Nya europeiska riktlinjer för hypertoni; och vad gör vi när blodtrycket inte når målvärde

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Kardiovskulära riskmottagningen och
European Society of Hypertension Center of Excellence

- *Behandlingens mål är att minska risken för framtida hjärt-kärlsjukdom*
- *Opportunistisk screening rekommenderas*
- *Prevention är effektiv!*
- *Riskalgoritmer skattar risk för framtida komplikationer bättre än enskilda riskfaktorer*
- *En global kardiovaskulär riskbedömning avgör vilken behandling som ska erbjudas*

Schematisk riskstratifiering enligt SCORE

Mycket hög risk

- Klinisk aterosklerotisk CV sjukdom (t ex CHD, revaskularisering, TIA/stroke, aortasjukdom, PAD) – *sekundär prevention*
- Bilddiagnostik med prognostiskt viktig aterosklerossjukdom (t ex signifikant koronar flerkärlssjukdom eller carotissjukdom (men ej ökad CCA-IMT)
- Diabetes med mikrovaskulära komplikationer, flera riskfaktorer eller T1DM med lång duration
- CKD med GFR < 30 ml/min/1,73 m^2
- FH med aterosklerossjukdom eller annan riskfaktor
- Beräknad 10 års risk för CV död enligt SCORE ***≥10 %***

Hög risk

- Markant förhöjning av enskilda riskfaktorer (fr a TC >8 mmol/L, LDL >4,9 mmol/L, SBP>180 och/eller DBP≥110 mm Hg, rökare med >20 paketår (paket à 20 per dag x år) före eller under behandling
- CKD med GFR 30-59 ml/min/1,73 m^2
- Hypertensiv hjärtsjukdom (LV hypertrofi)
- De flesta med diabetes
- Beräknad 10 års risk för CVD död enligt SCORE ***5-9 %***

Måttlig risk

- Många med minst måttlig hypertoni
- Diabetes hos unga eller med kort duration
- Beräknad 10 års risk för CV död enligt SCORE ***1-4 %***

Låg risk

- Beräknad 10 års risk för kardiovaskulär död enligt SCORE ***<1 %***

✓ SCORE finns även digitalt: www.hearscore.org
✓ Vid diabetes, använd riskskattning enligt NDR: www.ndr.nu/risk

Information från Läkemedelsverket 2014;25(5):20-33; Williams B et al. *Eur Heart J* 2018;39:3021-3104; Mach F et al. *Eur Heart J* 2020;41:111-88

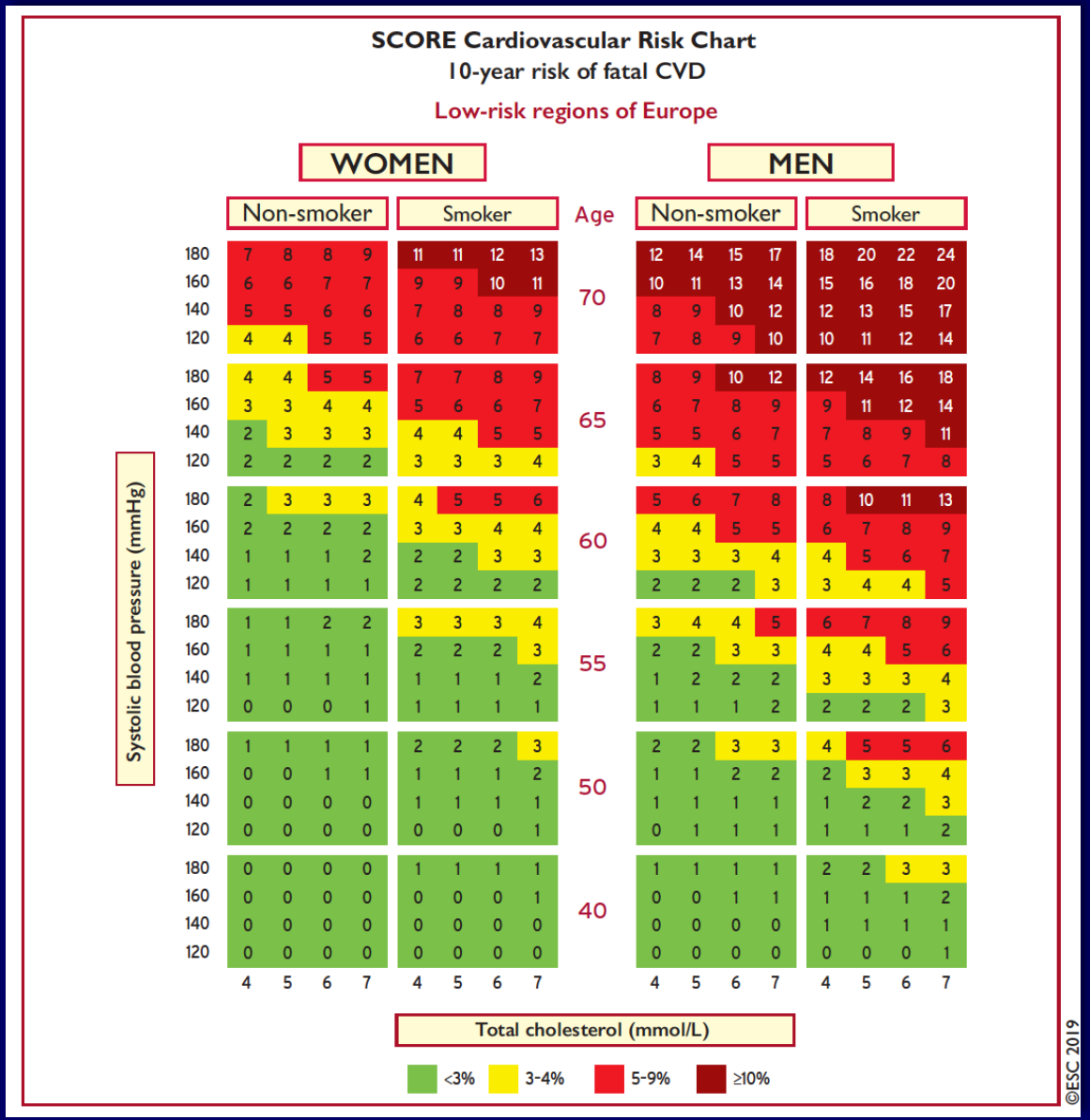
T Kahan 2020

10-Year Risk of Fatal CVD: SCORE Low-Risk Regions

- ✓ Digital (superior) version on www.hearscore.org

To convert the risk of fatal to total CV disease, multiply *x* 3 in men and *x* 4 in women, and slightly less in older people.

This SCORE risk chart differ slightly from 2016 ESC/EAS Guidelines: (i) age extended to age 70; (ii) the interaction between age and other risk factors has been incorporated; and (iii) cholesterol band of 8 mmol/L has been removed.



Mach F et al. *Eur Heart J* 2020;41:111-88

T Kahan 2020

Risk Evaluation in ESC/ESH 2018 Hypertension Guidelines: Modifiying Factors for SCORE Estimates

Very high risk	**People with any of the following:**
	Documented CVD, either clinical or unequivocal on imaging. • **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. ≥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 m^2) • **A calculated 10 year SCORE of ≥10%**
High risk	**People with any of the following:** • **Marked elevation of a single risk factor**, particularly cholesterol >8 mmol/L (>310 mg/dL), e.g. familial hypercholesterolaemia or grade 3 hypertension (BP ≥180/110 mmHg) • **Most other people with diabetes mellitus** (except some young people with type 1 diabetes mellitus and without major risk factors, who may be at moderate-risk)
	Hypertensive LVH
	Moderate CKD eGFR 30-59 mL/min/1.73 m^2)
	A calculated 10 year SCORE of 5-10%
Moderate risk	**People with:** • **A calculated 10 year SCORE of ≥1 to <5%** • **Grade 2 hypertension** • **Many middle-aged people belong to this category**
Low risk	**People with:** • **A calculated 10 year SCORE of <1%**

TABLE 7. Correction factors for the Systemic COronary Risk Evaluation (SCORE) cardiovascular risk estimates in first-generation immigrants to Europe [35]

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
Southern America	0.7

TABLE 6. Risk modifiers increasing cardiovascular risk estimated by the Systemic COronary Risk Evaluation (SCORE) system [35]

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

Williams B et al. *Eur Heart J* 2018;39:3021-3104; *J Hypertens* 2018;36:1953-2041

T Kahan 2018

Treatment Based on Global Risk Evaluation in ESC/ESH 2018 Hypertension Guidelines

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

FIGURE 1 Classification of hypertension stages according to blood pressure levels, presence of cardiovascular risk factors, hypertension-mediated organ damage, or comorbidities. Cardiovascular risk is illustrated for a middle-aged male. The cardiovascular risk does not necessarily correspond to the actual risk at different ages. The use of the SCORE system is recommended for formal estimation of cardiovascular risk for treatment decisions. BP, blood pressure; CKD, chronic kidney disease; DBP, diastolic blood pressure; HMOD, hypertension-mediated organ damage; SBP, systolic blood pressure; SCORE, Systematic COronary Risk Evaluation.

TABLE 4. Factors influencing cardiovascular risk in patients with hypertension

Demographic characteristics and laboratory parameters

- Sex[a] (men >women)
- Age[a]
- Smoking (current or past history)[a]
- Total cholesterol[a] and HDL-C
- Uric acid
- Diabetes[a]
- 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/min)

Asymptomatic HMOD

- Arterial stiffening:
- Pulse pressure (in older people) ≥60 mmHg
- Carotid–femoral PWV >10 m/s
- ECG LVH (Sokolow–Lyon index >35 mm, or R in aVL ≥11 mm; Cornell voltage duration product >2440 mm*ms, or Cornell voltage >28 mm in men or >20 mm in women)
- Echocardiographic LVH [left ventricular mass index: men >50 g/m$^{2.7}$; women >47 g/m$^{2.7}$ (height in m$^{2.7}$); indexation for BSA may be used in normal-weight patients; left ventricular mass/BSA g/m^2 >115 (men) and >95 (women)]
- Microalbuminuria (30–300 mg/24 h), or elevated albumin–creatinine ratio (30–300 mg/g; 3.4–34 mg/mmol) (preferentially on morning spot urine)[b]
- Moderate CKD with eGFR 30–59 ml/min/1.73 m^2 (BSA)[b]
- Ankle-brachial index <0.9
- Advanced retinopathy: haemorrhages or exudates, papilloedema

Established cardiovascular 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

BSA, body surface area; CAD, coronary artery disease; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HDL-C, HDL cholesterol; HFpEF, heart failure with preserved ejection fraction; HMOD, hypertension-mediated organ damage; LVH, left ventricular hypertrophy; PWV, pulse wave velocity; SCORE, Systematic COronary Risk Evaluation; TIA, transient ischaemic attack.
[a]CV risk factors included in the SCORE system.
[b]Proteinuria and reduced eGFR are independent risk factors. See Table 6 for cardiovascular risk modifiers.

Williams B et al. *Eur Heart J* 2018;39:3021-3104; *J Hypertens* 2018;36:1953-2041

T Kahan 2018

Strategies to Identify Patients for Antihypertensive Treatment

Strategies to identify patients for antihypertensive treatment

Elevated blood pressure is the major risk factor for disease and premature death globally, and the association between blood pressure and fatal cardiovascular complications is strong.[1,2] Antihypertensive treatment can reduce cardiovascular morbidity and all-cause mortality and, supported by evidence summarised in 2018,[3] lower target blood pressure values have been introduced into existing recommendations on the management of hypertension.[4,5] However, the absolute benefit of antihypertensive treatment in reducing cardiovascular events is determined by the overall cardiovascular risk of the individual. Therefore, a strategy to identify patients to be offered antihypertensive treatment based on cardiovascular risk might be superior to a strategy that offers treatment on the basis of threshold blood pressure values alone.

In *The Lancet*, Emily Herrett and colleagues[6] report on the eligibility and outcomes of offering antihypertensive treatment on the basis of cardiovascular risk compared with those of strategies relying on blood pressure level. This retrospective cohort study in the UK collected information from primary care, diagnoses, and procedures from hospital-based care, and mortality data for 1 222 670 people (57% women) aged 30–79 years with no previous cardiovascular disease. Herrett and colleagues compared four strategies to define treatment eligibility: a blood pressure of 140/90 mm Hg or higher alone, existing (2011) and proposed (2019) UK National Institute for Health and Care Excellence (NICE) guidelines on the management of hypertension, and an absolute risk strategy based on a predicted 10-year cardiovascular event risk (according to QRISK2) of 10% or greater. The primary outcome was a first cardiovascular diagnosis of coronary artery disease or cerebrovascular disease. Median age at entry was 51 years (IQR 41–62), blood pressure was 129/78 mm Hg, and 18% of participants were on antihypertensive treatment. During a median follow-up of 4·3 years (IQR 2·5–5·2), 7·1 cardiovascular events per 1000 person-years were diagnosed.

Jim Varney/Science Photo Library

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See Articles page 663

on the basis of cardiovascular risk might be superior to treating people on the basis of blood pressure values alone.[7,8] Nevertheless, we should always recommend lifestyle modifications and consider drug treatment (when appropriate) for dyslipidaemia and glucose intolerance, as well as support smoking cessation to reduce cardiovascular risk. Notably, only 43–70% of the patients eligible for treatment under any of the four strategies received antihypertensive treatment, and only half of those treated achieved blood pressure lower than 140/90 mm Hg. Therefore, and corroborating the findings of other studies,[4,5] adherence by care providers to guideline recommendations to treat blood pressure to target levels needs to be improved, along with treatment strategies based on cardiovascular risk.

Some limitations of Herrett and colleagues' study should be considered. First, a target blood pressure of 130/80 mm Hg or lower in patients aged 65 years or younger is recommended, but the additional benefits of a blood pressure lower than 120/70 mm Hg is less certain and might associate with an increased cardiovascular risk.[4,5] Furthermore, the evidence supporting a reduction in cardiovascular risk being superior to eligibility based on blood pressure alone would most likely persist.

In conclusion, the work of Herrett and colleagues shows the importance of assessing cardiovascular risk in the management of hypertension, and suggests that a strategy to offer antihypertensive therapy based on absolute cardiovascular risk might prevent more cardiovascular disease than a strategy based on blood pressure alone.

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1 Rapsomaniki E, Timmis A, George J, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people. *Lancet* 2014; 383: 1899–911.

Eligibility and subsequent burden of cardiovascular disease of four strategies for blood pressure-lowering treatment: a retrospective cohort study

Emily Herrett, Sarah Gadd, Rod Jackson, Krishnan Bhaskaran, Elizabeth Williamson, Tjeerd van Staa, Reecha Sofat, Adam Timmis, Liam Smeeth

Summary

Background Worldwide treatment recommendations for lowering blood pressure continue to be guided predominantly by blood pressure thresholds, despite strong evidence that the benefits of blood pressure reduction are observed in patients across the blood pressure spectrum. In this study, we aimed to investigate the implications of alternative strategies for offering blood pressure treatment, using the UK as an illustrative example.

Methods We did a retrospective cohort study in primary care patients aged 30–79 years without cardiovascular disease, using data from the UK's Clinical Practice Research Datalink linked to Hospital Episode Statistics and Office for National Statistics mortality. We assessed and compared four different strategies to determine eligibility for treatment: using 2011 UK National Institute for Health and Care Excellence (NICE) guideline, or proposed 2019 NICE guideline, or blood pressure alone (threshold ≥140/90 mm Hg), or predicted 10-year cardiovascular risk alone (QRISK2 score ≥10%). Patients were followed up until the earliest occurrence of a cardiovascular disease diagnosis, death, or end of follow-up period (March 31, 2016). For each strategy, we estimated the proportion of patients eligible for treatment and number of cardiovascular events that could be prevented with treatment. We then estimated eligibility and number of events that would occur during 10 years in the UK general population.

Findings Between Jan 1, 2011, and March 31, 2016, 1 222 670 patients in the cohort were followed up for a median of 4·3 years (IQR 2·5–5·2). 271 963 (22·2%) patients were eligible for treatment under the 2011 NICE guideline, 327 429 (26·8%) under the proposed 2019 NICE guideline, 481 859 (39·4%) on the basis of a blood pressure threshold of 140/90 mm Hg or higher, and 357 840 (29·3%) on the basis of a QRISK2 threshold of 10% or higher. During follow-up, 32 183 patients were diagnosed with cardiovascular disease (overall rate 7·1 per 1000 person-years, 95% CI 7·0–7·2). Cardiovascular event rates in patients eligible for each strategy were 15·2 per 1000 person-years (95% CI 15·0–15·5) under the 2011 NICE guideline, 14·9 (14·7–15·1) under the proposed 2019 NICE guideline, 11·4 (11·3–11·6) with blood pressure threshold alone, and 16·9 (16·7–17·1) with QRISK2 threshold alone. Scaled to the UK population, we estimated that 233 152 events would be avoided under the 2011 NICE guideline (28 patients needed to treat for 10 years to avoid one event), 270 233 under the 2019 NICE guideline (29 patients), 301 523 using a blood pressure threshold (38 patients), and 322 921 using QRISK2 threshold (27 patients).

Interpretation A cardiovascular risk-based strategy (QRISK2 ≥10%) could prevent over a third more cardiovascular disease events than the 2011 NICE guideline and a fifth more than the 2019 NICE guideline, with similar efficiency regarding number treated per event avoided.

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Introduction

Randomised trials[1,2] have shown that blood pressure reductions, whether by diet, lifestyle, or drug therapy, patient's clinic blood pressure is between 140/90 and 159/99 mm Hg and they have one or more of the following: an absolute 10-year cardiovascular risk of

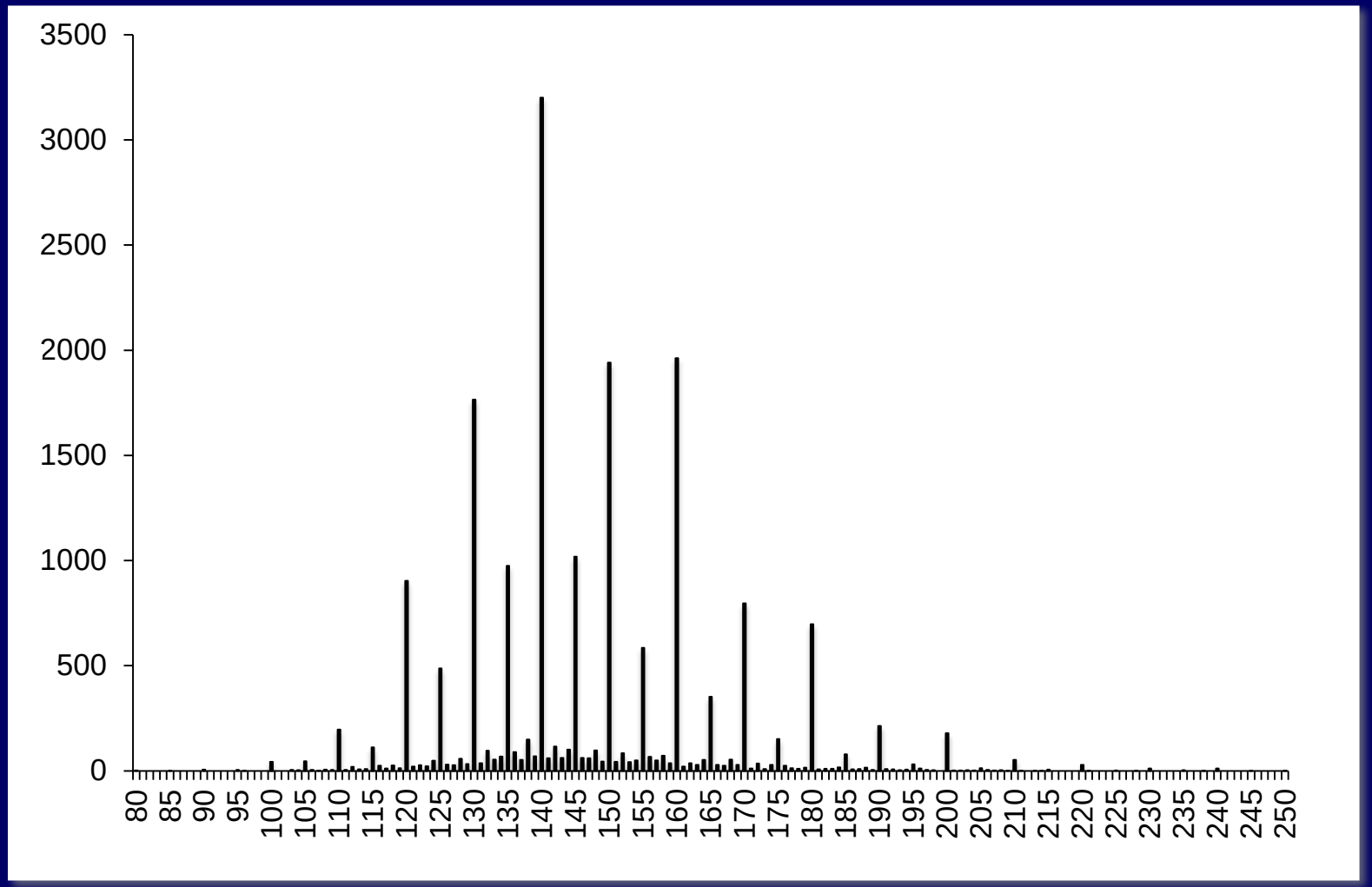
Herrett E et al. *Lancet* 2019;394:663-671.
Kahan T. *Lancet* 2019;394:615-617.

T Kahan 2019

Hur ställs diagnosen hypertoni?

- Viktigt att *mäta blodtrycket rätt;* validerad utrustning
- Bekvämt sittande (eller liggande) med stöd för armen vilande i hjärthöjd, ryggstöd och benen på golvet
- 3-5 min vila i lugn och ro
- Ej kaffe eller tobak de senaste 30 min
- Rätt manschett (12 cm om armomfång ≤32 cm, bredare vid större, smalare vid mindre)
- 3 mätningar, fler om >10 mm Hg initial skillnad, avlästa på närmast jämn siffra; medelvärde av de 2 senaste
- Mät i båda armar första gången. Välj sedan höger eller armen med högst tryck (>5-10 mm Hg skillnad)
- Stående efter 1 & 3 min hos äldre, vid diabetes, autonom neuropati eller ortostatisk hypotension mm

21 667 Hypertensive Patients in Swedish Primary Care



Qvarnström et al. *J Hum Hypertens* 2011;25:484-91

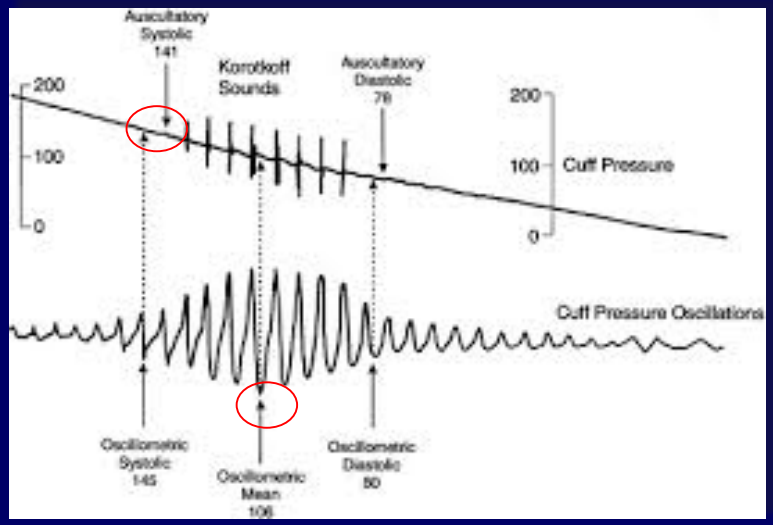
T Kahan 2011

Auscultatory or Oscillometric Measurements

sphygmomanometer |ˌsfigmōməˈnämitər|

noun

an instrument for measuring blood pressure, typically consisting of an inflatable rubber cuff that is applied to the arm and connected to a column of mercury next to a graduated scale, enabling the determination of systolic and diastolic blood pressure by increasing and gradually releasing the pressure in the cuff.



Ausculatatory

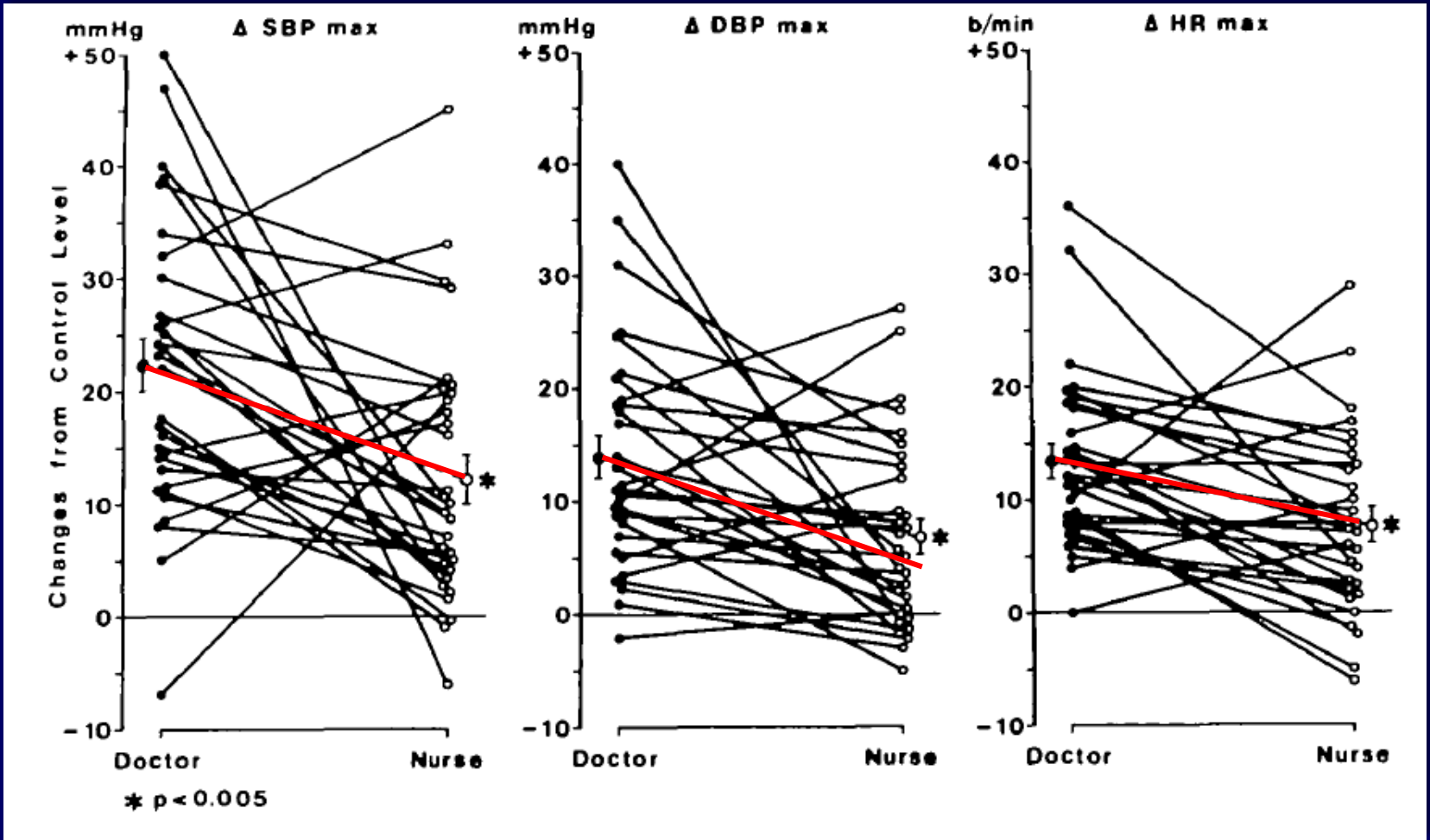
- Accurate
- Hg or aneroid meters
- Calibration
- Digit preference
- Training

Oscillometric

- Easy to use
- Calibration
- Little reader bias
- Arrhythmias
- Sometimes inaccurate

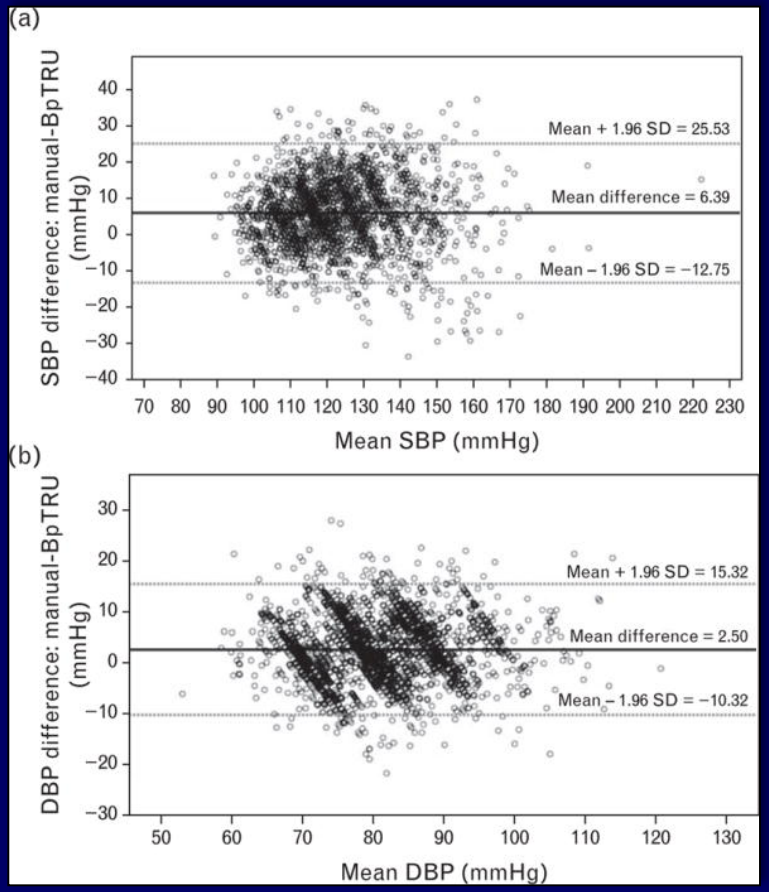
T Kahan 2014

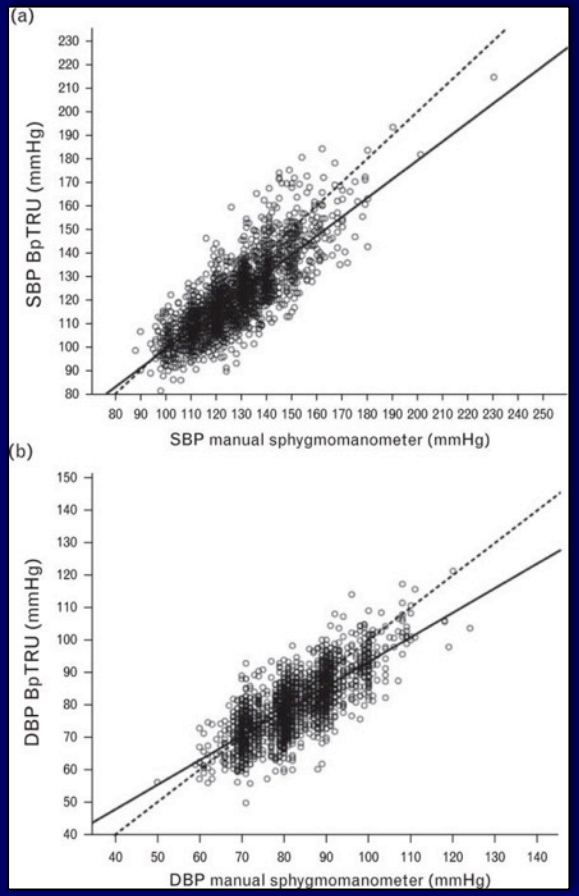
Alerting Reaction and Rise in Blood Pressure During Measurement by Physician and Nurse



Mancia G et al. *Hypertension* 1987;9:209-15

Automated Repeat Office BP Measurements (BpTRU) *vs* Standard Office BP Measurements





Solid line represents regression line, dashed line equity (y = x). Deviation from equity is increasing with increasing blood pressure

Random population sample of 2145 persons 25-64 ys. Manual auscultatory (mean of 2 last out of 3 recordings) and automated office BpTRU (5 unattended measurements at 1 min interval) recordings. **131/85** mm Hg automated BP corresponds to **140/90** mm Hg manual BP.

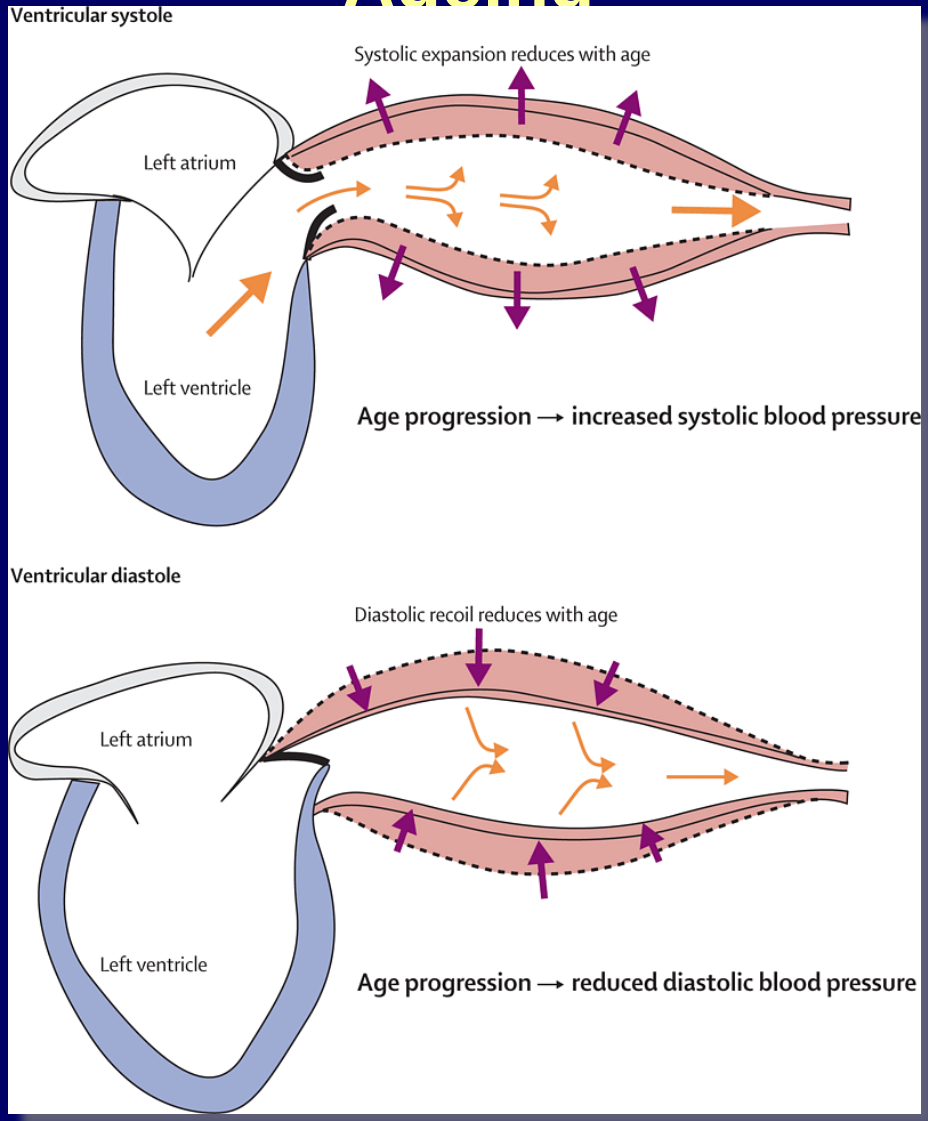
Wohlfart PG et al. *J Hypertens* 2016;34:2080-6

Hemblodtrycksmätning

- Använd validerad halvautomatisk utrustning på *överarm*
- Samma standardiserade betingelser som vid konventionell mätning
- Mät morgon och kväll, (2-) 3 mätningar varje gång, 1-2 min mellan
- Mät under minst 3 (men helst alla 7 dagar och exkludera dag 1) under 1 vecka för diagnostik, för att värdera läkemedelsförändringar eller inför mottagningsbesök; medelvärdesberäkna sedan alla mättillfällen
- Mät var 2-8 vecka vid långsiktig uppföljning
- Registrera värdet i loggbok eller elektroniskt direkt efter mätningen
- Patienten bör kontakta ansvarig läkare om resultaten är avvikande; och avråds ofta från att på egen hand förändra medicineringen
- Vid arytmi blir mätresultaten osäkra och flera mätningar kan krävas

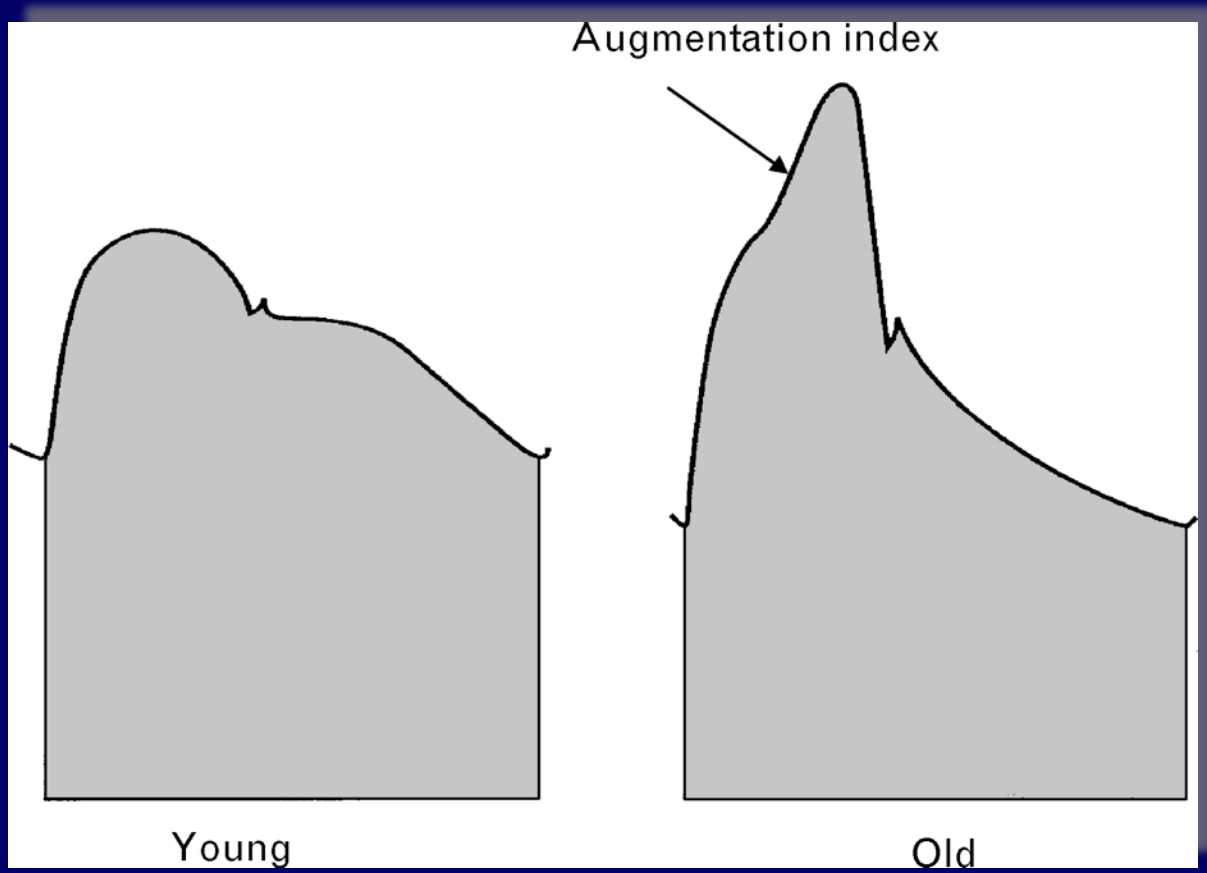
Modifierat efter Parati et al *J Hum Hypertens* 2010;24:779-85

Role of Aortic Compliance on Blood Pressure and Effect of Ageing



Kaplan & Opie. *Lancet* 2006;367:168-76

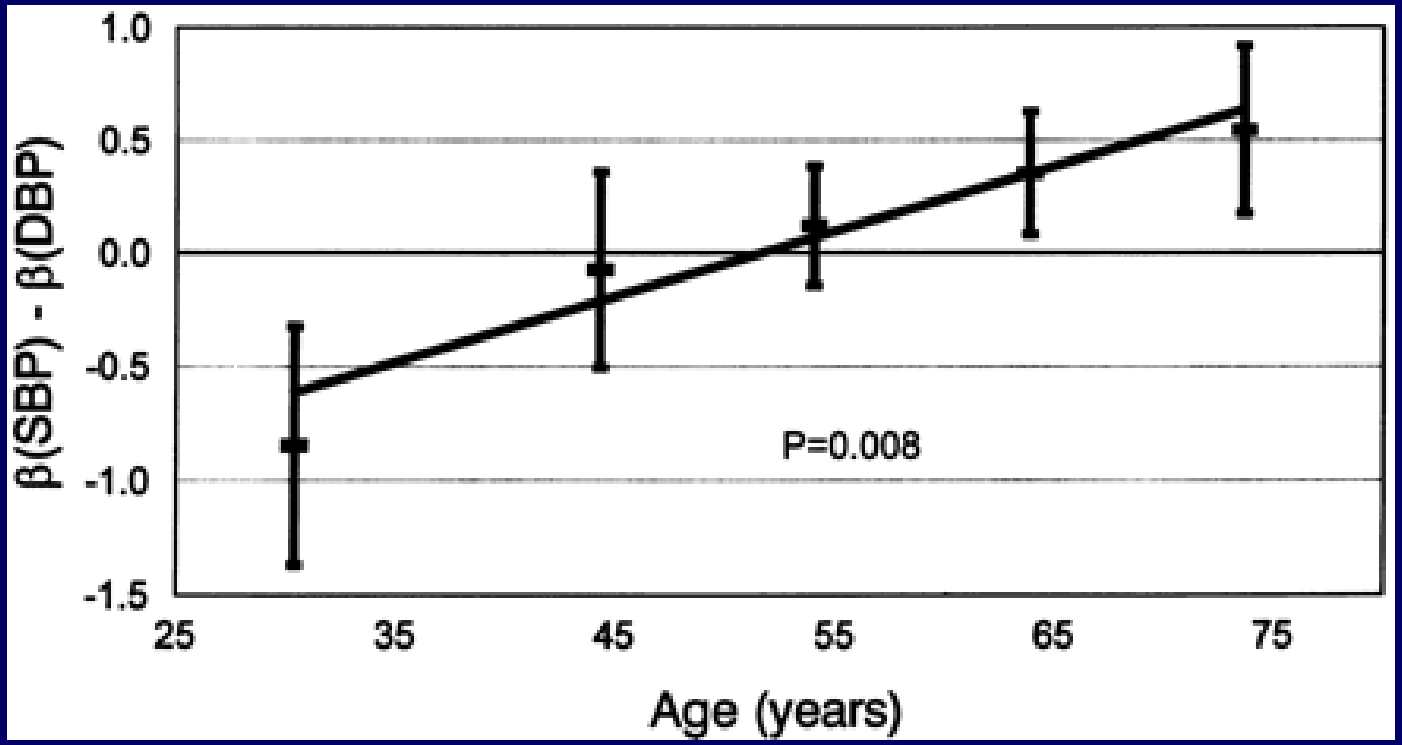
Aortic Blood Pressure, Vascular Structure, and Age



Traditional aspects of the shape of the aortic blood pressure curve in young (64 years) and old (> 65 years) subjects. Cardiac time as well as the areas under the curves are identical, implying the same mean arterial pressure.

Safar M, *J Hypertens* 2005;23:673-81

CHD Prediction by SBP and DBP



Difference in CHD prediction between SBP and DBP as function of age. Difference in ß coefficients (from Cox proportional-hazards regression) between SBP and DBP is plotted as function of age. Framingham: 3060 men and 3479 women 20-79 years of age who were free of CHD and were not on antihypertensive drug therapy at baseline.

Franklin et al. *Circulation* 2001;103:1245-9.

Age-Adjusted CV Mortality in 1999 Apparently Healthy Men

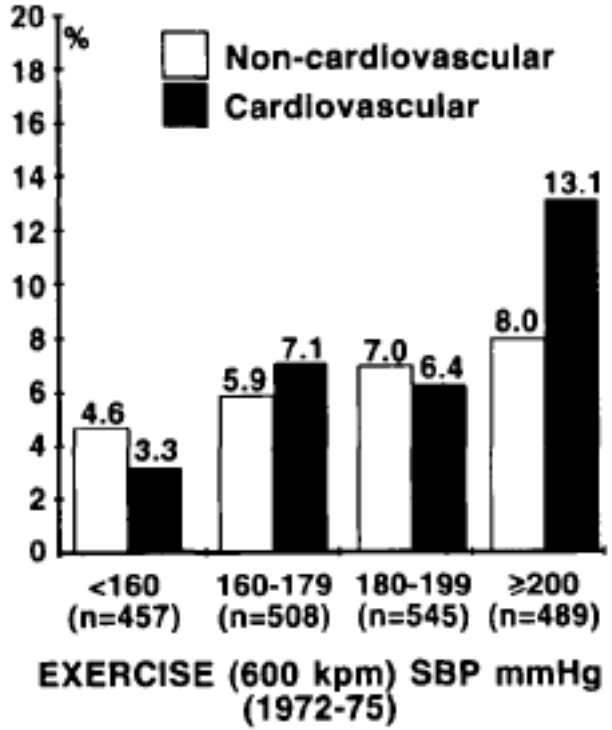
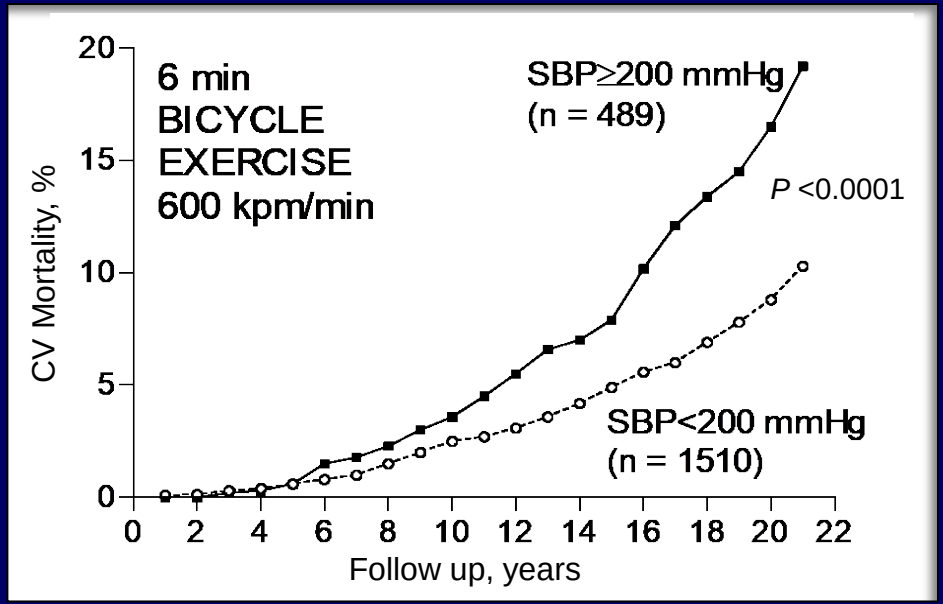


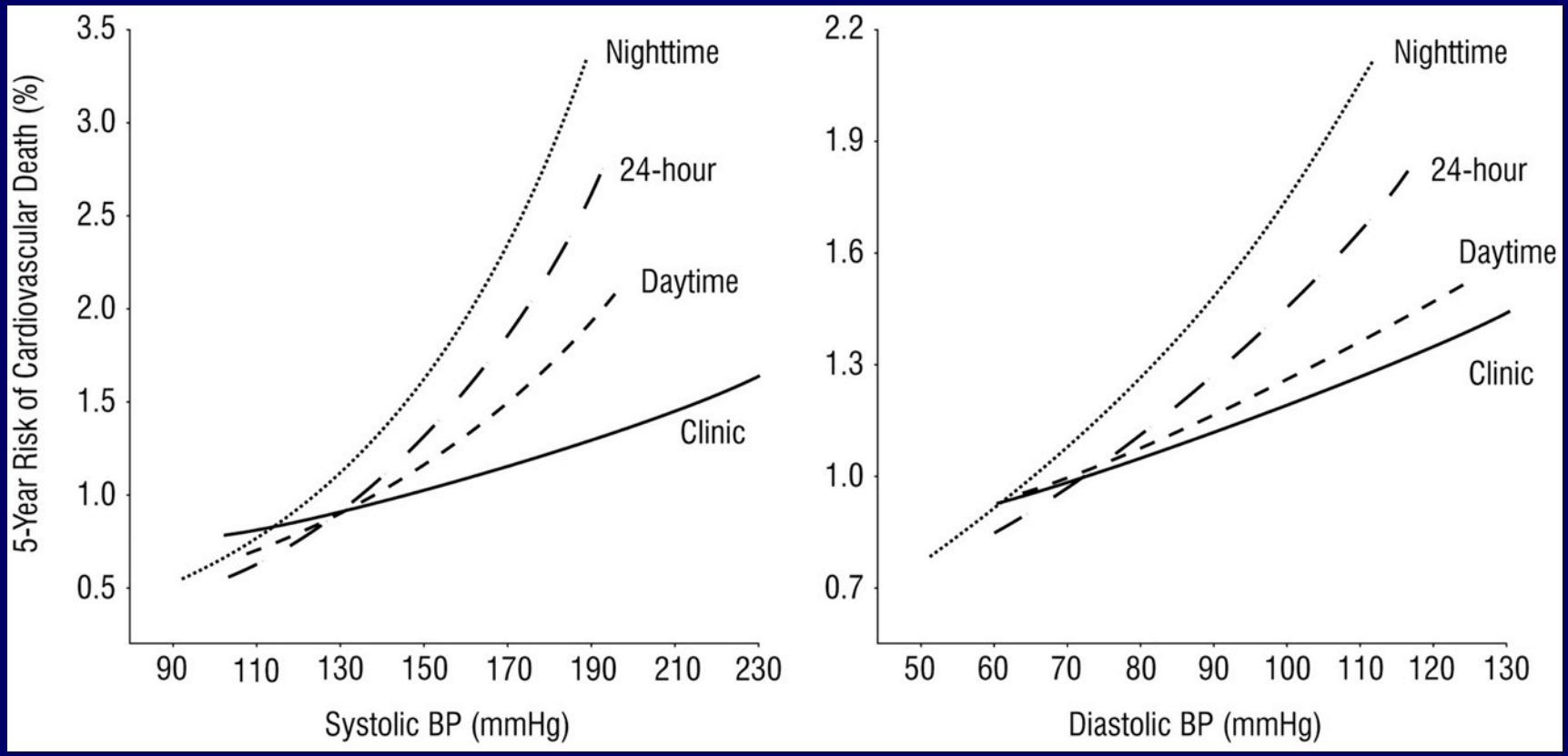
FIG 2. Bar graph shows 16-year crude cardiovascular and noncardiovascular death rates in relation to initial (1972 through 1975) peak exercise systolic blood pressure (SBP) at 600 kpm/min in middle-aged, apparently healthy men.

Mundal R et al. *Hypertens* 1994;24:56-62



Kjeldsen SE et al. *J Hypertens* 2001;91:1343-48

Adjusted 5-year Risk of Cardiovascular Death for CBP and ABP: the Dublin Outcome Study

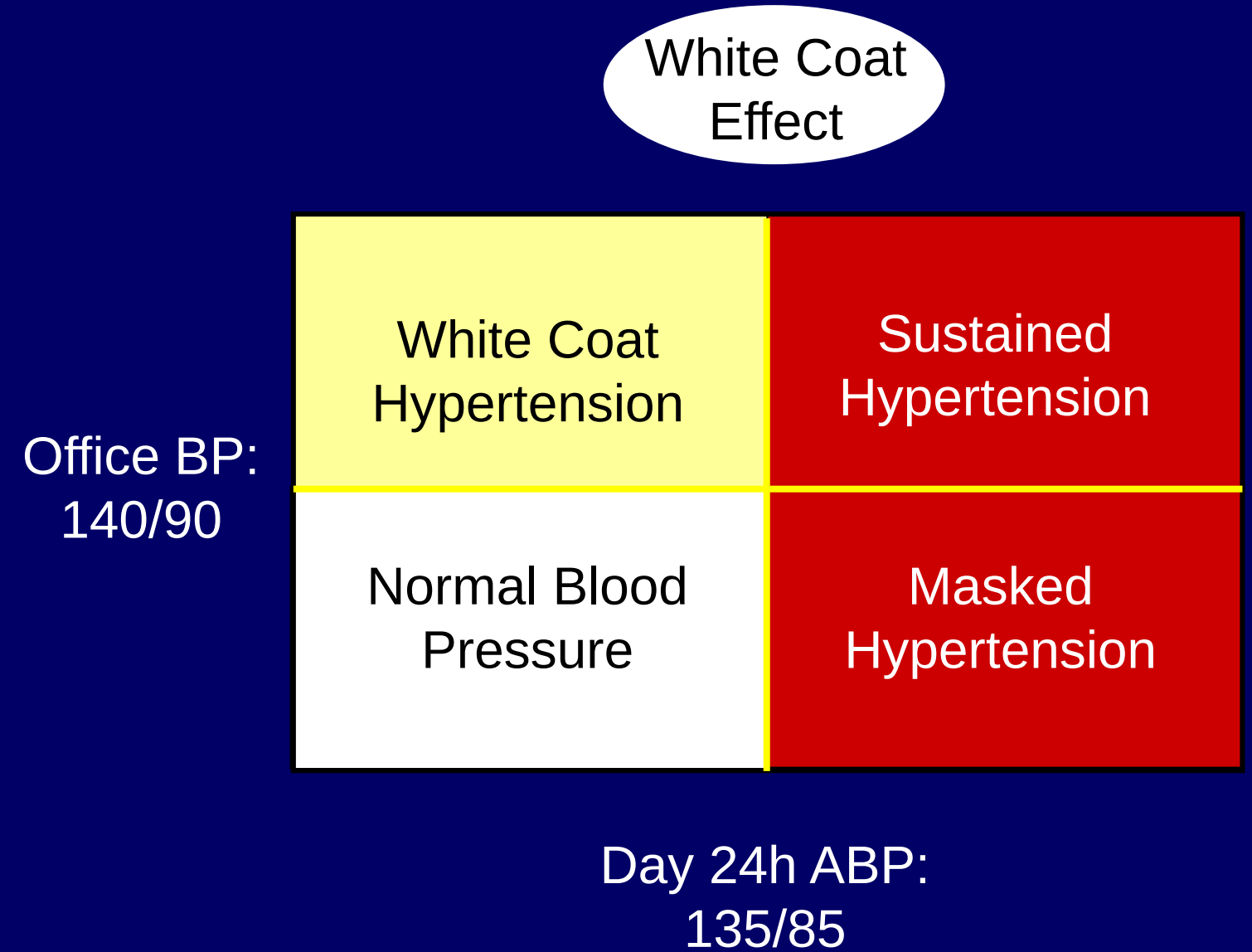


646 deaths in 5592 untreated hypertensive patients from 1980 to 2002

A ∆10 mm Hg increase in *night systolic ABP* causes a 20% increase in CV death risk.

Dolan et al. *Hypertension* 2005;46:156-161

Blood Pressure and Hypertension



T Kahan 2009

När och hur ska vi använda 24 timmars ambulatorisk blodtrycksmätning och hemblodtryck?

- Misstanke på vitrockshypertoni (*white coat hypertension)*, t ex mild hypertoni på mottagningen eller hypertoni hos individer med låg kardiovaskulär risk utan tecken på organpåverkan
- Misstanke på vitrockseffekt (*white coat effect*)
- Misstanke på maskerad hypertoni, t ex lätt förhöjda blodtryck på mottagningen eller individer med hög kardiovaskulär risk och tecken på organpåverkan eller patologisk blodtrycksstegring under arbete
- Oväntade symtom eller biverkningar
- Utvärdera och följa behandling
- Öka patientens delaktighet och följsamhet till behandling
- Högriskpatienter och gravida i behov av strikt kontroll
- Isolerad systolisk hypertoni
- Utredning av resistent hypertoni
- Mottagningsblodtryck, hemblodtryck och ambulatorisk blodtrycksmätning *ger komplementär information*

T Kahan 2013

Definition of Hypertension and Grade

Table 3 Classification of office blood pressure[a] and definitions of hypertension grade[b]

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension[b]	≥140	and	<90

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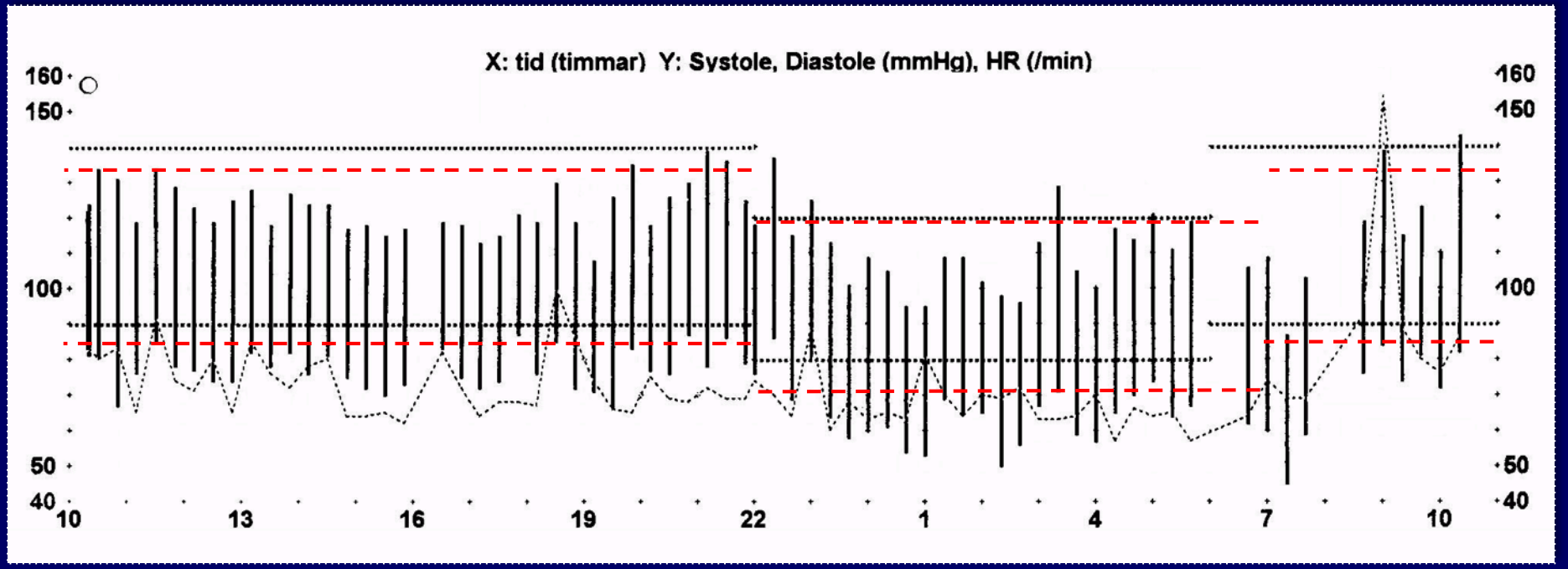
BP = blood pressure; SBP = systolic blood pressure.
[a]BP category is defined according to seated clinic BP and by the highest level of BP, whether systolic or diastolic.
[b]Isolated systolic hypertension is graded 1, 2, or 3 according to SBP values in the ranges indicated.
The same classification is used for all ages from 16 years.

Mild
Måttlig
Svår

ABPM day	≥135	and/or	≥85	Home BP	≥135	and/or	≥85
ABPM night	≥120	and/or	≥70				
ABPM 24 h	≥130	and/or	≥80				

Williams B et al. *Eur Heart J* 2018;39:3021-3104; *J Hypertens* 2018;36:1953-2041

Ambulatory Blood Pressure Monitoring



- Quality of registration
- 24h/day/night mean SBP and DBP
- White coat effect
- Night/day ratio (”dipping”)
- Pulse pressure
- BP variability (*eg* SD night)
- Heart rate
- Symptoms
- Interpretation

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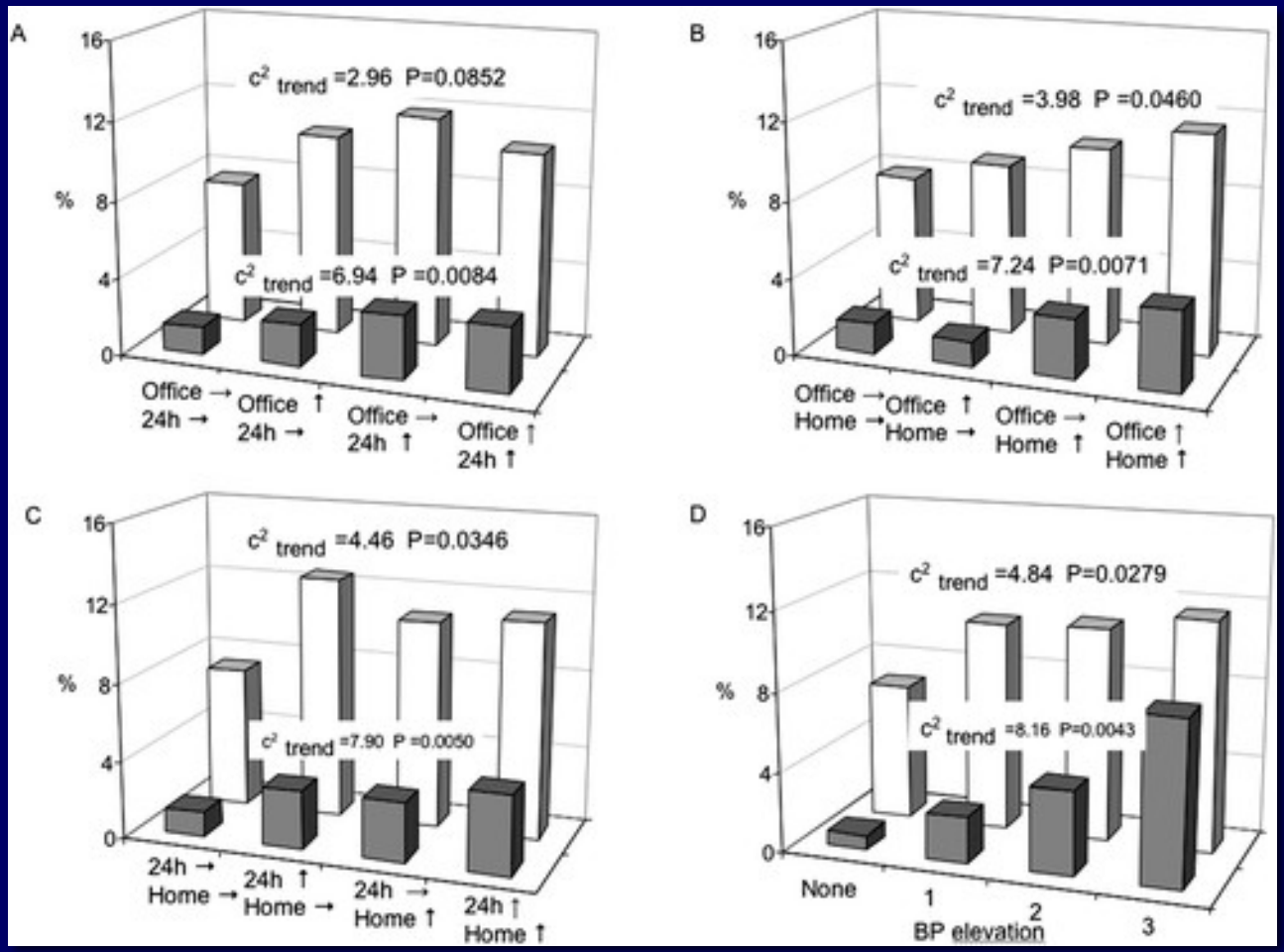
Office BP, Home BP, or ABPM



PAMELA, 2051 subjects 25-74 years of age who were representative of the general population of Monza. Percentage incidence of CV (filled) and all-cause death (open) over an average follow-up of 148 months in subjects with various combinations of normality or elevation in BP.

Mancia G et al. Hypertension 2006;47:846-53

ESC European Society of Cardiology

European Heart Journal (2018) **00**, 1–98
doi:10.1093/eurheartj/ehy339

ESC/ESH GUIDELINES

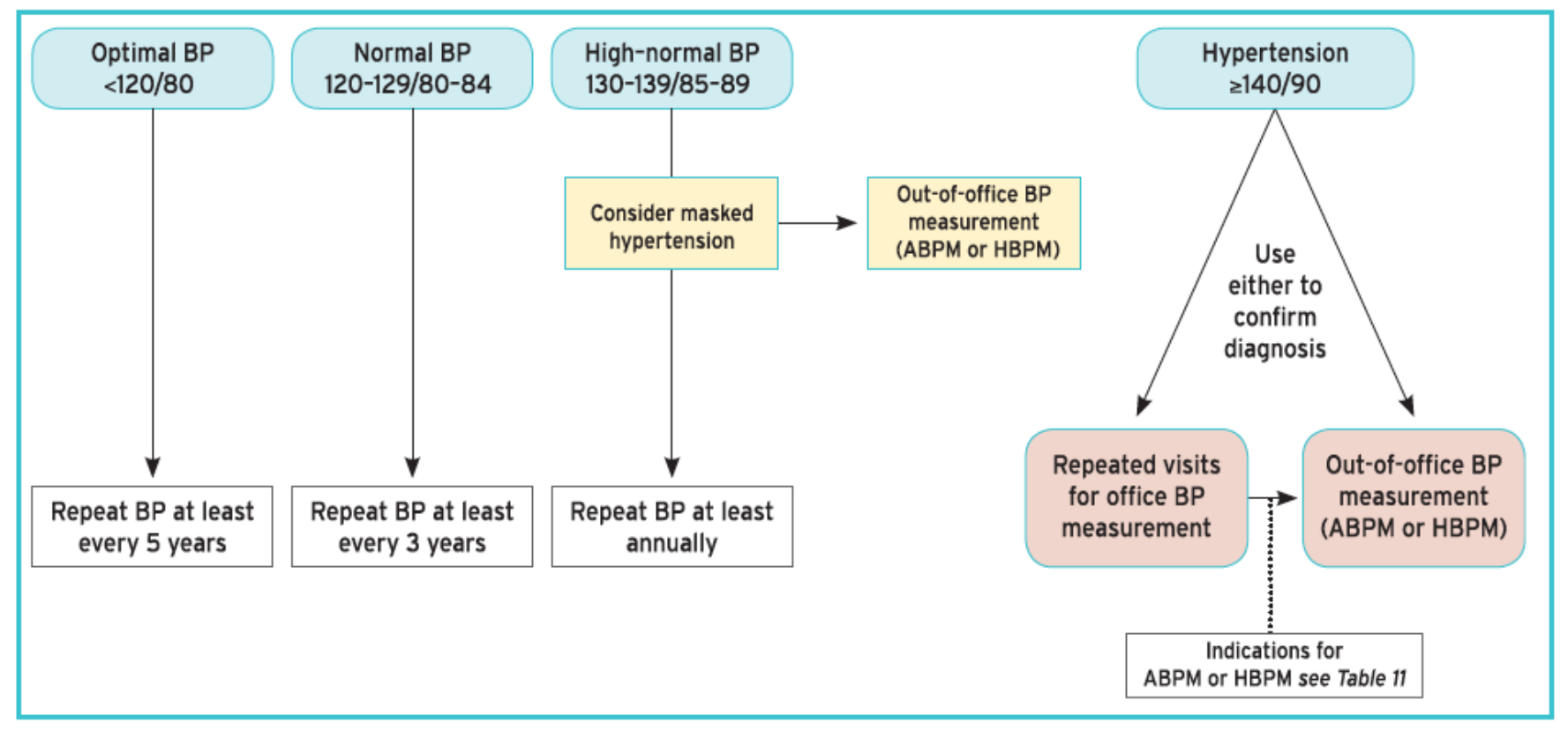
2018 ESC/ESH Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH)

Authors/Task Force Members: Bryan Williams* (ESC Chairperson) (UK), Giuseppe Mancia* (ESH Chairperson) (Italy), Wilko Spiering (The Netherlands), Enrico Agabiti Rosei (Italy), Michel Azizi (France), Michel Burnier (Switzerland), Denis L. Clement (Belgium), Antonio Coca (Spain), Giovanni de Simone (Italy), Anna Dominiczak (UK), Thomas Kahan (Sweden), Felix Mahfoud (Germany), Josep Redon (Spain), Luis Ruilope (Spain), Alberto Zanchetti† (Italy), Mary Kerins (Ireland), Sverre E. Kjeldsen (Norway), Reinhold Kreutz (Germany), Stephane Laurent (France), Gregory Y. H. Lip (UK), Richard Mcmanus (UK), Krzysztof Narkiewicz (Poland), Frank Ruschitzka (Switzerland), Roland E. Schmieder (Germany), Evgeny Shlyakhto (Russia), Costas Tsioufis (Greece), Victor Aboyans (France), Ileana Desormais (France)

Williams B et al. *Eur Heart J* 2018;39:3021-3104; *J Hypertens* 2018;36:1953-2041

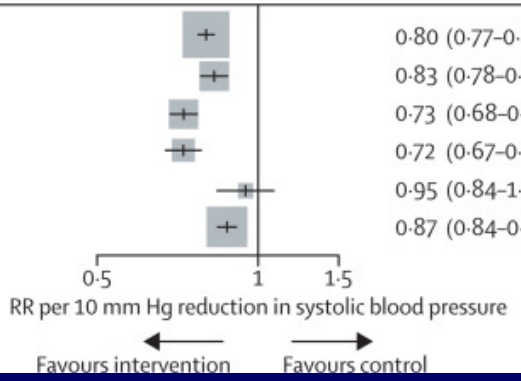
Screening and Diagnosis of Hypertension
ESC/ESH 2018 Hypertension Guidelines

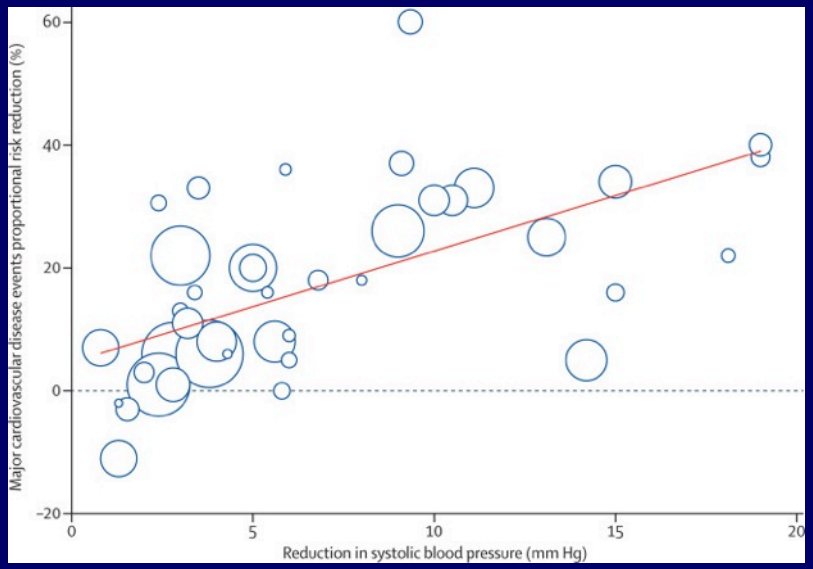


Williams B et al. *Eur Heart J* 2018;39:3021-3104; *J Hypertens* 2018;36:1953-2041

Standardised Effects of a 10 mm Hg Reduction in SBP

	Studies	Intervention		Control		RR (95% CI) per 10 mm Hg reduction in systolic blood pressure
		Events	Participants	Events	Participants	
Major cardiovascular events	55	13209	137319	14068	128259	0·80 (0·77–0·83)
Coronary heart disease	56	4862	136986	5301	128548	0·83 (0·78–0·88)
Stroke	54	4635	136682	5378	128641	0·73 (0·68–0·77)
Heart failure	43	3284	115411	3760	107440	0·72 (0·67–0·78)
Renal failure	16	890	39888	834	39043	0·95 (0·84–1·07)
All-cause mortality	57	9775	138298	9998	129700	0·87 (0·84–0·91)





Meta-analysis of 123 trials
with 613 815 subjects

Ettehad et al. *Lancet* 2016;387:957-67

Risk Reduction in Blood Pressure Lowering Trials

Outcome	Trials (n)	Difference SBP/DBP (mmHg)	Events (n/patients) Treated	Events (n/patients) Controls	RR (95% CI)	Standardized RR (95% CI)	Absolute Risk reduction 1000 pts/5 years (95% CI)	NNT 5 years (95% CI)
Stroke	31	−9.0/−4.8	1262/51179	1869/56326	0.68 (0.62–0.75)	0.63 (0.56–0.71)	−15 (−18, −12)	67 (57, 84)
CHD	35	−9.0/−4.8	1443/52168	1723/56868	0.82 (0.77–0.88)	0.78 (0.72–0.85)	−8 (−11, −6)	118 (94, 171)
HF	20	−10.6/−4.8	231/21517	415/20605	0.55 (0.46–0.65)	0.54 (0.45–0.64)	−12 (−14, −10)	81 (70, 101)
Stroke + CHD	32	−9.0/−4.8	2632/50705	3471/55848	0.77 (0.73–0.81)	0.75 (0.71–0.79)	−17 (−20, −15)	57 (50, 68)
Stroke + CHD + HF	22	−11.2/−5.4	1969/31902	2536/30979	0.73 (0.68–0.80)	0.74 (0.69–0.81)	−25 (−31, −19)	40 (32, 52)
CV death	33	−9.1/−4.8	1473/51245	1778/56402	0.82 (0.76–0.89)	0.80 (0.73–0.88)	−7 (−10, −5)	134 (100, 221)
All-cause death	37	−9.0/−4.8	2913/53140	3335/58288	0.89 (0.84–0.94)	0.88 (0.82–0.93)	−8 (−12, −5)	124 (83, 212)

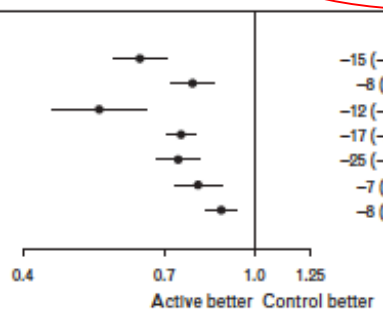


FIGURE 3 Relative and absolute risk reduction of various outcomes in the blood-pressure-lowering trials. Sensitivity analysis including intentional trials exclusively in hypertensive patients.. Standardized RR is to a SBP/DBP reduction of 10/5 mmHg. The column absolute risk reduction reports the number (and 95% CI) of events prevented every 1000 patients treated for 5 years with a standardized RR. NNT is the numbers (and 95% CI) of patients needed to treat for 5 years to prevent one event. CHD, coronary heart disease; CI, confidence interval; CV, cardiovascular; HF, heart failure; *n*, number; NNT, number needed to treat; pts, patients; RR, Mantel–Haenszel risk ratios.

Meta-analysis of all 68 published randomized controlled blood pressure lowering trials in hypertensive patients 1966-2013; n=245 885. Standardised RR to a reduction of 10/5 mm Hg

Thomopoulos C et al. *J Hypertens* 2014;32:2285-95

Meta-Analysis of Intensive *vs* Standard Blood Pressure Targets

Consistent with other recent meta-analyses which demonstrate that BP lowering reduced the risk of CV morbidity and mortality regardless of meta-analytic method, comorbid condition, or mean age of patient.

Additionally, BP lowering to a target of <130 mm Hg may reduce the risk of several outcomes including MI, stroke, heart failure, and major CV events.

Intensive *vs* any standard target BP

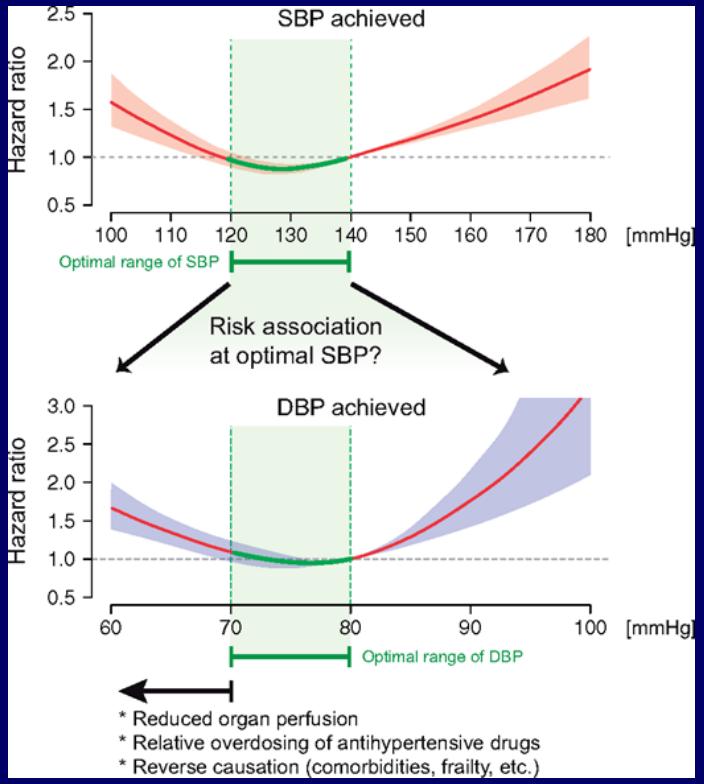
Outcome	Studies included, N	Study participants included, N	Events, N (%)		RR	(95% CI)	Heterogeneity	
			Intensive BP target	Standard BP target			I^2 (%)	*P*-value
All-cause mortality	15	49,934	952 (4.0)	1,001 (4.3)	0.89	(0.77, 1.02)	49.30	0.02
CVD mortality	10	40,266	268 (1.3)	504 (2.5)	0.86	(0.67, 1.12)	46.44	0.06
Major Cardiovascular Disease Events	7[a]	23,617	682 (5.8)	828 (7.0)	0.81	(0.70, 0.94)	41.34	0.12
Fatal or non-fatal myocardial infarction	11	31,926	415 (2.6)	419 (2.7)	0.86	(0.76, 0.99)	0.00	0.99
Fatal or non-fatal stroke	12	33,018	389 (2.3)	475 (2.9)	0.77	(0.65, 0.91)	26.43	0.18
Fatal or non-fatal heart failure	8	23,066	222 (1.9)	278 (2.4)	0.75	(0.56, 0.99)	49.12	0.06
Renal Events	8[b]	18,286	334 (3.8)	353 (4.2)	1.01	(0.89, 1.15)	0.00	0.80

<130 mm Hg *vs* any standard target BP

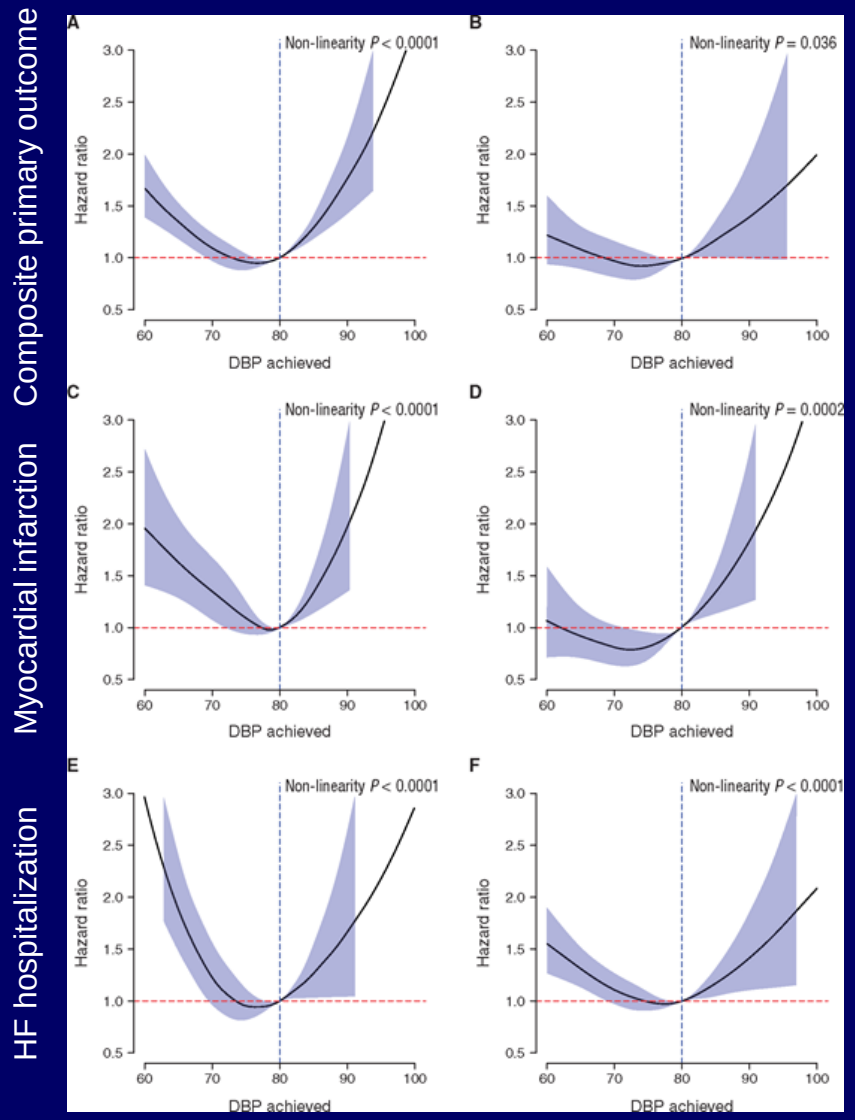
Outcome	Studies included, N	Study participants included, N	Events, N (%)		RR	(95% CI)	Heterogeneity	
			Intensive BP target	Standard BP target			I^2 (%)	*P*-value
All-cause mortality	9[a]	24,569	493 (4.0)	546 (4.4)	0.92	(0.79, 1.06)	15.59	0.30
CVD mortality	5[b]	19,039	117 (1.2)	145 (1.5)	0.81	(0.58, 1.14)	31.42	0.21
Major Cardiovascular Disease Events	5[a]	19,814	610 (6.2)	724 (7.3)	0.84	(0.73, 0.99)	40.70	0.15
Fatal or non-fatal myocardial infarction	6	22,077	269 (2.4)	316 (2.9)	0.85	(0.73, 1.00)	0.00	0.99
Fatal or non-fatal stroke	7	23,169	274 (2.4)	339 (2.9)	0.82	(0.70, 0.96)	0.00	0.45
Fatal or non-fatal heart failure	4	16,296	175 (2.2)	220 (2.7)	0.81	(0.58, 1.14)	53.42	0.09
Renal Events	5[b]	9,641	347 (7.4)	346 (7.0)	1.01	(0.89, 1.16)	0.00	0.99

Reboussin DM et al. *J Am Coll Cardiol* 2018;71:2176-98

Target DBP in Patients Achieving 130-139 mm Hg SBP in *ONTARGET and TRANSCEND*



Patients >55 ys with CV disease randomized to ramipril, telmisartan, or the combination. 16099 of 31546 patients achieved 120-139 mm Hg SBP. Adjusted for heart rate, age, sex, BMI, renal function, physical activity, education, alcohol consumption, tobacco use, history of hypertension, history of diabetes, myocardial infarction, stroke, TIA, heart rhythm, concomitant medications, study and study medications.



Böhm M et al. *Eur Heart J* 2018;3:3105-14

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Target Office Blood Pressure Ranges
ESC/ESH 2018 Guidelines

Age group	Office SBP treatment target ranges (mmHg)					Office DBP treatment target range (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke[a]/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[b]	**Target to 130–139** *if tolerated*	**Target to 130–139** *if tolerated*	**Target to 130–139** *if tolerated*	**Target to 130–139** *if tolerated*	**Target to 130–139** *if tolerated*	70–79
≥80 years[b]	**Target to 130–139** *if tolerated*	**Target to 130–139** *if tolerated*	**Target to 130–139** *if tolerated*	**Target to 130–139** *if tolerated*	**Target to 130–139** *if tolerated*	70–79
Office DBP treatment target range (mmHg)	70–79	70–79	70–79	70–79	70–79	

CAD, coronary artery disease; CKD, chronic kidney disease (includes diabetic and nondiabetic CKD); DBP, diastolic blood pressure; SBP, systolic blood pressure; TIA, transient ischaemic attack.
[a]Refers to patients with previous stroke and does not refer to blood pressure targets immediately after acute stroke.
[b]Treatment decisions and blood pressure targets may need to be modified in older patients who are frail and independent.

Williams B et al. *Eur Heart J* 2018;39:3021-3104; *J Hypertens* 2018;36:1953-2041

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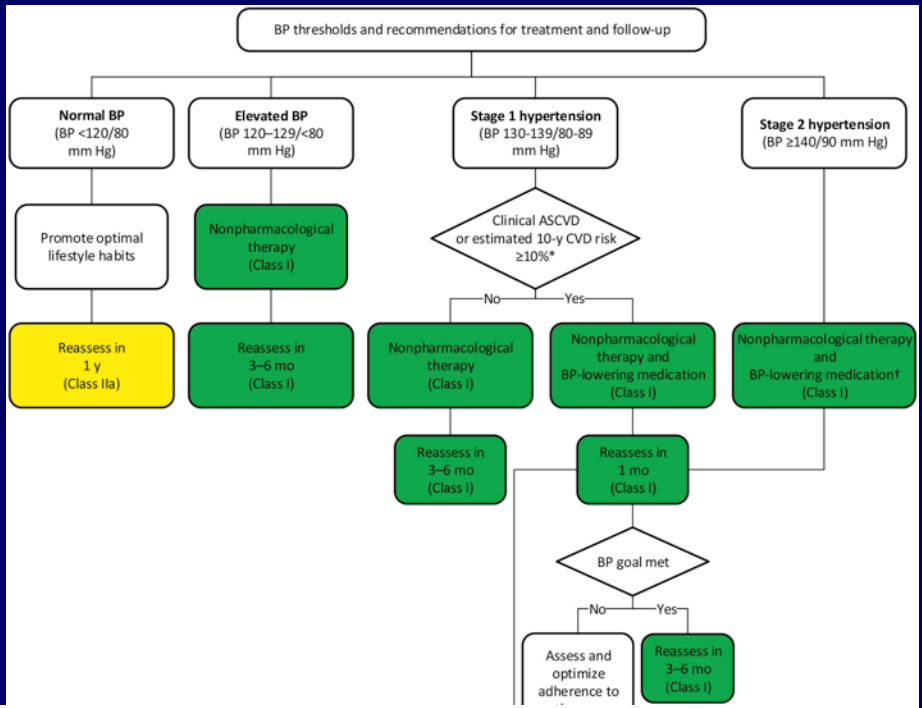
Initiation of Antihypertensive Treatment and Target Blood Pressures: *ACC/AHA 2018 Guidelines*

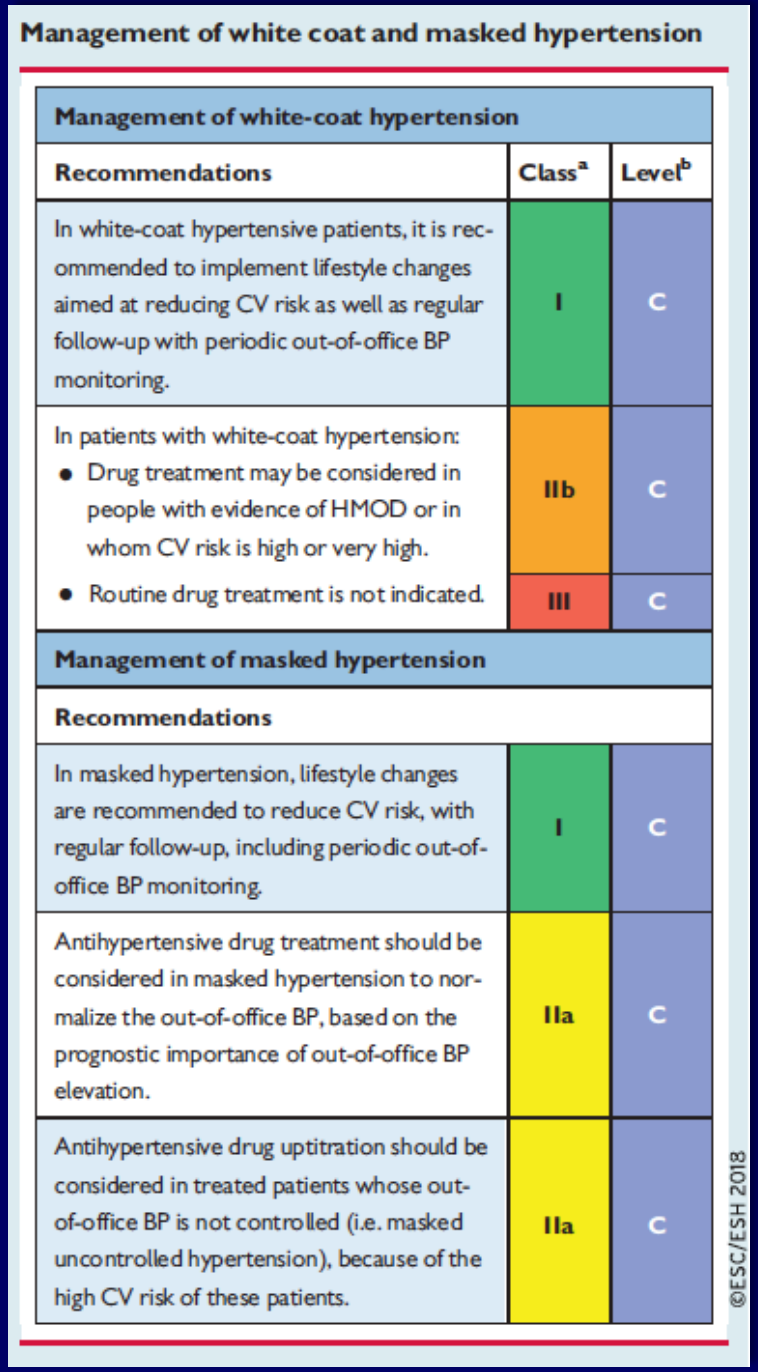


COR	LOE	RECOMMENDATIONS
I	SBP: B-R[SR] DBP: C-EO	1. For adults with confirmed hypertension and known CVD or 10-year ASCVD event risk of 10% or higher (see Section 8.1.2), a BP target of less than 130/80 mm Hg is recommended (S8.1.5-1–S8.1.5-5).
IIb	SBP: B-NR DBP: C-EO	2. For adults with confirmed hypertension, without additional markers of increased CVD risk, a BP target of less than 130/80 mm Hg may be reasonable (S8.1.5-6–S8.1.5-9).

COR	LOE	RECOMMENDATIONS
I	A	1. Treatment of hypertension with a SBP treatment goal of less than 130 mm Hg is recommended for noninstitutionalized ambulatory community-dwelling adults (≥65 years of age) with an average SBP of 130 mm Hg or higher (S10.3.1-1).
IIa	C-EO	2. 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.

Whelton PK et al. *J Am Coll Cardiol* 2018;71:e127-e248

T Kahan 2019



Management of white coat and masked hypertension

Management of white-coat hypertension		
Recommendations	**Class[a]**	**Level[b]**
In white-coat hypertensive patients, it is recommended to implement lifestyle changes aimed at reducing CV risk as well as regular follow-up with periodic out-of-office BP monitoring.	I	C
In patients with white-coat hypertension: • Drug treatment may be considered in people with evidence of HMOD or in whom CV risk is high or very high.	IIb	C
• Routine drug treatment is not indicated.	III	C
Management of masked hypertension		
Recommendations		
In masked hypertension, lifestyle changes are recommended to reduce CV risk, with regular follow-up, including periodic out-of-office BP monitoring.	I	C
Antihypertensive drug treatment should be considered in masked hypertension to normalize the out-of-office BP, based on the prognostic importance of out-of-office BP elevation.	IIa	C
Antihypertensive drug uptitration should be considered in treated patients whose out-of-office BP is not controlled (i.e. masked uncontrolled hypertension), because of the high CV risk of these patients.	IIa	C

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Management of White Coat and Masked Hypertension

ESC/ESH 2018 Guidelines

Williams B et al. *Eur Heart J* 2018;39:3021-3104; *J Hypertens* 2018;36:1953-2041

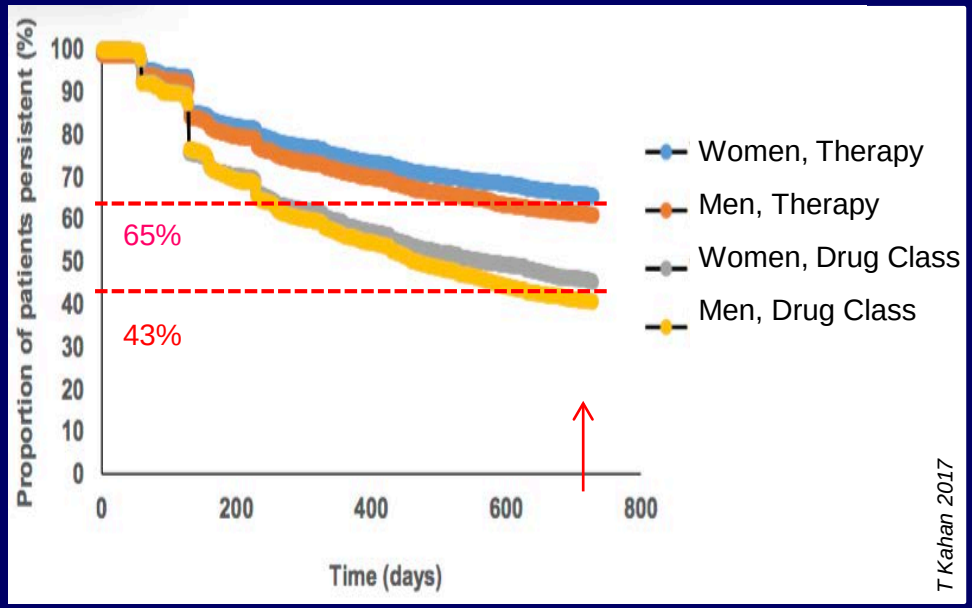
Associations with Discontinuation 2 years After Initiation: *Adjusted Hazard Ratios*

Significant association	*Hazard ratio [95% CI]*	*P (trend)*
Male gender	1.19 [1.07–1.32]	0.002
Young age (eg 30-49 *vs* 50-59 ys)	1.37 [1.20–1.59]	<0.001
Diabetes	0.77 [0.60–0.99]	0.040
Low SBP (eg <140 *vs* 160-179 mm Hg	1.39 [1.11–1.75]	<0.001
Country of birth (outside Nordic countries)	2.11 [1.79–2.48]	<0.001
Low income (eg Q1 *vs* Q4)	1.24 [0.96–1.32]	<0.001

No association to CV comorbidity, number of other drugs, DBP, educational level

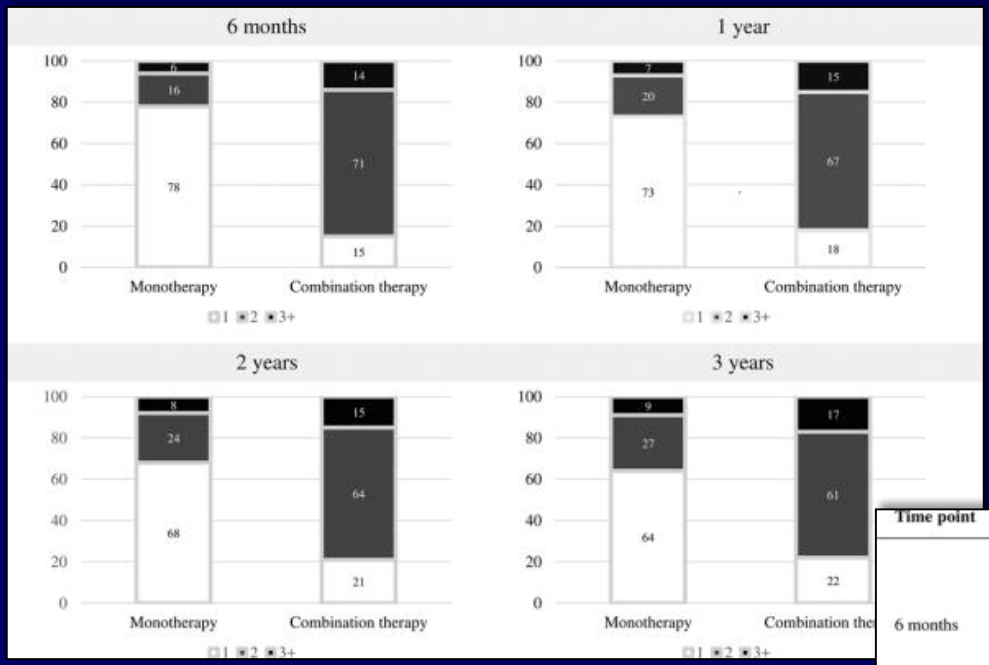
Switching estimated to 19-25%

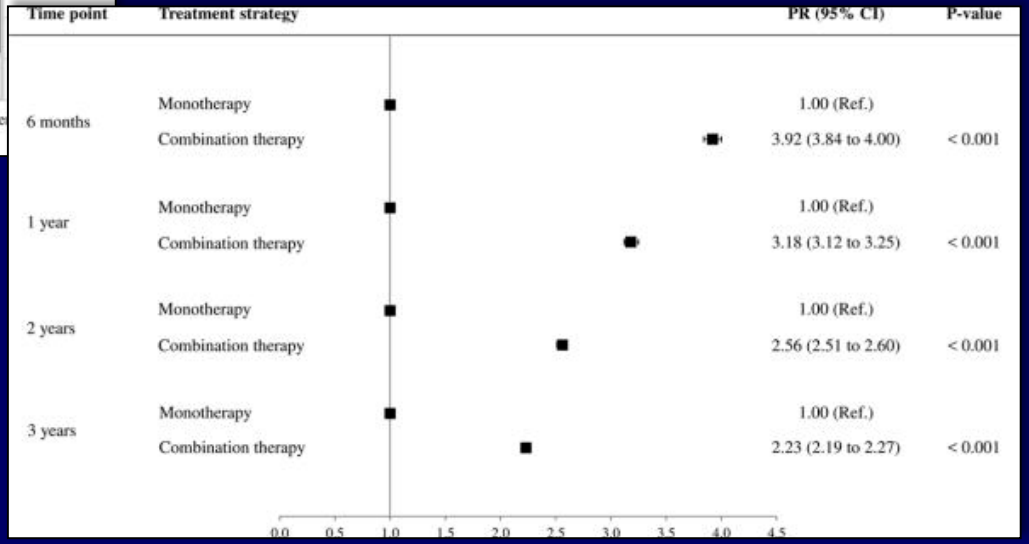
5225 hypertensive patients with newly started therapy, mean age 61 ys, mean BP 166/95 mm Hg. First prescription never purchased by 1%, 14% discontinued after first prescription.



Qvarnström M et al. *Eur J Clin Pharmacol* 2013;369:1955-64. Ibid *Medicine* 2016;95:e4908

Initial Antihypertensive Treatment Strategies and Therapeutic Inertia

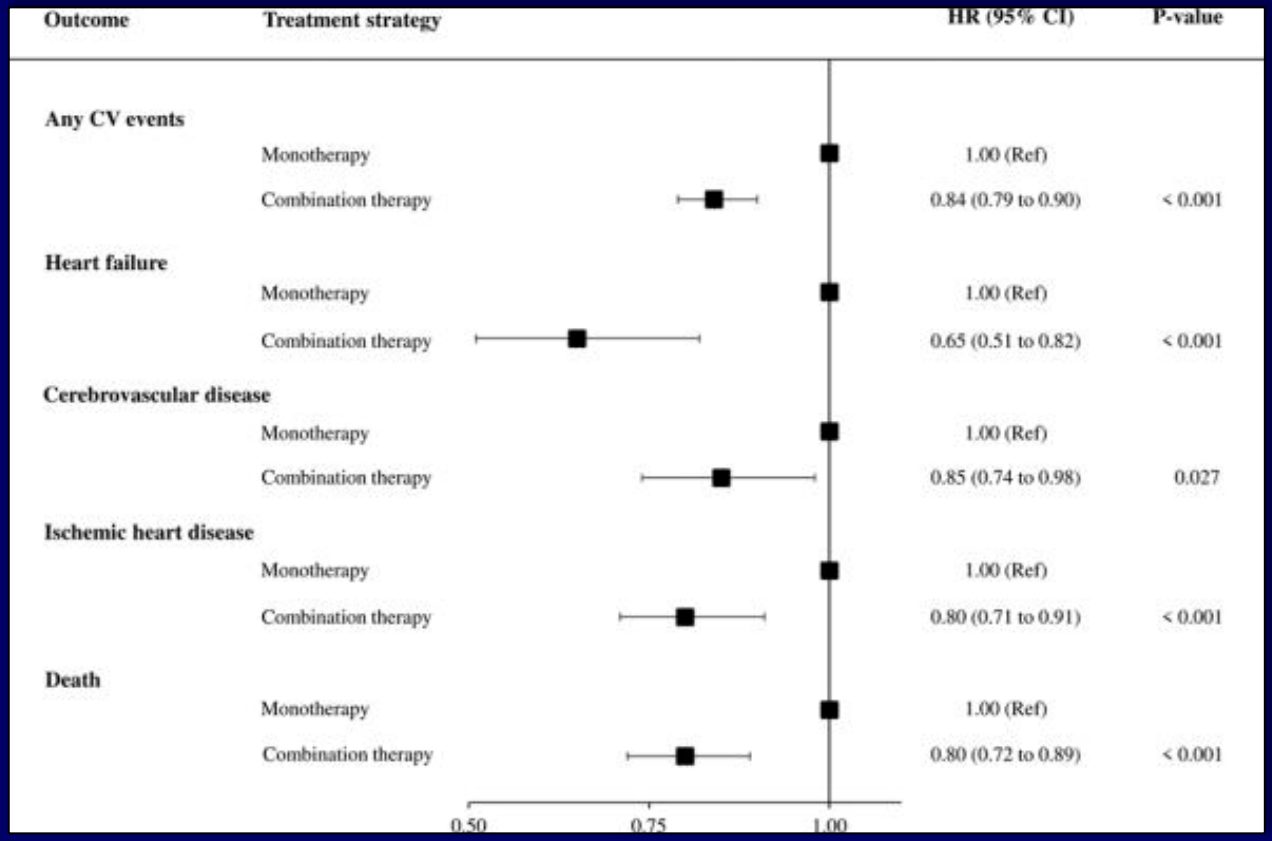




Data from health care utilization data-bases in Lombardy (Italy), where 100.962 patients (age 40-65 years) started anti-hypertensive treatment on 1 drug and 24.653 on ≥2 drugs (fixed dose or free combinations).

Rea F et al. *Hypertension* 2018;72:846-53

Initial Antihypertensive Treatment Strategies and Therapeutic Inertia

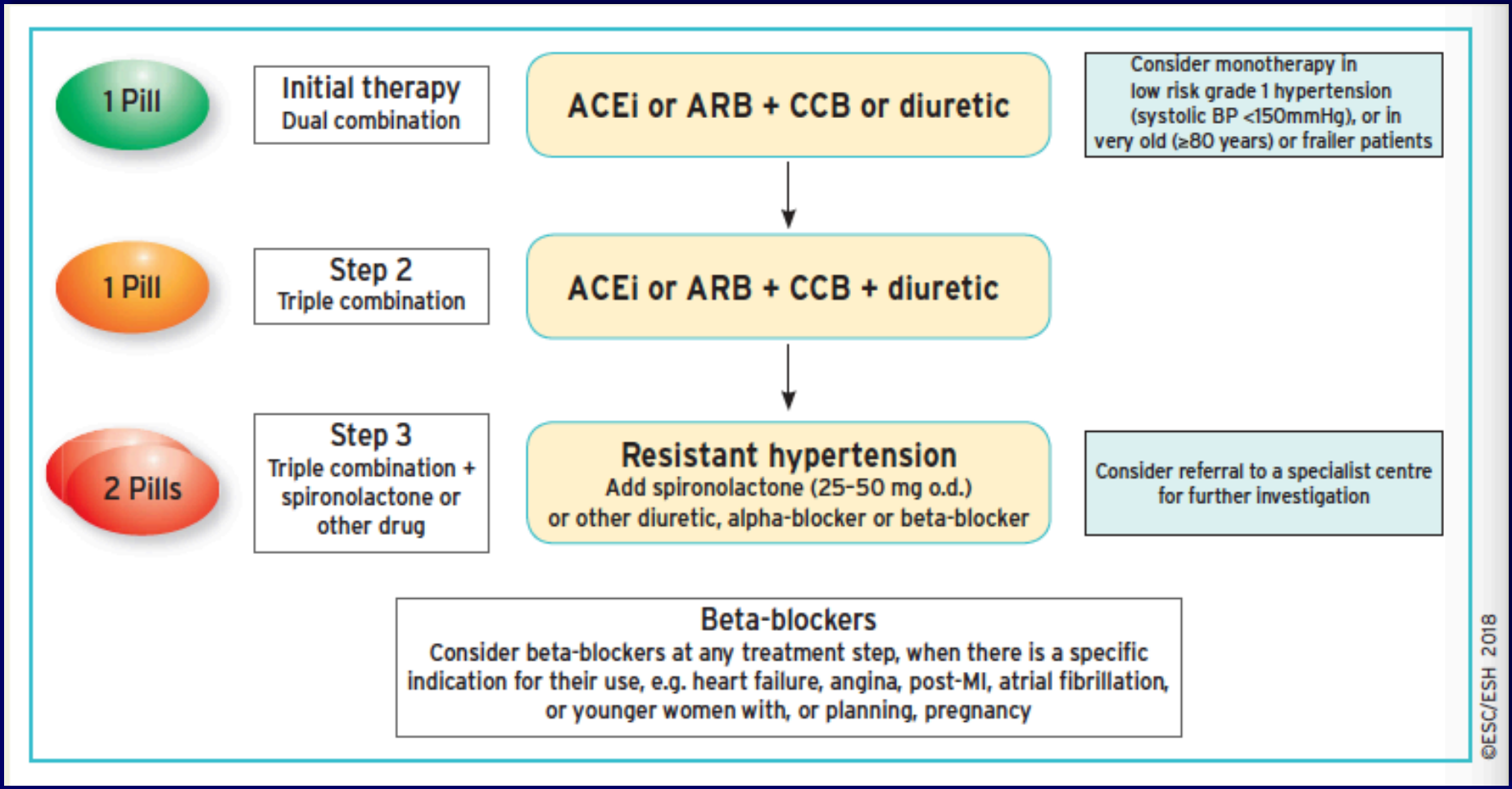


Data from health care utilization data-bases in Lombardy (Italy), where 100.962 patients (age 40-65 years) started tretament on 1 drug and 24.653 on ≥2 drugs. HR and 95% CI estimating the risk of CV outcomes and death during 3 years of follow-up. Patients were initially matched by high-dimensional propensity score.

Rea F et al. *Hypertension* 2018;72:846-53

T Kahan 2018

Core Drug Treatment Strategy in Hypertension
ESC/ESH 2018 Guidelines



Williams B et al. *Eur Heart J* 2018;39:3021-3104; *J Hypertens* 2018;36:1953-2041

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Läkemedel vid hypertoni

ACE-hämmare
- Ramipril 10 mg x 1
- Enalapril 20-40 mg x 1

Angiotensin-receptorblockerare
- Candesartan 32 mg x 1
- Losartan 100-150 mg x 1

Tiazider
- Hydroklortiazid 12,5-50 mg x 1
- Salures 2,5-5 mg x 1
- (Furosemid om eGFR < 30 ml/min/m^2)

Kalciumantagoninster
- Amlodipin 10 mg x1

Beta-receptorblockerare
- Metoprolol 50-100 mg x 1
- Bisoprolol 5-10 mg x 1

Mineralkortikoid-receptorantagonister
- Spironolakton 25-50 mg x 1

Alfa-receptorblockerare
- Doxazosin 8 mg x 1

✓ Njurfunktion (kreatinin, K)
✓ Hjärtfunktion (rytm, LVEF)
✓ Astma

✓ Individualisera preparatval
✓ Kloka kombinationer
✓ Ta hänsyn till samsjuklighet

T Kahan 2018

Therapeutic Strategies in Hypertensive Patients with Coronary Artery Disease

Recommendations	Class	Level
In patients with CAD receiving BP-lowering drugs, it is recommended:		
• To target SBP to ≤ 130 mmHg if tolerated, but not <120 mmHg.	I	A
• In older patients (aged ≥65 years), to target to an SBP range of 130–140 mmHg.	I	A
• To target DBP to <80 mmHg, but not <70 mmHg.	I	C
In hypertensive patients with a history of myocardial infarction, beta-blockers and RAS blockers are recommended as part of treatment.	I	A
In patients with symptomatic angina, beta-blockers and/or CCBs are recommended.	I	A

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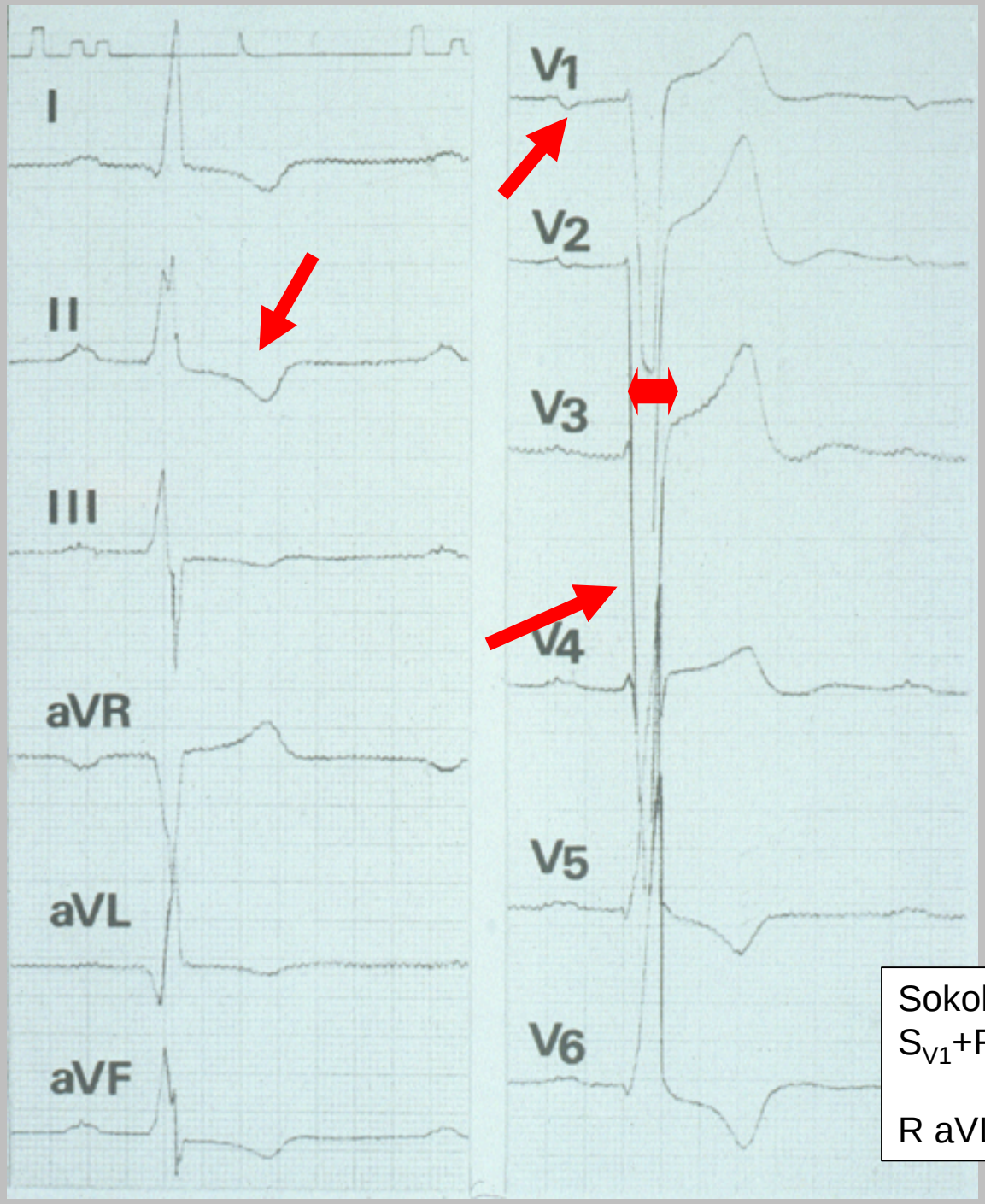
Williams B et al. *Eur Heart J* 2018;39:3021-3104; *J Hypertens* 2018;36:1953-2041

Therapeutic Strategies in Hypertensive Patients with Heart Failure or LV Hypertrophy

ESC/ESH 2018 Guidelines

	Recommendations	Class	Level
Heart failure	In hypertensive patients with heart failure (with reduced or preserved ejection fraction), BP-lowering treatment should be considered if BP is ≥140/90 mmHg.	IIa	B
HFrEF	In patients with HFrEF, it is recommended that BP-lowering treatment comprises an ACE inhibitor or ARB, and a beta-blocker and diuretic and/or MRA if required.	I	A
HFrEF	Dihydropyridine CCBs may be added if BP control is not achieved.	IIb	C
HFpEF	In patients with HFpEF, BP treatment threshold and target values should be the same as for HFrEF.	IIa	B
HFpEF	Because no specific drug has proven its superiority, all major agents can be used.	I	C
LV hypertrophy	In all patients with LVH: • It is recommended to treat with an RAS blocker in combination with a CCB or diuretic.	I	A
LV hypertrophy	• SBP should be lowered to a range of 120–130 mmHg.	IIa	B

Williams B et al. *Eur Heart J* 2018;39:3021-3104; *J Hypertens* 2018;36:1953-2041

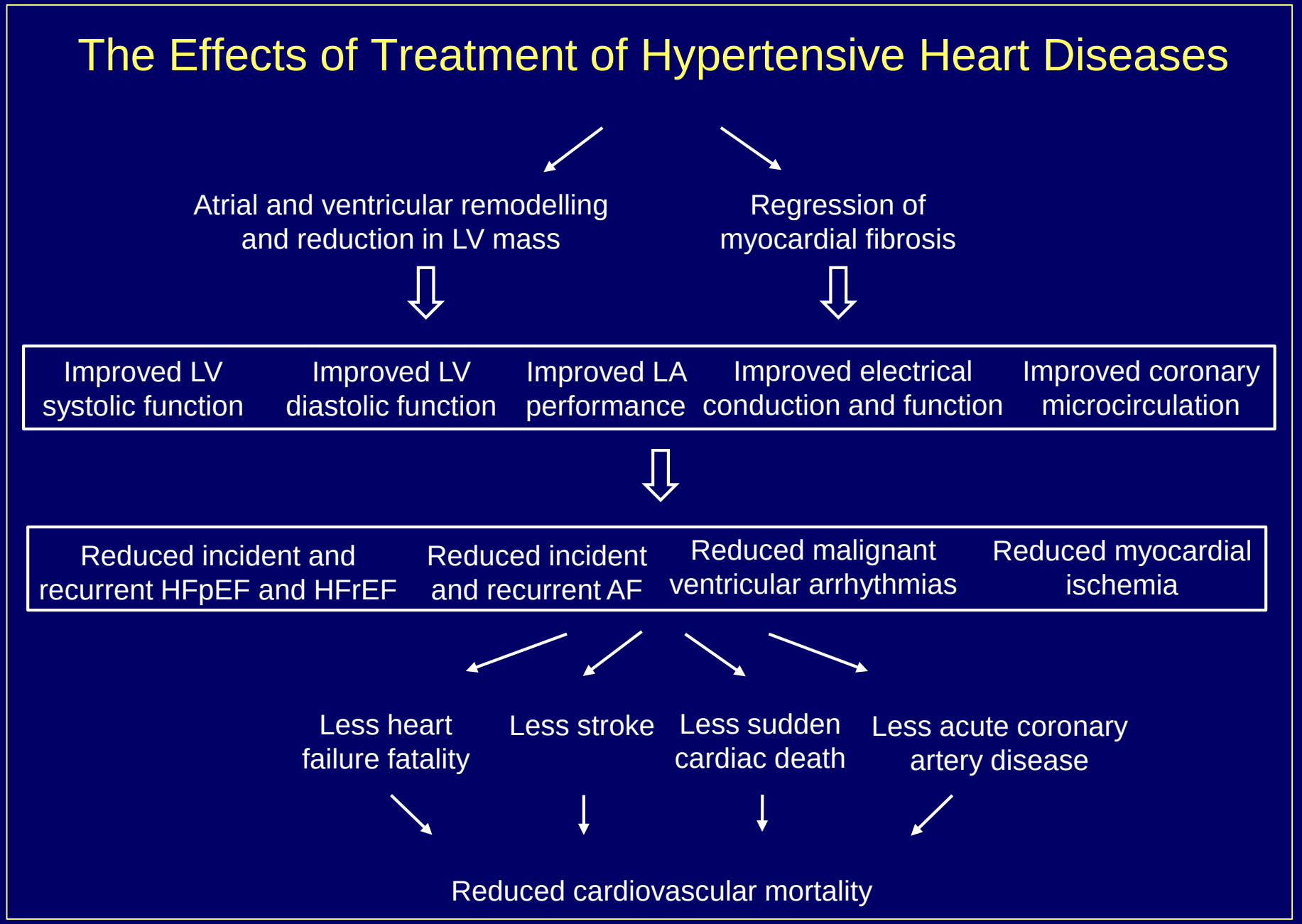


Sokolow-Lyon:
$S_{V1}+R_{V5}$ el R_{V6} >35 mm

R aVL $\geq$ 11 mm

T Kahan 2020

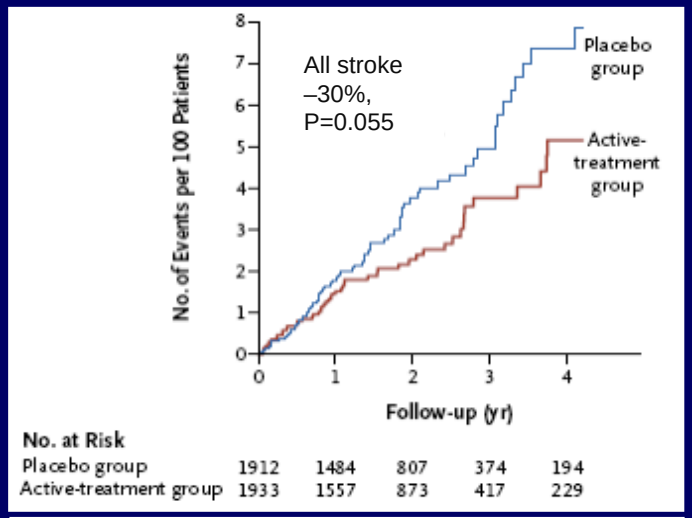
The Effects of Treatment of Hypertensive Heart Diseases

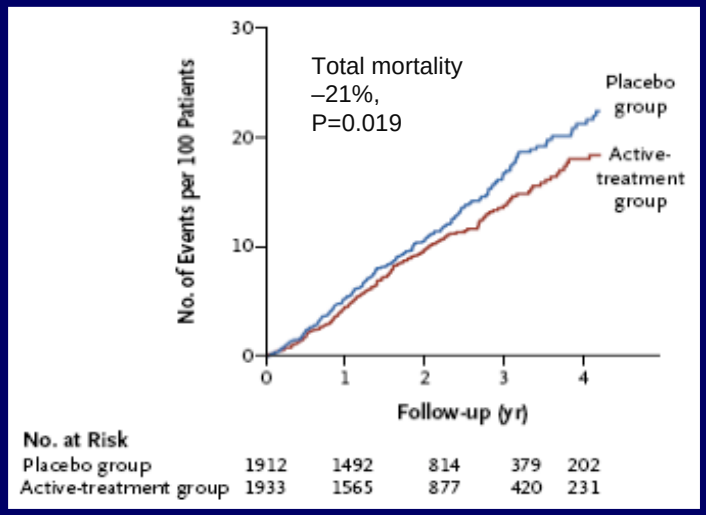


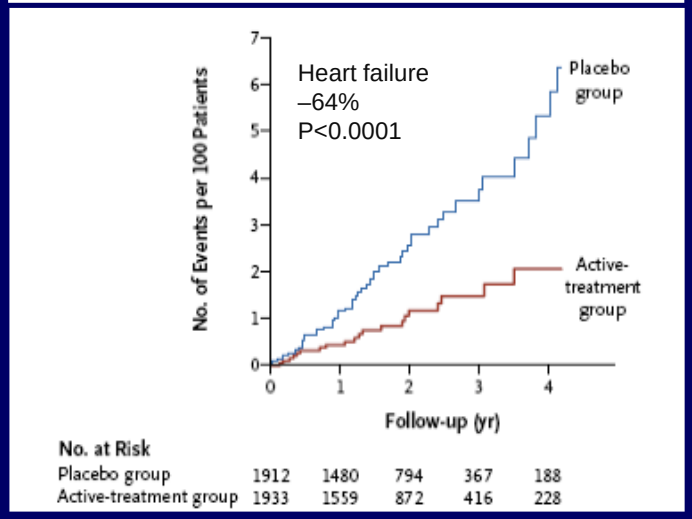
Jekell A, Nilsson PN, Kahan T. *Curr Pharmacol Des* 2018;24(37):4391-4396

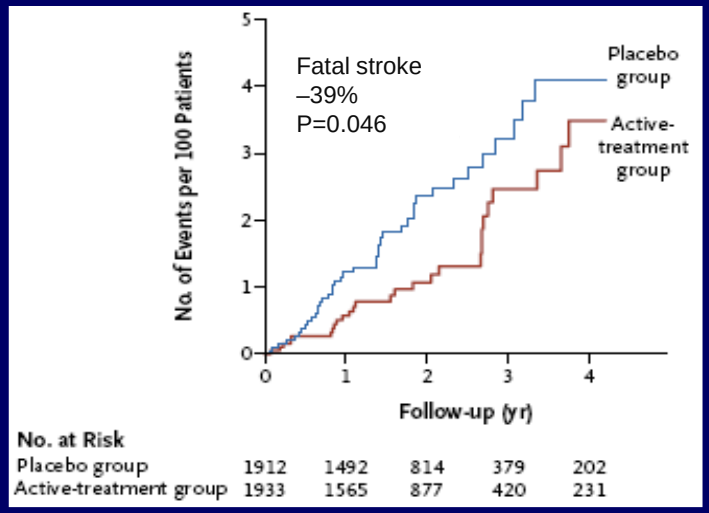
T Kahan 2018

Antihypertensive Treatment in Very Old Patients: HYVET









HYVET: n=3845, 60% women, 84 ys, 173/91 mm Hg, 12% with CV disease.
Target 150/80 mm Hg, achieved 144/78 mm Hg. Mean follow up 2.1 years.

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

Antihypertensive Treatment in Patients over 65 Years of Age

Meta-analysis of 18 randomized controlled studies in 114 584 hypertensive patients 65 years or older. Mean age 71.0 years and mean follow up 3.4 years.

Study	Year	Mean follow-up (years)	Medications used	N (treatment/ control)	Age	Control *Difference in SBP/ DBP from baseline (mm Hg)*	Treatment *Difference in SBP/ DBP from baseline (mm Hg)*
Coope J	1986	4.4	Atenolol and bendrofluazide	419/465	68.8	–14/–10	–32/–22
EWHPE	1985	4.6	Hydrochlorothiazide plus triamterene	416/424	72	–15/–11	–35/–16
HYVET	2008	2.08	Indapamide 1.5 mg ±perindopril	1933/1912	83.6	–14.5/–6.8	–29.5/–12.9
MRC (b-blocker)	1992	5.8	Atenolol 50 mg	1101/2212	70.3	–19.5/–6	–32.5/–15
MRC (diuretic)	1992	5.8	Hydrochlorothiazide 25–50 mg plus amiloride 2.5–5 mg daily	1081/2213	70.3	–19.5/–6	–34/–14.5
SHEP	1991	4.5	Chlorthalidone 12.5–25 mg and atenolol 25–50 mg	2365/2379	71.6	–15/–9	–27/–9
STONE	1996	2.5	Nifedipine	801/774	66.3	–12.31/–7.59	–21.65/–13.14
STOP-Hypertension	1991	2.1	Atenolol 50 mg or hydrochlorothiazide 25 mg plus amiloride 2–5 mg or metoprolol 100 mg or pindolol 5 mg	815/812	75.7	–2/–7	–29/–17
Syst-Eur	1997	2	Enalapril 5–20 mg daily and hydrochlorothiazide 12.5–25 mg	2398/2297	70.3	–13/–2	–23/–7
Syst-China	2000	2	Enalapril 5–20 mg daily and hydrochlorothiazide 12.5–25 mg daily	1253/1141	66.5	–11/–2	–20/–5
ACCOMPLISH	2008	3	Benazepril plus amlodipine or benazepril plus hydrochlorothiazide	5744/5762	68.4	–12.9/–5.6	–13.7/–6.8
ALLHAT (A vs C)	2002	4.9	Amlodipine 2.5–10 mg or chlorthalidone 12.5–25 mg	8784/5204	66.9	–11.5/–9.3	–12.3/–8.6
ALLHAT (L vs c)	2002	4.9	Lisinopril 10–40 mg or chlorthalidone 12.5–25 mg	8784/5185	66.9	–10.5/–8.7	–12.3/–8.6
ANBP-2	2003	4.1	ACE inhibitors or thiazide diuretics (enalapril or hydroclorthiazide recommended)	3044/3039	71.9	–26/–12	–26/–12
JATOS	2008	2	Strict or mild treatment (background medication was efonidipine)	2212/2206	73.6	–25.9/–11	–35.7/–14.3
INVEST	2003	2	Verapamil versus atenolol	11 267/11 309	66.1	–18.7/–10	–19/–10.2
LIFE	2002	4.7	Losartan or atenolol	586/609	67.4	–29/–16.8	–30.3/–16.6
STOP-2	1999	4	Atenolol 50 mg, metoprolol 100 mg, pindolol 5 mg or hydrochlorothiazide 25 mg plus amiloride 2.5 mg daily or enalapril 10 mg or lisinopril 10 mg, or felodipine 2.5 mg or isradipine 2–5 mg daily	4401/2213	76.0	–36/–17	–35/–17
VALISH	2010	3.07	Strict versus moderate control	1545/1534	76.1	–27.6/–4.7	–32.9/–6.9
VALUE	2004	4.2	Valsartan or amlodipine	7596/7649	67.3	–15.2/–8.2	–17.3/–9.9

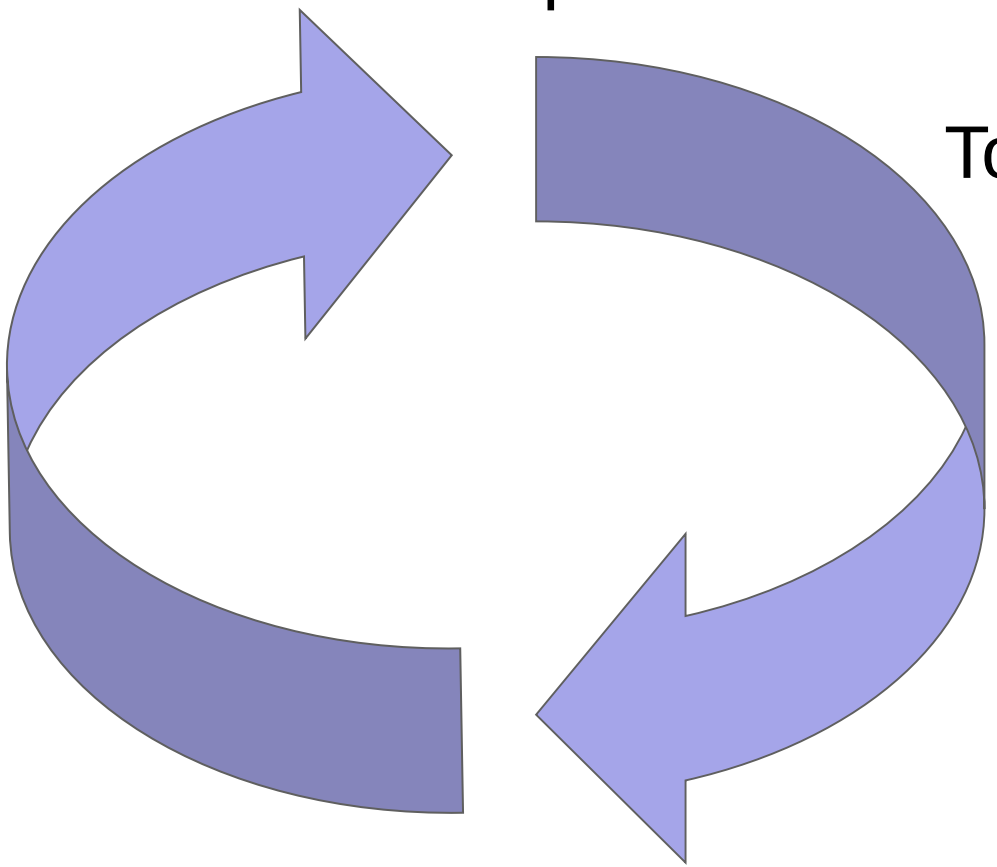
Briasoulis A et al. *Heart* 2014;100: 317–323

Kahan 2019

Hypertoni, uppföljning

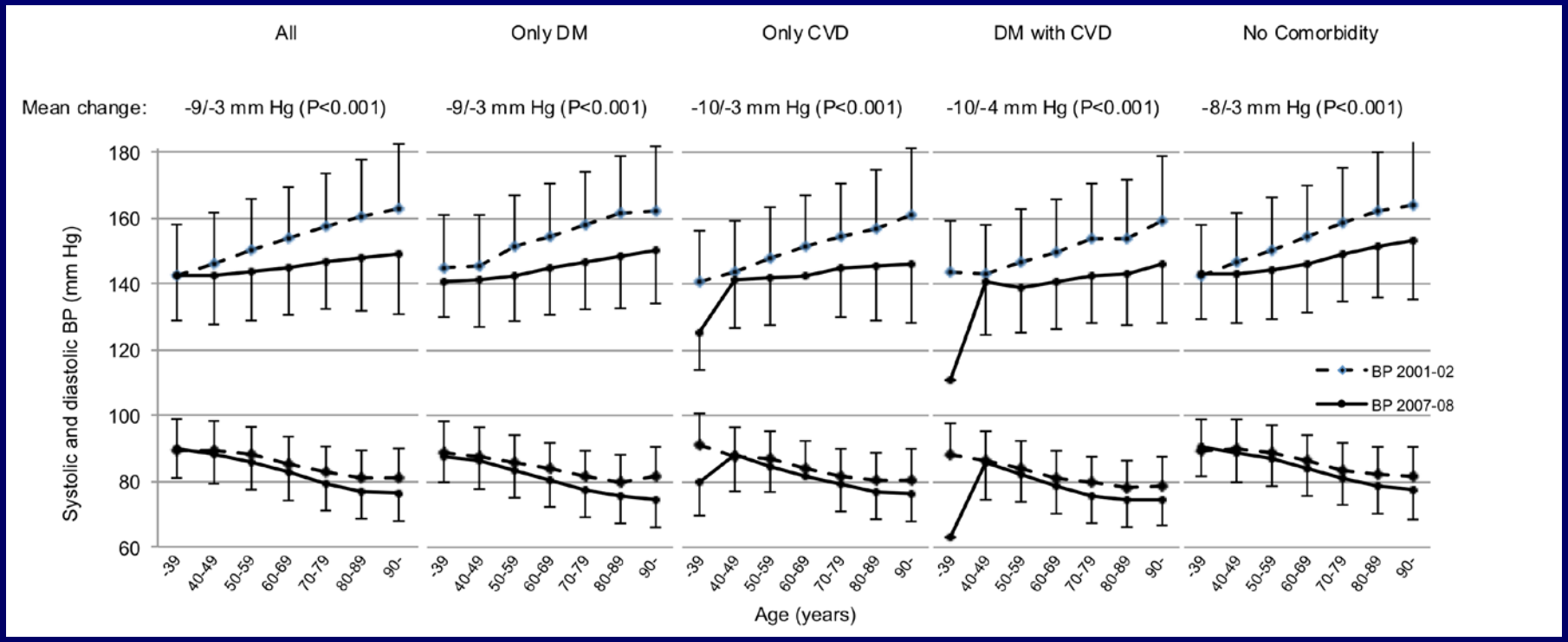
- Alla klasser sänker vid normaldosering blodtrycket med ca 10/5 mm Hg (placebojusterat)
- Uppföljning av påbörjad läkemedelsbehandling görs (i allmänhet av läkare) efter ett par månader
- Dessförinnan bör blodtryckskontroll, dostitrering, samt uppföljning av livsstilsåtgärder och biverkningar göras efter 2-4 veckor
- När blodtryck och riskfaktorer är under god kontroll rekommenderas 1-2 kontroller per år; aktiv uppföljning!
- Följ upp mikroalbuminuri (veckor-månader) och vänsterkammarhypertrofi (år; EKG ofta lämpligt) som ger viktig prognostisk information

Vårdprocessen



T Kahan 2008

Time Trends in BP Control by Age and Comorbidity



SPCCD data for 31523 hypertensive patients 2001-02 and 56459 in 2007-08 (overlap 25438) 30 ys or older, 57% women, mean age 68±12 years. Error bars are 95% CI.

Mean BP 2001-02 and 2007-08 were ***152/82 and 143/79 mm Hg (∆-9/-3 mm Hg) in women****; and* ***150/84 and 142/81 mm Hg (∆-8/-3 mm Hg) men***.

Mean BP in 19 9574 patients assessed ***both*** *2001-02 and 2007-08 were* ***152/83 and 143/79 mm Hg (∆-9/-4 mm Hg) in women****; and* ***150/84 and 141/80 mm Hg (∆-9/-4 mm Hg) men***.

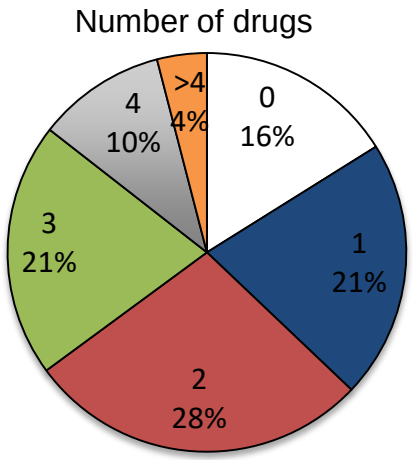
Holmquist C et al. *J Hypertens* 2017;35:2102-8

T Kahan 2017

Prescribed/Dispensed Antihypertensive Drugs 2002–14

The 5 most common drugs, %	Women	Men
Beta blockers	39	38
CCB	29	34
ACE inhibitors	27	36
ARB	30	29
Diuretics	30	21
The 5 most common combinations, %		
ARB + Diuretics	16	15
Beta blockers + diuretics	16	13
Beta blockers + CCB	13	16
ACE inhibitors + diuretics	12	15
ACE inhibitors + beta blockers	11	16
ACE inhibitor + CCB	8	14

P<0.01 for all differences between women and men.



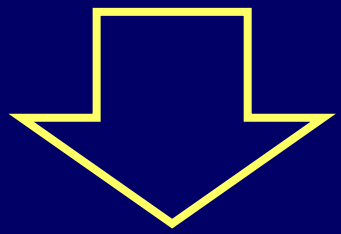
Contemporary Swedish cohort studies reporting on ≥10 000 hypertensive patients

	Current study	HyperQ[18]	SPCCD[26]	QregPV[41]
Year of survey	2013	2002–2005	2007–2008	2014
Patients, No.	292 623	6537	62 407	223 663
Men/women, %	47/53	48/52	44/56	48/53
Age (range), y	68 ± 13 (20–109)	66 ± 12–	69 ± 13 (37–106)	69 ± 12 (15–113)
Systolic/diastolic blood pressure, mm Hg	–	147 ± 17/82 ± 9	143 ± 18/80 ± 10	136 ± 16/79 ± 13
Atrial fibrillation/flutter, %	11	–	8	–
Ischemic heart disease, %	14	–	15	15
Heart failure, %	8	–	8	–
Diabetes mellitus, %	21	22	24	22
Cerebrovascular disease, %	6	–	8	–
No cardiovascular disease, %	59	–	56	–
Data on medicines used	Dispensed	Prescribed	Prescribed	Dispensed
ACEIs, women, %	27	18	32	25
ACEIs, men, %	36	27	44	35
ARBs, women, %	30	34	23	30
ARBs, men, %	29	35	23	30
ACEIs and/or ARBs, women, %	57	51	55	54
ACEIs and/or ARBs, men, %	65	62	67	64
CCBs, women, %	29	26	30	32
CCBs, men, %	34	34	35	31
β-Blockers, women, %	39	54	51	41
β-Blockers, men, %	38	51	49	39
Diuretics, women, %	38	64	48	37
Diuretics, men, %	32	48	37	32

292 623 patients, mean age 68±13 (range 20-109) years, 53% women in Greater Stockholm (2.1 million people) who were alive at the end of 2013.

Wallentin F et al. *J Clin Hypertens* 2018;20:106–14

Assessment of a Patient Referred for Refractory (Resistant) Hypertension



Consider Reasons for Hypertension Remaining Uncontrolled

1. Care giver is not acting (*care giver inertia*)
2. Drug adherence and treatment persistence
3. White coat effect
4. Secondary hypertension
5. True resistant hypertension

Why does Blood Pressure Remain Elevated?

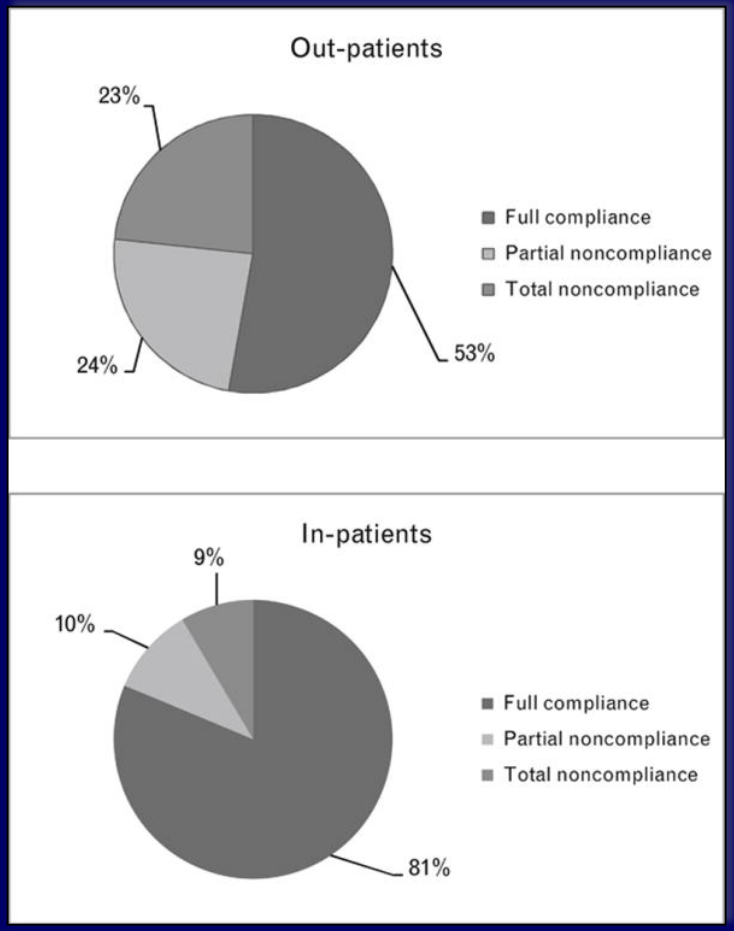
1. Care giver is not acting (*care giver inertia*)

- ✓ Different focus
- ✓ Lack of knowledge
- ✓ Poor evidence
- ✓ Side effects
- ✓ Old patient
- ✓ Serious co-morbidity
- ✓ Care giver organisation (e.g. treatment algorithms, continuity, follow up, educational level, incentives)
- ✓ …

Further Reasons Uncontrolled Blood Pressure

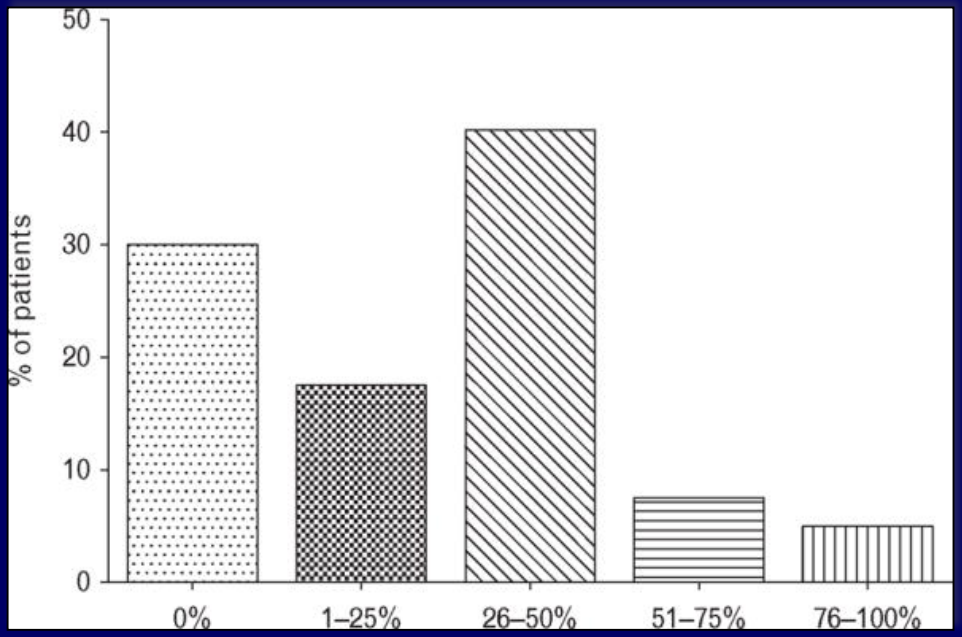
1. Care giver is not acting (*care giver inertia*)
2. **Drug adherence, treatment persistence**

Assessment of Non-Compliance in Resistant Hypertension Using Toxicological Analysis



Unanticipated blood sampling for serum LC/MS in 176 hospitalized patients and 163 out-patients referred for resistant hypertension.

Strauch B et al. *J Hypertens* 2013;31:2455-61

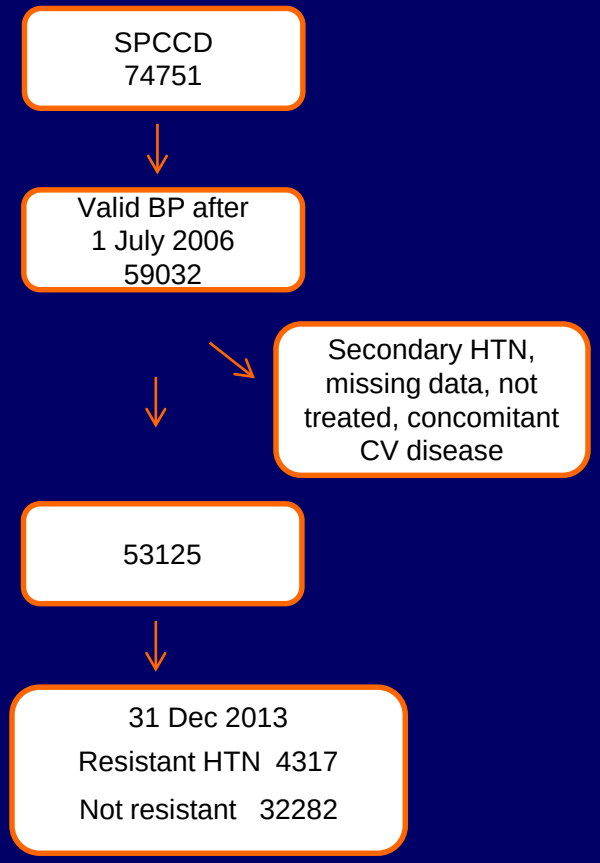


375 patients referred for apparent resistant hypertension; 76 remained uncontrolled on ≥4 drugs after drug optimization and exclusion of secondary causes including white coat effect. Percentage of drugs taken by 76 patients; according to urine LC/MS.

Jung et al. *J Hypertens* 2013;31:766-74

T Kahan 2014

Prognosis in Apparent Resistent Hypertension



Death/hospitalization	*HR [95% CI]*	*%*
CV Mortality	1.20 [1.03–1.40]	3.2
All casue mortality	1.11 [1.03–1.23]	10.5
Heart failure	1.34 [1.17–1.54]	4.0
IHD	1.16 [1.04–1.30]	6.7
Stroke	1.03 [0.90–1.19]	4.5
TIA	1.12 [0.86–1.46]	1.3

Any definition of resistant HTN (12%). BP 152/80 vs 141/80 mm Hg. Mean follow up 4.3 ys. Adjusted for age, sex, smoking, BMI, AF, BP, diabetes, and socioeconomic factors. Similar results when BP was excluded form the model.

Holmqvist L et al. *J Hypertens* 2018;36:402-9

T Kahan 2017

Further Reasons for Uncontrolled Blood Pressure

1. Care giver is not acting (*care giver inertia*)
2. Drug adherence, treatment persistence
3. **White coat effect**

Åke, 1935 (6)

SVAR FYSIOLOGI

Sida 1 (2)

Slutsvar

FRÅN

Danderyds Sjukhus AB
Hjärtkliniken

182 88 Stockholm
Tel 08-123 564 60

B: 11010-231-M05
S: 11010-231-M05
F: 11010-231-M05
R:
L: DS15-2732

TILL

Danderyds Sjukhus AB
Hjärt-kärlcentrum Nord
Svärdvägen 11 pl 4
182 33 Danderyd
Tel: 08-123 56460 Fax: 08-123 577 88

Patienten bör undersökas på:
Patienten kallas från:

Remissdatum:

Remittent: Thomas Kahan

Remiss ej gjord i Take Care.

SVAR

Undersökningsdatum: 2015-02-03
Undersökning: 24 h blodtrycksm på hjärtmott

Utlåtande:

9126 24 H BLODTRYCKSM PÅ HJÄRTMOTT 2015-02-03 (NR: 15-2732)
24-timmars ambulatorisk blodtrycksmätning (24 h ABP)

Spacelabs 90207 utrustning.

Ambulatorisk blodtrycksmätning 3 ggr/timme under 24,0 timmar med början 15-02-03 kl 11:16. Registrering är av god teknisk kvalitet.

Med auskultatorisk metodik uppmät 240/130 mmHg vid uppkoppling.

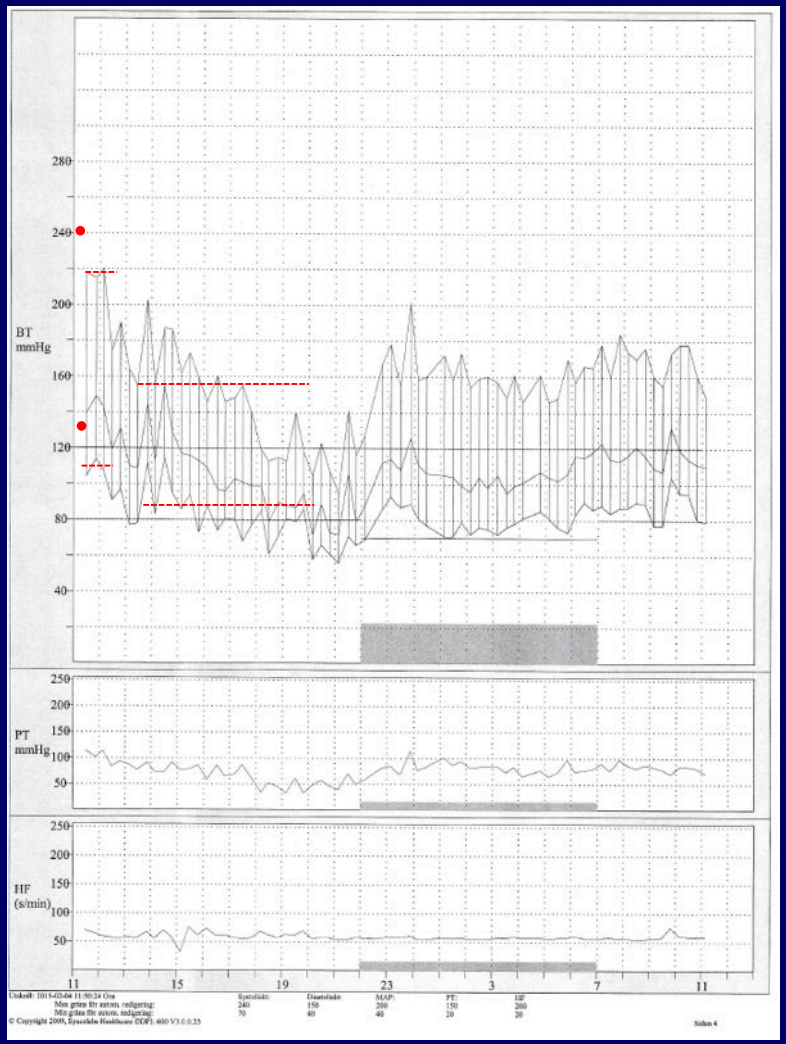
Medelvärdesbildat blodtryck för hela registreringsperioden är 158/82 mmHg. Motsvarande värde för perioden kl 07.00 - 22.00 är 157/84 mmHg. För perioden kl 22.00 - 07.00 är det medelvärdesbildade blodtrycket 160/79 mmHg. Variabiliteten (SD) för SBP dagtid är 31 mmHg, natt 14 mmHg.

Den initiala timmen kraftigt förhöjda blodtryck omkring 220/110, som sedan successivt sjunker för att mellan kl 18 och kl 22 ligga på omkring 120/70. Därefter stiger blodtrycket åter i samband med att patienten lägger sig kl 22.30 och förblir därefter stabilt på ungefär 160/85. Stiger upp kl 09. Systoliska blodtryck är måttligt förhöjda, medan diastoliska trycken ligger strax under övre referensområdesgränsen. Blodtrycket påverkas inte av nattvila och man ser här en kraftigt förhöjd systolisk och lätt förhöjd diastolisk medelblodtryck. Variabiliteten är sannolikt ökad. Hjärtfrekvens så som vid pågående betablockad. Inga subjektiva besvär.

Bil: Medelvärdesbildade blodtryck för var timme under registreringsperioden.
Referensvärden (mmHg):<135/85 dag, <120/70 natt, <130/80 24 h; variabilitet <16 dagtid och <12 nattetid.

SIGNERAT 2015-02-06 Specläkare kardiologi Thomas Kahan /1PHM

----------slut----------



Further Reasons for Uncontrolled Blood Pressure

1. Care giver is not acting (*care giver inertia*)
2. Drug adherence, treatment persistence
3. White coat effect
4. **Secondary hypertension**

Common Causes of Secondary Hypertension

Cause	Prevalence in hypertensive patients	Suggestive symptoms and signs	Screening Investigations
Obstructive sleep apnoea	5–10%	Snoring; obesity (can be present in non obese); morning headache; daytime somnolence	Epworth score and ambulatory polygraphy
Renal parenchymal disease	2–10%	Mostly asymptomatic; diabetes; haematuria, proteinuria, nocturia; anaemia, renal mass in adult polycystic CKD	Plasma creatinine and electrolytes, eGFR; urine dipstick for blood and protein, urinary albumin:creatinine ratio; renal ultrasound
Renovascular disease			
Atherosclerotic renovascular disease	1–10%	Older; widespread atherosclerosis (especially PAD); diabetes; smoking; recurrent flash pulmonary oedema; abdominal bruit	Duplex renal artery Doppler or CT angiography or MR angiography
Fibromuscular dysplasia		Younger; more common in women; abdominal bruit	
Endocrine causes			
Primary Aldosteronism	5–15%	Mostly asymptomatic; muscle weakness (rare)	Plasma aldosterone and renin, and aldosterone: renin ratio; hypokalaemia (in a minority): note hypokalaemia can depress aldosterone levels
Phaeochromocytoma	<1%	Episodic symptoms (the 5 'Ps'): paroxysmal hypertension, pounding headache, perspiration, palpitations, and pallor; labile BP; BP surges precipitated by drugs (e.g. beta-blockers, metoclopramide, sympathomimetics, opioids, and tricyclic antidepressants)	Plasma or 24 h urinary fractionated metanephrines
Cushing's syndrome	<1%	Moon face, central obesity, skin atrophy, striae and bruising; diabetes; chronic steroid use	24 h urinary-free cortisol
Thyroid disease (hyperthyroidism or hypothyroidism)	1–2%	Signs and symptoms of hyperthyroidism or hypothyroidism	Thyroid function tests
Hyperparathyroidism	<1%	Hypercalcaemia, hypophosphataemia	Parathyroid hormone, Ca^{2+}
Other causes			
Coarctation of the aorta	<1%	Usually detected in children or adolescence; different BP (≥20/10 mmHg) between upper–lower extremities and/or between right–left arm and delayed radial-femoral femoral pulsation; low ABI interscapular ejection murmur; rib notching on chest X-ray	Echocardiogram

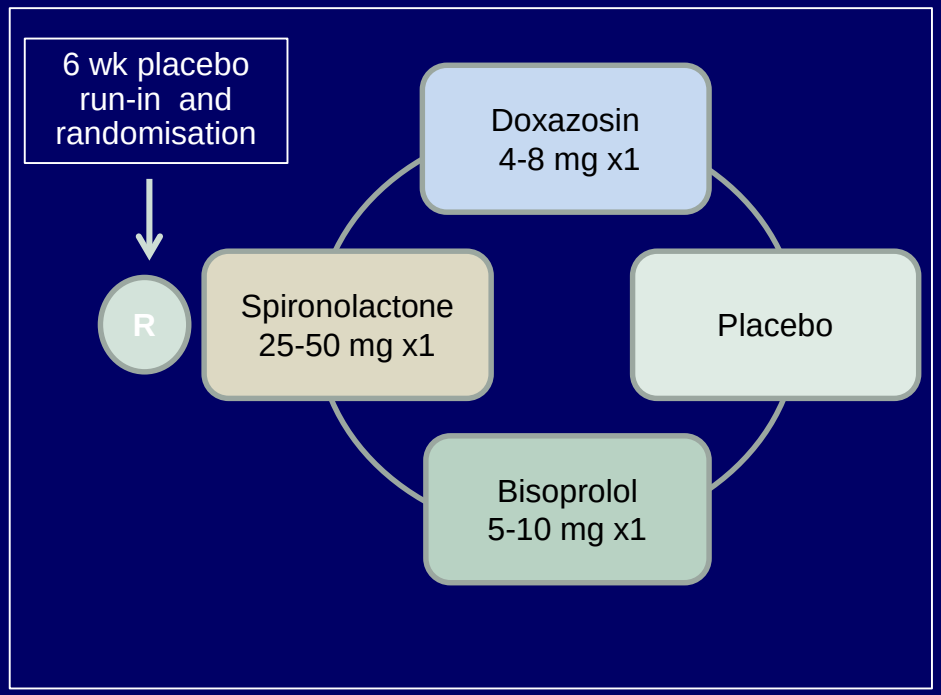
Williams B et al. *Eur Heart J* 2018;39:3021-3104; *J Hypertens* 2018; ;36:1953-2041

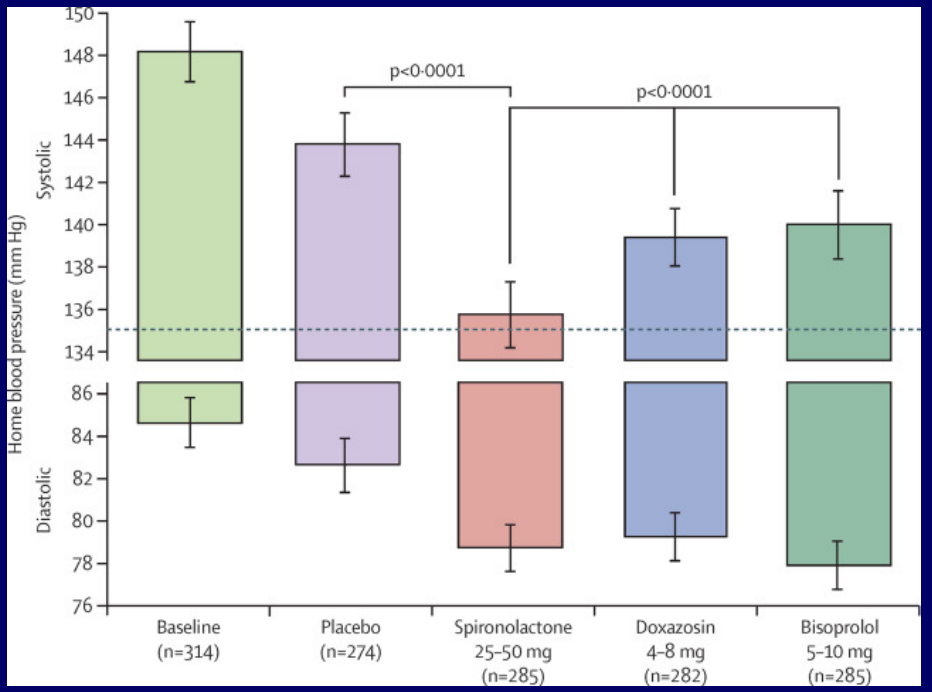
T Kahan 2018

Further Reasons for Uncontrolled Blood Pressure

1. Care giver is not acting (*care giver inertia*)
2. Drug adherence, treatment persistence
3. White coat effect
4. Secondary hypertension
5. **True resistant hypertension**

Treatment in Resistent Hypertension : PATHWAY 2





314 Patients with resistent hypertension (157/90 mm Hg), treated with ACEI/ARB, CCB, and thiazide; 12 wk treatment periods

Spironolactone *vs* placebo
8·70 (−9·72 to −7·69); p<0·0001

Spironolactone *vs* mean bisoprolol and doxazosin
−4·26 (−5·13 to −3·38); p<0·0001

Spironolactone *vs* doxazosin
−4·03 (−5·04 to −3·02); p<0·0001

Spironolactone *vs* bisoprolol
−4·48 (−5·50 to −3·46); p<0·0001

Williams B et al. *Lancet* 2015;386:2059-68

T Kahan 2016

Sammanfattning, aktuella riktlinjer vid hypertoni

- ✓ Betoning på riskevaluering
- ✓ Större vikt vid *out-of-office* mätningar
- ✓ Nya behandlingsmål (med intervall)
- ✓ Lägre målvärden och mer aktiv behandling hos äldre
- ✓ *Adherence* till behandling är fortsatt stort problem
- ✓ Proaktiv behandlingsstart är viktig, ofta behövs 2 klasser; och fasta kombinationer är fördel
- ✓ Evidensbaserad behandling vid sann terapiresistent hypertoni rekommenderas
- ✓ Behandla risken, inte bara blodtrycket