

Overview of Hypertension Management

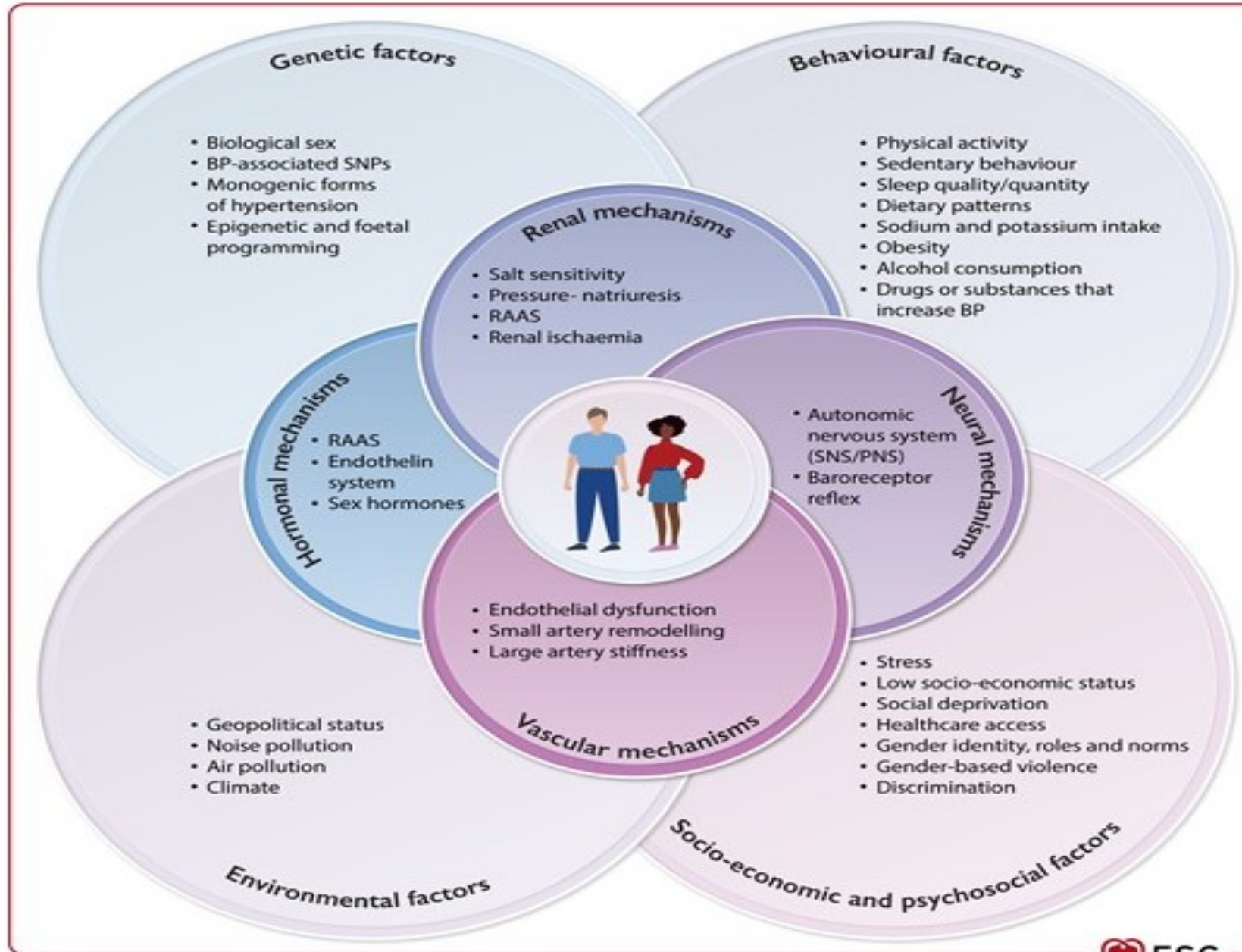
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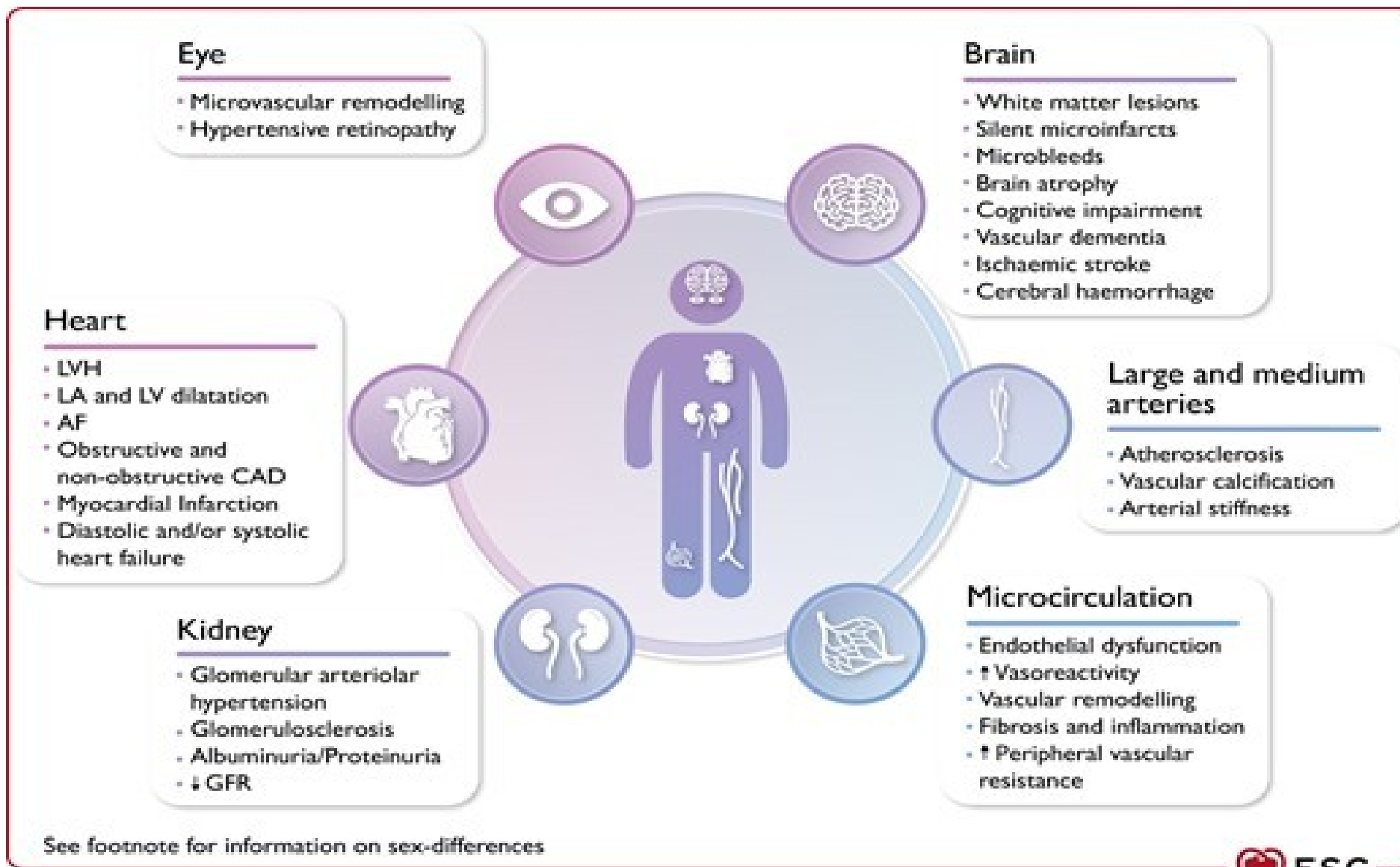
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Epidemiology

- Hypertension is the leading global risk factor for cardiovascular mortality and disability in adult women and men.
- Hypertension becomes progressively more common with advancing age, with a prevalence of >60% in people aged >60 years.
- It is estimated that the number of people with hypertension will reach close to 1.5 billion in 2025.
- It is the most important modifiable risk factor for all-cause and CVD morbidity and mortality globally.
- Most patients with hypertension have essential or primary hypertension (90%-95%), while an estimated (5%-10%) have secondary hypertension

Pathophysiology of Hypertension





Hypertension-mediated organ damage and cardiovascular diseases

Office blood pressure measurement

1



Measure after 5 min seated comfortably in a quiet environment

2



Use a validated device with an appropriate cuff size based on arm circumference

3



Place the BP cuff at the level of the heart with the patient's back and arm supported

8



Assess for orthostatic hypotension at 1st visit and thereafter by symptoms



www.validatebp.org

4



Measure BP three times (1–2 min apart) and average the last 2 readings

7



Record heart rate and exclude arrhythmia by pulse palpation

6



Measure BP in both arms at the 1st visit to detect between arm differences

5



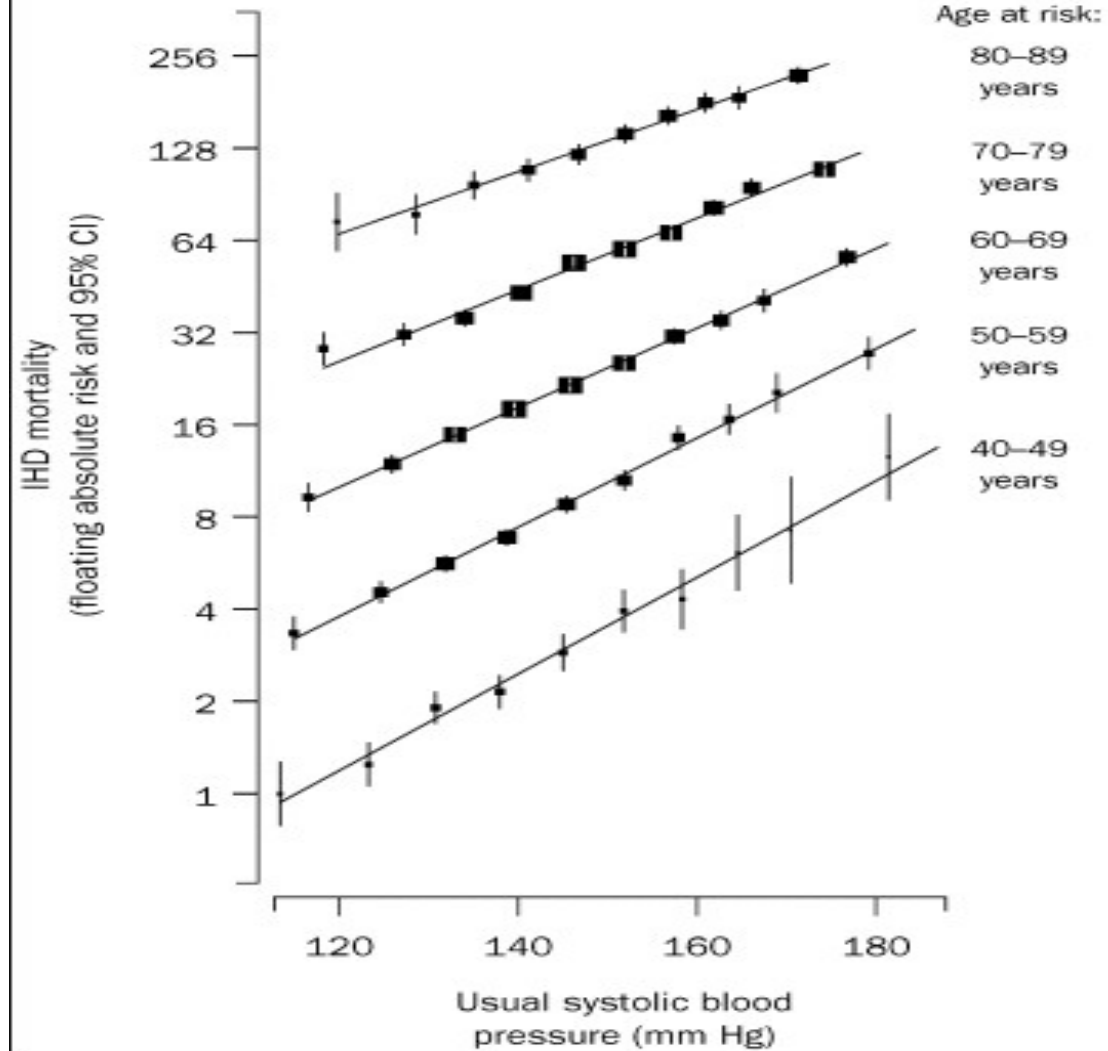
Obtain further measurements if the readings differ by >10 mmHg

- Systolic BP appears to be a stronger determinant of CVD risk than diastolic BP
- incremental pulse pressure is associated with an increased risk of CVD events, including coronary heart disease and heart failure
- non-dipping status is considered an independent cardiovascular risk factor, and has been associated with an increased risk of all-cause mortality in older hypertensive adults
- BP variability (short term & long term) is associated with higher risk of CVD events.

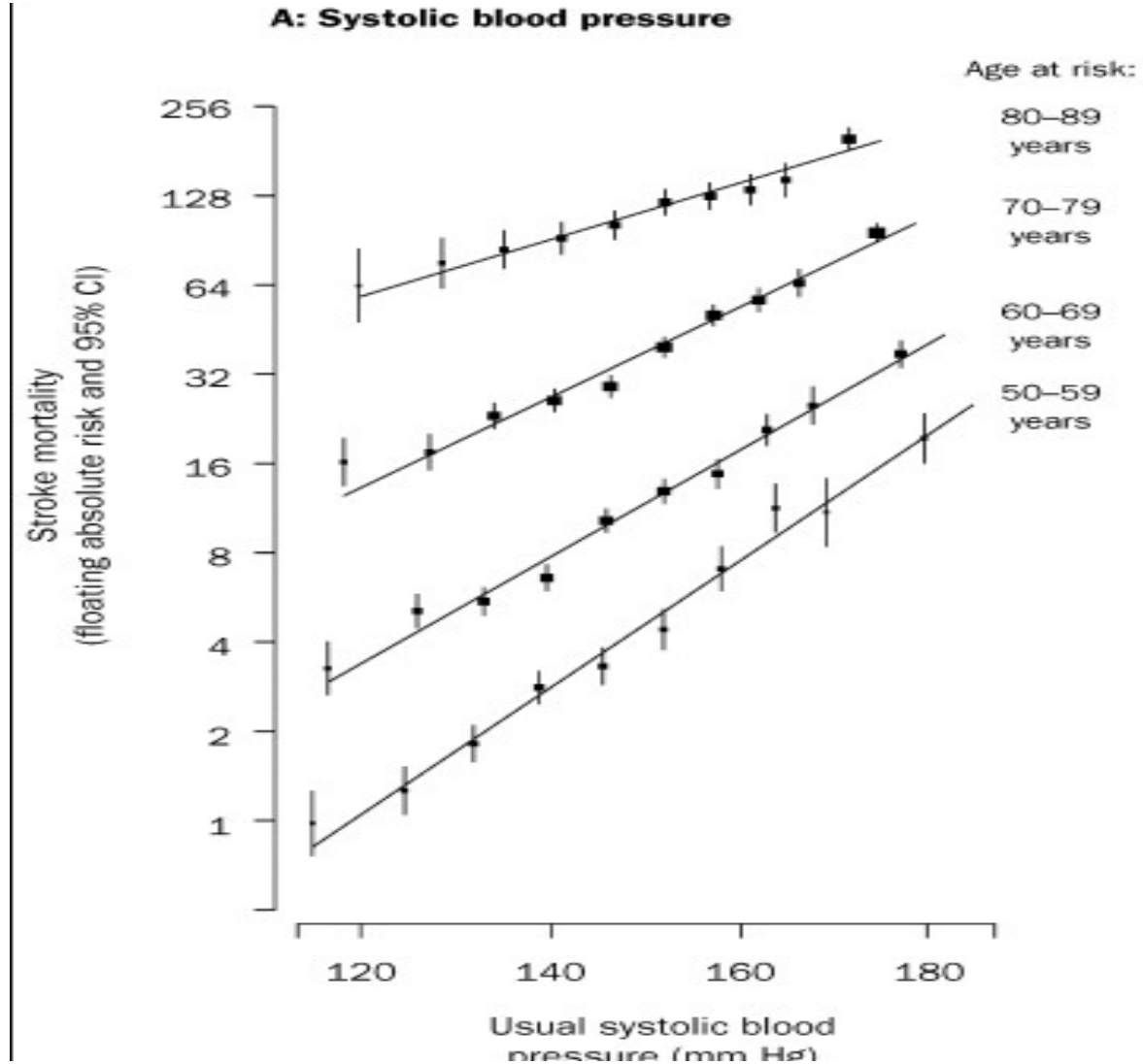
Hypertension & CVD Risk

- In many meta-analyses, the hazard ratios for CHD and stroke were between
 - * 1.1 and 1.5 for SBP/DBP of 120–129/80–84 mm Hg versus <120/80 mm Hg
 - * 1.5 and 2.0 for SBP/DBP of 130–139/85–89 mm Hg versus <120/80 mm Hg.
- CVD risk begins below thresholds used to define hypertension and the risk increases with higher blood pressure levels

A meta-analysis of individual data for one million adults in 61 prospective studies



Ischaemic heart disease (IHD) mortality rate in each decade of age versus usual blood pressure at the start of that decade



Stroke mortality rate in each decade of age versus usual blood pressure at the start of that decade

TABLE 6 **Categories of BP in Adults***

BP Category	SBP		DBP
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120–129 mm Hg	and	<80 mm Hg
Hypertension			
Stage 1	130–139 mm Hg	or	80–89 mm Hg
Stage 2	≥140 mm Hg	or	≥90 mm Hg

ACC 2017

Table 5 Comparison of office, home, and ambulatory blood pressure measurement thresholds for elevated blood pressure and hypertension

	Office BP (mmHg) ^a	Home BP (mmHg)	Daytime ABPM (mmHg)	24 h ABPM (mmHg)	Night-time ABPM (mmHg)
Reference					
Non-elevated BP	<120/70	<120/70	<120/70	<115/65	<110/60
Elevated BP	120/70–<140/90	120/70–<135/85	120/70–<135/85	115/65–<130/80	110/60–<120/70
Hypertension	≥140/90	≥135/85	≥135/85	≥130/80	≥120/70

Cardiovascular Risk Stratification

- Both guidelines recommend CVD risk assessment.
- The ESC guideline: Systematic Coronary Risk Evaluation 2 (SCORE2) tool to estimates 10-year risk of both fatal and nonfatal CVD events in adults 40-69 years , Older Persons (SCORE2-OP), for adults ≥ 70 years of age.
- The ACC/AHA guideline: the Pooled Cohort Equation (PCE) to estimate 10-year risk of fatal and nonfatal CVD events in adults 40-79 years of age

Conditions with sufficient CVD risk



Established clinical
cardiovascular disease

Atherosclerotic cardiovascular disease^a
Heart failure



Moderate or severe
CKD

eGFR <60 mL/min/1.73 m² or
albuminuria ≥30 mg/g (≥3 mg/mmol)



Other forms of hypertension-
mediated organ damage

Cardiac^b
Vascular^b



Diabetes
mellitus

Type 1 and type 2 diabetes mellitus^c



Familial
hypercholesterolaemia

Probable or definite familial hypercholesterolaemia

Recommendations	Class ^a	Level ^b	
In individuals with increased CVD risk where their screening office BP is 120–139/70–89 mmHg, it is recommended to measure BP out of office, using ABPM and/or HBPM or, if not logistically feasible, by making repeated office BP measurements on more than one visit. ^{70,238–241}	I	B	ESC 2024
Where screening office BP is 140–159/90–99 mmHg, it is recommended that the diagnosis of hypertension should be based on out-of-office BP measurement with ABPM and/or HBPM. If these measurements are not logistically or economically feasible, then diagnosis can be made on repeated office BP measurements on more than one visit. ^{70,238–241}	I	B	
Where screening office BP is $\geq 160/100$ mmHg: It is recommended that BP 160–179/100–109 mmHg be confirmed as soon as possible (e.g. within 1 month) preferably by either home or ambulatory BP measurements;	I	C	

Table 6 Comparison of ambulatory and home blood pressure monitoring

Ambulatory monitoring

Advantages

- Can identify white-coat and masked hypertension
- Measurement in real-life settings and during usual activities
- Stronger prognostic evidence
- Night-time readings
- Abundant information from a single investigation, including short-term diurnal BP variability
- Additional BP phenotyping (e.g. nocturnal dipping status)

Disadvantages

- Relatively expensive and sometimes limited availability
- Can be uncomfortable and affect sleep

Home monitoring

Advantages

- Identify white-coat and masked hypertension
- Cheap and widely available
- Measurement at home, which may be more relaxed than at doctor's office
- Patient engagement in BP measurement and telemedicine potential
- Easily repeated and used over longer periods to assess day-to-day BP variability

Disadvantages

- Only static BP at rest is typically available
- Potential for measurement error due to improper measurement technique or unvalidated or poorly calibrated device
- Nocturnal readings not usually possible

Table S2 Key information to be collected in medical history

Risk factors

Family and personal history of hypertension, CVD, or renal disease.

Family and personal history of associated CVD risk factors.

Smoking history (including vaping).

Dietary history (including but not exclusive to salt intake).

Alcohol consumption.

Physical activity/sedentary lifestyle.

History of erectile dysfunction.

Migraine with aura.

Autoimmune inflammatory diseases.

Human immunodeficiency virus.

Sleep history, snoring, sleep apnoea.

Psychosocial factors (chronic stress, depression, social deprivation, low socio-economic status, discrimination, gender-based violence).

Previous hypertension in pregnancy/pre-eclampsia and other pregnancy-related complications (gestational diabetes, miscarriage/stillbirth, pre-term labour).

Early menopause, polycystic ovary disease.

History and symptoms suggesting HMOD, established CVD, and renal disease

Brain and eyes: syncope, impaired vision, TIA, sensory or motor deficit, stroke, carotid revascularization, cognitive impairment, dementia.

Heart: chest pain, shortness of breath, oedema, myocardial infarction, coronary revascularization, history of palpitations, arrhythmias (especially AF), heart failure.

Kidneys: polyuria, nocturia, haematuria, urinary tract infections, patient or family history of CKD (e.g. polycystic kidney disease).

Peripheral arteries: cold extremities, intermittent claudication, leg ulcers, peripheral revascularization.

History and symptoms suggesting secondary hypertension

All causes:

BP > 160/100 mmHg in young adults (<40 years), BP > 180/110 mmHg irrespective of age.

Sudden development of hypertension or rapidly worsening BP.

Resistant hypertension.

Hypertensive emergency.

Table S3 Key steps in physical examination

Anthropometric measures

Weight and height for BMI calculation.
Waist circumference.

Signs of HMOD or established CVD

Neurological examination and cognitive status (based on clinical suspicion).²¹¹
Palpation and auscultation of heart and carotid arteries.
Auscultation of abdominal aorta, iliac, and femoral arteries.
Palpation of peripheral arteries.
Comparison of BP in both arms (at least once).

Signs of secondary hypertension

Skin inspection: cafe-au-lait patches of neurofibromatosis (phaeochromocytoma/paraganglioma).
Kidney palpation for signs of renal enlargement (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, inter-arm BP difference in young individuals with aortic coarctation (aortic murmur may also be heard).
Signs of Cushing's disease or acromegaly.
Signs of thyroid or parathyroid disease.
Neck circumference of >40 cm in men, >35 cm in women (OSAS).

BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; HMOD, hypertension-mediated organ damage; OSAS, obstructive sleep apnoea syndrome. Adapted from the 2018 ESC/ESH Guidelines for the management of arterial hypertension.²¹⁰

Table 8 Routine tests recommended in the initial work-up of a patient with elevated blood pressure or hypertension

Routine test	Clinical utility
Fasting blood glucose (and HbA1c if fasting blood glucose is elevated)	Assessing CVD risk and comorbidities
Serum lipids: total cholesterol, LDL cholesterol, HDL and non-HDL cholesterol, triglycerides	Assessing CVD risk
Blood sodium and potassium, haemoglobin and/or haematocrit, calcium, and TSH	Screening secondary hypertension (primary aldosteronism, Cushing's disease, polycythaemia, hyperparathyroidism, and hyperthyroidism)
Blood creatinine and eGFR; urinalysis and urinary albumin-to-creatinine ratio	Assessing CVD risk and HMOD Guiding treatment choice Screening secondary hypertension (renoparenchymal and renovascular)
12-lead ECG	Assessing HMOD (left atrial enlargement, left ventricular hypertrophy) Assessing irregular pulse and other comorbidities (AF, previous acute myocardial infarction)

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AF, atrial fibrillation; CVD, cardiovascular disease; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; HbA1c, glycated haemoglobin; HDL, high-density lipoprotein; HMOD, hypertension-mediated organ damage; LDL, low-density lipoprotein; TSH, thyroid-stimulating hormone.

Optional Tests to improve CVD risk stratification

Optional test	Clinical utility
Echocardiography	Assessing HMOD (hypertensive heart disease) Assessing established CVD (previous acute myocardial infarction, heart failure) Assessing thoracic aorta dilation
CAC by cardiac CT or carotid or femoral artery ultrasound imaging	Assessing HMOD (atherosclerotic plaque)
Large artery stiffness (carotid–femoral or brachial–ankle PWV)	Assessing HMOD (arterial stiffness)
High-sensitivity cardiac troponin and/or NT-proBNP	Assessing HMOD
Ankle–brachial index	Assessing established CVD (lower-extremity arterial disease)
Abdominal ultrasound	Assessing established CVD (abdominal aneurysm)
Fundoscopy	Assessing HMOD (hypertensive retinopathy) Diagnosing hypertensive emergency/ malignant hypertension (haemorrhages and exudates, papilloedema)

Echocardiography is recommended in patients with hypertension and ECG abnormalities, or signs or symptoms of cardiac disease. ^{14,31,292}	I	B
Echocardiography may be considered in patients with elevated BP, particularly when it is likely to change patient management. ^{31,291}	IIb	B

Preventing and Treating Elevated Blood Pressure and Hypertension

- The ultimate goal is to reduce CVD, to improve quality of life, and to prevent premature death.
- Besides BP, other CVD risk factors need to be comprehensively addressed

TABLE 15 Best Proven Nonpharmacological Interventions for Prevention and Treatment of Hypertension*

	Nonpharmacological Intervention	Dose	Approximate Impact on SBP		
			Hypertension	Normotension	Reference
Weight loss	Weight/body fat	Best goal is ideal body weight, but aim for at least a 1-kg reduction in body weight for most adults who are overweight. Expect about 1 mm Hg for every 1-kg reduction in body weight.	−5 mm Hg	−2/3 mm Hg	(S6.2-1)
Healthy diet	DASH dietary pattern	Consume a diet rich in fruits, vegetables, whole grains, and low-fat dairy products, with reduced content of saturated and total fat.	−11 mm Hg	−3 mm Hg	(S6.2-6,S6.2-7)
Reduced intake of dietary sodium	Dietary sodium	Optimal goal is <1500 mg/d, but aim for at least a 1000-mg/d reduction in most adults.	−5/6 mm Hg	−2/3 mm Hg	(S6.2-9,S6.2-10)
Enhanced intake of dietary potassium	Dietary potassium	Aim for 3500–5000 mg/d, preferably by consumption of a diet rich in potassium.	−4/5 mm Hg	−2 mm Hg	(S6.2-13)
Physical activity	Aerobic	■ 90–150 min/wk ■ 65%–75% heart rate reserve	−5/8 mm Hg	−2/4 mm Hg	(S6.2-18,S6.2-22)
	Dynamic resistance	■ 90–150 min/wk ■ 50%–80% 1 rep maximum ■ 6 exercises, 3 sets/exercise, 10 repetitions/set	−4 mm Hg	−2 mm Hg	(S6.2-18)
	Isometric resistance	■ 4 × 2 min (hand grip), 1 min rest between exercises, 30%–40% maximum voluntary contraction, 3 sessions/wk ■ 8–10 wk	−5 mm Hg	−4 mm Hg	(S6.2-19,S6.2-31)
Moderation in alcohol intake	Alcohol consumption	In individuals who drink alcohol, reduce alcohol† to: ■ Men: ≤2 drinks daily ■ Women: ≤1 drink daily	−4 mm Hg	−3 mm Hg	(S6.2-22–S6.2-24)

Men and women are recommended to drink less alcohol than the upper limit, which is about 100 g/week of pure alcohol. How this translates into number of drinks depends on portion size (the standards of which differ per country), but most drinks contain 8–14 g of alcohol per drink. Preferably, it is recommended to avoid alcohol to achieve the best health outcomes.^{170,419,440,441}

I

B

It is recommended to restrict free sugar consumption, in particular sugar-sweetened beverages, to a maximum of 10% of energy intake. It is also recommended to discourage consumption of sugar-sweetened beverages, such as soft drinks and fruit juices, starting at a young age.^{425–427}

I

B

It is recommended to stop tobacco smoking, initiate supportive care and refer to smoking cessation programmes, as tobacco use strongly and independently causes CVD, CVD events, and all-cause mortality.^{428,429,431,437}

I

A

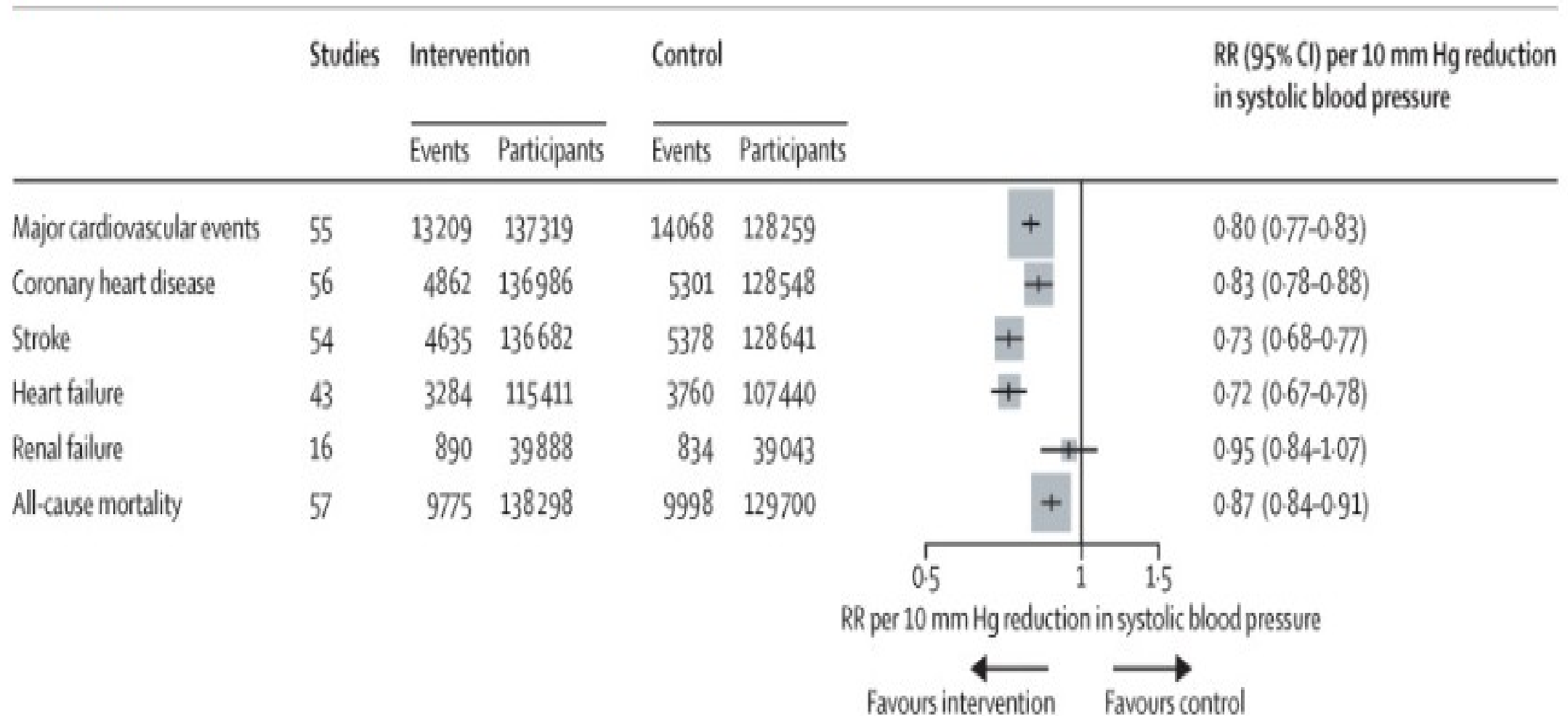
It is recommended to aim for a stable and healthy BMI (e.g. 20–25 kg/m²) and waist circumference values (e.g. <94 cm in men and <80 cm in women) to reduce BP and CVD risk.^{399–401}

I

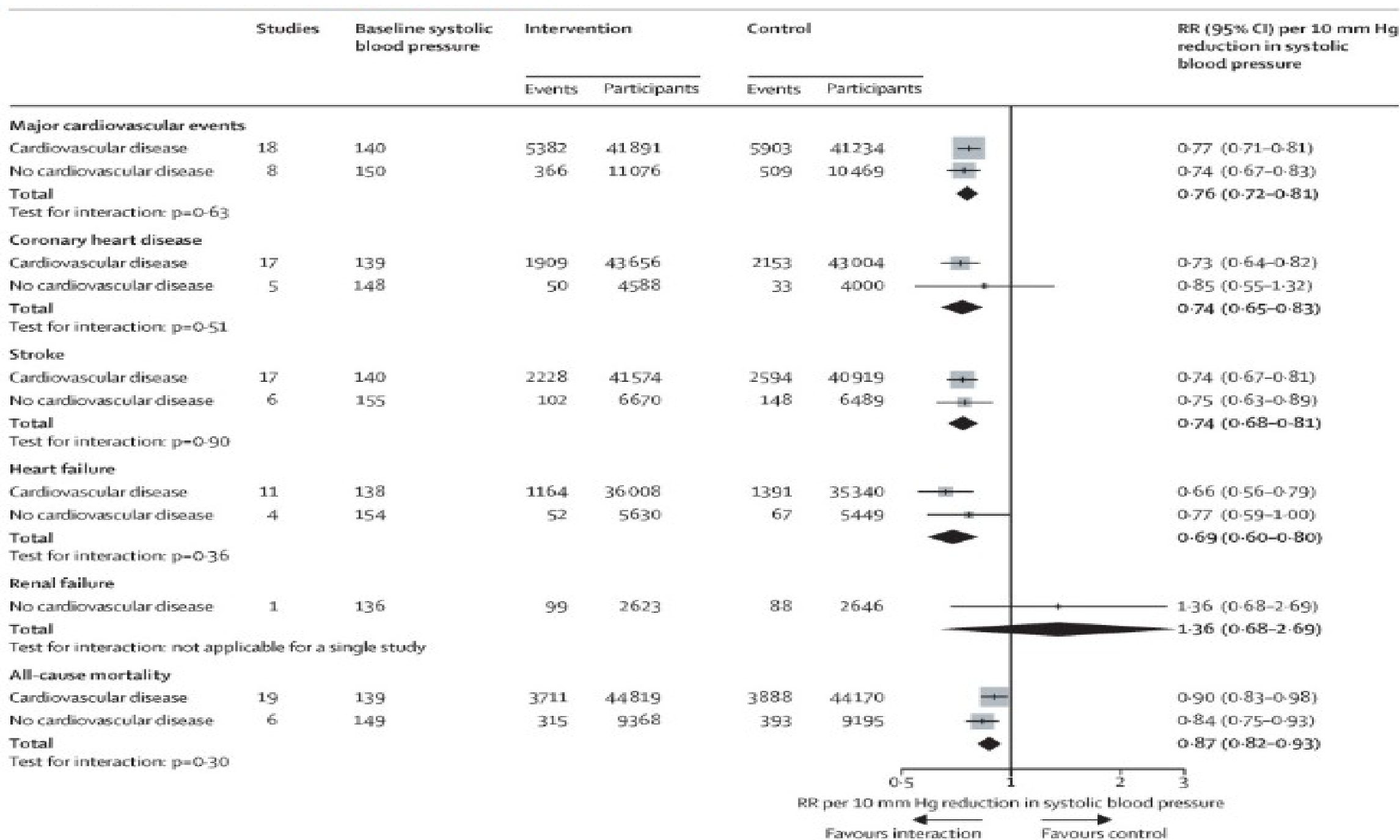
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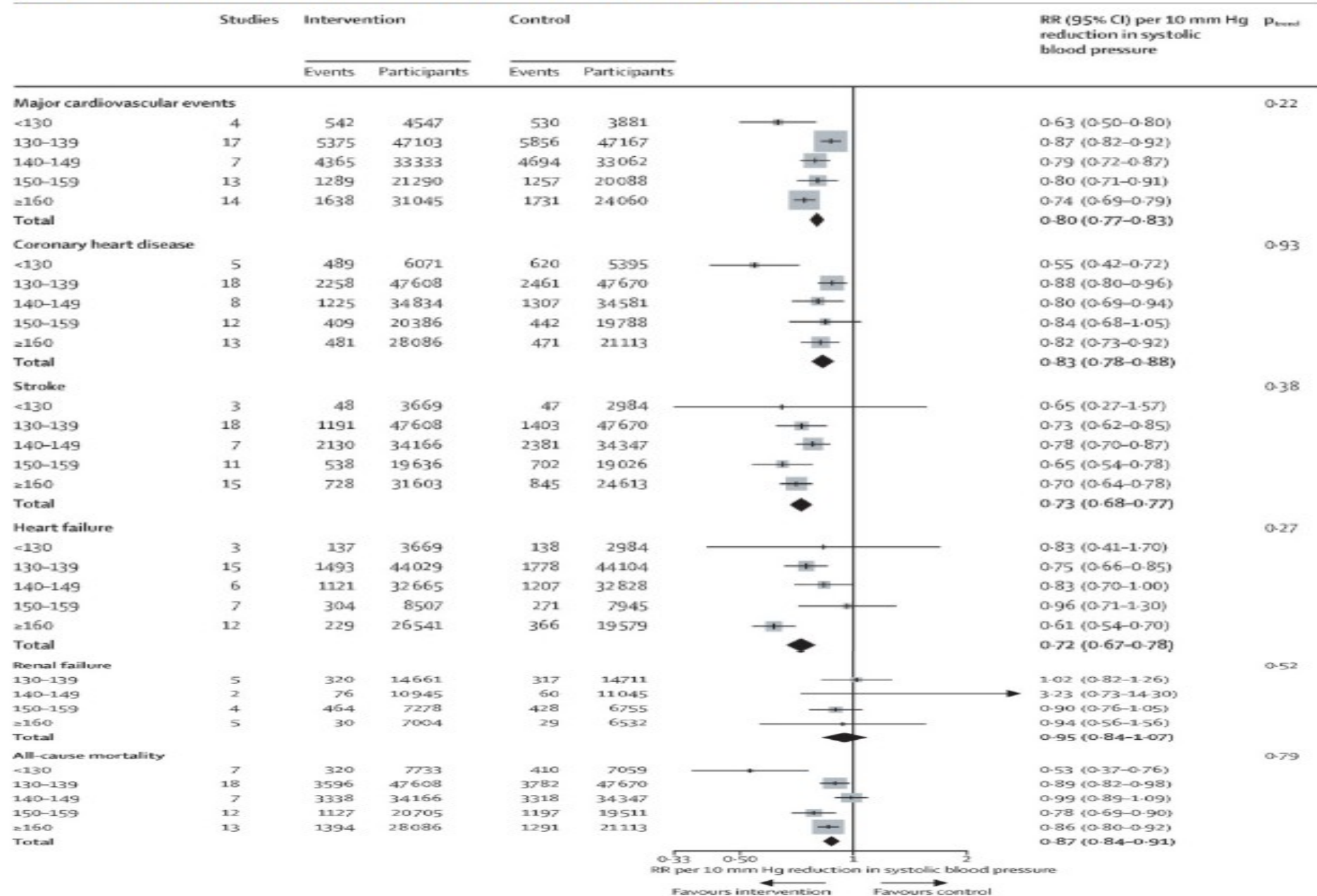
Pharmacologic Management of Hypertension

- There is a clear relationship between the intensity of BP lowering and the relative and absolute reduction in risk of CVD events for all adults, regardless of age, sex, prior CVD, diabetes, or AF.
- The higher the patient's baseline absolute risk for CVD, the greater the net benefit from BP-lowering treatment and, at the population level, the lower the estimated number needed to treat (NNT).



Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis of 68 RCTs. Lancet 2016, Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, et al.





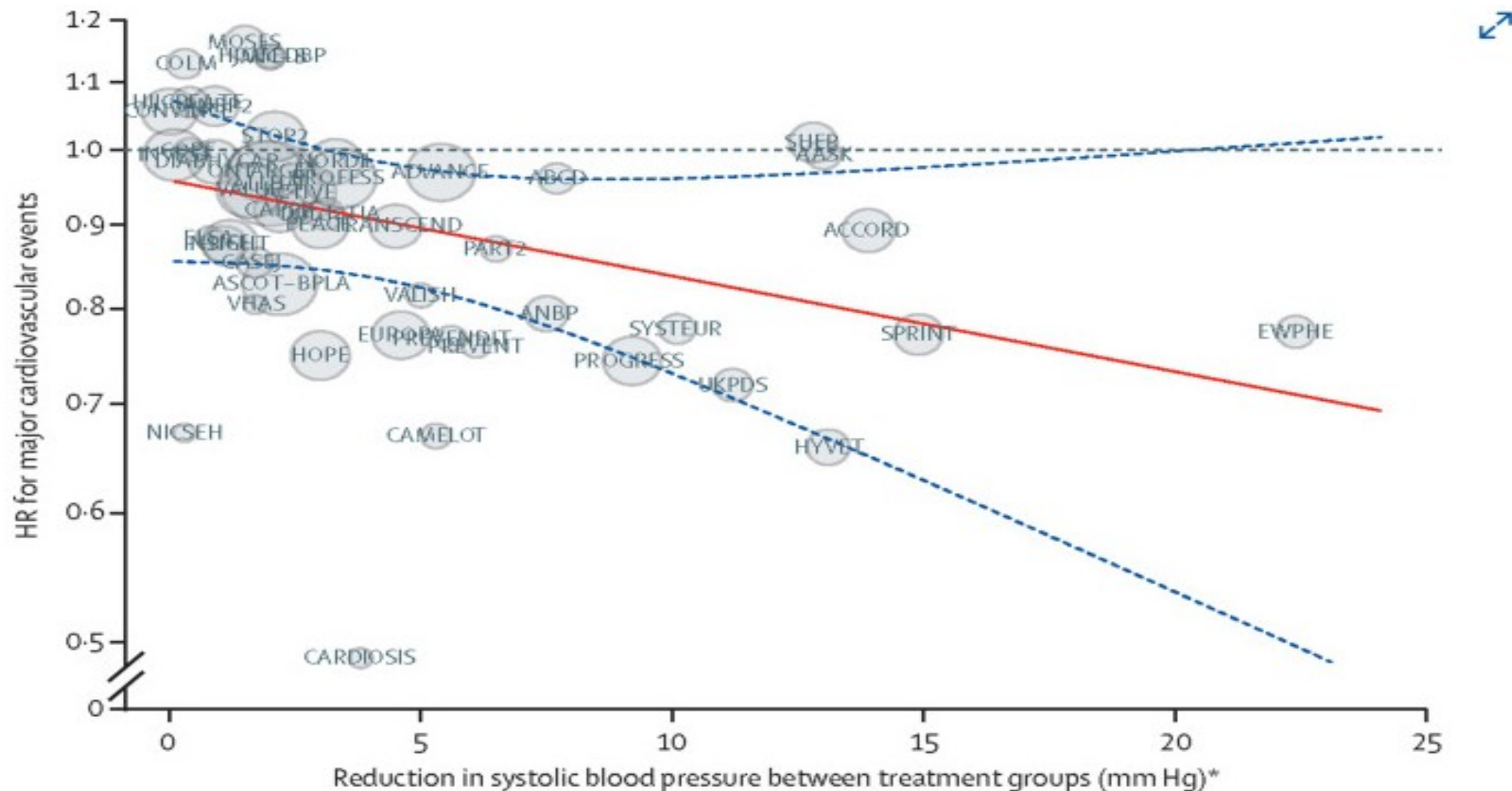


Figure 2 Association between the intensity of blood pressure reduction and relative treatment effects for prevention of major cardiovascular events

Meta-regression analyses of 48 trials, The Blood Pressure Lowering Treatment Trialists' Collaboration Lancet, 2021

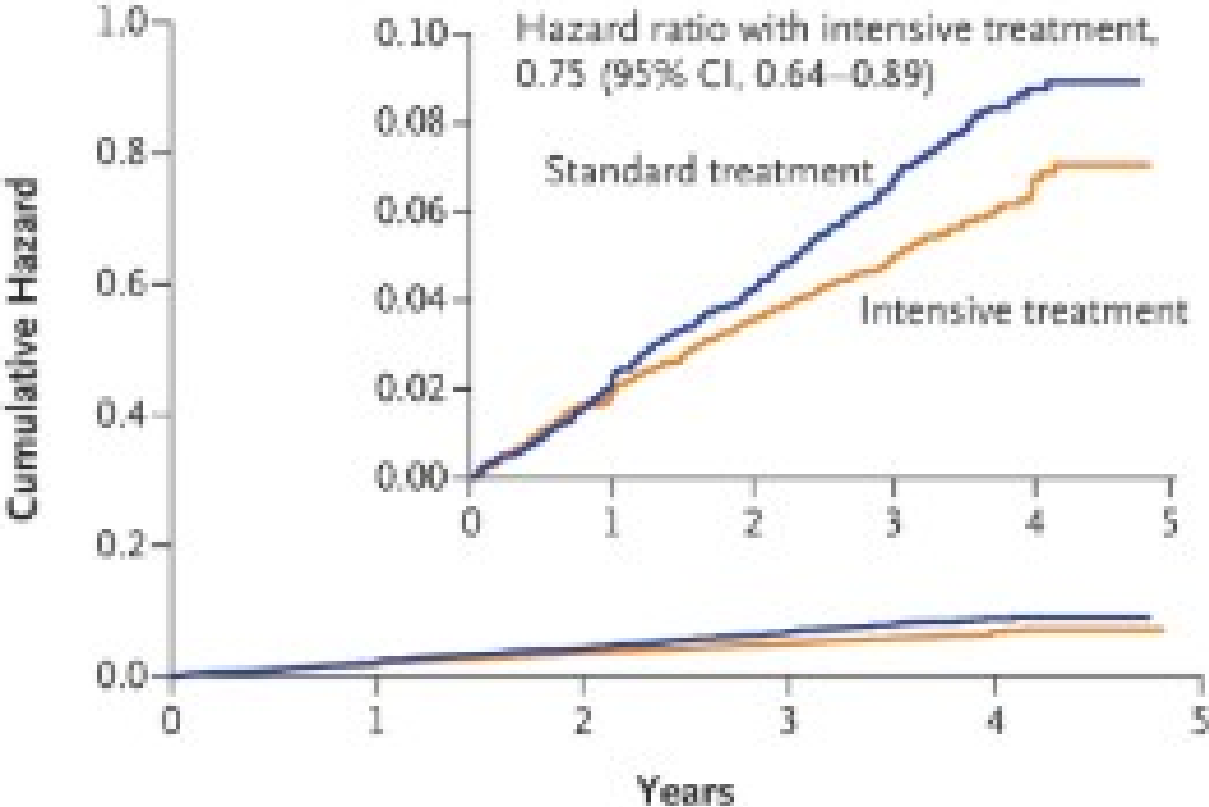
SPRINT

Trial design: Patients with systolic BP ≥ 130 mm Hg and at least one risk factor were randomized in a 1:1 fashion to either intensive SBP lowering (target <120 mm Hg) or routine SBP management (target <140 mm Hg). Patients were followed for 5 years.

Primary end point: myocardial infarction, other acute coronary syndromes, stroke, heart failure, or death from cardiovascular causes.

the mean systolic blood pressure was 121.4 mm Hg in the intensive-treatment group and 136.2 mm Hg in the standard-treatment group

A Primary Outcome



No. at Risk					
Standard treatment	4683	4437	4228	2829	721
Intensive treatment	4678	4436	4256	2900	779

Table 2. Primary and Secondary Outcomes and Renal Outcomes.*

Outcome	Intensive Treatment		Standard Treatment		Hazard Ratio (95% CI)	P Value
	no. of patients (%)	% per year	no. of patients (%)	% per year		
All participants	(N = 4678)		(N = 4683)			
Primary outcome†	243 (5.2)	1.65	319 (6.8)	2.19	0.75 (0.64–0.89)	<0.001
Secondary outcomes						
Myocardial infarction	97 (2.1)	0.65	116 (2.5)	0.78	0.83 (0.64–1.09)	0.19
Acute coronary syndrome	40 (0.9)	0.27	40 (0.9)	0.27	1.00 (0.64–1.55)	0.99
Stroke	62 (1.3)	0.41	70 (1.5)	0.47	0.89 (0.63–1.25)	0.50
Heart failure	62 (1.3)	0.41	100 (2.1)	0.67	0.62 (0.45–0.84)	 0.002
Death from cardiovascular causes	37 (0.8)	0.25	65 (1.4)	0.43	0.57 (0.38–0.85)	 0.005
Death from any cause	155 (3.3)	1.03	210 (4.5)	1.40	0.73 (0.60–0.90)	 0.003
Primary outcome or death	332 (7.1)	2.25	423 (9.0)	2.90	0.78 (0.67–0.90)	 <0.001
Participants with CKD at baseline	(N = 1330)		(N = 1316)			
Composite renal outcome‡	14 (1.1)	0.33	15 (1.1)	0.36	0.89 (0.42–1.87)	0.76
≥50% reduction in estimated GFR§	10 (0.8)	0.23	11 (0.8)	0.26	0.87 (0.36–2.07)	0.75
Long-term dialysis	6 (0.5)	0.14	10 (0.8)	0.24	0.57 (0.19–1.54)	0.27
Kidney transplantation	0		0			
Incident albuminuria¶	49/526 (9.3)	3.02	59/500 (11.8)	3.90	0.72 (0.48–1.07)	0.11
Participants without CKD at baseline 	(N = 3332)		(N = 3345)			
≥30% reduction in estimated GFR to <60 ml/min/1.73 m²§	127 (3.8)	1.21	37 (1.1)	0.35	3.49 (2.44–5.10)	 <0.001
Incident albuminuria¶	110/1769 (6.2)	2.00	135/1831 (7.4)	2.41	0.81 (0.63–1.04)	0.10

Blood Pressure (BP) Thresholds and Recommendations for Treatment and Follow-Up

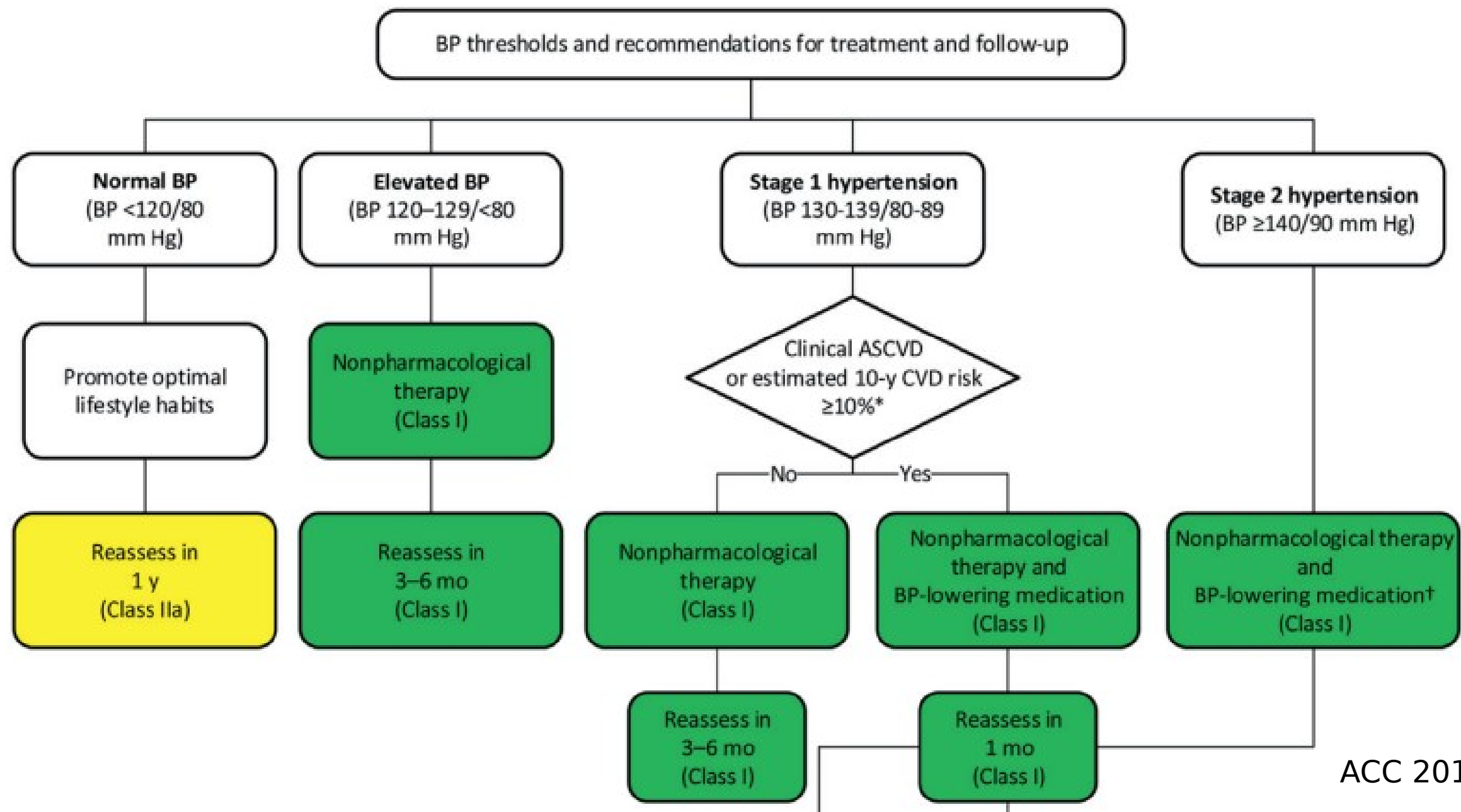


Table 14 Initiation of blood pressure-lowering treatment based on confirmed blood pressure category and cardiovascular disease risk

Blood pressure (mmHg)	Non-elevated BP (<120/70)	Elevated BP (120/70 to 139/89)		Hypertension (≥140/90)
Risk		(a) All adults with SBP 120–129 mmHg (b) SBP 130–139 AND 10-year estimated CVD risk <10% AND no high-risk conditions or risk modifiers or abnormal risk tool tests	(a) SBP 130–139 AND high-risk conditions (e.g. established CVD, diabetes mellitus, CKD, FH or HMOD) (b) SBP 130–139 AND 10-year estimated CVD risk ≥10% (c) SBP 130–139 AND 10-year estimated CVD risk 5% - <10% AND risk modifiers or abnormal risk tool tests	Assumed all at sufficiently high risk to benefit from pharmacological treatment
Treatment	Lifestyle measures for prevention Screen BP and CVD risk opportunistically	Lifestyle measures for treatment Monitor BP and CVD risk yearly	Lifestyle measures and pharmacological treatment (after 3-month delay). Monitor BP yearly once treatment control is established	Lifestyle measures and pharmacological treatment (immediate) Monitor BP yearly once treatment control is established
Target (mmHg)	Maintain BP <120/70	Aim BP 120–129/70–79 mmHg ^a		

BP, blood pressure; CKD, chronic kidney disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; FH, familial hypercholesterolaemia; HMOD, hypertension-mediated organ damage; SBP, systolic blood pressure.

^aCaution in adults with orthostatic hypotension, moderate-to-severe frailty, limited life expectancy, and older patients (aged ≥85 years).

- Moderate-to-severe frailty
- Symptomatic orthostatic hypotension
- Age ≥ 85 years

Established CKD,
moderate/severe CKD,
HMOD, DM, or FH
(Class I)

10-year predicted CVD risk

5%–10%

- Any of the following:
 - High-risk ethnicity
 - Family history of premature onset ASCVD
 - Socio-economic deprivation
 - Auto-immune diseases
 - Severe mental illness
 - HIV

- Any of the following:
 - Gestational diabetes
 - Gestational hypertension
 - Pre-eclampsia
 - Pre-term delivery
 - One or more still births
 - Recurrent miscarriage

- Any of the following meeting abnormal criteria:
 - CAC score
 - Carotid or femoral plaque
 - High-sensitivity cardiac troponin
 - NT-proBNP
 - Pulse wave velocity

Calculation
CORE- Diabetes
(Class 1b)

2010



1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2007, 2008, 2009, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017, 2018, 2019, 2020, 2021, 2022, 2023, 2024, 2025, 2026, 2027, 2028, 2029, 2030, 2031, 2032, 2033, 2034, 2035, 2036, 2037, 2038, 2039, 2040, 2041, 2042, 2043, 2044, 2045, 2046, 2047, 2048, 2049, 2050, 2051, 2052, 2053, 2054, 2055, 2056, 2057, 2058, 2059, 2060, 2061, 2062, 2063, 2064, 2065, 2066, 2067, 2068, 2069, 2070, 2071, 2072, 2073, 2074, 2075, 2076, 2077, 2078, 2079, 2080, 2081, 2082, 2083, 2084, 2085, 2086, 2087, 2088, 2089, 2090, 2091, 2092, 2093, 2094, 2095, 2096, 2097, 2098, 2099, 2100, 2101, 2102, 2103, 2104, 2105, 2106, 2107, 2108, 2109, 2110, 2111, 2112, 2113, 2114, 2115, 2116, 2117, 2118, 2119, 2120, 2121, 2122, 2123, 2124, 2125, 2126, 2127, 2128, 2129, 2130, 2131, 2132, 2133, 2134, 2135, 2136, 2137, 2138, 2139, 2140, 2141, 2142, 2143, 2144, 2145, 2146, 2147, 2148, 2149, 2150, 2151, 2152, 2153, 2154, 2155, 2156, 2157, 2158, 2159, 2160, 2161, 2162, 2163, 2164, 2165, 2166, 2167, 2168, 2169, 2170, 2171, 2172, 2173, 2174, 2175, 2176, 2177, 2178, 2179, 2180, 2181, 2182, 2183, 2184, 2185, 2186, 2187, 2188, 2189, 2190, 2191, 2192, 2193, 2194, 2195, 2196, 2197, 2198, 2199, 2200, 2201, 2202, 2203, 2204, 2205, 2206, 2207, 2208, 2209, 2210, 2211, 2212, 2213, 2214, 2215, 2216, 2217, 2218, 2219, 2220, 2221, 2222, 2223, 2224, 2225, 2226, 2227, 2228, 2229, 2230, 2231, 2232, 2233, 2234, 2235, 2236, 2237, 2238, 2239, 2240, 2241, 2242, 2243, 2244, 2245, 2246, 2247, 2248, 2249, 2250, 2251, 2252, 2253, 2254, 2255, 2256, 2257, 2258, 2259, 2260, 2261, 2262, 2263, 2264, 2265, 2266, 2267, 2268, 2269, 2270, 2271, 2272, 2273, 2274, 2275, 2276, 2277, 2278, 2279, 2280, 2281, 2282, 2283, 2284, 2285, 2286, 2287, 2288, 2289, 2290, 2291, 2292, 2293, 2294, 2295, 2296, 2297, 2298, 2299, 2300, 2301, 2302, 2303, 2304, 2305, 2306, 2307, 2308, 2309, 2310, 2311, 2312, 2313, 2314, 2315, 2316, 2317, 2318, 2319, 2320, 2321, 2322, 2323, 2324, 2325, 2326, 2327, 2328, 2329, 2330, 2331, 2332, 2333, 2334, 2335, 2336, 2337, 2338, 2339, 2340, 2341, 2342, 2343, 2344, 2345, 2346, 2347, 2348, 2349, 2350, 2351, 2352, 2353, 2354, 2355, 2356, 2357, 2358, 2359, 2360, 2361, 2362, 2363, 2364, 2365, 2366, 2367, 2368, 2369, 2370, 2371, 2372, 2373, 2374, 2375, 2376, 2377, 2378, 2379, 2380, 2381, 2382, 2383, 2384, 2385, 2386, 2387, 2388, 2389, 2390, 2391, 2392, 2393, 2394, 2395, 2396, 2397, 2398, 2399, 2400, 2401, 2402, 2403, 2404, 2405, 2406, 2407, 2408, 2409, 2410, 2411, 2412, 2413, 2414, 2415, 2416, 2417, 2418, 2419, 2420, 2421, 2422, 2423, 2424, 2425, 2426, 2427, 2428, 2429, 2430, 2431, 2432, 2433, 2434, 2435, 2436, 2437, 2438, 2439, 2440, 2441, 2442, 2443, 2444, 2445, 2446, 2447, 2448, 2449, 2450, 2451, 2452, 2453, 2454, 2455, 2456, 2457, 2458, 2459, 2460, 2461, 2462, 2463, 2464, 2465, 2466, 2467, 2468, 2469, 2470, 2471, 2472, 2473, 2474, 2475, 2476, 2477, 2478, 2479, 2480, 2481, 2482, 2483, 2484, 2485, 2486, 2487, 2488, 2489, 2490, 2491, 2492, 2493, 2494, 2495, 2496, 2497, 2498, 2499, 2500, 2501, 2502, 2503, 2504, 2505, 2506, 2507, 2508, 2509, 2510, 2511, 2512, 2513, 2514, 2515, 2516, 2517, 2518, 2519, 2520, 2521, 2522, 2523, 2524, 2525, 2526, 2527, 2528, 2529, 2530, 2531, 2532, 2533, 2534, 2535, 2536, 2537, 2538, 2539, 2540, 2541, 2542, 2543, 2544, 2545, 2546, 2547, 2548, 2549, 2550, 2551, 2552, 2553, 2554, 2555, 2556, 2557, 2558, 2559, 2560, 2561, 2562, 2563, 2564, 2565, 2566, 2567, 2568, 2569, 2570, 2571, 2572, 2573, 2574, 2575, 2576, 2577, 2578, 2579, 2580, 2581, 2582, 2583, 2584, 2585, 2586, 2587, 2588, 2589, 2590, 2591, 2592, 2593, 2594, 2595, 2596, 2597, 2598, 2599, 2600, 2601, 2602, 2603, 2604, 2605, 2606, 2607, 2608, 2609, 2610, 2611, 2612, 2613, 2614, 2615, 2616, 2617, 2618, 2619, 2620, 2621, 2622, 2623, 2624, 2625, 2626, 2627, 2628, 2629, 2630, 2631, 2632, 2633, 2634, 2635, 2636, 2637, 2638, 2639, 2640, 2641, 2642, 2643, 2644, 2645, 2646, 2647, 2648, 2649, 2650, 2651, 2652, 2653, 2654, 2655, 2656, 2657, 2658, 2659, 2660, 2661, 2662, 2663, 2664, 2665, 2666, 2667, 2668, 2669, 2670, 2671, 2672, 2673, 2674, 2675, 2676, 2677, 2678, 26

After 3 months of lifestyle measures, pharmacological treatment for patients with $\geq 130/80$ mmHg (Class II)



TABLE 23
BP Thresholds for and Goals of Pharmacological Therapy in Patients With Hypertension 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	$\geq 140/90$	$< 130/80$
Peripheral artery disease	$\geq 130/80$	$< 130/80$

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

Table 23 Office blood pressure treatment target range

Age group	Office SBP treatment target ranges (mmHg)					Office DBP treatment target range (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke ³ /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	

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Table 14 Initiation of blood pressure-lowering treatment based on confirmed blood pressure category and cardiovascular disease risk

Blood pressure (mmHg)	Non-elevated BP (<120/70)	Elevated BP (120/70 to 139/89)		Hypertension (≥140/90)
Risk		(a) All adults with SBP 120–129 mmHg (b) SBP 130–139 AND 10-year estimated CVD risk <10% AND no high-risk conditions or risk modifiers or abnormal risk tool tests	(a) SBP 130–139 AND high-risk conditions (e.g. established CVD, diabetes mellitus, CKD, FH or HMOD) (b) SBP 130–139 AND 10-year estimated CVD risk ≥10% (c) SBP 130–139 AND 10-year estimated CVD risk 5% - <10% AND risk modifiers or abnormal risk tool tests	Assumed all at sufficiently high risk to benefit from pharmacological treatment
Treatment	Lifestyle measures for prevention Screen BP and CVD risk opportunistically	Lifestyle measures for treatment Monitor BP and CVD risk yearly	Lifestyle measures and pharmacological treatment (after 3-month delay). Monitor BP yearly once treatment control is established	Lifestyle measures and pharmacological treatment (immediate) Monitor BP yearly once treatment control is established
Target (mmHg)	Maintain BP <120/70	Aim BP 120–129/70–79 mmHg ³		

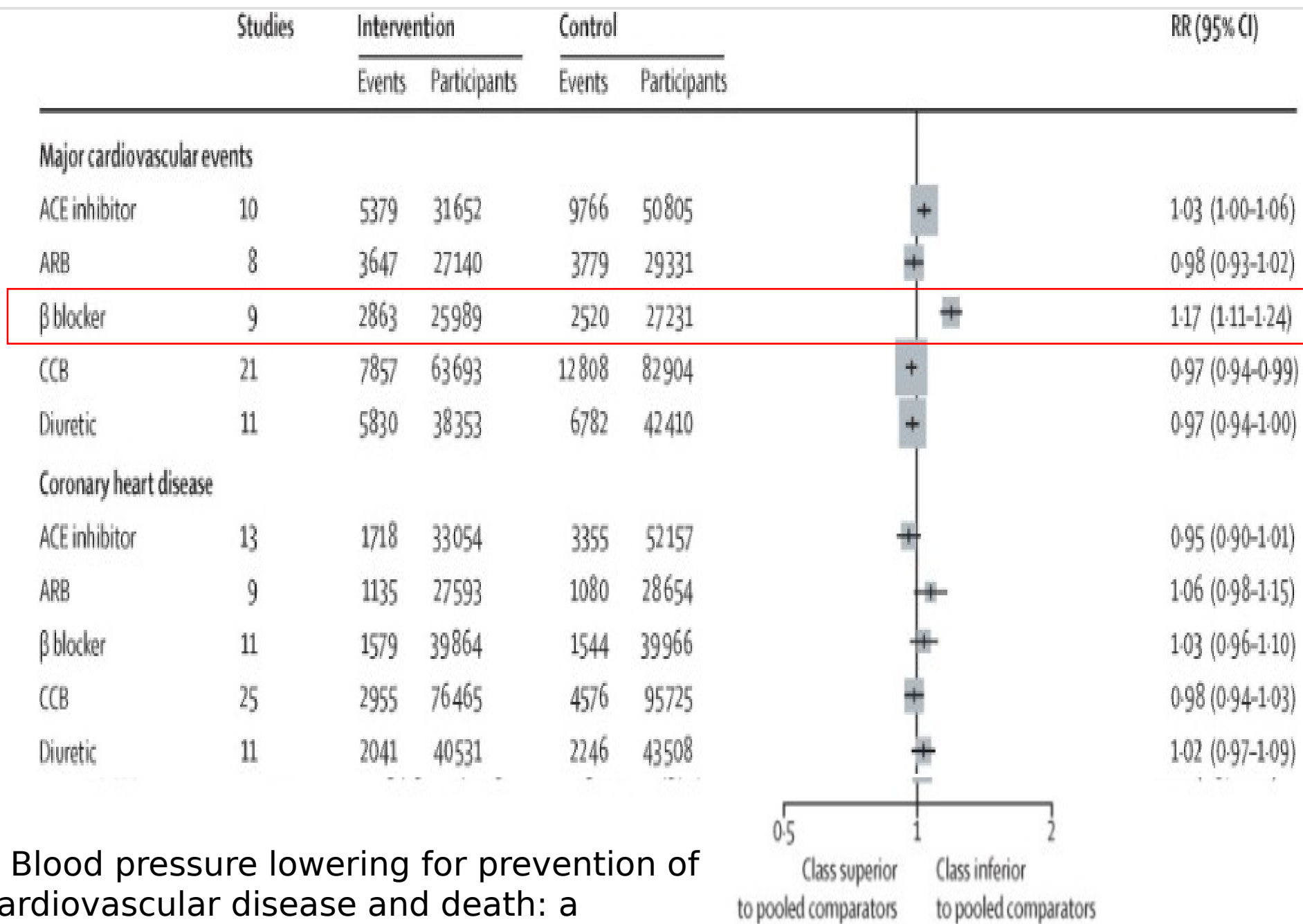
© ESC 2024

BP, blood pressure; CKD, chronic kidney disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; FH, familial hypercholesterolaemia; HMOD, hypertension-mediated organ damage; SBP, systolic blood pressure.

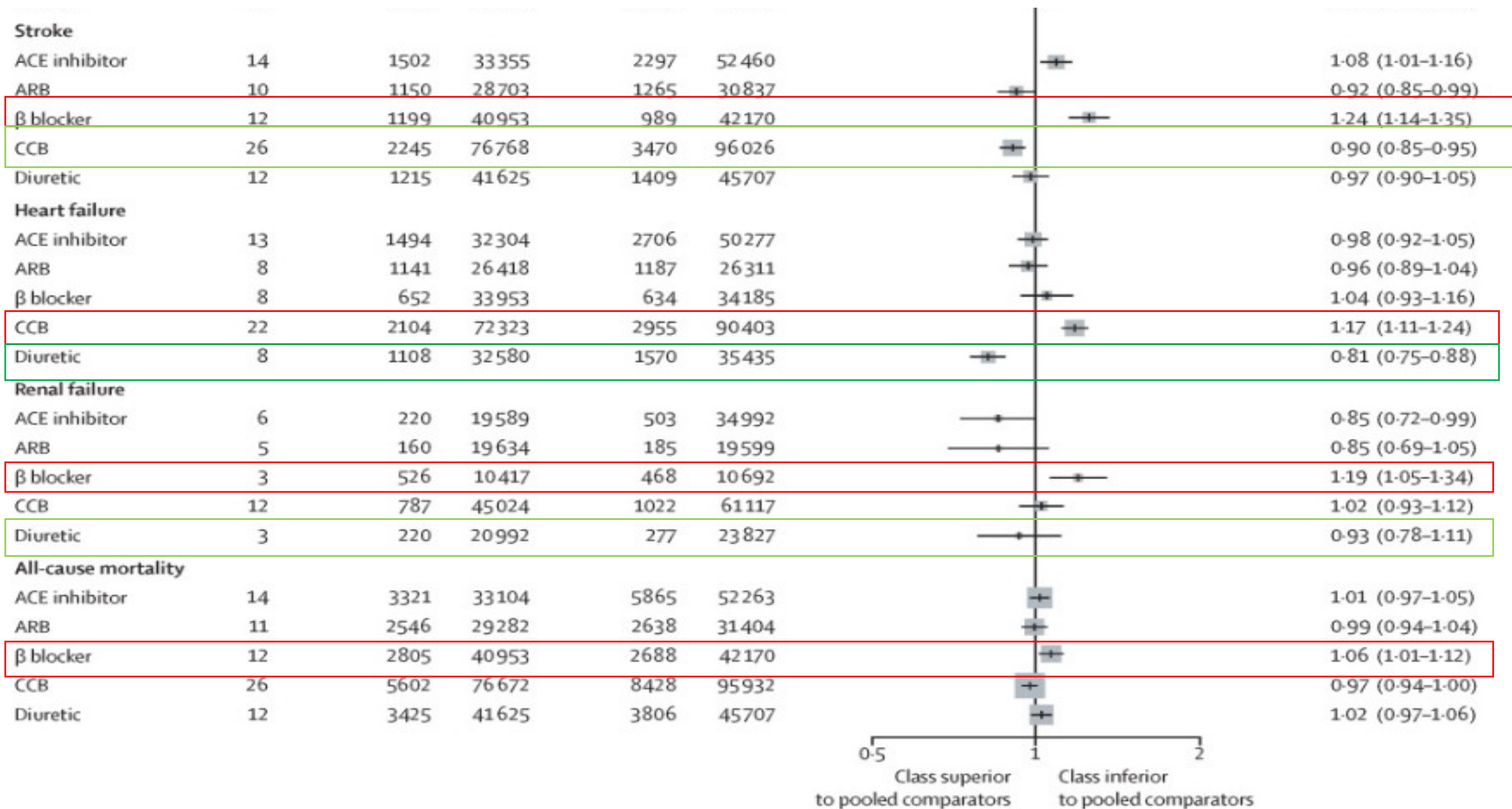
³Caution in adults with orthostatic hypotension, moderate-to-severe frailty, limited life expectancy, and older patients (aged ≥85 years).

‘the lower the better, but within reason’ paradigm

- The major drug classes with robust evidence for **BP-mediated reduction in CVD events** are **ACE inhibitors, ARBs, dihydropyridine CCBs, diuretics** (thiazides and thiazide-like diuretics such as hydrochlorothiazide, chlorthalidone, and indapamide), and **beta-blockers**
- The magnitude of BP reduction achieved with these main classes of BP-lowering medications as monotherapy is similar overall
- beta-blockers are less effective than ACE inhibitors, ARBs, CCBs, or diuretics at preventing stroke, and have a higher discontinuation rate due to side effects.
- Clinical outcome evidence from trials for other BP-lowering drug classes, such as alpha-blockers, hydralazine, minoxidil, other potassium-sparing diuretics, and centrally acting agents, is less compelling and caution regarding adverse effects is warranted.



. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis of 68 RCTs. Lancet 2016



Recommendations	Class ^a	Level ^b
Among all BP-lowering drugs, ACE inhibitors, ARBs, dihydropyridine CCBs, and diuretics (thiazides and thiazide-like drugs such as chlorthalidone and indapamide) have demonstrated the most effective reduction of BP and CVD events, and are therefore recommended as first-line treatments to lower BP. ^{122,446}	I	A
It is recommended that beta-blockers are combined with any of the other major BP-lowering drug classes when there are other compelling indications for their use, e.g. angina, post-myocardial infarction, heart failure with reduced ejection fraction, or for heart rate control. ^{122,448–450}	I	A
It is recommended to take medications at the most convenient time of day for the patient to establish a habitual pattern of medication taking to improve adherence. ^{246,513}	I	B

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Table S10 Choice of starting blood pressure-lowering treatment, depending on comorbidity

Comorbidity	Initial drug class
Diabetes mellitus Metabolic syndrome	ACE inhibitor ARB CCB
Chronic kidney disease Proteinuria/albuminuria	ACE inhibitor ARB Diuretic CCB SGLT2 inhibitors
Post-myocardial infarction	Beta-blocker ACE inhibitor ARB MRA
AF	Beta-blocker ACE inhibitor ARB
Heart failure	ACE inhibitor ARB MRA Beta-blocker SGLT2 inhibitor Diuretic

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ACE, angiotensin-converting enzyme; AF, atrial fibrillation; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; MRA, mineralocorticoid receptor blocker; SGLT2, sodium–glucose co-transporter 2.

Combination Versus single drug treatment for Hypertension

- Combining drugs from different drug classes can have additive or synergistic effects and lead to greater BP reduction than increasing the dose of one drug.
- If combination BP-lowering therapy is pursued, single-pill combinations are preferred.

Value of low dose combination treatment with blood pressure lowering drugs: analysis of 354 randomised trials, BMJ, 2003

Table 3. Efficacy: effects of two different drugs on blood pressure separately and in combination (summary results from 119 randomised placebo controlled comparisons; adapted from Law et al⁷)

Treatment	Average (SE) fall in blood pressure (mm Hg) (treated minus placebo)	
	Systolic	Diastolic
Observed		
"First" drug alone	7.0 (0.4)	4.1 (0.3)
"Second" drug alone	8.1 (0.3)	4.6 (0.3)
Both drugs together	14.6 (0.5)	8.6 (0.4)
Expected		
Sum of first and second drugs alone	15.1	8.7
Difference between observed and expected (95% CI)	-0.5 (-1.4 to 0.4)	-0.1 (-1.0 to 0.8)

Table 3 shows that the sum of the average reductions in blood pressure with each drug used alone is close to the observed effect of the two drugs used in combination, indicating an additive effect.

Table 4. Efficacy: blood pressure lowering effects of drugs when used at half standard dose separately and in combination

	Blood pressure reduction* (95% CI)		
	One drug	Two drugs	Three drugs
Systolic blood pressure (mm Hg)	6.7 (6.1 to 7.2)	13.3 (12.4 to 14.1)	19.9 (18.5 to 21.3)
Diastolic blood pressure (mm Hg)	3.7 (3.1 to 4.3)	7.3 (6.2 to 8.3)	10.7 (9.1 to 12.4)

↵*Reductions in blood pressure adjusted to a usual pretreatment blood pressure of 150/90 mm Hg, the average blood pressure in people aged 50–69 years who have a stroke or ischaemic heart disease event.⁷

Table 7. Effects of blood pressure lowering drugs on reducing the incidence of stroke and ischaemic heart disease events when used separately and in combination at half standard dose*

Disease	Percentage (95% CI) reduction in incidence		
	One drug	Two drugs	Three drugs
Stroke	29 (26 to 31)	49 (42 to 55)	63 (55 to 70)
Ischaemic heart disease events	19 (17 to 21)	34 (29 to 40)	46 (39 to 53)

↵*Calculated from reductions in blood pressure in table 4 and estimates of association between blood pressure and disease events at age 60–69 years from the Prospective Studies Collaboration.¹

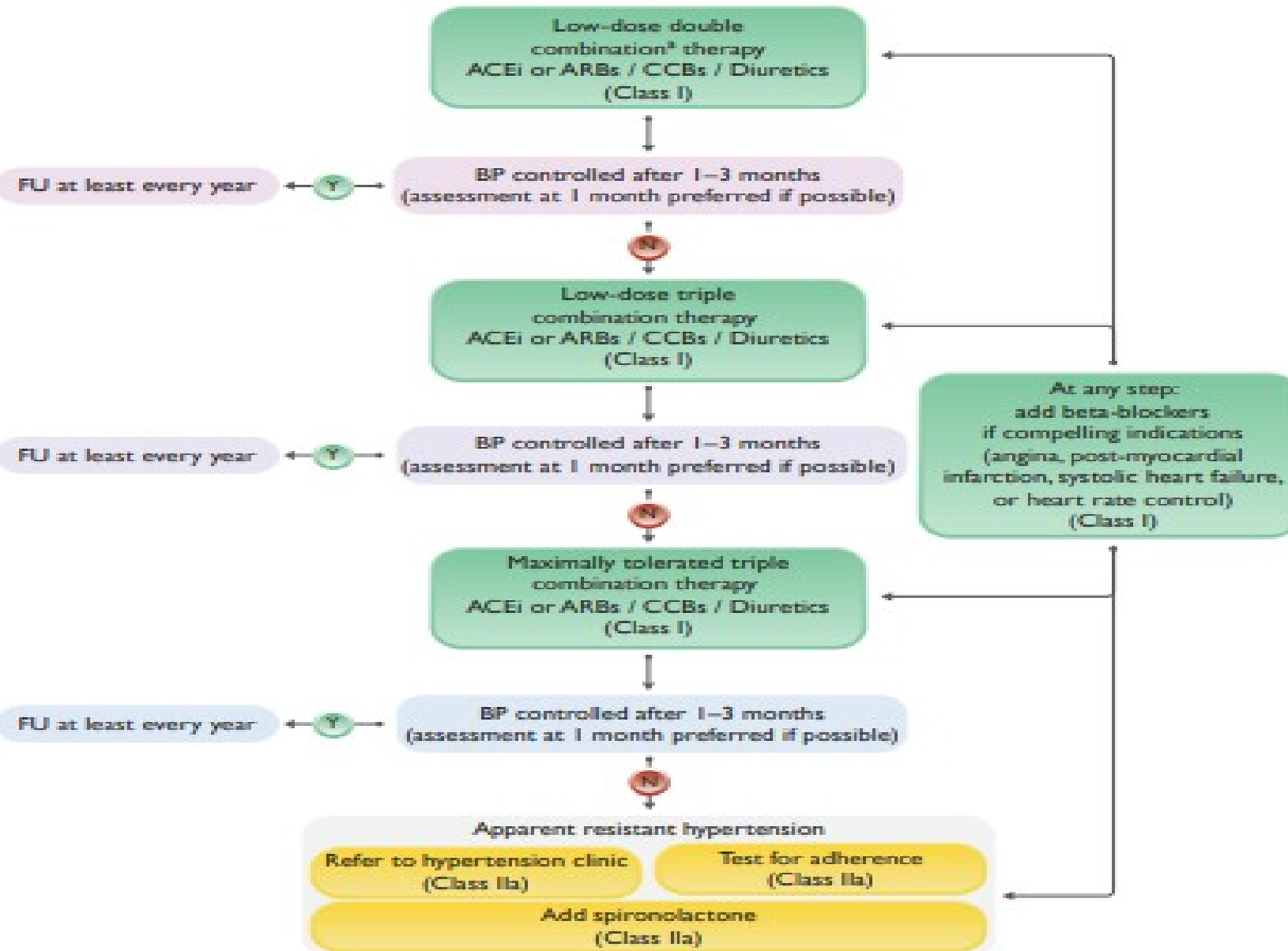
Side-Effect

- In 33 trial arms two drugs together caused symptoms which was significantly lower than the value expected with an additive effect.
- One drug does not therefore potentiate the adverse effects of another.

**Value of low dose combination treatment
with blood pressure lowering drugs: analysis
of 354 randomised trials, BMJ, 2003**

***Initial monotherapy preferred**

- Elevated BP category (120/70–139/89 mmHg)
- Moderate-to-severe frailty
- Symptomatic orthostatic hypotension
- Age ≥ 85 years



Recommendations for Choice of Initial Monotherapy Versus Initial Combination Drug Therapy*

COR	LOE	RECOMMENDATIONS
I	C-EO	1. 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.
IIa	C-EO	2. 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.

*Fixed-dose combination antihypertensive medications are listed in [Online Data Supplement D](#).

Conclusion

- CVD risk begins below thresholds used to define hypertension and the risk increases with higher blood pressure levels
- BP lowering can significantly reduce major cardiovascular outcomes
- The major drug classes with robust evidence for BP-mediated reduction in CVD events should be used as first line agents.
- Combining drugs from different drug classes can have additive or synergistic effects and lead to greater BP reduction.
- The lower the BP the better.