In the name of God

Update on Management of HTN in Adults With Type 2 Diabetes Mellitus

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Case-Study-1

- L.N. is a 49-year-old white woman with a history of type 2 diabetes,obesity, hypertension, and migraine headaches. The patient was diagnosed with type 2 diabetes 9 years ago when she presented with mild polyuria and polydipsia.
- Initial treatment for her diabetes consisted of an oral sulfonylurea with metformin. Her diabetes has been under fair control with a most recent hemoglobin A_{1c} of 7.4%.
- Hypertension was diagnosed 5 years ago when blood pressure (BP) measured in the office was noted to be consistently elevated in the range of 160/90 mmHg on three occasions. L.N. was initially treated with valsartan, starting at 80mg daily and increasing to 160 mg daily, yet her BP control has fluctuated.

Cont…

- One year ago, microalbuminuria was detected on an annual urine screen, with 194 mg/dl of microalbumin identified on a spot urine sample. L.N. comes into the office today for her usual follow-up visit for diabetes. Physical examination reveals an obese woman with a BP of 154/86 mmHg
- **Questions**

1. What are the effects of controlling BP in people with diabetes?
2. What is the target BP for patients with diabetes and hypertension?
3. Which antihypertensive agents are recommended for patients with diabetes?

Introduction

- Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of morbidity and mortality for individuals with diabetes and results in an estimated $37.3 billion in cardiovascular-related spending per year associated with diabetes
- Common conditions coexisting with type 2 diabetes (e.g., hypertension and dyslipidemia) are clear risk factors for ASCVD, and diabetes itself confers independent risk
- Numerous studies have shown the efficacy of controlling individual cardiovascular risk factors in preventing or slowing ASCVD in people with diabetes. Furthermore, large benefits are seen when multiple cardiovascular risk factors are addressed simultaneously

Cardiometabolic Risk Factors

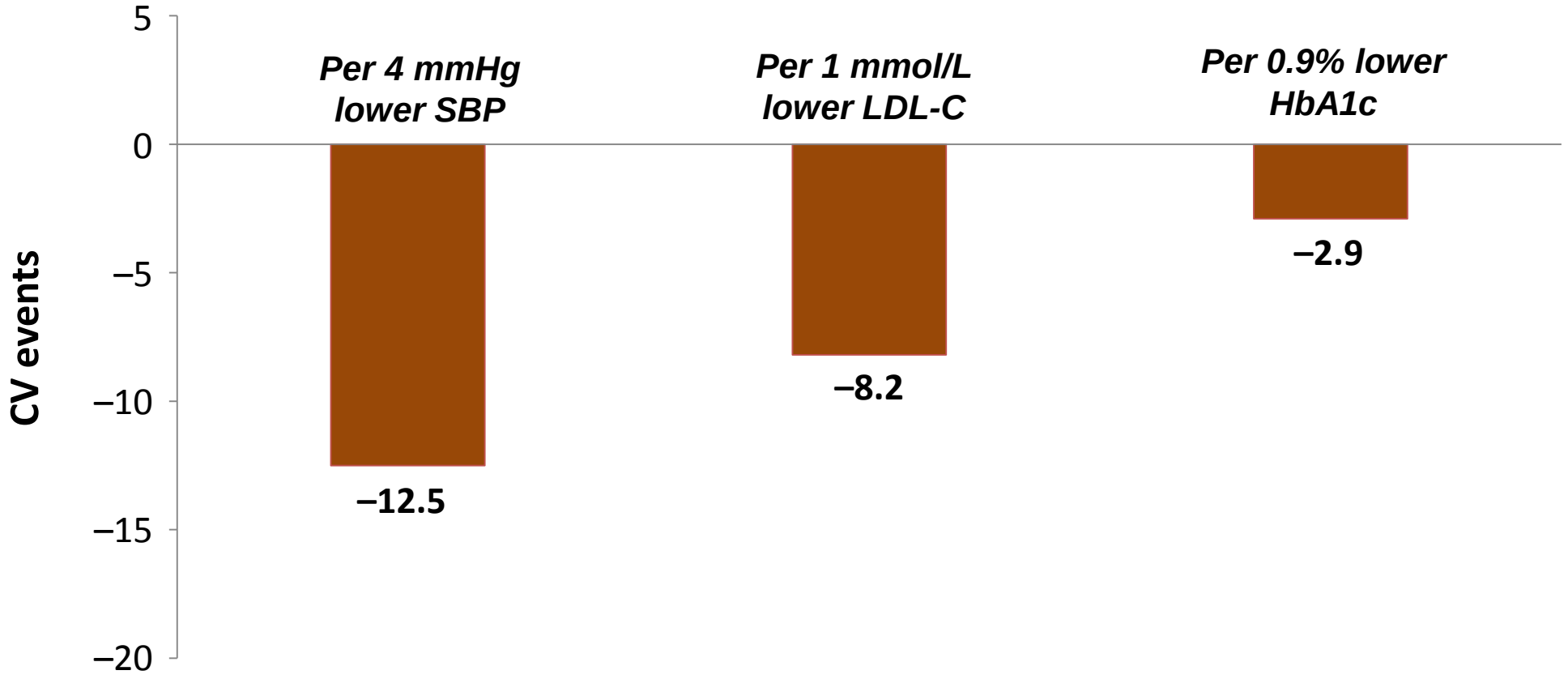
Modifiable

- Overweight
- Abnormal lipid metabolism
- Inflammation, hypercoagulation
- Hypertension
- Smoking
- Physical inactivity
- Unhealthy diet
- Insulin resistance

Non-modifiable

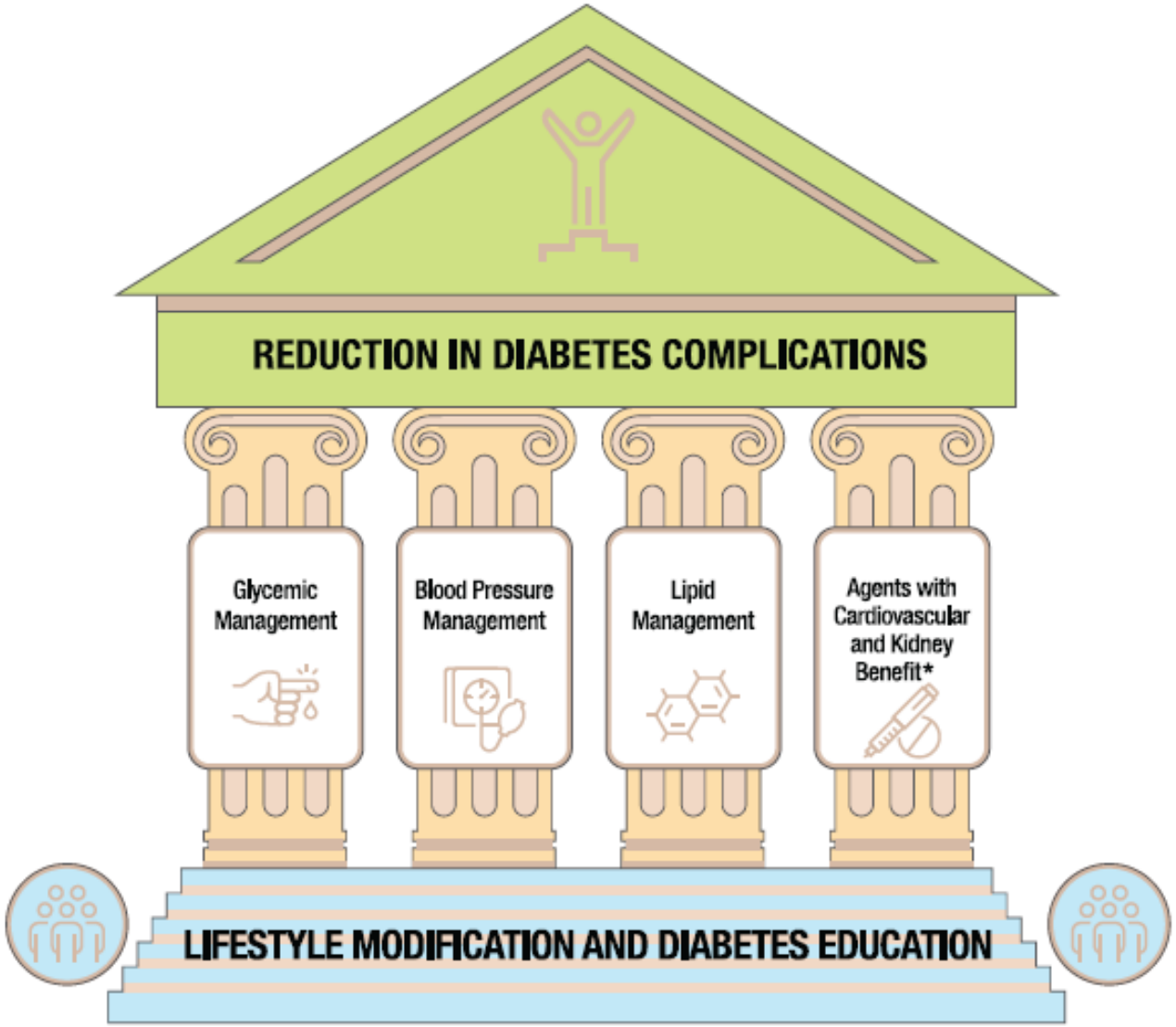
- Age
- Race/ethnicity
- Gender
- Family history

Benefit of different interventions per 200 individuals with diabetes treated for 5 years



Ray KK, et al. Lancet. 2009;373:1765–72

Multifactorial approach to reduction in risk of diabetes complications



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Recommendations:

- Blood pressure should be measured at every routine clinical visit. Patients found to have elevated blood pressure (≥130/80 mmHg) should have blood pressure confirmed using multiple readings, including measurements on a separate day, to diagnose hypertension. A
- Patients with blood pressure ≥ 180/110 mmHg and cardiovascular disease could be diagnosed with hypertension at a single visit. E
- All hypertensive patients with diabetes should monitor their blood pressure at home. (white coat or masked hypertension). A

Treatment Goals , ADA 2024

- Blood pressure targets should be individualized through a shared decision-making process that addresses cardiovascular risk, potential adverse effects of antihypertensive medications, and patient preferences. B

- People with diabetes and hypertension qualify for antihypertensive drug therapy when the blood pressure is persistently elevated ≥130/80 mmHg. B

- The on-treatment target blood pressure goal is <130/80 mmHg, if it can be safely attained. B

Treatment Goals , ADA 2024

- In pregnant individuals with diabetes and chronic hypertension, a blood pressure threshold of 140/90 mmHg (no less than 90/60) for initiation or titration of therapy is associated with better pregnancy outcomes. A

- In pregnant patients with diabetes and preexisting hypertension, a blood pressure target of 110–135/85 mmHg is suggested in the interest of reducing the risk for accelerated maternal hypertension. A

In type 1 diabetes,

hypertension is often the result of underlying nephropathy, while in type 2 diabetes it usually coexists with other cardiometabolic risk factors.

There is an absence of high-quality data available to guide blood pressure targets in type 1 diabetes

JAMA. 2015 Feb 10;313(6):603-15. Blood pressure lowering in type 2 diabetes: a systematic review and meta-analysis.

- **OBJECTIVE:** To determine the associations between BP-lowering treatment and vascular disease in type 2 diabetes.
- **DATA SOURCES AND STUDY SELECTION:** We searched MEDLINE for large-scale randomized controlled trials of BP-lowering treatment including patients with diabetes, published between January 1966 and October 2014.
- **MAIN OUTCOMES AND MEASURES:** All-cause mortality, cardiovascular events, coronary heart disease events, stroke, heart failure, retinopathy, new or worsening albuminuria, and renal failure.

JAMA. 2015 Feb 10;313(6):603-15. Blood pressure lowering in type 2 diabetes: a systematic review and meta-analysis.

- **RESULTS:** 100,354 participants were included.

Each 10-mm Hg lower systolic BP was associated with a significantly lower risk of :

- Mortality (relative risk [RR], 0.87; 95% CI, 0.78-0.96); 13% ↓
- CVD(RR, 0.89 [95% CI, 0.83-0.95]; 11% ↓
- CHD(RR, 0.88 [95% CI, 0.80-0.98]; 12% ↓
- **Stroke (RR, 0.73 [95% CI, 0.64-0.83]; 27% ↓**
- Albuminuria (RR, 0.83 [95% CI, 0.79-0.87]; 17% ↓
- Retinopathy (RR, 0.87 [95% CI, 0.76-0.99]; 13% ↓
- When trials were stratified by mean baseline ,lower RRs observed among those with baseline BP of ≥ 140 mm Hg

Tight BP Control : Large RCTs

Table 9.1—Randomized controlled trials of intensive versus standard hypertension treatment strategies

Clinical trial	Population	Intensive	Standard	Outcomes
ACCORD BP (16)	4,733 participants with T2D aged 40–79 years with prior evidence of CVD or multiple cardiovascular risk factors	Systolic blood pressure target: <120 mmHg Achieved (mean) systolic/diastolic: 119.3/64.4 mmHg	Systolic blood pressure target: 130–140 mmHg Achieved (mean) systolic/diastolic: 133.5/70.5 mmHg	• No benefit in primary end point: composite of nonfatal MI, nonfatal stroke, and CVD death • Stroke risk reduced 41% with intensive control, not sustained through follow-up beyond the period of active treatment • Adverse events more common in intensive group, particularly elevated serum creatinine and electrolyte abnormalities
ADVANCE BP (17)	11,140 participants with T2D aged 55 years and older with prior evidence of CVD or multiple cardiovascular risk factors	Intervention: a single-pill, fixed-dose combination of perindopril and indapamide Achieved (mean) systolic/diastolic: 136/73 mmHg	Control: placebo Achieved (mean) systolic/diastolic: 141.6/75.2 mmHg	• Intervention reduced risk of primary composite end point of major macrovascular and microvascular events (9%), death from any cause (14%), and death from CVD (18%) • 6-year observational follow-up found reduction in risk of death in intervention group attenuated but still significant (142)
HOT (143)	18,790 participants, including 1,501 with diabetes	Diastolic blood pressure target: ≤80 mmHg	Diastolic blood pressure target: ≤90 mmHg	• In the overall trial, there was no cardiovascular benefit with more intensive targets • In the subpopulation with diabetes, an intensive diastolic target was associated with a significantly reduced risk (51%) of CVD events

SPRINT (43)	9,361 participants without diabetes	SBP target: <120 mmHg Achieved (mean): 121.4 mmHg	SBP target: <140 mmHg Achieved (mean): 136.2 mmHg	• Intensive SBP target lowered risk of the primary composite outcome 25% (MI, ACS, stroke, heart failure, and death due to CVD) • Intensive target reduced risk of death 27% • Intensive therapy increased risks of electrolyte abnormalities and AKI
STEP (34)	8,511 participants aged 60–80 years, including 1,627 with diabetes	SBP target: <130 mmHg Achieved (mean): 127.5 mmHg	SBP target: <150 mmHg Achieved (mean): 135.3 mmHg	• Intensive SBP target lowered risk of the primary composite outcome 26% (stroke, ACS [acute MI and hospitalization for unstable angina], acute decompensated heart failure, coronary revascularization, atrial fibrillation, or death from cardiovascular causes) • Intensive target reduced risk of cardiovascular death 28% • Intensive therapy increased risks of hypotension

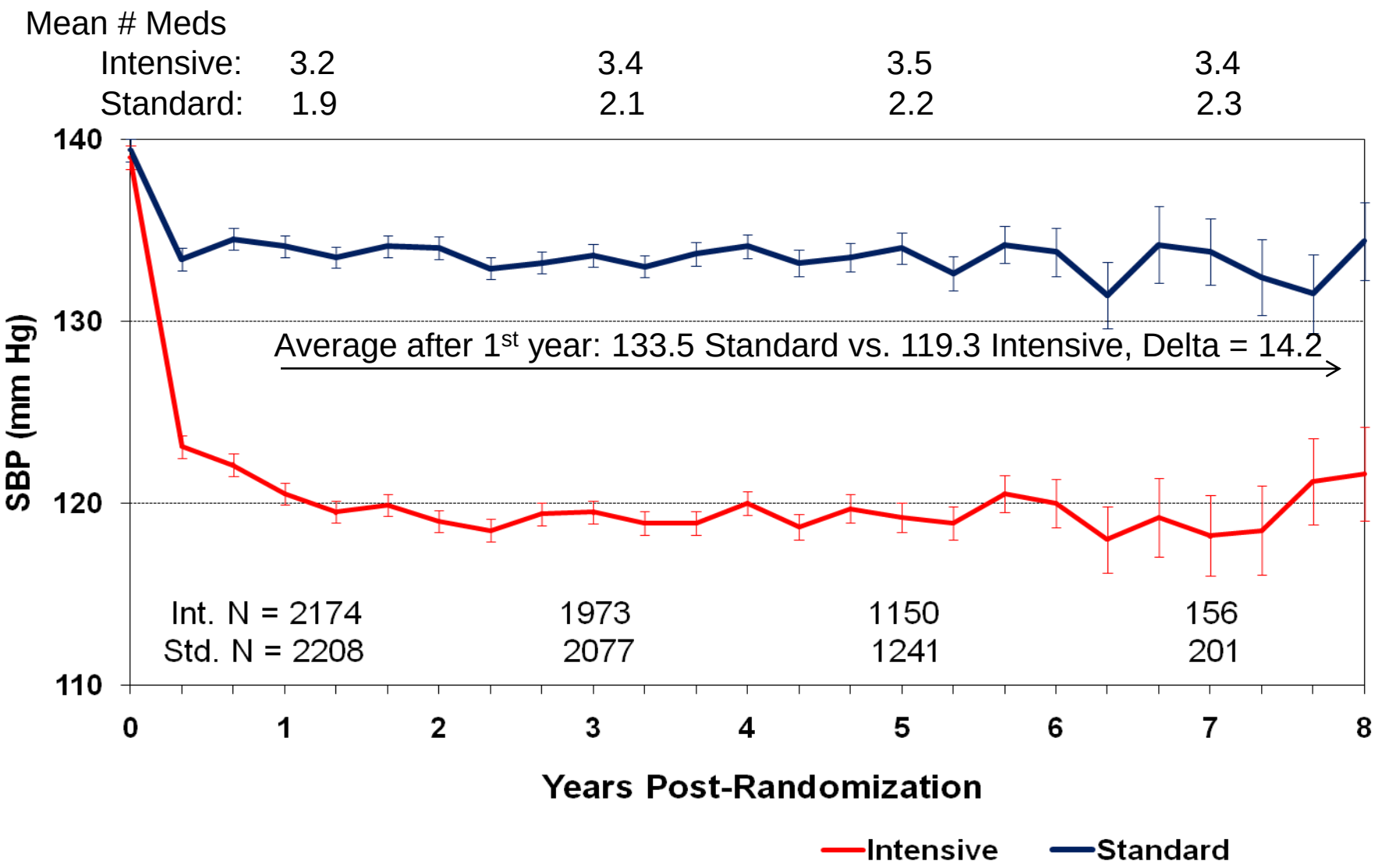
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus

The ACCORD Study Group*

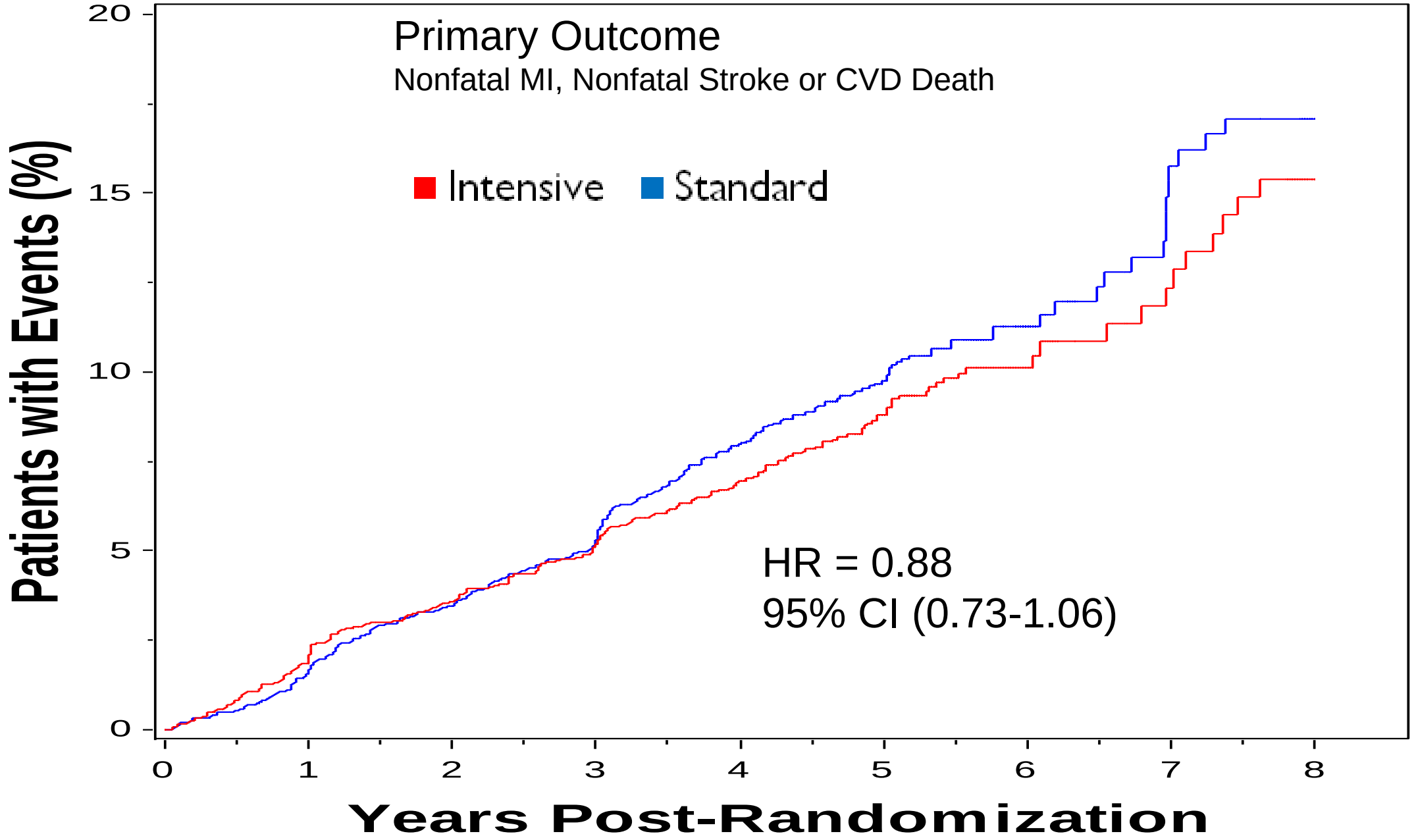
Systolic Pressures (mean + 95% CI)



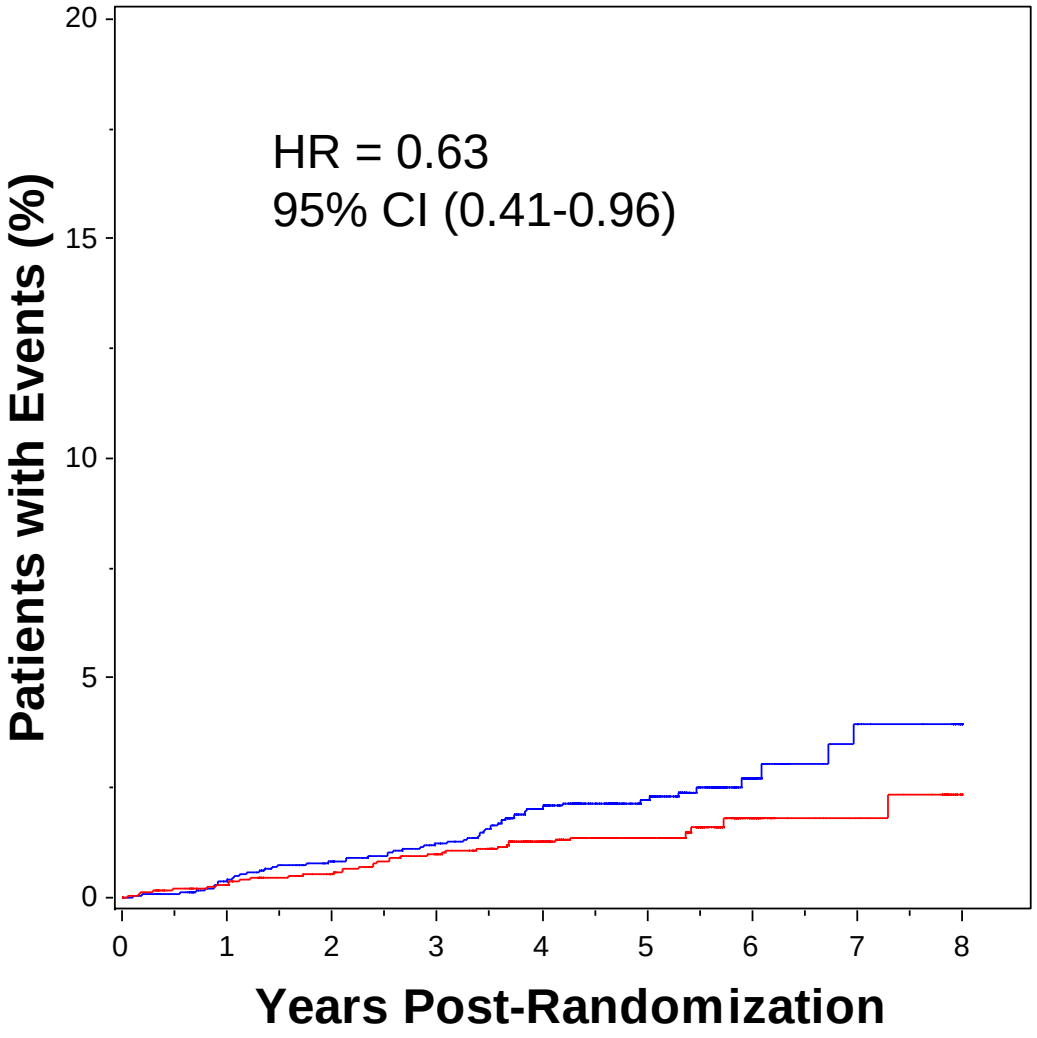
Primary & Secondary Outcomes

	Intensive Events (%/yr)	Standard Events (%/yr)	HR (95% CI)	P
Primary	208 (1.87)	237 (2.09)	0.88 (0.73-1.06)	0.20
Total Mortality	150 (1.28)	144 (1.19)	1.07 (0.85-1.35)	0.55
Cardiovascular Deaths	60 (0.52)	58 (0.49)	1.06 (0.74-1.52)	0.74
Nonfatal MI	126 (1.13)	146 (1.28)	0.87 (0.68-1.10)	0.25
Nonfatal Stroke	34 (0.30)	55 (0.47)	0.63 (0.41-0.96)	0.03
Total Stroke	36 (0.32)	62 (0.53)	0.59 (0.39-0.89)	0.01

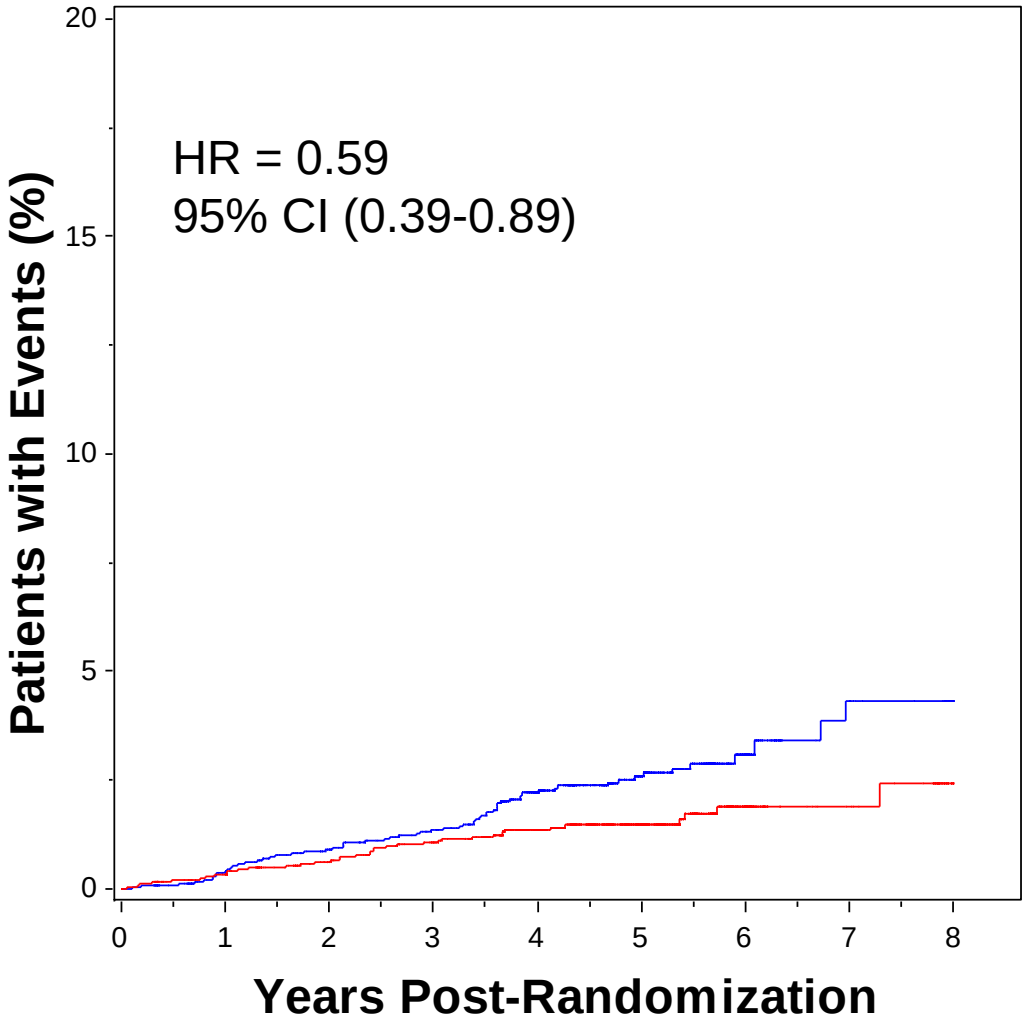
Also examined Fatal/Nonfatal HF (HR=0.94, p=0.67), a composite of fatal coronary events, nonfatal MI and unstable angina (HR=0.94, p=0.50) and a composite of the primary outcome, revascularization and unstable angina (HR=0.95, p=0.40)


Primary Outcome
Nonfatal MI, Nonfatal Stroke or CVD Death
Intensive
Standard
HR = 0.88
95% CI (0.73-1.06)
Patients with Events (%)
0
5
10
15
20
0
1
2
3
4
5
6
7
8
Years Post-Randomization

Nonfatal Stroke



Total Stroke



Intensive Standard

Stroke Results

- Intensive BP management reduced the rate of two closely correlated secondary end points: total stroke (p=0.01) and nonfatal stroke (p=0.03)

Assuming that this finding was real, the **number needed** to treat to the lower SBP level to prevent one stroke over 5 years was **89**

Conclusions

- The ACCORD BP trial evaluated the effect of targeting a SBP goal of 120 mm Hg, compared to a goal of 140 mm Hg, in patients with type 2 diabetes at increased cardiovascular risk.

- The results provide **no conclusive evidence** that the intensive BP control strategy reduces the rate of a composite of major CVD events in such patients.

Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial): a randomised controlled trial

ADVANCE Collaborative Group*

We assessed the effects of the routine administration of an angiotensin converting enzyme (ACE) inhibitor-diuretic combination on serious vascular events in patients with diabetes, irrespective of initial blood pressure levels or the use of other blood pressure lowering drugs.

The primary endpoints were composites of major macrovascular and microvascular events, defined as death from CVD analysis ,non-fatal stroke or non-fatal MI, and new or worsening renal or diabetic eye disease, and was by intention-to-treat.

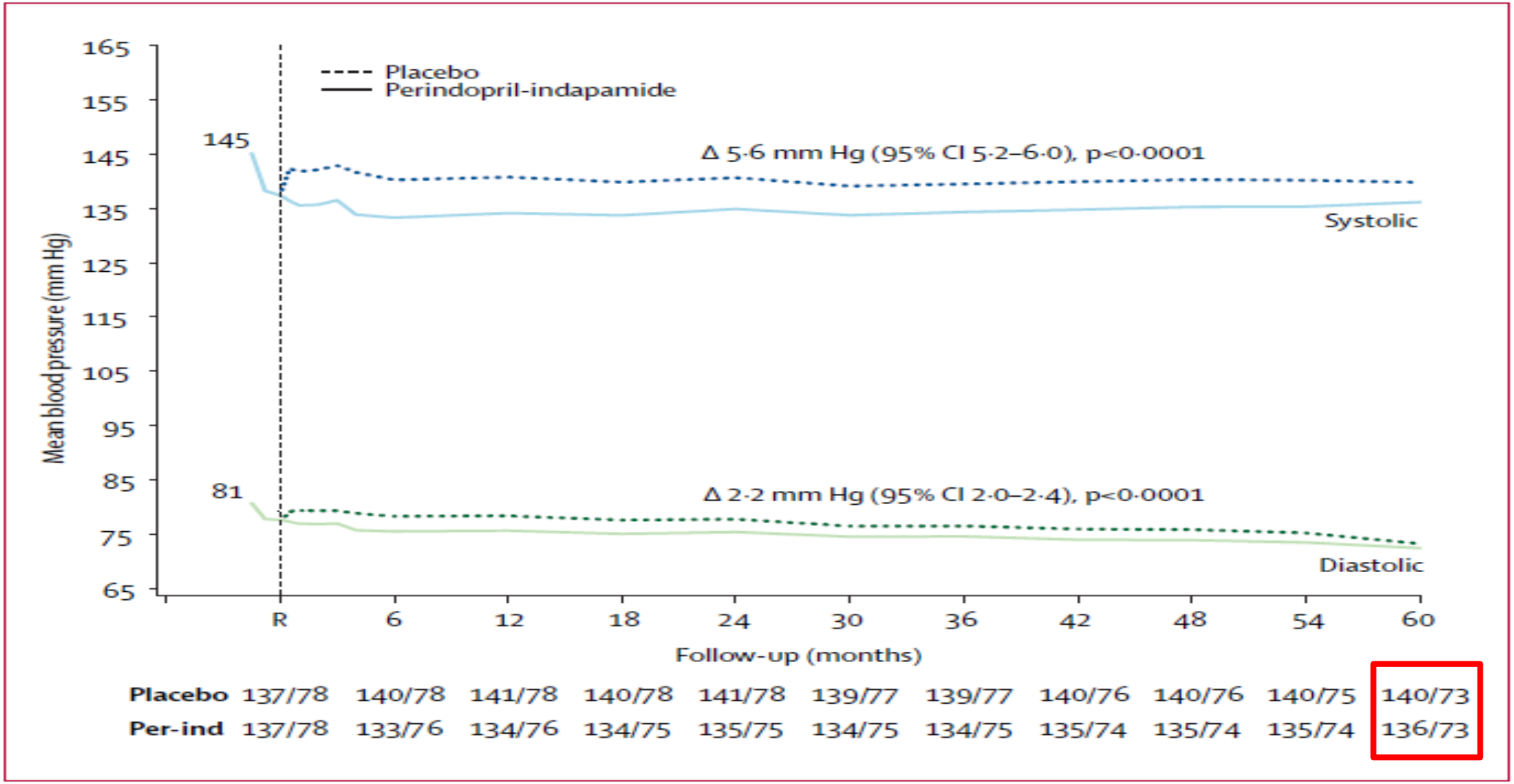
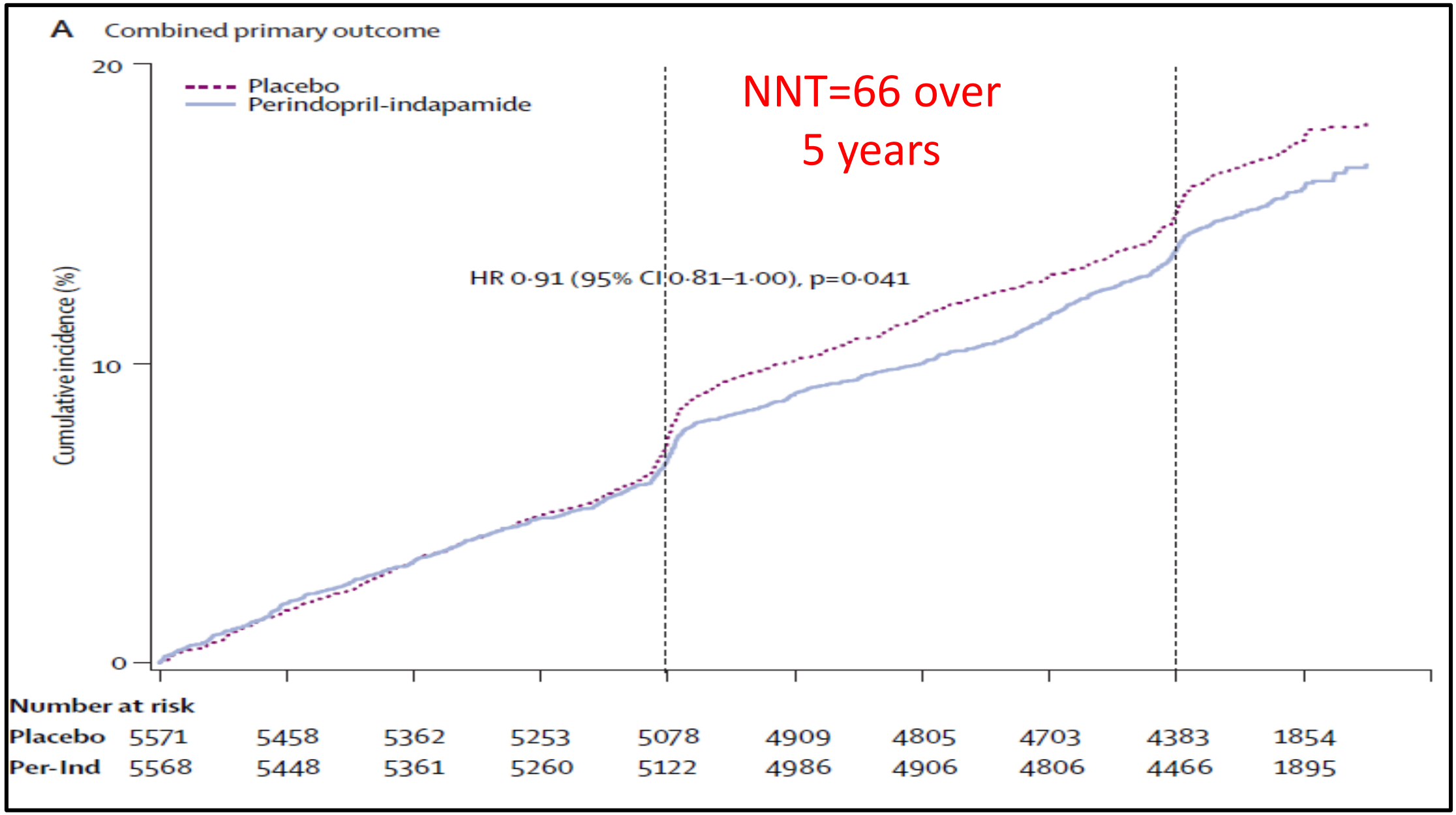
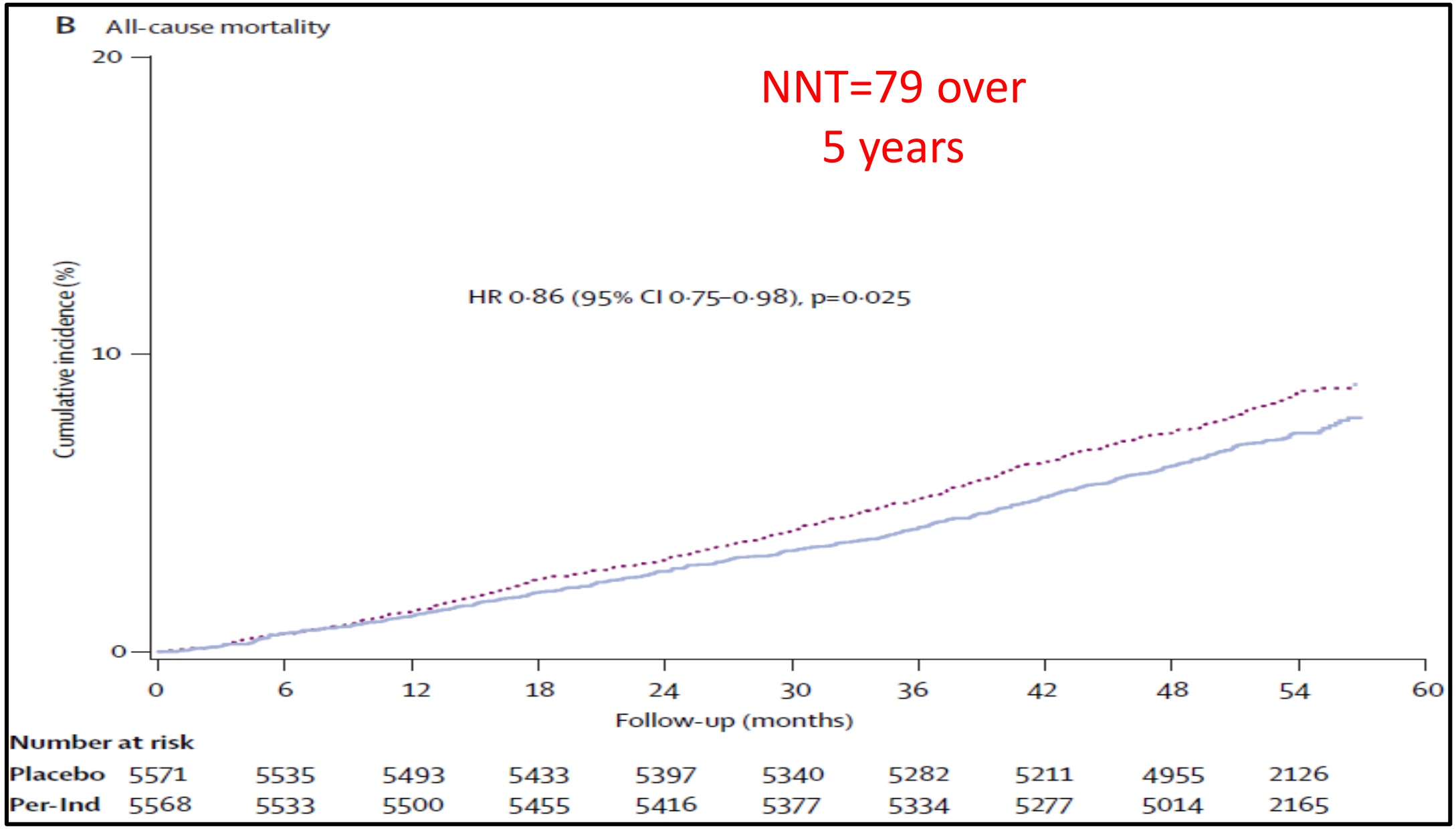


Figure 2: **Mean systolic and diastolic blood pressure during run-in on active treatment and after randomisation to active treatment or placebo**

Δ=average difference between randomised groups during follow-up. R=randomisation. Per-ind=perindopril-indapamide.


A Combined primary outcome
Placebo
Perindopril-indapamide
NNT=66 over
5 years
HR 0·91 (95% CI 0·81–1·00), p=0·041
Cumulative incidence (%)
20
10
0
Number at risk
Placebo 5571 5458 5362 5253 5078 4909 4805 4703 4383 1854
Per-Ind 5568 5448 5361 5260 5122 4986 4906 4806 4466 1895


B All-cause mortality
NNT=79 over
5 years
HR 0·86 (95% CI 0·75–0·98), p=0·025
Cumulative incidence (%)
20
10
0
0
6
12
18
24
30
36
42
48
54
60
Follow-up (months)
Number at risk
Placebo 5571 5535 5493 5433 5397 5340 5282 5211 4955 2126
Per-Ind 5568 5533 5500 5455 5416 5377 5334 5277 5014 2165

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Follow-up of Blood-Pressure Lowering and Glucose Control in Type 2 Diabetes

S. Zoungas, J. Chalmers, B. Neal, L. Billot, Q. Li, Y. Hirakawa, H. Arima, H. Monaghan, R. Joshi, S. Colagiuri, M.E. Cooper, P. Glasziou, D. Grobbee, P. Hamet, S. Harrap, S. Heller, L. Lisheng, G. Mancia, M. Marre, D.R. Matthews, C.E. Mogensen, V. Perkovic, N. Poulter, A. Rodgers, B. Williams, S. MacMahon, A. Patel, and M. Woodward, for the ADVANCE-ON Collaborative Group*

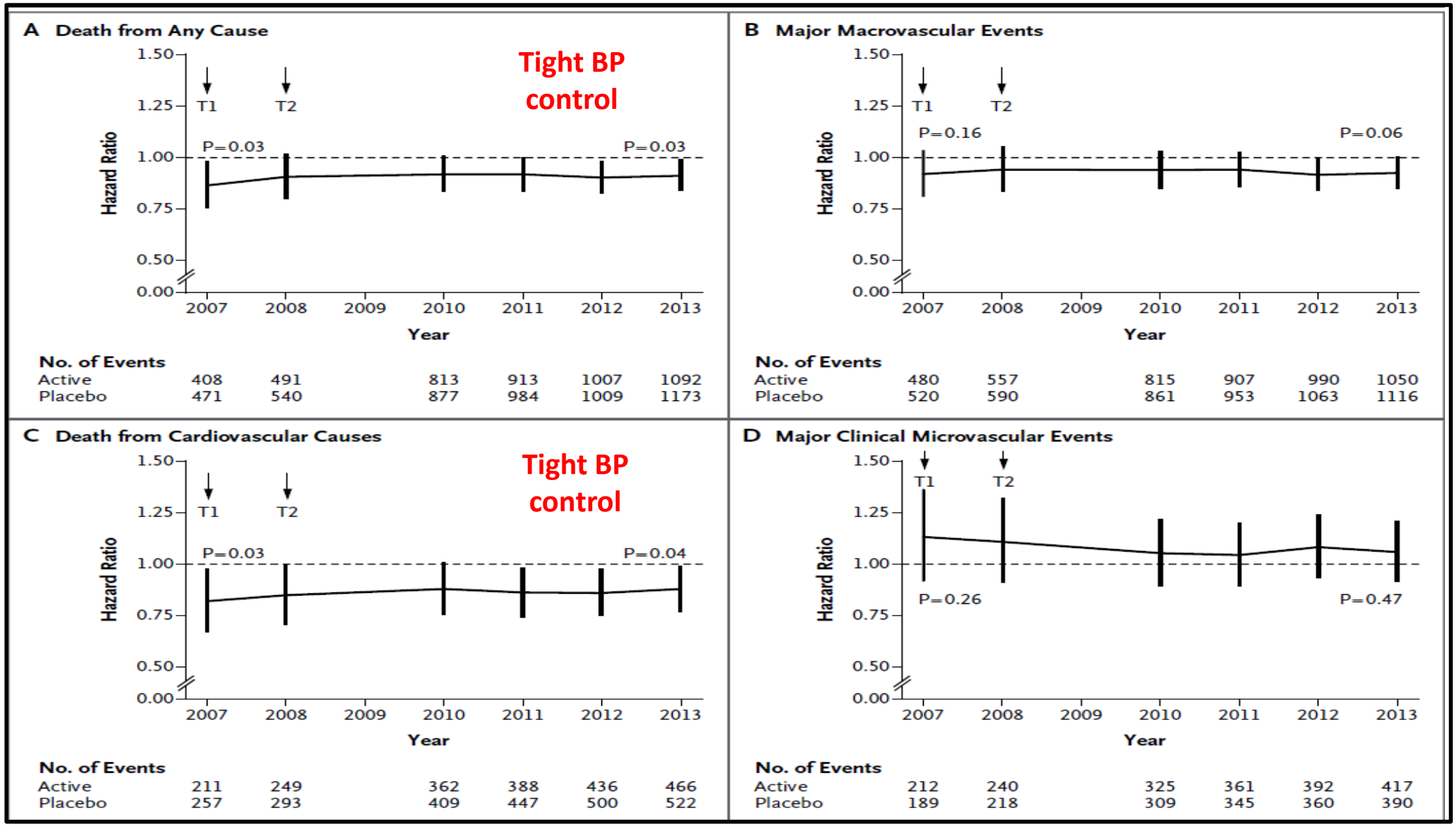
ABSTRACT

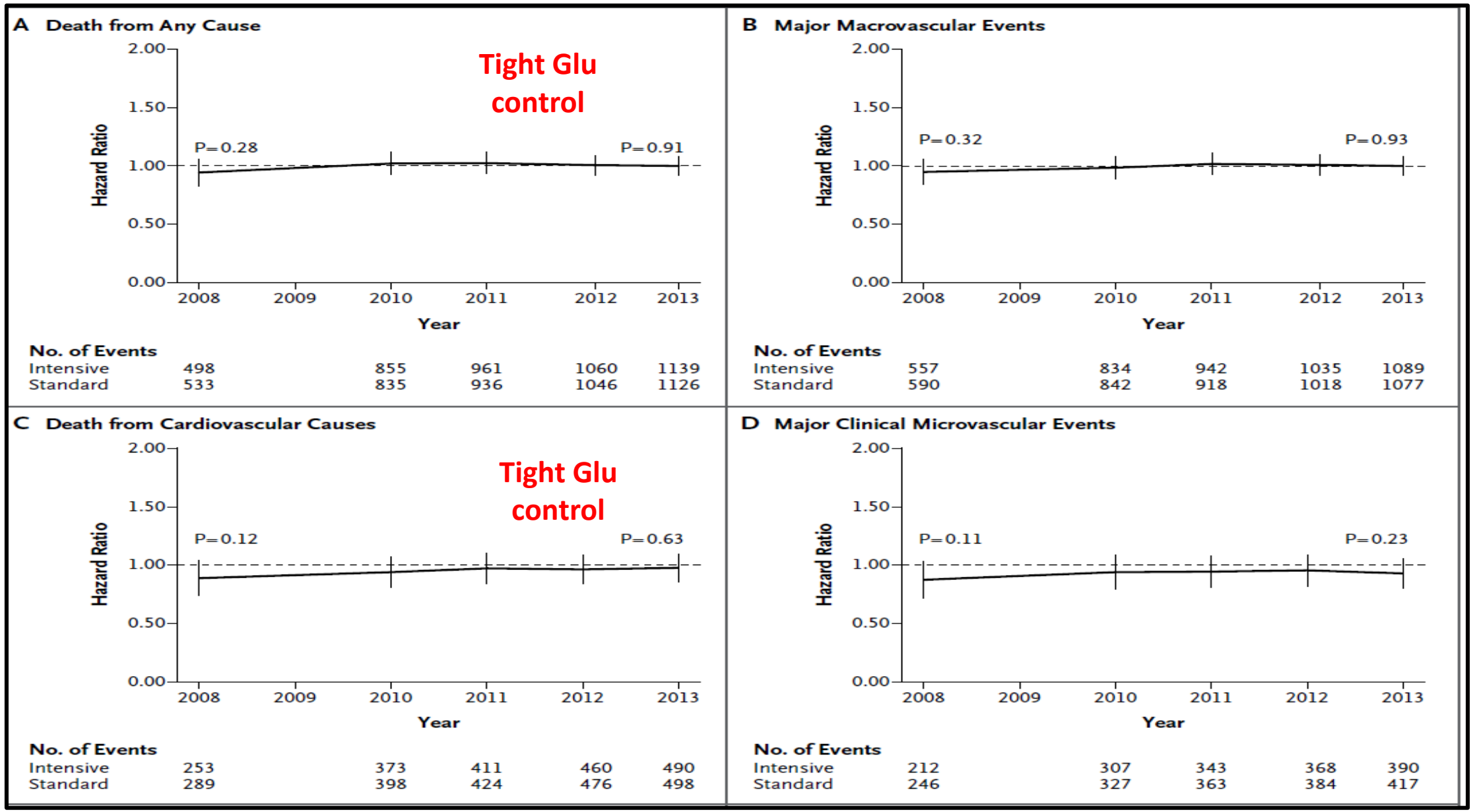
BACKGROUND

In the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) factorial trial, the combination of perindopril and indapamide reduced mortality among patients with type 2 diabetes, but intensive glucose control, targeting a glycated hemoglobin level of less than 6.5%, did not. We now report results of the 6-year post-trial follow-up.

METHODS

We invited surviving participants, who had previously been assigned to perindopril–indapamide or placebo and to intensive or standard glucose control (with the glucose-control comparison extending for an additional 6 months), to participate in a post-trial follow-up evaluation. The primary end points were death from any cause and major macrovascular events.


A Death from Any Cause
Tight BP control
Hazard Ratio
1.50
1.25
1.00
0.75
0.50
0.00
T1
T2
P=0.03
P=0.03
2007
2008
2009
2010
2011
2012
2013
Year
No. of Events
Active 408 491 813 913 1007 1092
Placebo 471 540 877 984 1009 1173
B Major Macrovascular Events
Hazard Ratio
T1
T2
P=0.16
P=0.06
Year
No. of Events
Active 480 557 815 907 990 1050
Placebo 520 590 861 953 1063 1116
C Death from Cardiovascular Causes
Tight BP control
Hazard Ratio
T1
T2
P=0.03
P=0.04
Year
No. of Events
Active 211 249 362 388 436 466
Placebo 257 293 409 447 500 522
D Major Clinical Microvascular Events
Hazard Ratio
T1
T2
P=0.26
P=0.47
Year
No. of Events
Active 212 240 325 361 392 417
Placebo 189 218 309 345 360 390


A Death from Any Cause
Tight Glu control
Hazard Ratio
2.00
1.50
1.00
0.50
0.00
P=0.28
P=0.91
2008
2009
2010
2011
2012
2013
Year
No. of Events
Intensive 498 855 961 1060 1139
Standard 533 835 936 1046 1126
B Major Macrovascular Events
Hazard Ratio
2.00
1.50
1.00
0.50
0.00
P=0.32
P=0.93
2008
2009
2010
2011
2012
2013
Year
No. of Events
Intensive 557 834 942 1035 1089
Standard 590 842 918 1018 1077
C Death from Cardiovascular Causes
Tight Glu control
Hazard Ratio
2.00
1.50
1.00
0.50
0.00
P=0.12
P=0.63
2008
2009
2010
2011
2012
2013
Year
No. of Events
Intensive 253 373 411 460 490
Standard 289 398 424 476 498
D Major Clinical Microvascular Events
Hazard Ratio
2.00
1.50
1.00
0.50
0.00
P=0.11
P=0.23
2008
2009
2010
2011
2012
2013
Year
No. of Events
Intensive 212 307 343 368 390
Standard 246 327 363 384 417

Meta-Analyses of RCTs

ADA 2024

- Based on these analyses, antihypertensive treatment appears to be beneficial when mean baseline blood pressure is ≥140/90 mmHg

- More intensive reduction to <130 mmHg was associated with a further reduction in stroke, retinopathy, and albuminuria, but not other cardiovascular events

Individualization of Treatment Targets

Specific factors to consider are
1. Absolute risk of cardiovascular events
2. Risk of progressive kidney disease, as reflected by albuminuria,
3. Adverse effects (hypotension, syncope, falls, acute kidney injury, and electrolyte abnormalities)
4. Age
5. Overall treatment burden

- Patients who patients with diabetes and either clinically diagnosed ASCVD (particularly stroke) or 10-year ASCVD risk ≥15%, if it can be attained safely may be best suited to intensive blood pressure control (<130/80 mmHg)

Diabetes Care 2017;40:1273–1284

Individualization of Treatment Targets

- In contrast, patients with conditions more common in older adults, such as functional limitations, polypharmacy, multimorbidity , loss of autonomy and orthostatic hypotension may be best suited to less intensive blood pressure control. (higher SBP goals should be considered)

- Patients with low absolute cardiovascular risk (10-year ASCVD risk <15%) or with a history of adverse effects of intensive blood pressure control or at high risk of adverse effects should have a higher blood pressure target. In such patients, a blood pressure target of <140/90 mmHg is recommended, if it can be safely attained.

Diabetes Care 2020;40:1273–1284

Treatment Strategies

- **Nonpharmacological therapy** is reasonable in individuals with diabetes and mildly elevated BP (>120/80 mmHg).
- Smoking cessation
- Weight reduction (The loss of 1 kg in body weight has been associated with a decrease in blood pressure of 1 mmHg)
- Increase physical activity
- moderation of alcohol intake
- Psychological factors and stress
- Dietary changesDietary Approaches to Stop Hypertension (DASH)-style eating pattern

- reducing sodium(<2,300 mg per day),
- increasing potassium intake
- vegetables (8–10 servings per day)
- low-fat dairy products (2–3 servings per day)

Look medication lists for agents that may raise blood pressure, including over-the-counter and herbal ones.
NSIAD drugs increase systolic blood pressure on average by 5 mmHg

Pharmacologic Antihypertensive Treatment

Combination therapy and management of REFRACTORY hypertension among diabetic patients

ADA 2024

- Patients with **confirmed office-based blood pressure ≥130/80** mmHg should, in addition to lifestyle therapy, have prompt initiation and timely titration of pharmacologic therapy. A
- Patients with **confirmed office-based blood pressure ≥150/90** mmHg should, in addition to lifestyle therapy, have prompt initiation and timely titration of two drugs or a single-pill combination of drugs. A

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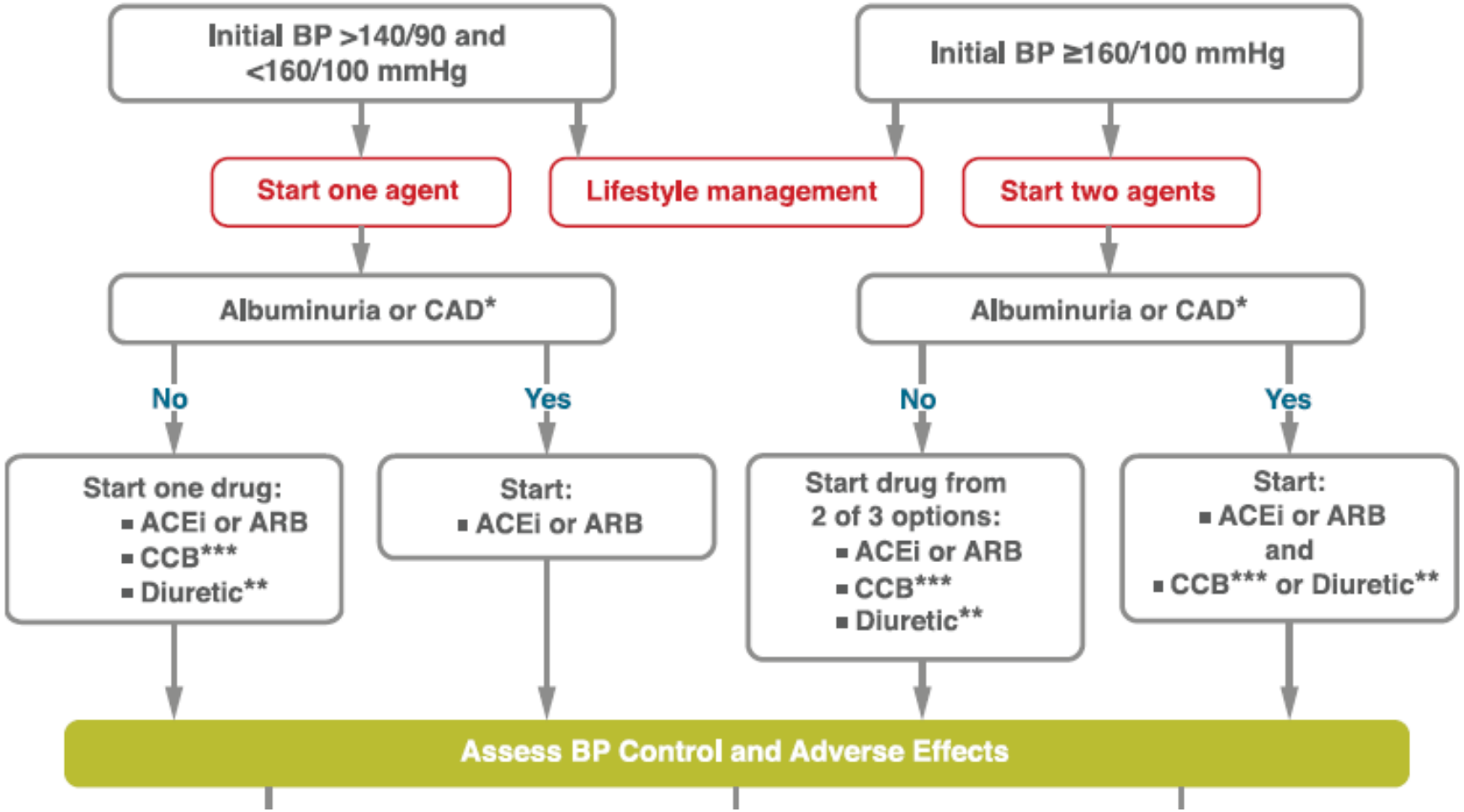
- Treatment for hypertension should include drug classes demonstrated to reduce cardiovascular events in patients with diabetes. A
- ACE inhibitors or angiotensin receptor blockers are recommended first-line therapy for hypertension in people with diabetes and coronary artery disease. A
- Multiple-drug therapy is generally required to achieve blood pressure targets. However, combinations of ACE inh. and ARB and combinations of ACE inh. or ARB with direct renin inhibitors should not be used. A

ADA 2024

- An ACE inh. or ARB, at the maximum tolerated dose is the recommended first-line treatment for hypertension in patients with diabetes and urinary albumin-to-creatinine ratio ≥300 mg/g creatinine A or 30–299 mg/g creatinine. B If one class is not tolerated, the other should be substituted. B
- For patients treated with an ACE inhibitor, ARB, mineralocorticoid receptor antagonist (MRA), or diuretic, serum creatinine/estimated glomerular filtration rate and serum potassium should be monitored at least annually. B

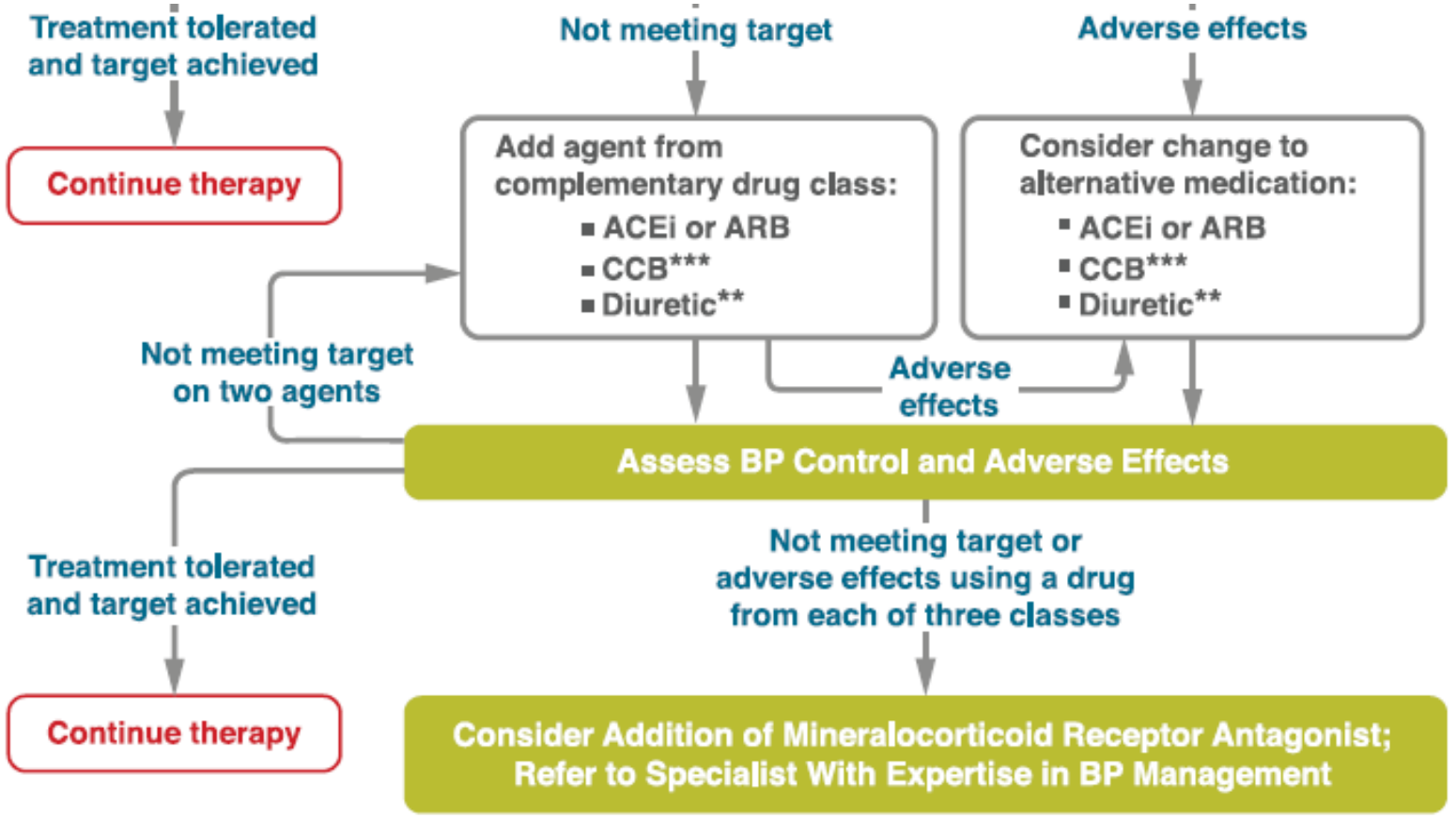
Recommendations



**Thiazide-like diuretic; long-acting agents shown to reduce cardiovascular events, such as chlorthalidone and indapamide, are preferred

***Dihydropyridine calcium channel blocker (CCB)

Recommendations



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- Initial treatment to reduce cardiovascular events in patients with diabetes: ACE inhibitors, angiotensin receptor blockers (ARBs), thiazide-like diuretics, or dihydropyridine calcium channel blockers
- Beta-Blockers are indicated in the setting of prior MI, active angina, or HfrEF but have not been shown to reduce mortality as blood pressure–lowering agents in the absence of these conditions (Among beta blockers, carvedilol, may have certain advantages compared with other beta blockers in patients with diabetes However, bisoprolol and metoprolol extended release are reasonable alternatives)

When RASBs prefer to other medications among patients with type 2 diabetes

- An ACE inhibitor or ARB are recommended first-line therapy for hypertension in people with diabetes and coronary artery disease
- An ACE inhibitor or ARB, at the maximum tolerated dose indicated for blood pressure treatment, is the recommended first-line treatment for hypertension in patients with diabetes and urine albumin-to creatinine ratio ≥300 mg/g creatinine (A) or 30–299 mg/g creatinine (B)

In order to reduce risk of progressive kidney disease

Diabetes Care 2017;40:1273–1284

Diabetes mellitus as a compelling indication for use of renin angiotensin system blockers: systematic review and meta-analysis of randomized trials

Sripal Bangalore,[1] Robert Fakheri,[1] Bora Toklu,[2] Franz H Messerli[3]

ABSTRACT

- **Objective :**To evaluate the outcomes with use of renin angiotensin system (RAS) blockers compared with other antihypertensive agents in people with diabetes.
- **Design**
- **Meta-analysis**
- **Data sources and study selection:** PubMed, Embase, and the Cochrane central register of controlled trials databases for randomized trials of RAS blockers versus other antihypertensive agents in people with diabetes mellitus.
- **Outcomes:** were death, cardiovascular death, myocardial infarction, angina, stroke, heart failure, revascularization, and ESRD.

BMJ. 2016 Feb 11;352:i438.

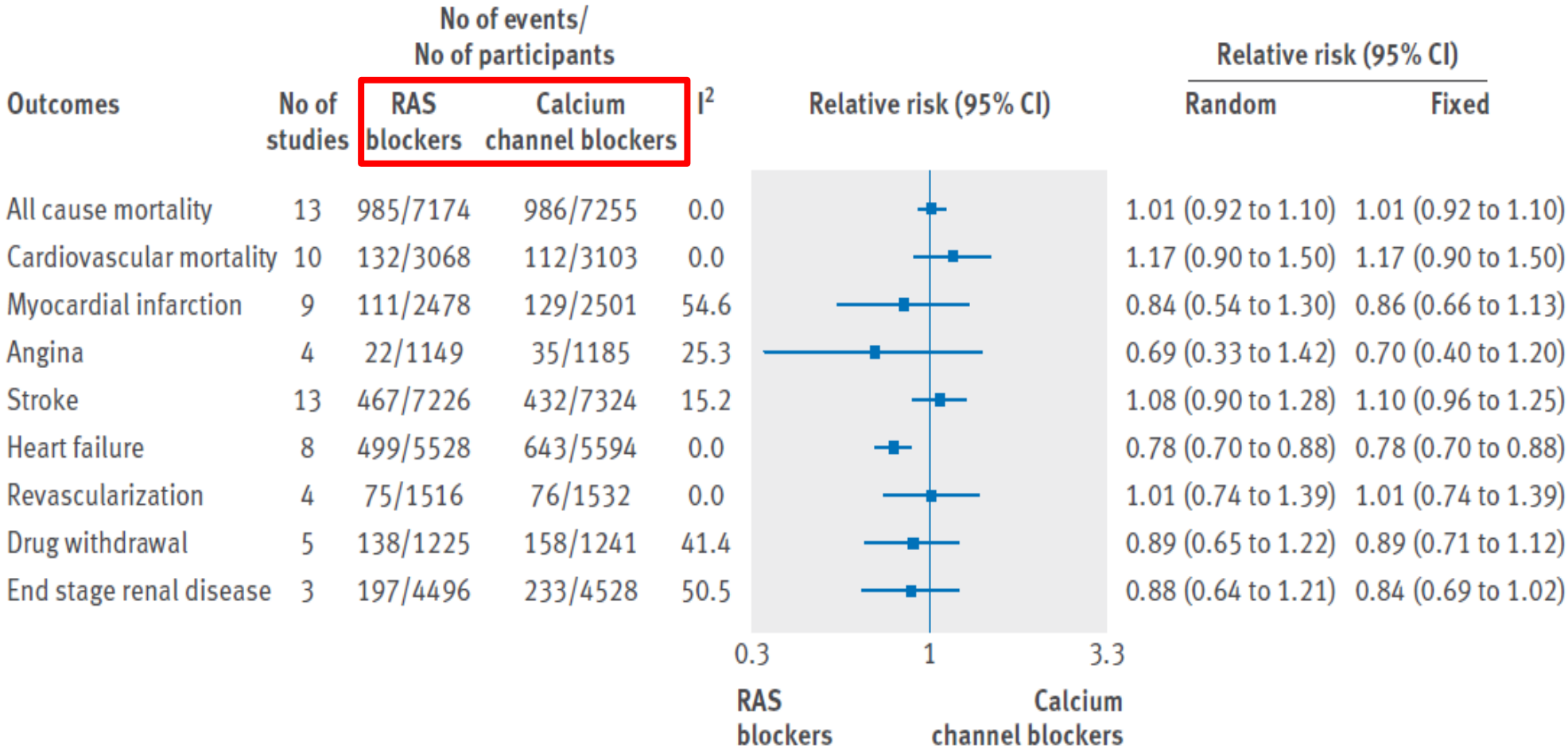

Fig 10 | Outcomes with renin angiotensin system (RAS) blockers compared with calcium channel blockers in people with diabetes

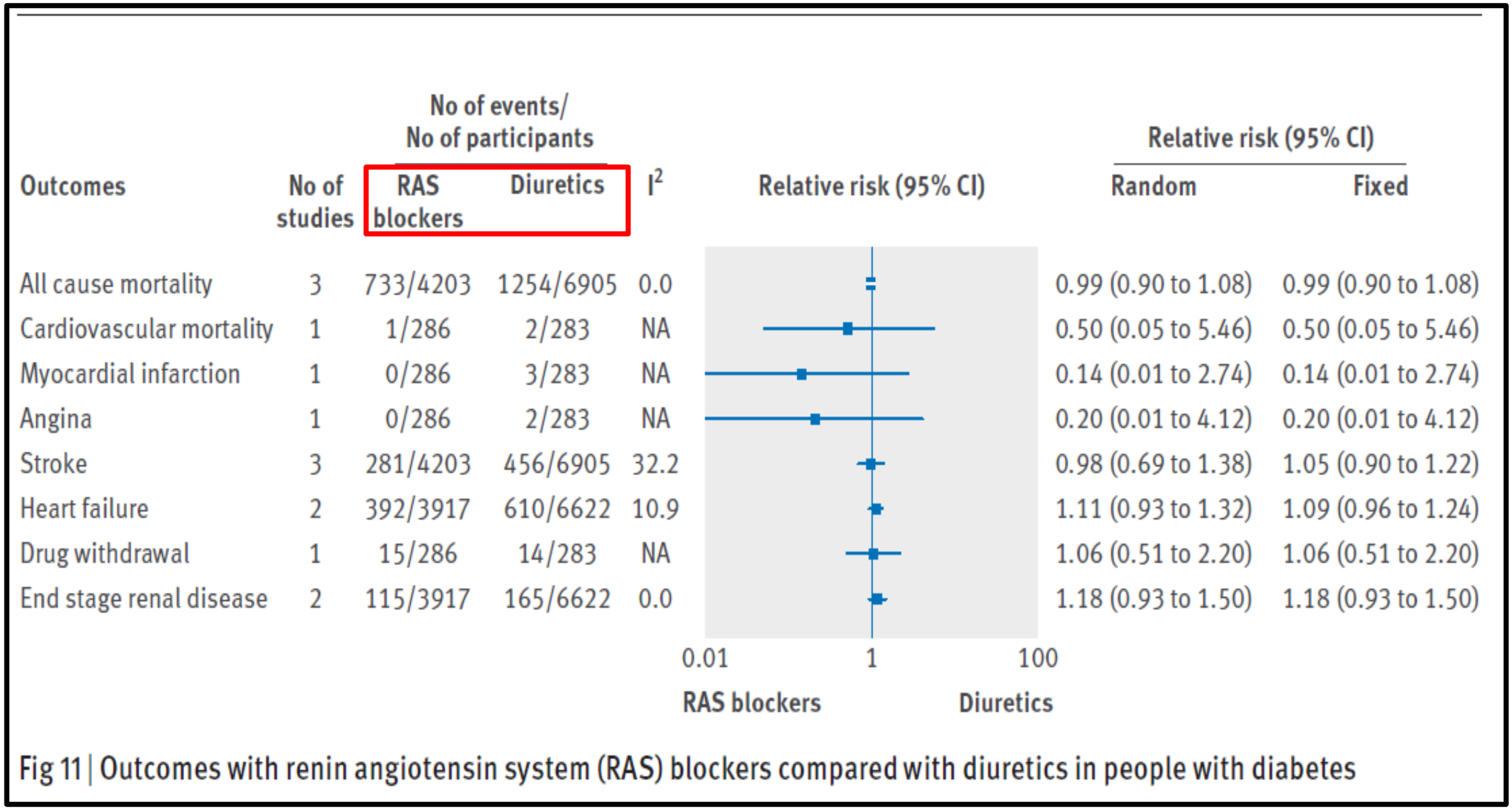

Fig 11 | Outcomes with renin angiotensin system (RAS) blockers compared with diuretics in people with diabetes

Outcomes	No of studies	No of events/ No of participants: RAS blockers	No of events/ No of participants: β blockers	I^2	Relative risk (95% CI)	Relative risk (95% CI): Random	Relative risk (95% CI): Fixed
All cause mortality	2	138/986	163/967	84.1		0.84 (0.47 to 1.51)	0.83 (0.66 to 1.04)
Cardiovascular mortality	2	77/986	90/967	73.3		0.87 (0.47 to 1.60)	0.84 (0.61 to 1.14)
Myocardial infarction	2	102/986	96/967	24.8		1.02 (0.73 to 1.40)	1.02 (0.77 to 1.35)
Angina	2	50/986	55/967	0.0		0.89 (0.60 to 1.30)	0.89 (0.60 to 1.30)
Stroke	2	72/986	82/967	0.0		0.88 (0.64 to 1.21)	0.88 (0.64 to 1.21)
Heart failure	1	12/400	9/358	NA		1.19 (0.50 to 2.83)	1.19 (0.50 to 2.83)
Revascularization	1	62/586	70/609	NA		0.92 (0.65 to 1.30)	0.92 (0.65 to 1.30)
Drug withdrawal	2	90/986	134/967	37.4		0.51 (0.23 to 1.14)	0.61 (0.47 to 0.80)
End stage renal disease	1	4/400	4/358	NA		0.90 (0.22 to 3.58)	0.90 (0.22 to 3.58)

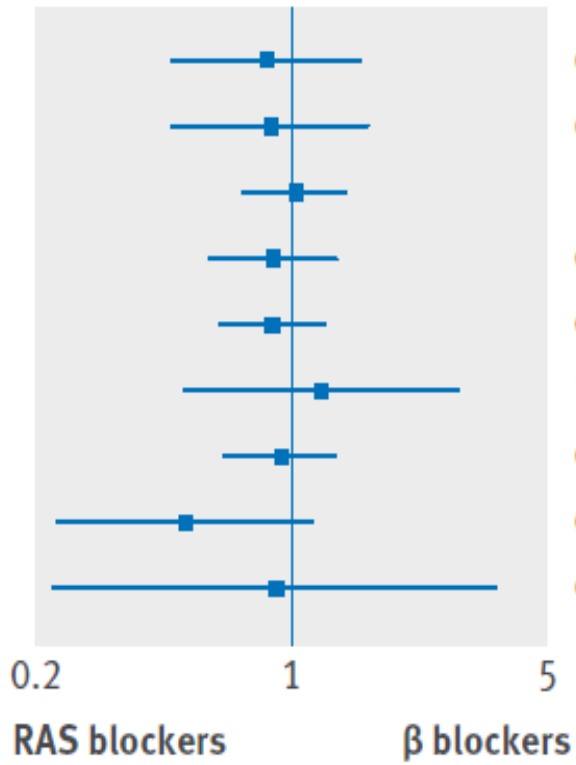

Fig 12 | Outcomes with renin angiotensin system (RAS) blockers compared with β blockers in people with diabetes

In the absence of albuminuria, risk of progressive kidney disease is low, and ACE inhibitors and ARBs have not been found to afford superior cardioprotection when compared with other antihypertensive agents .

The combination of both ACE inhibitors and ARBs is not recommended given the lack of added ASCVD benefit and increased rate of hyperkalemia, syncope, and acute kidney injury.

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Cardiovascular Events During Differing Hypertension Therapies in Patients With Diabetes

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Avoiding Cardiovascular Events Through COMbination Therapy in Patients Living With Systolic Hypertension

Aim: To determine which combination therapy in patients with hypertension and diabetes most effectively decreases cardiovascular event

Trial compared the outcomes effects of a renin-angiotensin system blocker, benazepril, combined with amlodipine (BA) or hydrochlorothiazide (BH).
A total of 6,946 patients with diabetes were randomized to treatment with BA or BH. A subgroup of 2,842 diabetic patients at very high risk (previous cardiovascular or stroke events) was also analyzed, as were 4,559 patients without diabetes

J Am Coll Cardiol. 2010 Jun 29;56(1):77-85

Study procedures

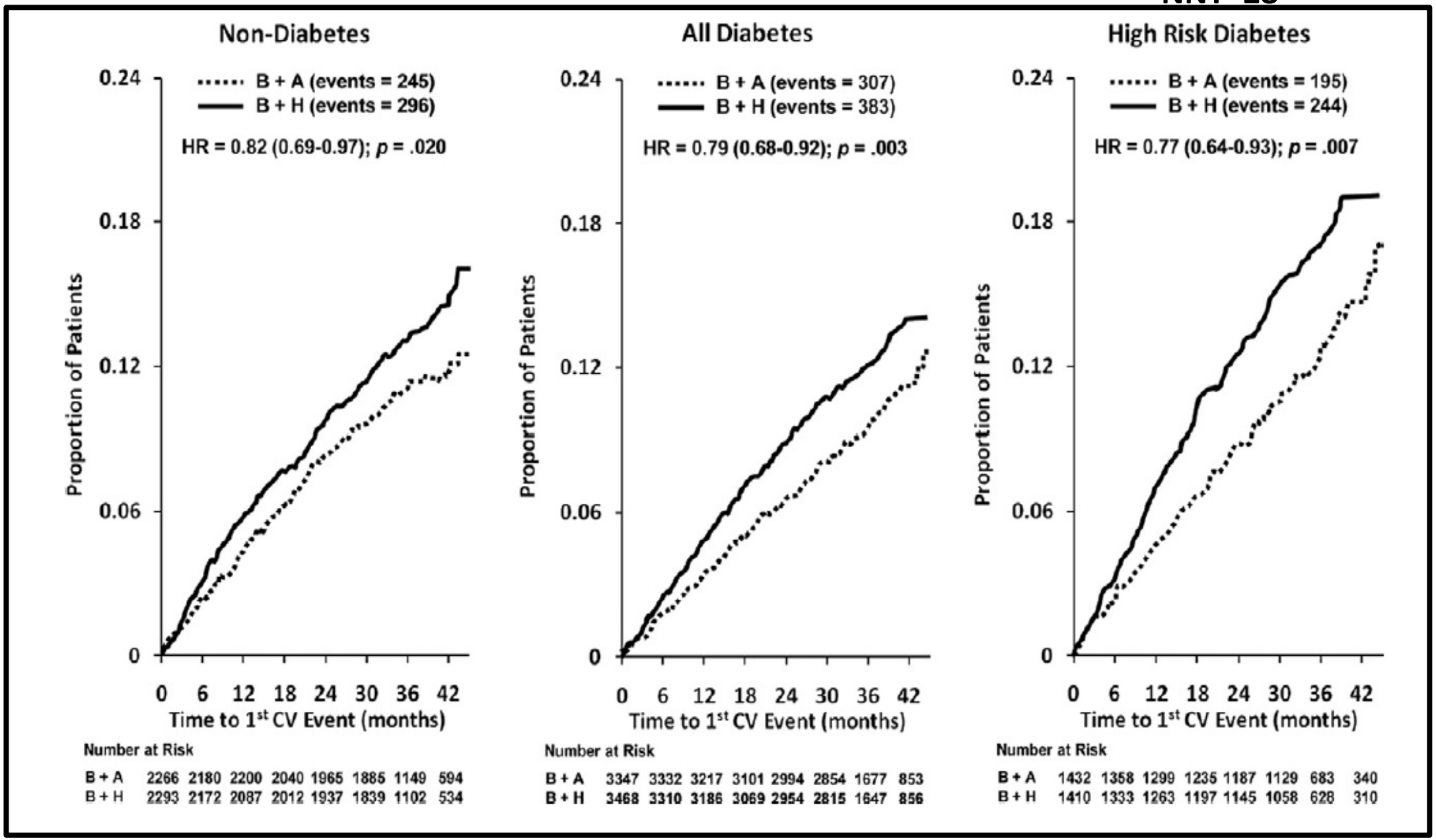
- The starting doses were benazepril 20 mg/day + either amlodipine 5 mg/day or HCT 12.5 mg/day.
- The study protocol then mandated an increase in the benazepril dose to 40 mg/day in both treatment arms.
- Thereafter, the amlodipine dose could be increased to 10 mg/day or the HCT dose to 25 mg/day if required to achieve a target blood pressure goal of 140/90 mm Hg.
- For the diabetic patients (who represent the principal cohort of this report) or for patients with chronic kidney disease, a target blood pressure of 130/80 mm Hg was recommended, but not mandated.

Table 3 24-h Systolic Blood Pressure Averages in Patients With Diabetes

Characteristic	B+A	B+H	Mean Difference	p Value
Patients	185	168	—	—
24-h mean	125.3	123.7	1.6	0.262
Daytime (6:00 AM–10:00 PM)	126.9	125.2	1.7	0.249
Nighttime (10:00 PM–6:00 AM)	119.9	118.9	1.0	0.528

Data obtained by ambulatory monitoring in patients with diabetes treated with BA or BH after 2 years of treatment.

NNT= 48 **NNT=46** **NNT=28**



Key messages

- In patients with diabetes and hypertension, combining a renin-angiotensin system blocker with amlodipine, compared with hydrochlorothiazide, was superior in reducing cardiovascular events and could influence future management of hypertension in patients with diabetes.
- Other such trials are needed to confirm these outcomes and assess other antihypertensive medication combinations

Bedtime Dosing

- prior analyses of randomized clinical trials found a benefit to evening versus morning dosing of antihypertensive medications

- these results have not been reproduced in subsequent trials. Therefore, preferential use of antihypertensives at bedtime is not recommended

Resistant hypertension
is defined as
blood pressure ≥140/90 mmHg
despite a therapeutic strategy that includes appropriate lifestyle management plus a diuretic and two other antihypertensive drugs belonging to different classes at adequate doses.

Table 3—Conditions to exclude before making the diagnosis of resistant hypertension

Conditions	Definition
Secondary hypertension (136)*	Hypertension elicited or exacerbated by other drugs or diseases
Pseudoresistance (136,137)	Apparent hypertension due to lack of medication adherence, poor blood pressure measurement technique
Masked hypertension (137)	Clinic blood pressure <140/90 mmHg; daytime blood pressure ≥135 or ≥85 mmHg
White-coat hypertension (137)	Clinic blood pressure ≥140 or ≥90 mmHg; daytime blood pressure <135/85 mmHg

*Secondary causes of hypertension include endocrine issues, renal arterial disease, excessive edema in advanced kidney disease, and hormones, such as testosterone. Drugs that increase blood pressure include NSAIDs, decongestants, and some illicit substances.

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Key Message

- Studies show that spironolactone was by far the most effective blood pressure-lowering treatment for patients with resistant hypertension.
- These findings suggest that the predominant underlying pathophysiological cause of resistant hypertension is sodium retention, despite existing baseline diuretic therapy.
- This conclusion is supported by the finding that the response to spironolactone had a clear inverse relation with plasma renin, was especially effective at lower plasma renin levels, and yet the most effective drug throughout the range of plasma renin

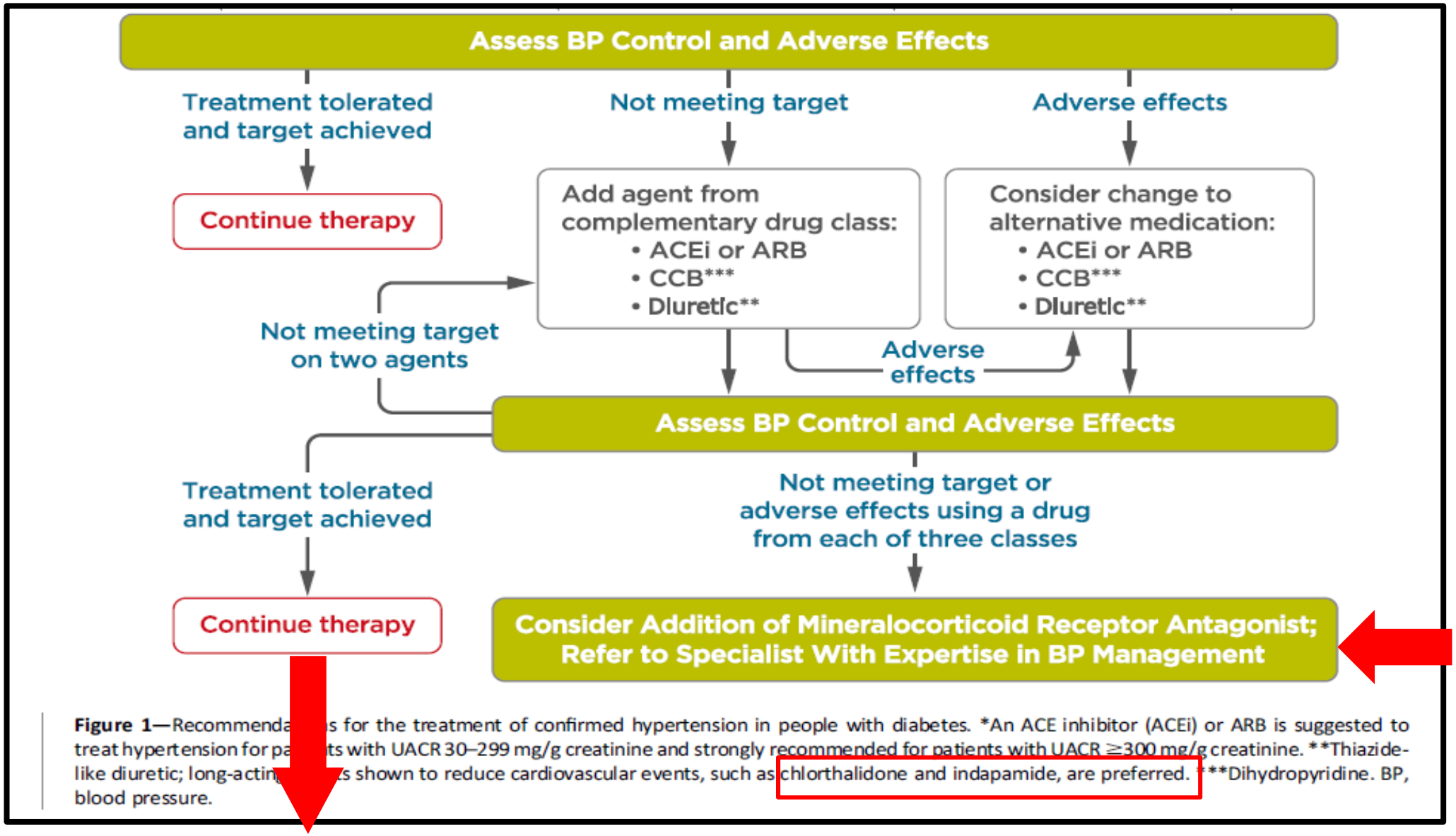

Figure 1—Recommenda s for the treatment of confirmed hypertension in people with diabetes. *An ACE inhibitor (ACEi) or ARB is suggested to treat hypertension for pa ts with UACR 30–299 mg/g creatinine and strongly recommended for patients with UACR ≥300 mg/g creatinine. **Thiazide-like diuretic; long-actin s shown to reduce cardiovascular events, such as chlorthalidone and indapamide, are preferred. ***Dihydropyridine. BP, blood pressure.

Reduce sympathetic nerve activity Reduce albuminuria and have additional cardiovascular benefits

In patients receiving pharmacologic antihypertensive treatment, home blood pressure should be measured to promote patient engagement in treatment and adherence and may better correlate with ASCVD risk than office measurements .B

ADA 2024

- Adding a mineralocorticoid receptor antagonist to a regimen including an ACE inhibitor or ARB may increase the risk for hyperkalemia, emphasizing the importance of regular monitoring for serum creatinine and potassium in these patients.

- and long-term outcome studies are needed to better evaluate the role of mineralocorticoid receptor antagonists in blood pressure management.

In people with diabetic kidney disease, hyperkalemia risk dramatically increases when the eGFR is < 45 mL/min/1.73 m2 or serum K is > 4.5 mEq/L while the patient is already receiving a diuretic.

The combination of reduced eGFR and elevated K in a given patient can raise the risk ***8*** fold for hyperkalemia development if spironolactone and an ACE inhibitor or ARB are added

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Case-Study-2

57 A 34-year-old man with a 4-year history of type 2 diabetes mellitus presents for follow-up. He eats a well-balanced diet, but he has not been exercising regularly (less than 1 hour per week of activity greater than 2 metabolic equivalents). His most recent hemoglobin A_{1c} measurement is 7.4% (57 mmol/mol). He has no diabetes-related complications, including no history of atherosclerotic cardiovascular disease. He does not smoke cigarettes and drinks 1 to 2 alcoholic beverages a week. He takes metformin, 1000 mg twice daily.

On physical examination, his blood pressure is 138/94 mm Hg (repeated 144/92 mm Hg) and pulse rate is 88 beats/min. His height is 70 in (178 cm), and weight is 230 lb (104.5 kg) (BMI = 33 kg/m^2). There are no carotid bruits. His heart rate and rhythm are regular. No murmurs are appreciated. Bilateral radial, dorsalis pedis, and posterior tibial pulses are palpable (2+).

Laboratory test results:

Complete metabolic panel, normal
LDL cholesterol = 92 mg/dL (<100 mg/dL [optimal]) (SI: 2.38 mmol/L [<2.59 mmol/L])
Triglycerides = 165 mg/dL (<150 mg/dL [optimal]) (SI: 1.86 mmol/L [<1.70 mmol/L])
Urine albumin-to-creatinine ratio = 22 mg/g creat (<30 mg/g creat)

Cont…

In addition to initiating an exercise program, which of the following should be recommended as the best next step to reduce this patient's risk of cardiovascular disease?

A. No further intervention now
B. Start atorvastatin
C. Start aspirin
D. Start icosapent ethyl
E. Start lisinopril


Thanks for
your patience,
dear colleagues!