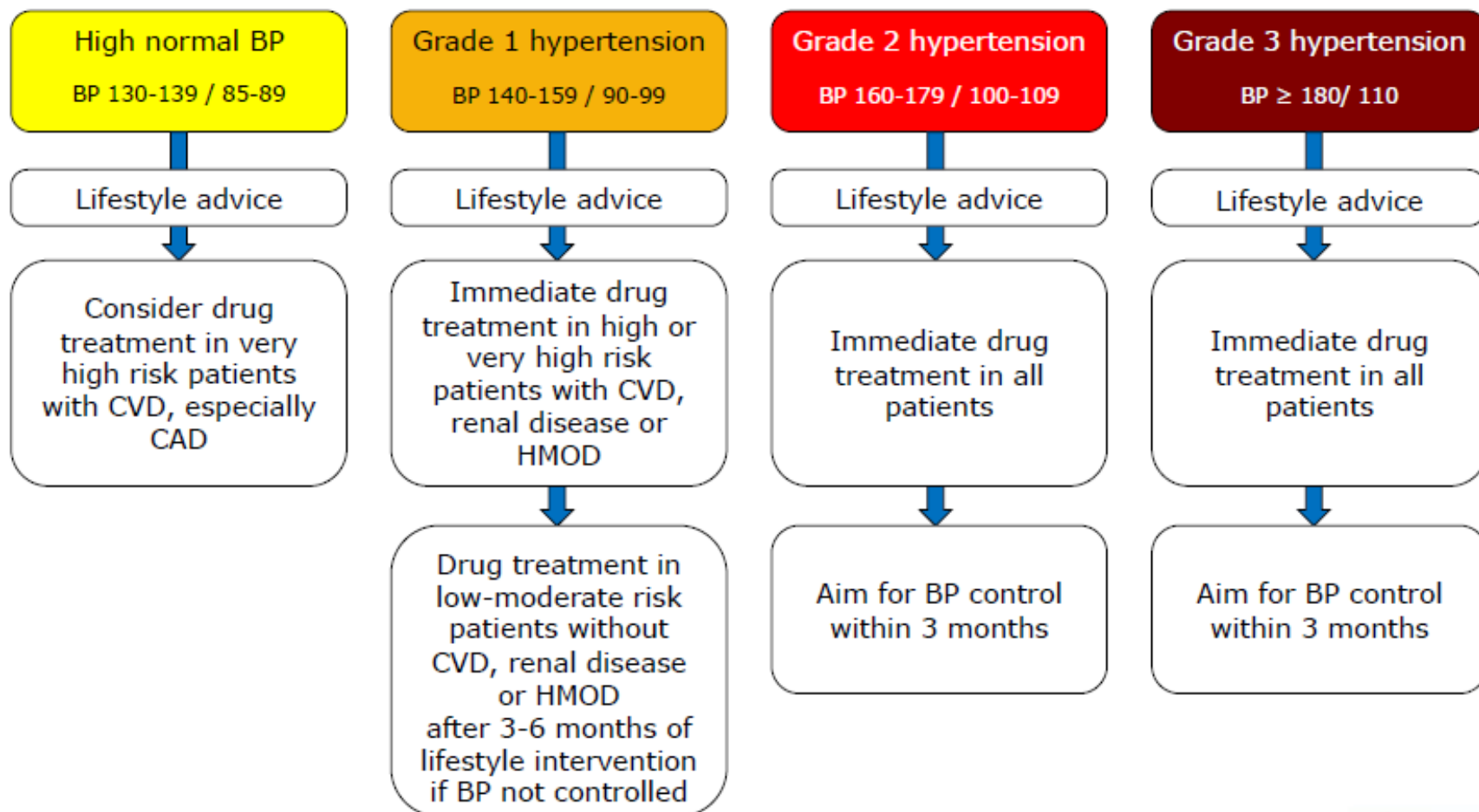
eGFR indicates estimated glomerular filtration rate.

TREATMENT INITIATION

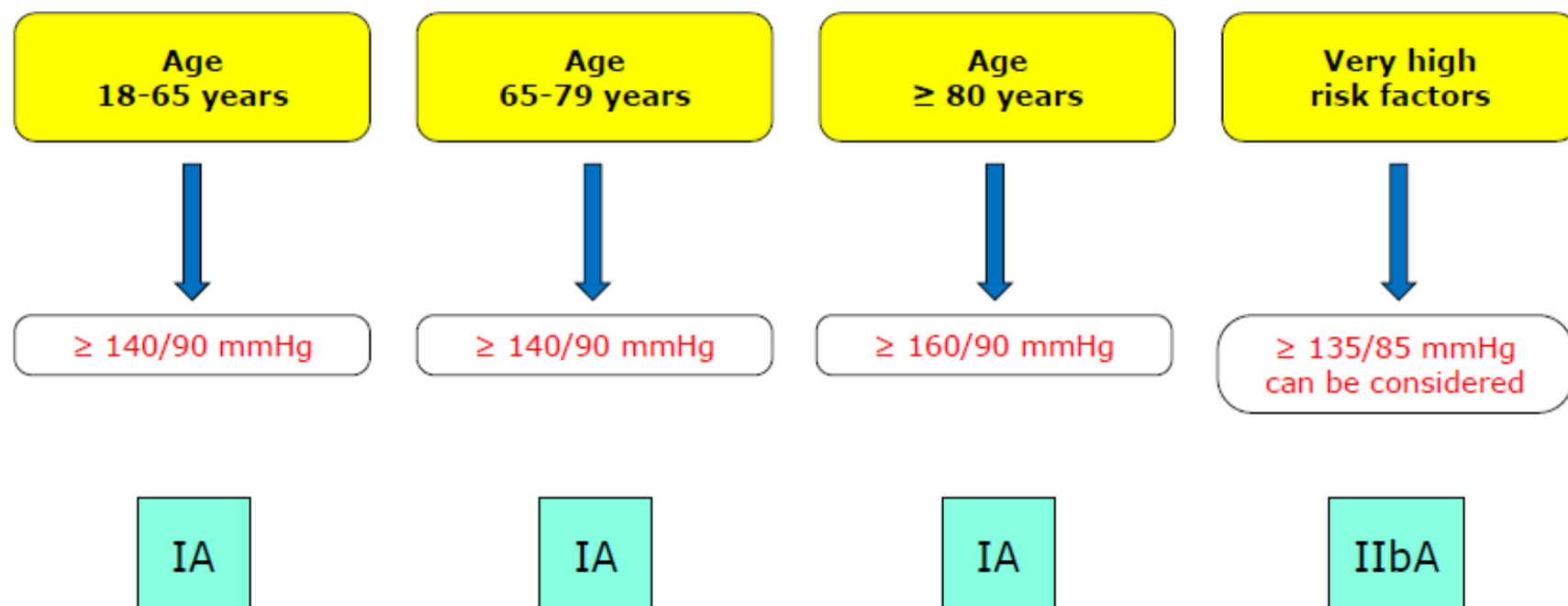
?



Initiation of BP-lowering treatment (lifestyle changes and medication) at different initial office BP levels



Summary of office BP thresholds for treatment



BP Treatment Threshold and the Use of CVD Risk Estimation to Guide Drug Treatment of Hypertension

| COR | LOE | Recommendations for BP Treatment Threshold and Use of Risk Estimation* to Guide Drug Treatment of Hypertension |
|-----|-----------|--|
| I | SBP: A | Use of BP-lowering medications is recommended for secondary prevention of recurrent CVD events in patients with clinical CVD and an average SBP of 130 mm Hg or higher or an average DBP of 80 mm Hg or higher , and for primary prevention in adults with an estimated 10-year atherosclerotic cardiovascular disease (ASCVD) risk of 10% or higher and an average SBP 130 mm Hg or higher or an average DBP 80 mm Hg or higher. |
| | DBP: C-EO | |
| I | C-LD | Use of BP-lowering medication is recommended for primary prevention of CVD in adults with no history of CVD and with an estimated 10-year ASCVD risk <10% and an SBP of 140 mm Hg or higher or a DBP of 90 mm Hg or higher. |

* ACC/AHA Pooled Cohort Equations (<http://tools.acc.org/ASCVD-Risk-Estimator/>) to estimate 10-year risk of atherosclerotic CVD.

BP TARGETS

?

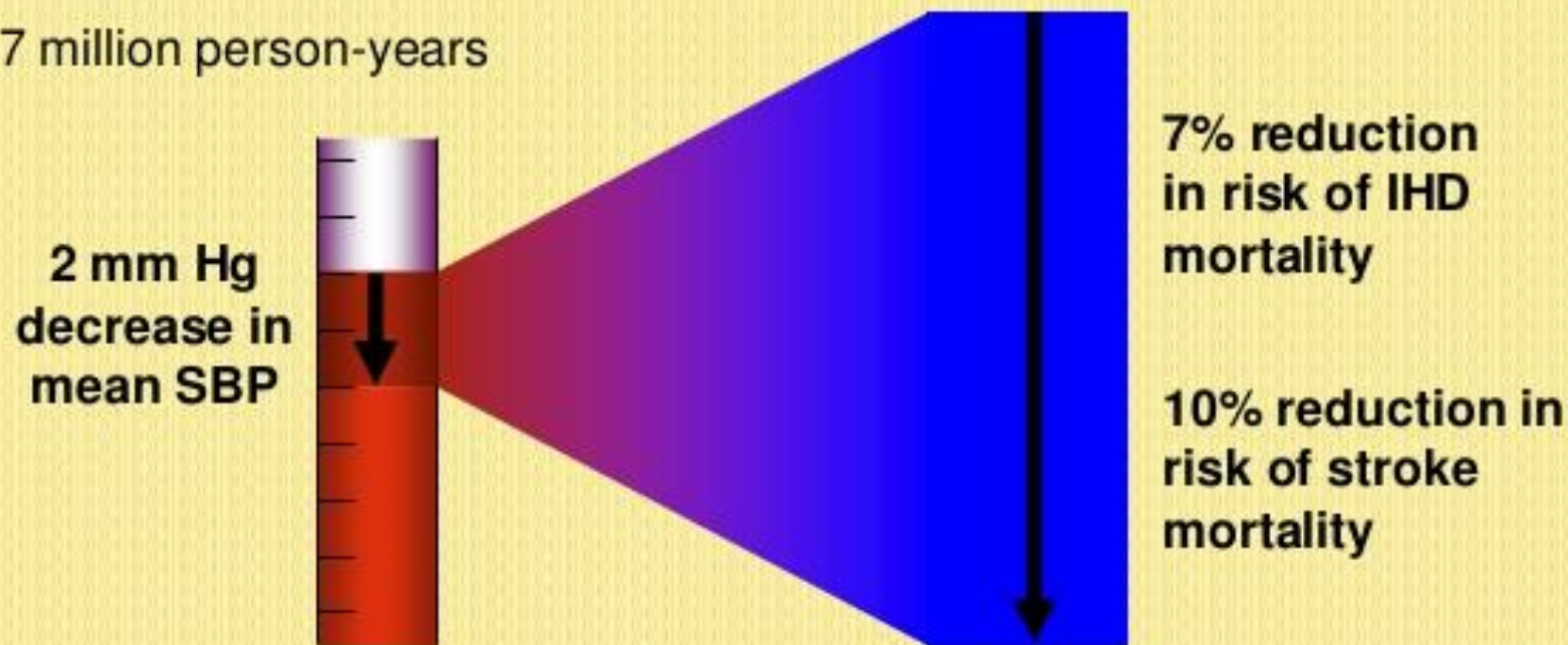


BP REDUCTION IS CRITICAL THE LOWER, THE BETTER

Meta-analysis of 61 prospective, observational studies*

1 million adults

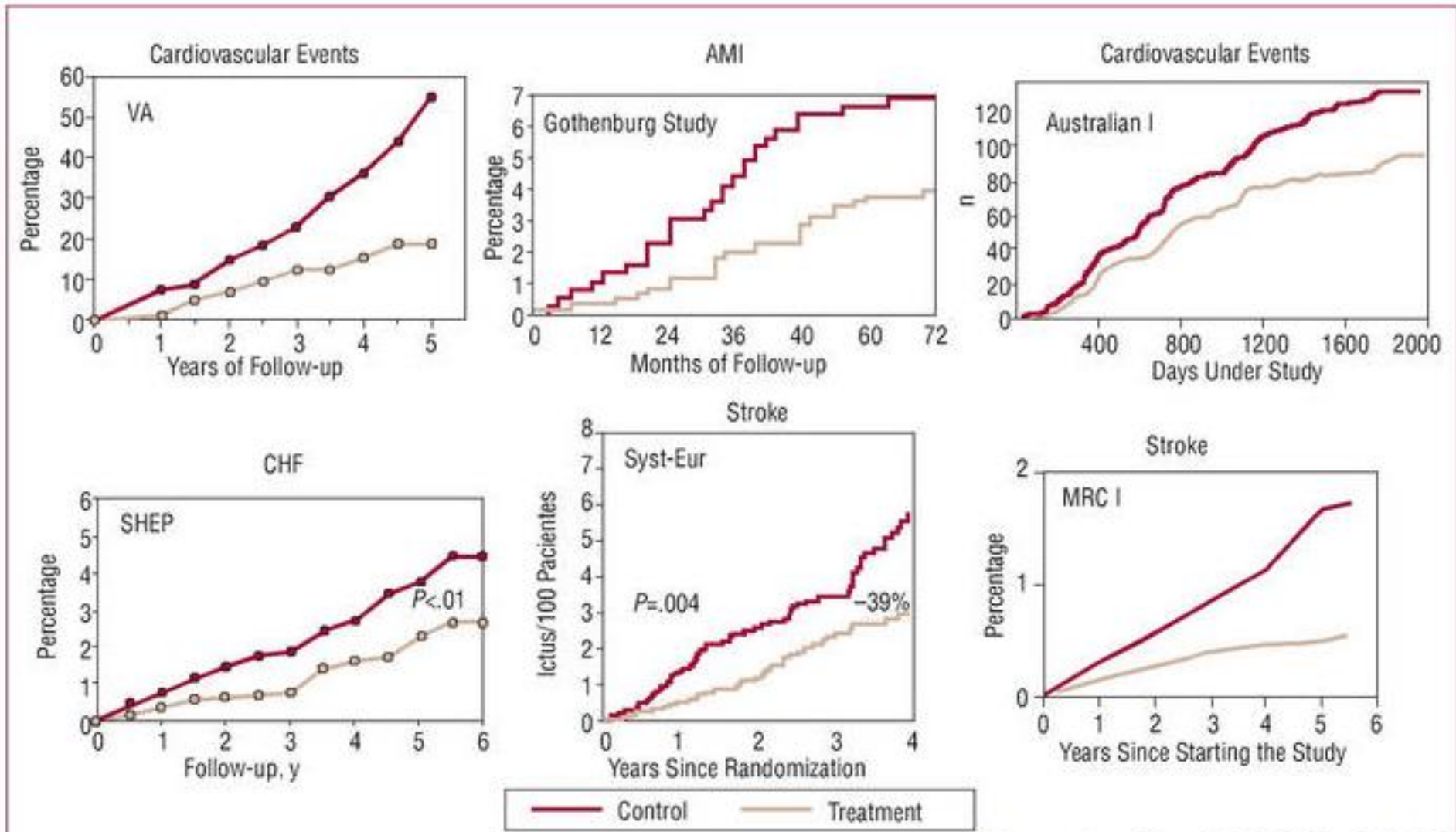
12.7 million person-years



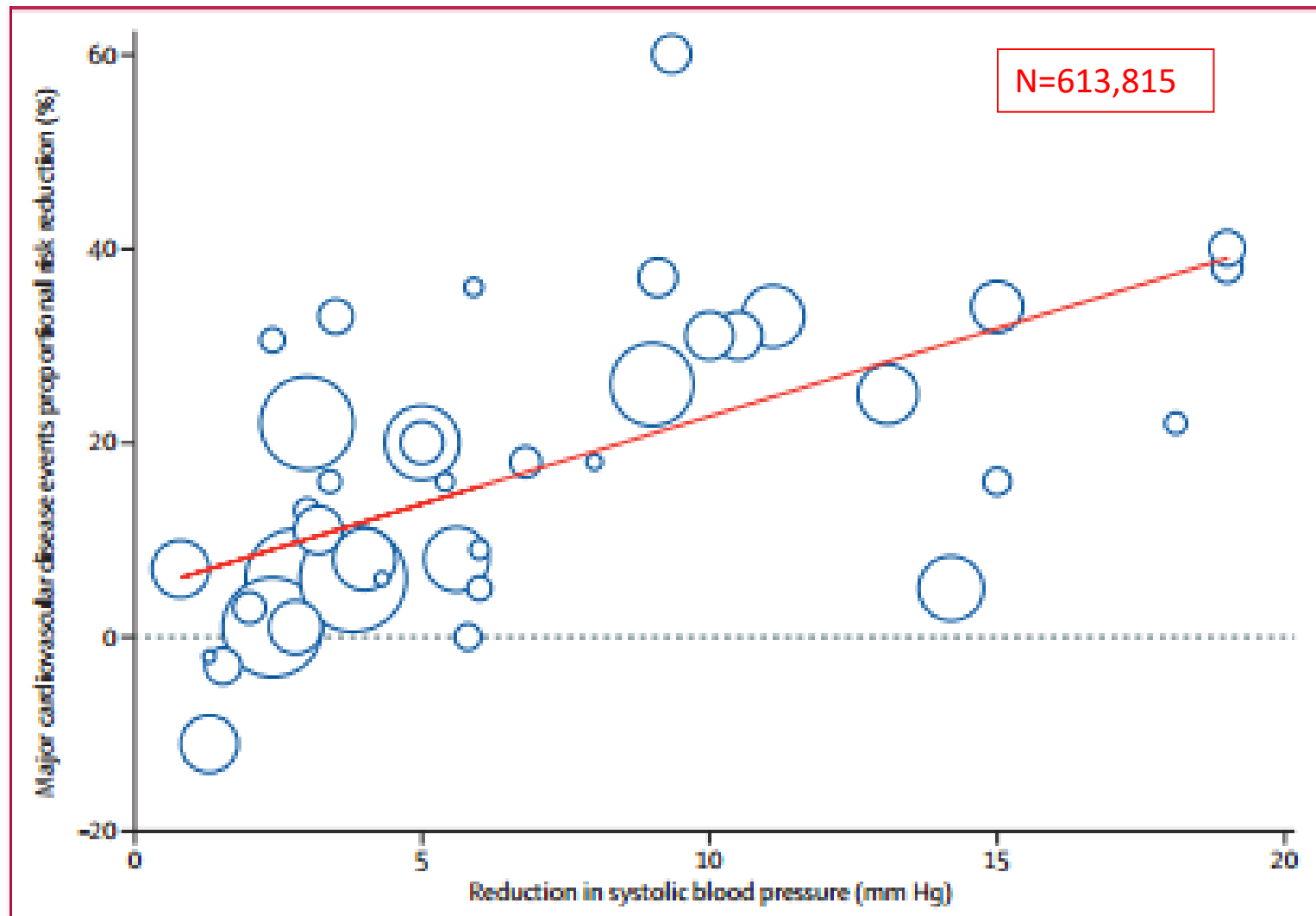
*Epidemiologic studies, not clinical trials of HTN agents.
BP, blood pressure; IHD, ischemic heart disease.
Lewington S et al. *Lancet* 2002;360:1903-1913.



Early clinical benefit of antihypertensive treatment



Meta-regression analyses showed relative risk reductions proportional to the magnitude of the BP reductions achieved



BP lowering significantly reduces vascular risk across various baseline BP levels and comorbidities. Our results provide strong support for lowering BP to SBP < than 130 mm Hg and providing BP lowering treatment to individuals with a history of CVD, CAD, stroke, DM, HF and CKD

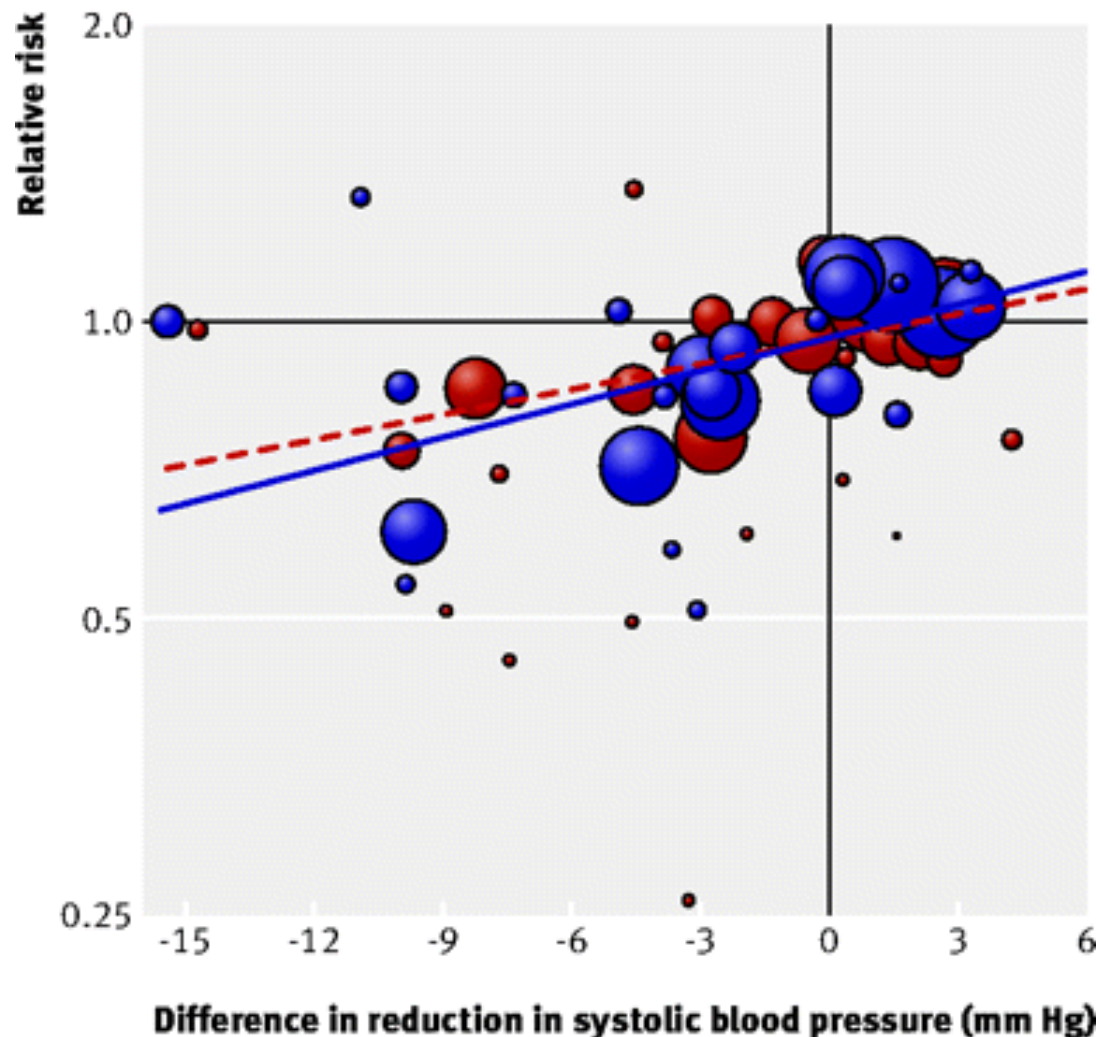
Associations of reduction in BP with risk reduction for total MACE for adults aged <65 and ≥65

Reduction in risk for each 5 mm Hg reduction in systolic blood pressure:

—●— Age <65: 11.9% (5.3% to 18.0%)

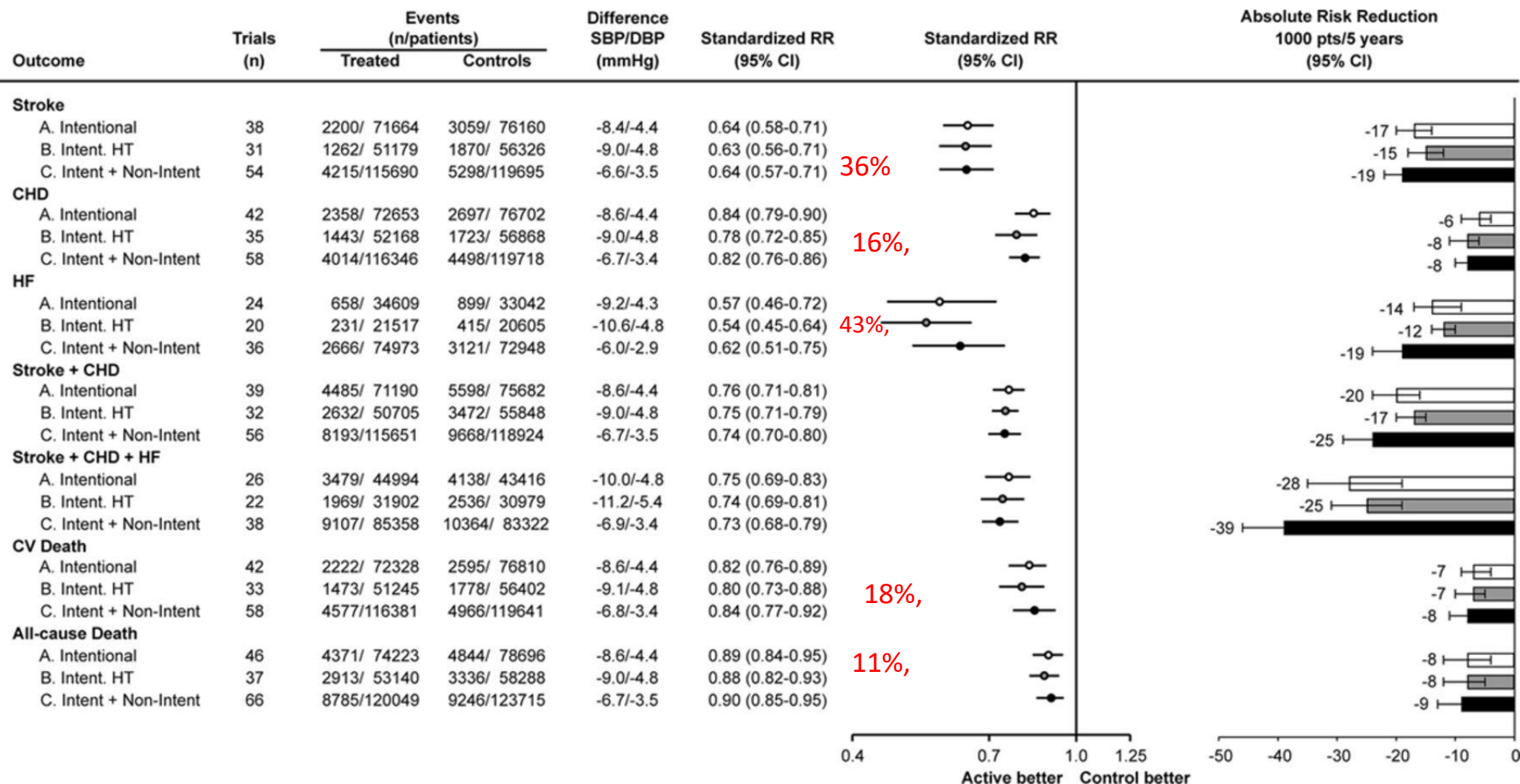
-●- Age ≥65: 9.1% (3.6% to 14.3%)

P for heterogeneity of slopes = 0.38



Relative and absolute risk reduction of various outcomes in trials of BP lowering

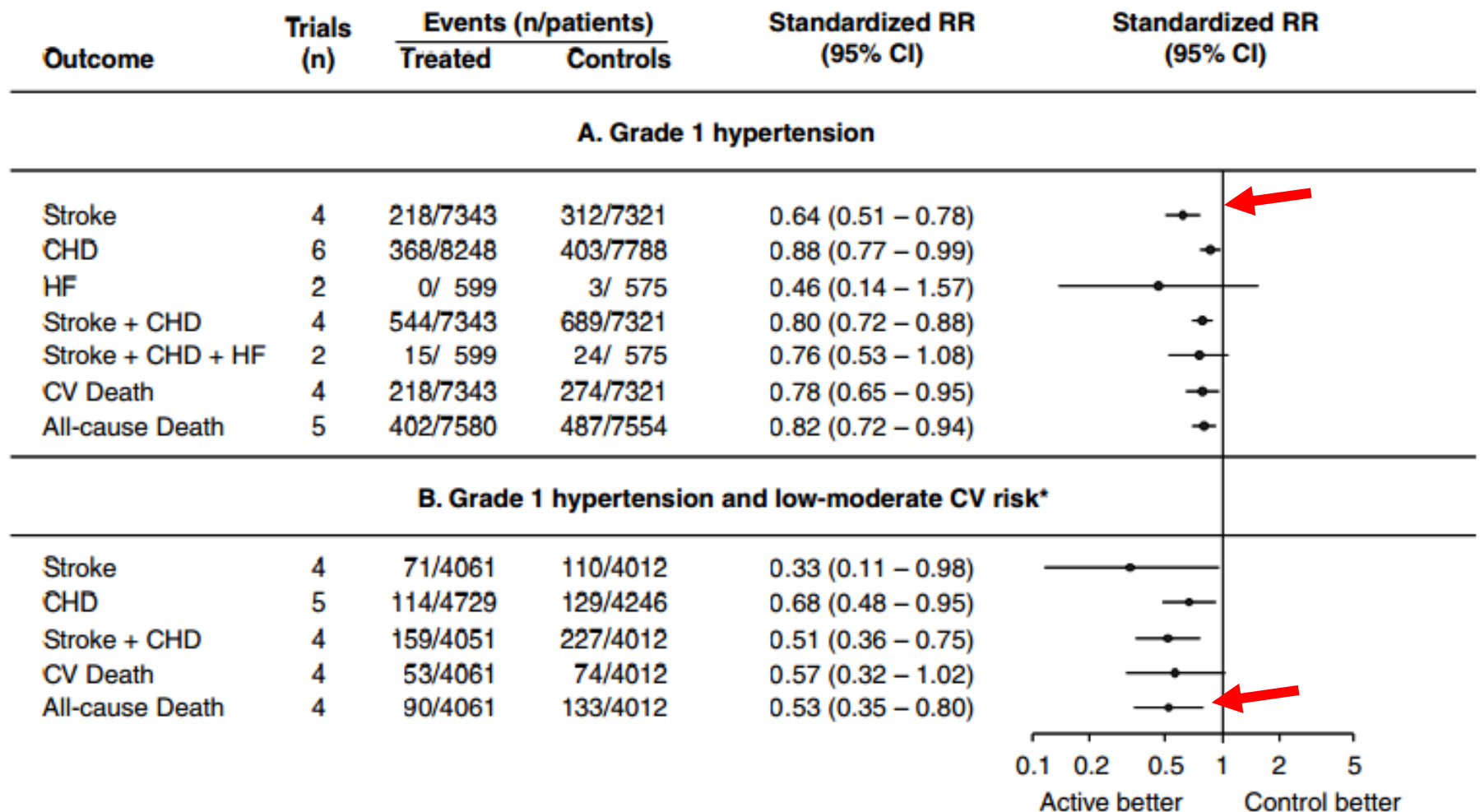
standardized SBP/DBP difference between active and control groups of 10/5 mm Hg



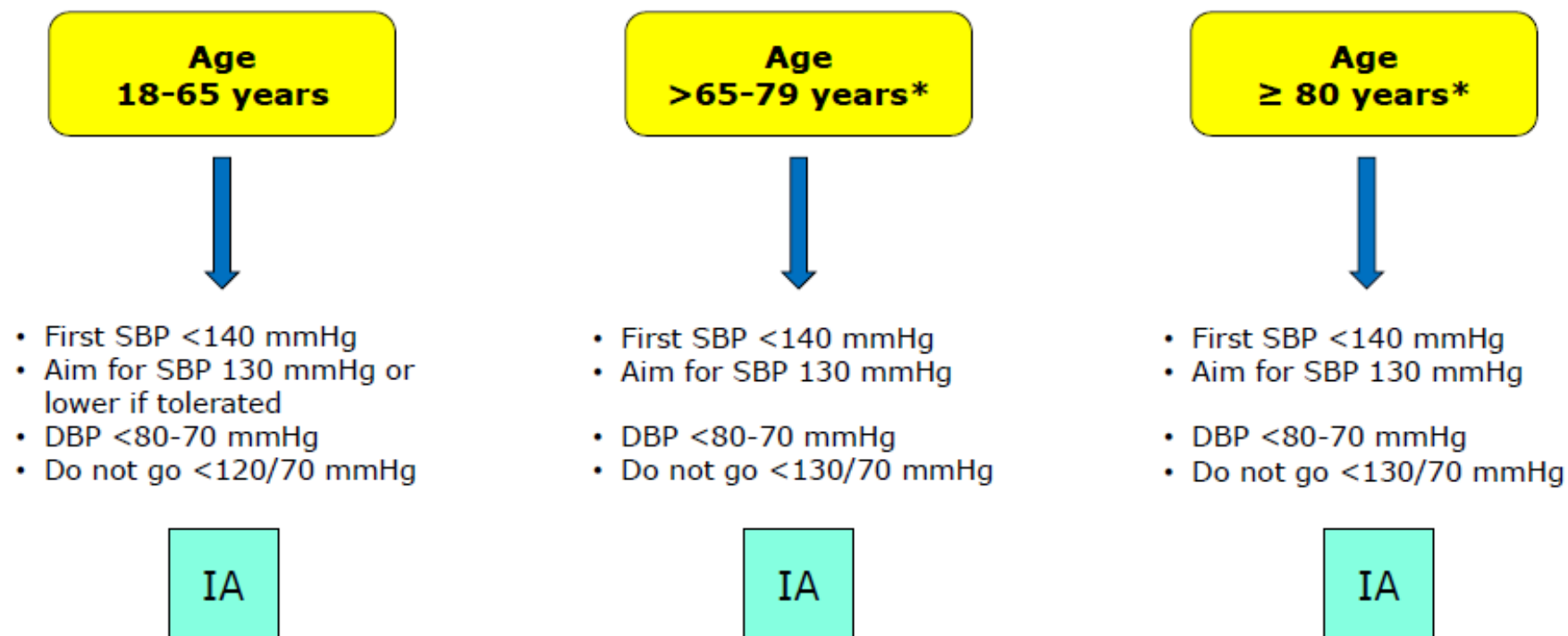
Zanchetti A, Thomopoulos C et al. Circ Res. 2015

absolute risk reduction reports the number of events prevented for every 1000 patients treated for 5 years with a standardized RR

Effects of BP lowering in trials of grade 1 HTN



Office BP treatment target range



* Consider frailty/independence/tolerability of treatment

Office BP treatment target range

| Age group | Office SBP treatment target ranges (mmHg) | | | | | Office DBP treatment target range (mmHg) |
|--|---|---|--|---|---|--|
| | Hypertension | + Diabetes | + CKD | + CAD | + Stroke/TIA | |
| 18–65 years | Target to 130 or lower if tolerated Not < 120 | Target to 130 or lower if tolerated Not < 120 | Target to < 140 to 130 if tolerated | Target to 130 or lower if tolerated Not < 120 | Target to 130 or lower if tolerated Not < 120 | 70–79 |
| 65–79 years | Target to < 140 to 130 if tolerated | Target to < 140 to 130 if tolerated | Target to < 140 to 130 if tolerated | Target to < 140 to 130 if tolerated | Target to < 140 to 130 if tolerated | 70–79 |
| ≥ 80 years | Target to < 140 to 130 if tolerated | Target to < 140 to 130 if tolerated | Target to < 140 to 130 if tolerated | Target to < 140 to 130 if tolerated | Target to < 140 to 130 if tolerated | 70–79 |
| Office DBP treatment target range (mmHg) | 70–79 | 70–79 | 70–79 | 70–79 | 70–79 | |

Highlight #3: Bp target goal now <130/80 mm Hg for almost everyone

| Recommendations for BP Goal for Patients with Hypertension | | |
|--|---------------|---|
| COR | LOE | Recommendations |
| I | SBP : B-R | For adults with confirmed hypertension and known CVD or greater than or equal to 10% 10-year ASCVD event risk, a BP target of less than 130/80 mm Hg is recommended. |
| | DBP : C-EO | |
| IIb | SBP : B-NR | For adults with confirmed hypertension, without additional markers of increased CVD risk, a BP target of less than 130/80 mm Hg may be reasonable. |
| | DBP : C-EO | |

| Recommendations for Treatment of Hypertension in Older Persons | | |
|--|------|--|
| COR | LOE | Recommendations |
| I | A | Treatment of hypertension is recommended for noninstitutionalized ambulatory community-dwelling adults (≥65 years of age), with an average SBP greater than or equal to 130 mmHg with SBP treatment goal of less than 130 mm Hg . |
| IIa | C-EO | For older adults (≥65 years of age) with hypertension and a high burden of comorbidity and limited life expectancy, clinical judgment, patient preference, and a team-based approach to assess risk/benefit is reasonable for decisions regarding intensity of BP-lowering and choice of antihypertensive drugs. |

ACC/AHA 2017

BP Thresholds for and Goals of Pharmacological Therapy in Patients With HTN According to Clinical Conditions


| Clinical Condition(s) | BP Threshold, mm Hg | BP Goal, mm Hg |
|--|---------------------|----------------|
| General | | |
| Clinical CVD or 10-year ASCVD risk $\geq 10\%$ | $\geq 130/80$ | $< 130/80$ |
| No clinical CVD and 10-year ASCVD risk $< 10\%$ | $\geq 140/90$ | $< 130/80$ |
| Older persons (≥ 65 years of age; noninstitutionalized, ambulatory, community-living adults) | ≥ 130 (SBP) | < 130 (SBP) |
| Specific comorbidities | | |
| Diabetes mellitus | $\geq 130/80$ | $< 130/80$ |
| Chronic kidney disease | $\geq 130/80$ | $< 130/80$ |
| Chronic kidney disease after renal transplantation | $\geq 130/80$ | $< 130/80$ |
| Heart failure | $\geq 130/80$ | $< 130/80$ |
| Stable ischemic heart disease | $\geq 130/80$ | $< 130/80$ |
| Secondary stroke prevention | $\geq 140/90$ | $< 130/80$ |
| Secondary stroke prevention (lacunar) | $\geq 130/80$ | $< 130/80$ |
| Peripheral arterial disease | $\geq 130/80$ | $< 130/80$ |

ASCVD indicates atherosclerotic cardiovascular disease; BP, blood pressure; CVD, cardiovascular disease; and SBP, systolic blood pressure.

ACC/AHA 2017

Optimal Blood Pressure Goals Recommended by the Latest Hypertension Guidelines

LATEST HYPERTENSION GUIDELINES 2017/2018

| Hypertension Definitions | BP Treatment Goal is the Same |
|--------------------------------------|---|
| <u>2018</u> ESC / ESH > 140/90 mm Hg |  < 130/80 mm Hg |
| <u>2017</u> ACC / AHA > 130/80 mm Hg | |

Optimal Blood Pressure Goals Recommended by the Latest Hypertension Guidelines

Eur Heart J. 2018;39(33):3012-3016. doi:10.1093/eurheartj/ehy494

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Nonpharmacological Interventions



Adoption of lifestyle changes in patients with hypertension











| Recommendations | Class | Level |
|---|-------|-------|
| Salt restriction to < 5 g per day is recommended. | I | A |
| It is recommended to restrict alcohol consumption to: <ul style="list-style-type: none"> • Less than 14 units per week for men. • Less than 8 units per week for women. | I | A |
| It is recommended to avoid binge drinking. | III | C |
| Increased consumption of vegetables, fresh fruits, fish, nuts, unsaturated fatty acids (olive oil), low consumption of red meat, and consumption of low-fat dairy products are recommended. | I | A |
| Body-weight control is indicated to avoid obesity (BMI > 30 kg/m ² or WC > 102 cm in men and > 88 cm in women) and aim at a healthy BMI (about 20–25 kg/m ²) and WC values (< 94 cm in men and < 80 cm in women) to reduce BP and CV risk. | I | A |
| Regular aerobic exercise (e.g. at least 30 min of moderate dynamic exercise on 5–7 days per week) is recommended. | I | A |
| Smoking cessation and supportive care and referral to smoking cessation programs are recommended. | I | B |

Strategies to Promote Lifestyle Modification

| COR | LOE | Recommendation for Strategies to Promote Lifestyle Modification |
|-----|------|---|
| I | C-EO | Effective behavioral and motivational strategies to achieve a healthy lifestyle (i.e., tobacco cessation, weight loss, moderation in alcohol intake, increased physical activity, reduced sodium intake, and consumption of a healthy diet) are recommended for adults with hypertension. |

ACC/AHA 2017

Management of mild hypertension in adults

| RECOMMENDATION | | DESCRIPTION | | APPROXIMATE SYSTOLIC BP REDUCTION RANGE |
|--|---|--|---|---|
| DASH eating plan |  | Diet rich in fruits, vegetables, and low fat dairy with reduced fat intake |  | 8-14 mm Hg |
| Exercise |  | Regular aerobic activity at least 30 minutes a day |  | 4-9 mm Hg |
| Reduced dietary sodium intake |  | No more than 2400 mg (ideally 1600 mg) of sodium daily |  | 2-8 mm Hg |
| Moderation of alcohol drinking as needed |  | Maximum 2 ounces ethanol/day for men; maximum 1 ounce/day for women (approximately 1 ounce is contained in a 12 oz beer, 5 oz glass of wine, or 1.5 oz shot of liquor) |  | 2-4 mm Hg |
| Weight loss if warranted |  | Achieve/maintain body mass index of 18.5-24.9 |  | 3 mm Hg per 4-8% bodyweight reduction |

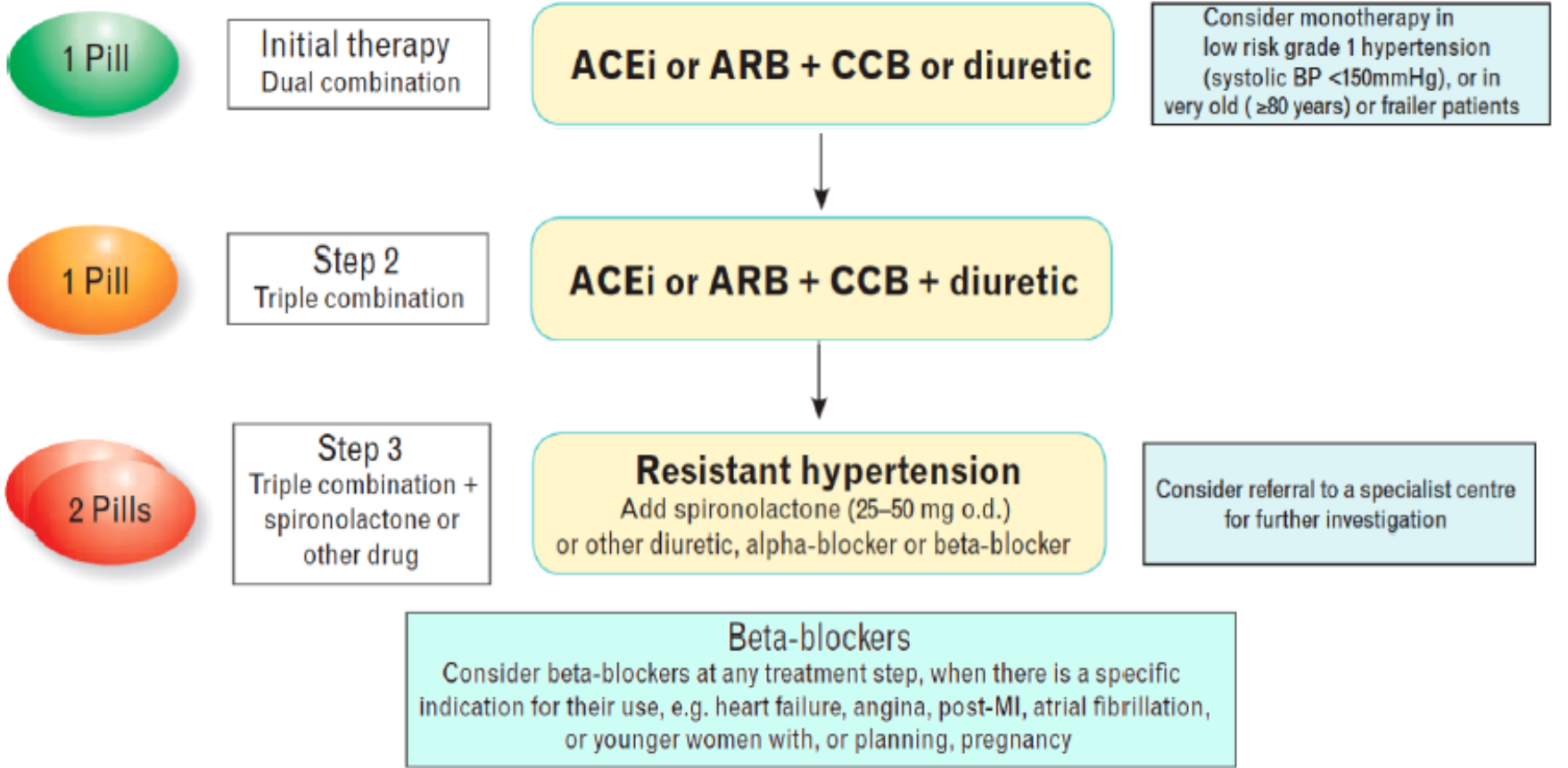
Anthony J Viera, et al *BMJ* 2016 *BMJ* 2016;

ESH/ESC 2018 IA
ACC/AHA 2017 IA

MEDICATIONS

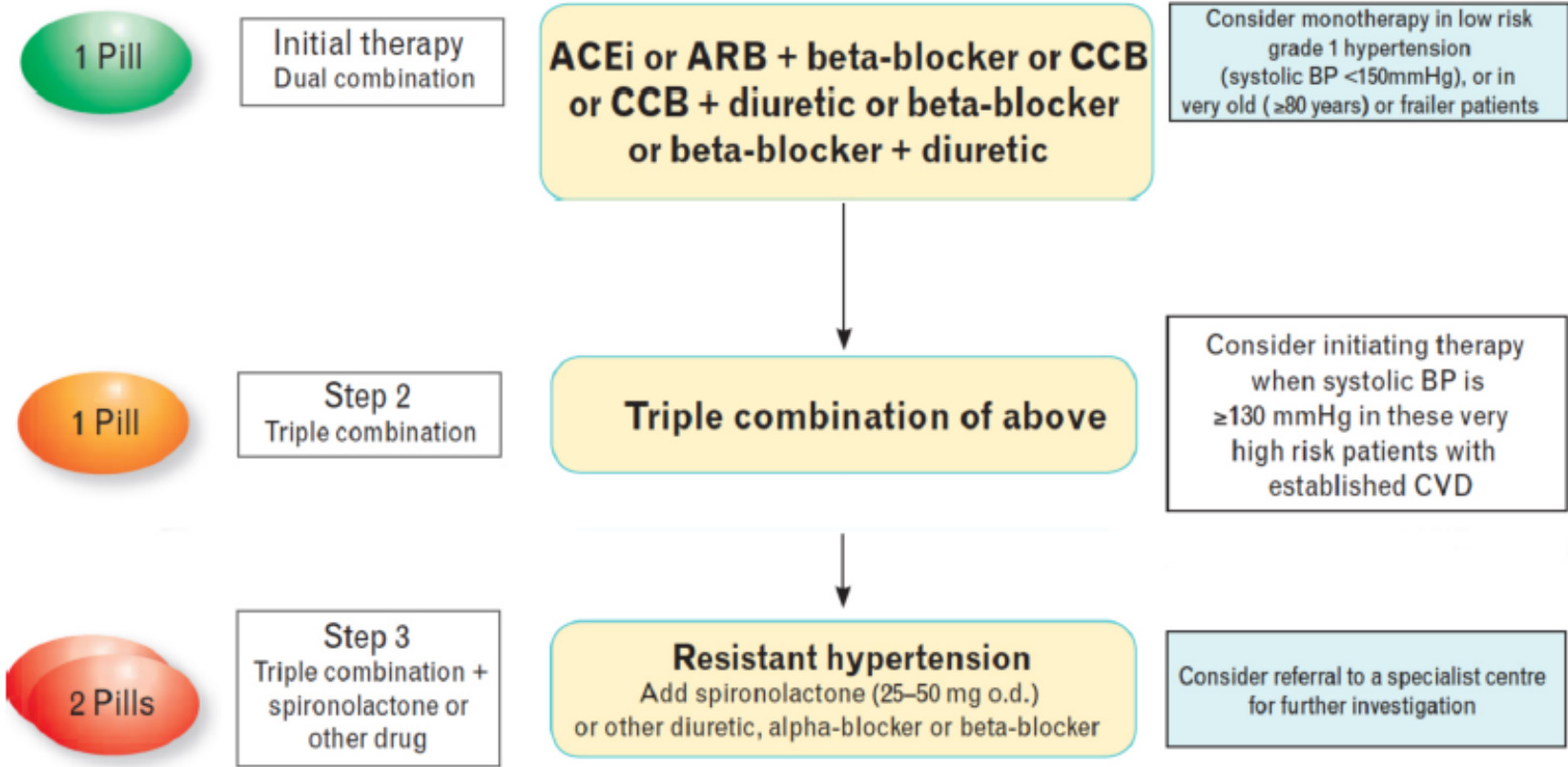


Core drug-treatment strategy for uncomplicated hypertension



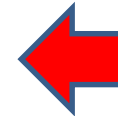
The core algorithm is also appropriate for most patients with HMOD, cerebrovascular disease, diabetes, or PAD

Drug-treatment strategy for hypertension and CAD

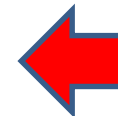


Recommendation for Choice of Initial Medication

| COR | LOE | Recommendation for Choice of Initial Medication |
|-----|-----------------|---|
| I | A ^{SR} | For initiation of antihypertensive drug therapy, first-line agents include thiazide diuretics, CCBs, and ACE inhibitors or ARBs. |



| COR | LOE | Recommendations for Choice of Initial Monotherapy Versus Initial Combination Drug Therapy* |
|-----|------|---|
| I | C-EO | Initiation of antihypertensive drug therapy with 2 first-line agents of different classes, either as separate agents or in a fixed-dose combination, is recommended in adults with stage 2 hypertension and an average BP more than 20/10 mm Hg above their BP target. |
| Ia | C-EO | Initiation of antihypertensive drug therapy with a single antihypertensive drug is reasonable in adults with stage 1 hypertension and BP goal <130/80 mm Hg with dosage titration and sequential addition of other agents to achieve the BP target. |



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General Principles of Drug Therapy

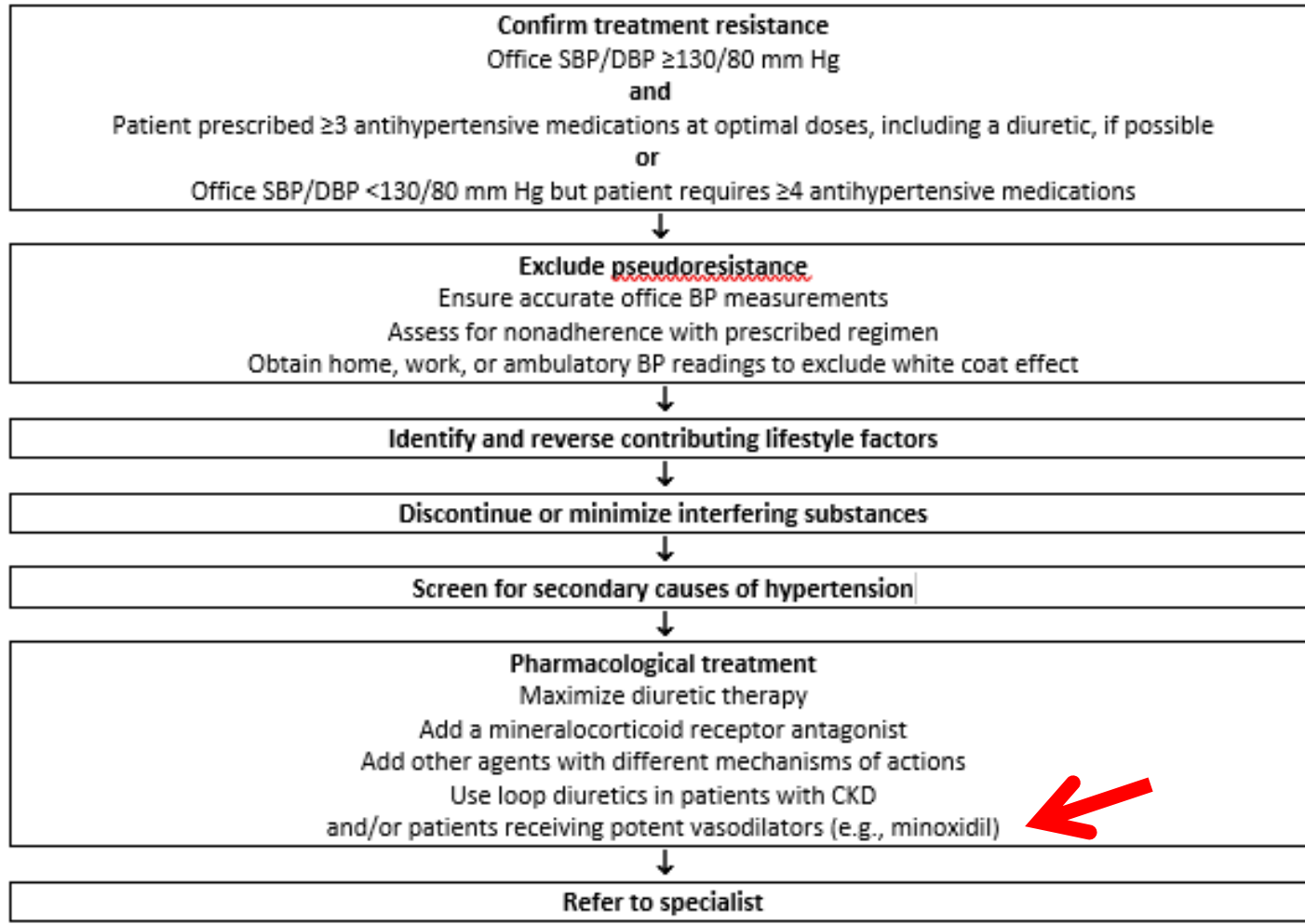
| COR | LOE | Recommendation for General Principle of Drug Therapy |
|----------------------|----------|--|
| III: Harm | A | Simultaneous use of an ACE inhibitor, ARB, and/or renin inhibitor is potentially harmful and is not recommended to treat adults with hypertension. |

ACC/AHA 2017

Resistant Hypertension: Diagnosis, Evaluation, and Treatment

ACC/AHA 2017

Figure 10. Resistant Hypertension: Diagnosis, Evaluation, and Treatment



BP indicates blood pressure; CKD, chronic kidney disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; NSAIDs, nonsteroidal anti-inflammatory drugs; and SBP, systolic blood pressure.

Adapted with permission from Calhoun et al.

Compelling and possible contraindications to the use of specific antihypertensive drugs

| Drug | Contraindications | |
|---|--|--|
| | Compelling | Possible |
| Diuretics (thiazides/thiazide-type, e.g. chlorthalidone and indapamide) | <ul style="list-style-type: none"> Gout | <ul style="list-style-type: none"> Metabolic syndrome Glucose intolerance Pregnancy Hypercalcemia Hypokalemia |
| Beta-blockers | <ul style="list-style-type: none"> Asthma Any high-grade sino-atrial or atrioventricular block Bradycardia (heart rate < 60 beats per min) | <ul style="list-style-type: none"> Metabolic syndrome Glucose intolerance Athletes and physically active patients |
| Calcium antagonists (dihydropyridines) | | <ul style="list-style-type: none"> Tachyarrhythmia Heart failure (HFrEF, class III or IV) Pre-existing severe leg oedema |
| Calcium antagonists (verapamil, diltiazem) | <ul style="list-style-type: none"> Any high-grade sino-atrial or AV block Severe LV dysfunction (LV EF < 40%) Bradycardia (heart rate < 60 beats per min) | <ul style="list-style-type: none"> Constipation |
| ACE inhibitors | <ul style="list-style-type: none"> Pregnancy Previous angioneurotic oedema Hyperkalemia (potassium > 5.5 mmol/L) Bilateral renal artery stenosis | <ul style="list-style-type: none"> Women of child-bearing potential without reliable contraception |
| ARBs | <ul style="list-style-type: none"> Pregnancy Hyperkalemia (potassium > 5.5 mmol/L) Bilateral renal artery stenosis | <ul style="list-style-type: none"> Women of child-bearing potential without reliable contraception |

Treatment of CV risk factors associated with hypertension

ESH 2018

| Recommendations | Class ^a | Level ^b |
|---|--------------------|--------------------|
| CV risk assessment with the SCORE system is recommended for hypertensive patients who are not already at high or very high risk due to established CVD, renal disease, or diabetes. ³³ | I | B |
| For patients at very high CV risk, statins are recommended to achieve LDL-C levels of <1.8 mmol/L (70 mg/dL), or a reduction of ≥50% if the baseline LDL-C is 1.8–3.5 mmol/L (70–135 mg/dL). ^{596,599,602} | I | B |
| For patients at high CV risk, statins are recommended to achieve an LDL-C goal of <2.6 mmol/L (100 mg/dL), or a reduction of ≥50% if the baseline LDL-C is 2.6–5.2 mmol/L (100–200 mg/dL). ^{599,602} | I | B |
| For patients at low–moderate CV risk, statins should be considered to achieve an LDL-C value of <3.0 mmol/L (115 mg/dL). ⁵⁹⁸ | IIa | C |
| Antiplatelet therapy, in particular low-dose aspirin, is recommended for secondary prevention in hypertensive patients. ^{35,604} | I | A |
| Aspirin is not recommended for primary prevention in hypertensive patients without CVD. ^{35,604} | III | A |

Strategies to Improve ADHERENCE



Interventions that may improve drug adherence in hypertension

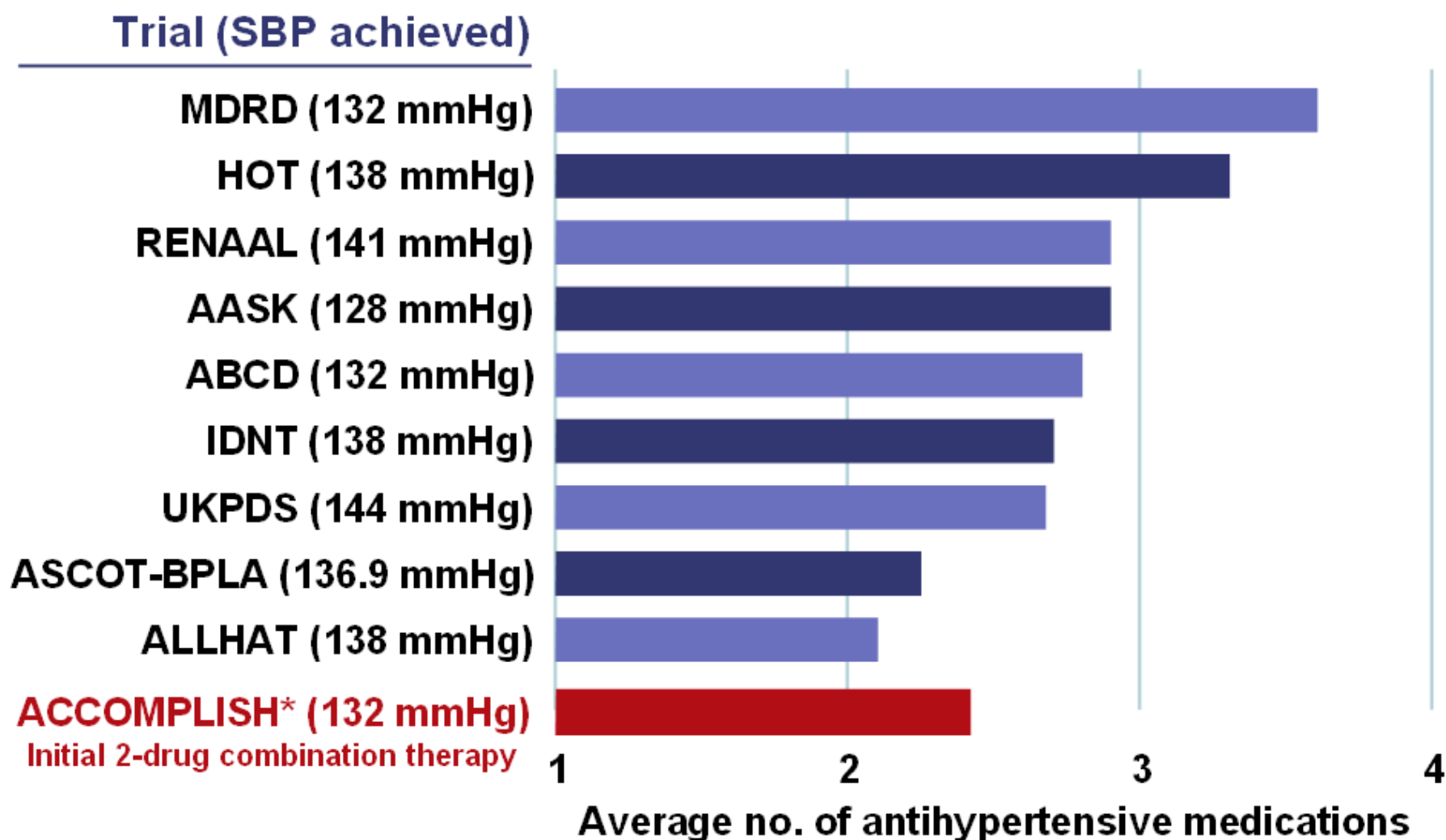
| |
|----------------------|
| Physician level |
| Patient level |
| Drug-treatment level |
| Health-system level |

Antihypertensive Medication Adherence Strategies

| COR | LOE | Recommendations for Antihypertensive Medication Adherence Strategies |
|-----|------|--|
| I | B-R | In adults with hypertension, dosing of antihypertensive medication once daily rather than multiple times daily is beneficial to improve adherence. |
| Ia | B-NR | Use of combination pills rather than free individual components can be useful to improve adherence to antihypertensive therapy. |

ACC/AHA 2017

Multiple Antihypertensive Agents are Needed to Reach BP Goal

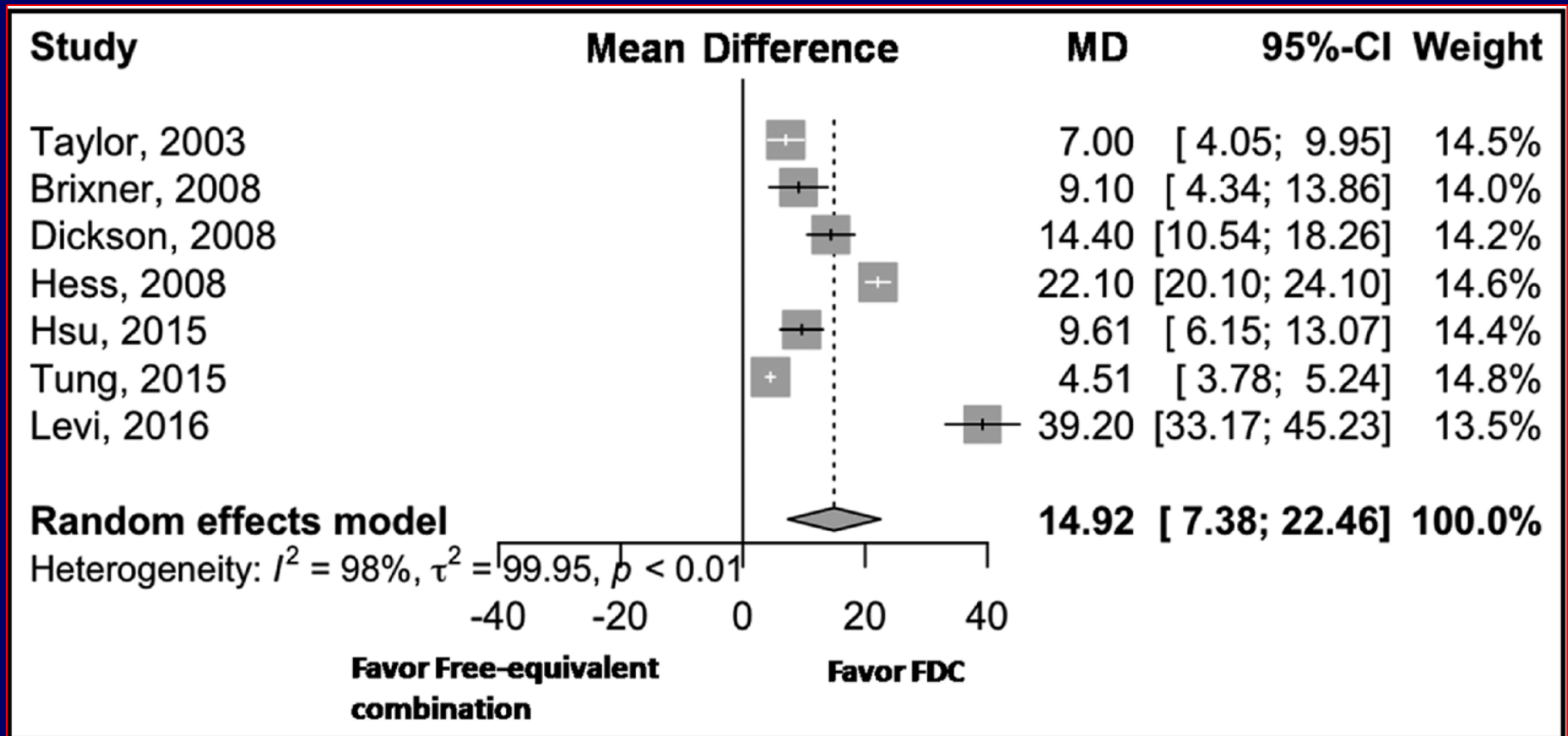


*Interim 6-month data

Bakris et al. Am J Med 2004;116(5A):30S–8
Dahlöf et al. Lancet 2005;366:895–906; Jamerson et al. Blood Press 2007;16:80–6

The impact of fixed-dose combination versus free-equivalent combination therapies on adherence for HTN: a meta-analysis

Forest plot for medication adherence



Du LP et al The Journal of Clinical Hypertension, 2018,

Forest plot of the association between antihypertensive medication adherence and stroke risk

