Management of HTN in pts with DM

Amir A. Nassiri, MD,DIU

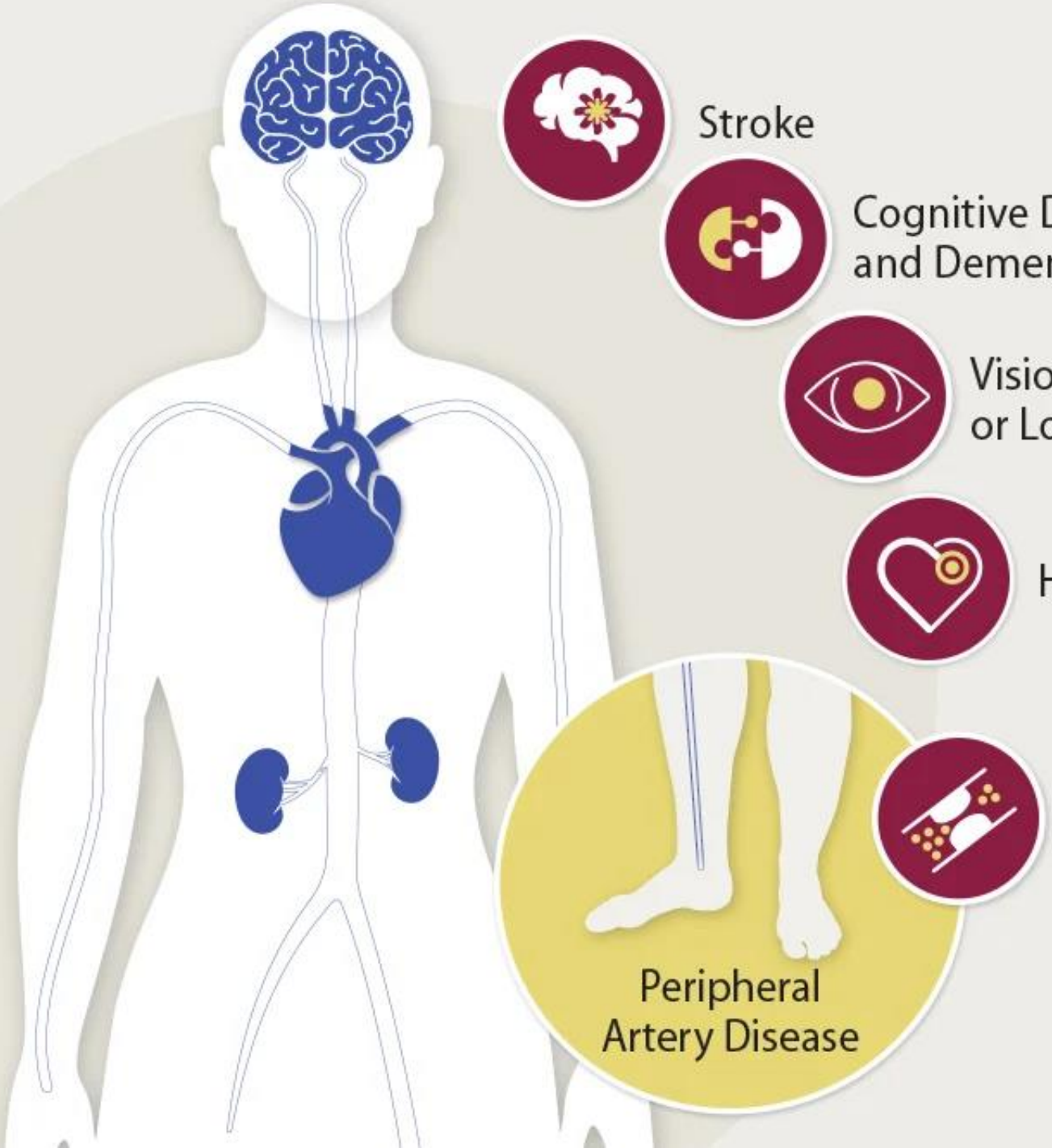
SBUMU

Tehran, 2025 Oct 13th

Introduction

- Reasons to control BP in DM (CVD / Renal protection)
- BP goals (120, 130, 140,…)
- What agents to use

Health Problems Caused by High Blood Pressure



Stroke

Cognitive Decline and Dementia

Vision Decline or Loss

Heart Disease

Peripheral Artery Disease

Chronic Kidney Disease

Pregnancy-Related Complications

Other Health Problems

CDC

Diabetes cardiovascular risk

Coronary heart disease

Prevalence: 14–21%[5,16]

Most frequently reported form of CVD and most lethal one.[5]
Risk of death from CHD is higher in women then in men (HR, 95% CI: 1.81 [1.27–2.59] versus 1.48[1.10–1.99]).[5]

Heart failure

Prevalence: 19–26%[20]

Second most common initial manifestation of CVD in T2DM.[16]
Risk of HF is up to 2-fold in men and 5-fold in women.[20]

Peripheral artery disease

Prevalence: 16–29%[15,16]

Most common initial manifestation of CVD in T2DM.[16]
Prevalence is 1.8-fold higher in women compared to men.[16]

Stroke

Prevalence: 8–12%[2,10]

Second more frequent cause of death in patients with T2DM after CHD[10]
Prevalence is similar in men and women.[21]

Retinopathy

Prevalence: 34%[29]

Most common microvascular complication of diabetes;[29] responsible of 2.6% of all cases of blindness worldwide.[29]
Prevalence rates are higher in TIDM compared to T2DM (77.3 vs. 25.2%).[31]

Neuropathy

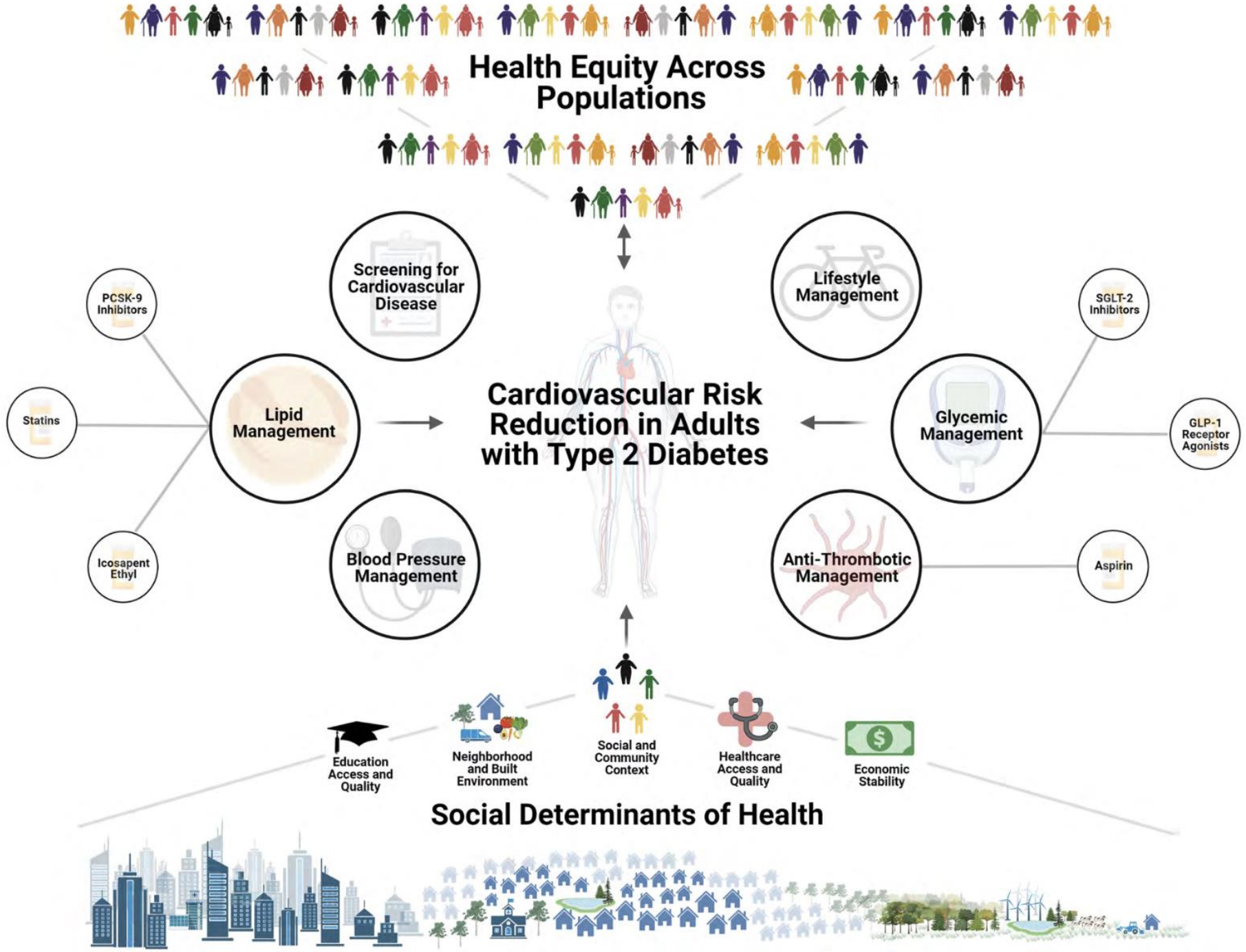
Cardiac autonomic neuropathy

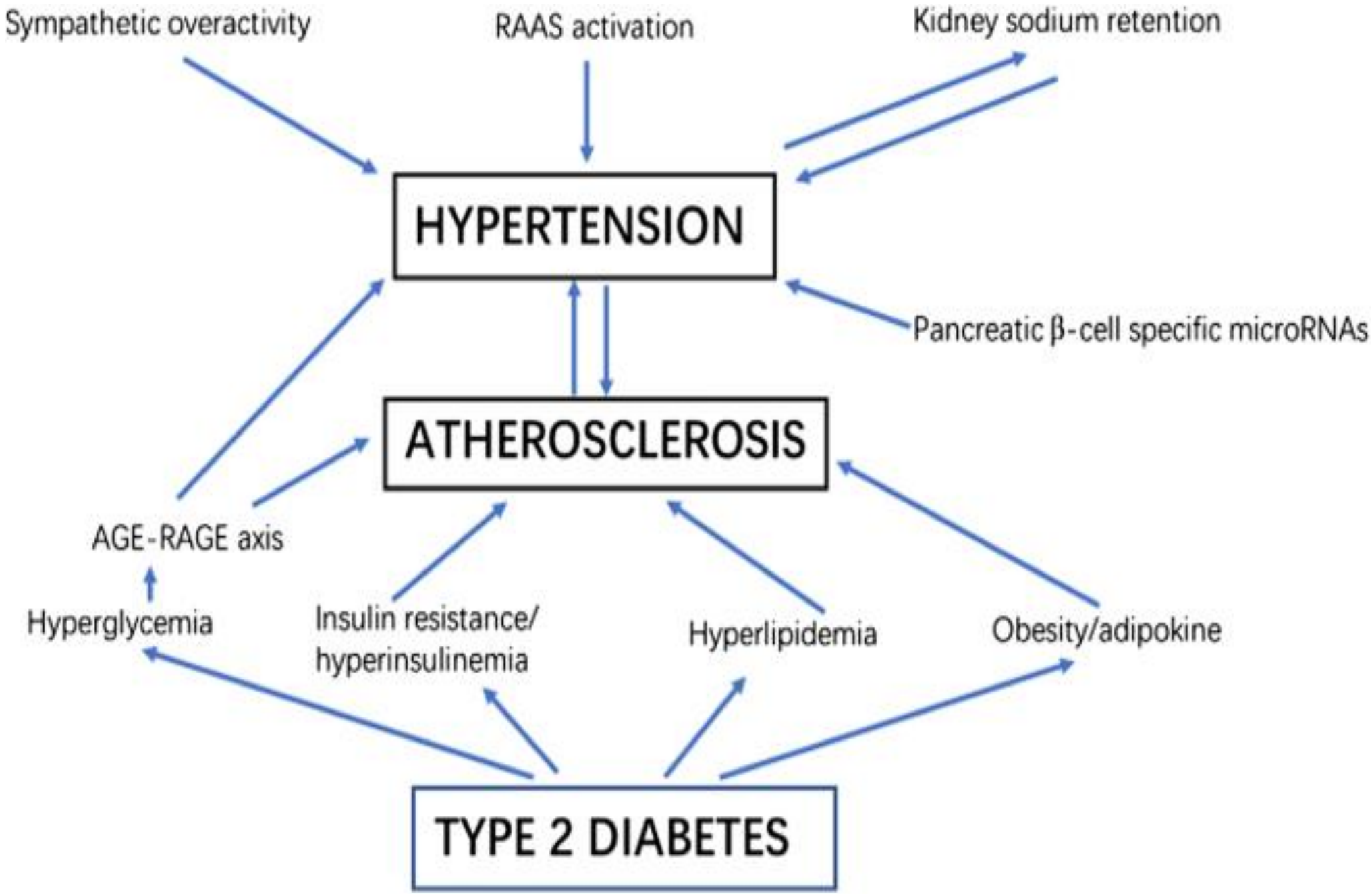
Prevalence: 31–73% in people with T2DM[32]
No difference in prevalence between men and women.[32]

Nephropathy

Prevalence: 29–61%[28]

Leading cause of end stage renal disease in the adult population worldwide.[2]
Female sex is a risk factor for nephropathy in T2DM.[28]


Health Equity Across Populations
Screening for Cardiovascular Disease
Lifestyle Management
PCSK-9 Inhibitors
SGLT-2 Inhibitors
Statins
Lipid Management
Cardiovascular Risk Reduction in Adults with Type 2 Diabetes
Glycemic Management
GLP-1 Receptor Agonists
Icosapent Ethyl
Blood Pressure Management
Anti-Thrombotic Management
Aspirin
Education Access and Quality
Neighborhood and Built Environment
Social and Community Context
Healthcare Access and Quality
Economic Stability
Social Determinants of Health


Sympathetic overactivity
RAAS activation
Kidney sodium retention
HYPERTENSION
Pancreatic β-cell specific microRNAs
ATHEROSCLEROSIS
AGE-RAGE axis
Hyperglycemia
Insulin resistance/
hyperinsulinemia
Hyperlipidemia
Obesity/adipokine
TYPE 2 DIABETES

ASCVD

32%
of all deaths in 2019
were due to CVD

- MI or other ACS
- Revascularization procedures
- TIA
- Stroke (ischemic)
- Athero. PAD (ABI<0.90)
- Other documented athero disease:

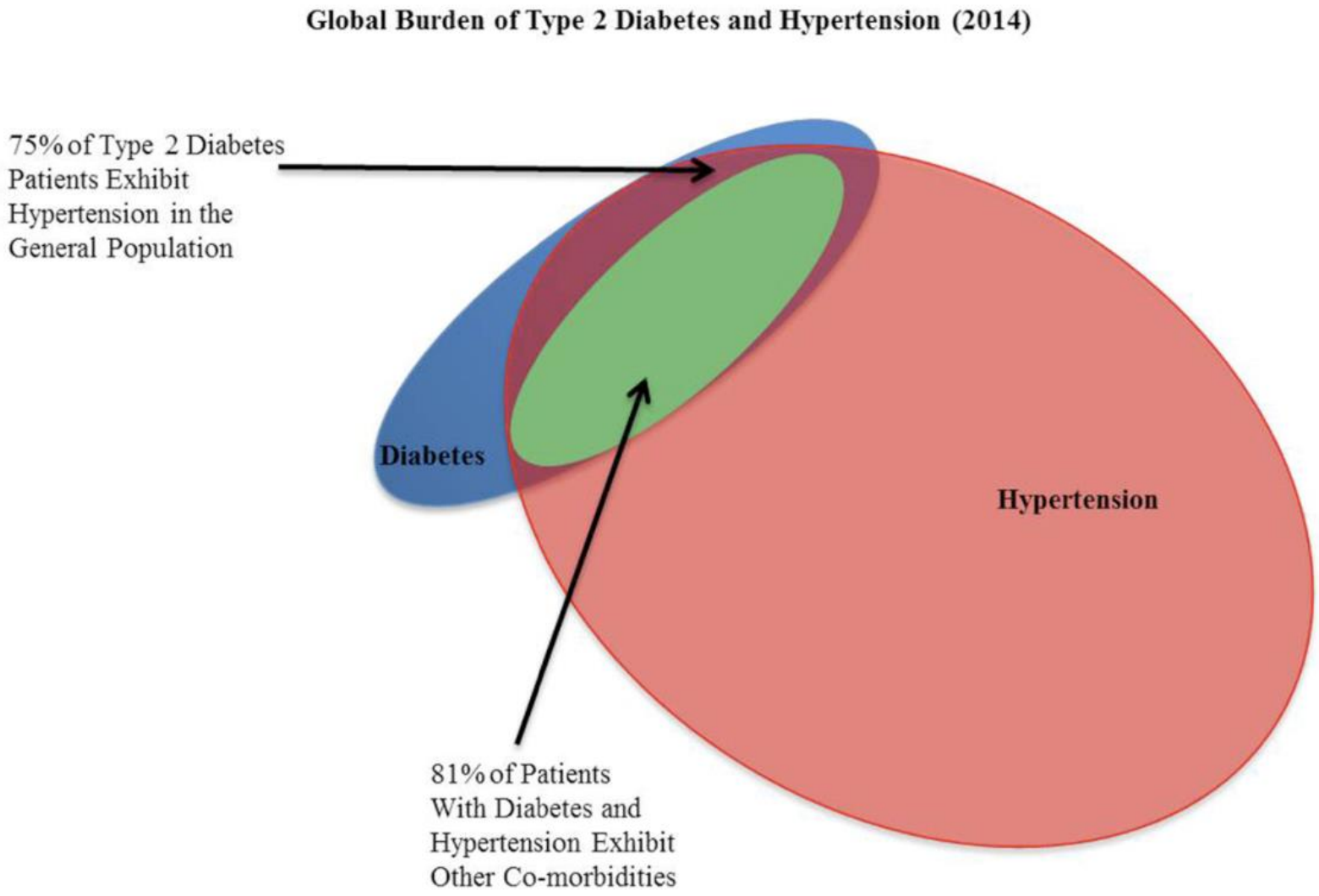
  1-Coro-atheroscl.

  2-Renal atheroscl.

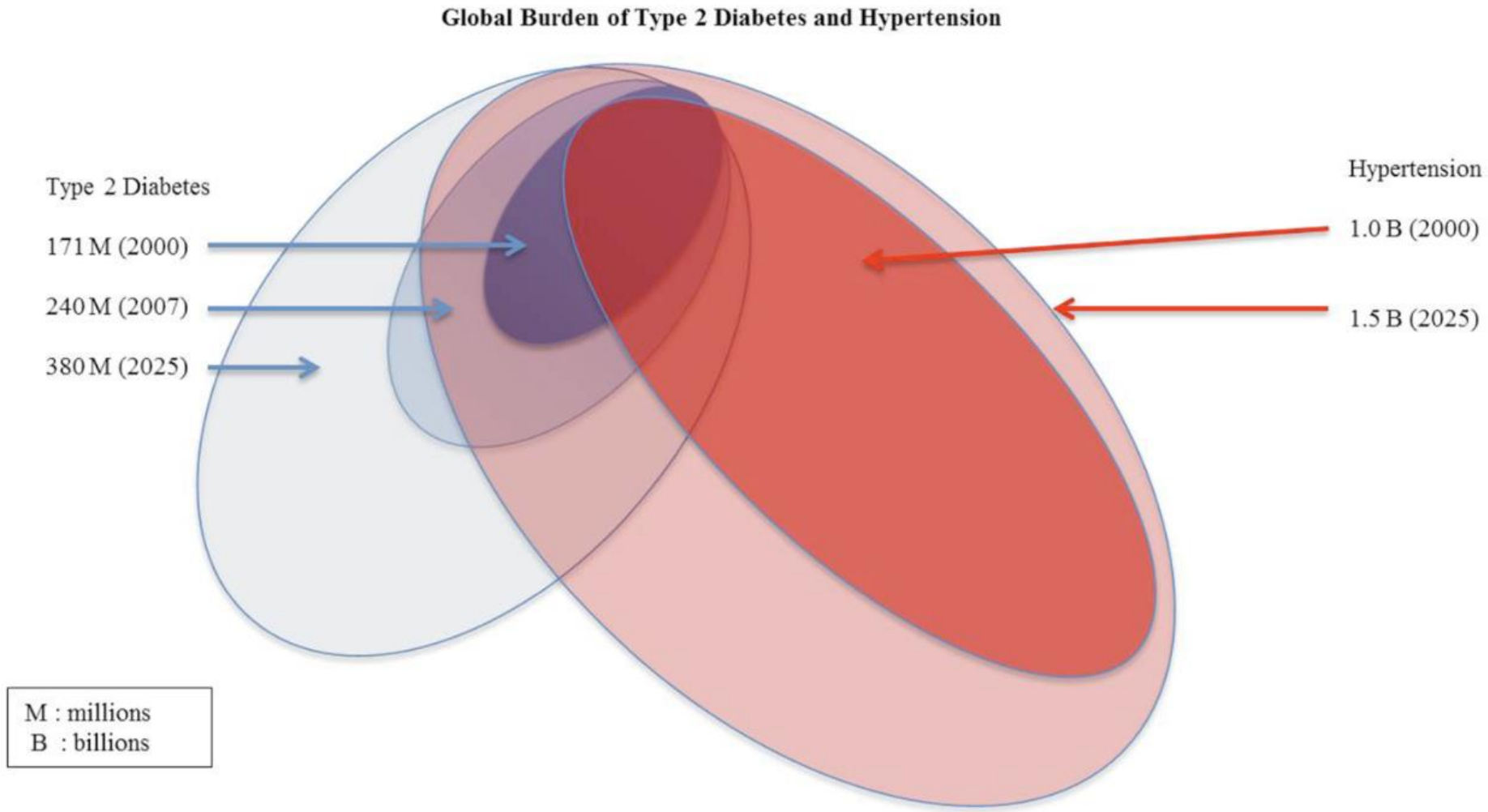
  3-Aortic aneurysm 2nd to atheroscl’

  4-Carotid plaque >50%

Current prevalence



Estimates for the future…



Why to manage HTN in DM ?

HTN is common in DM

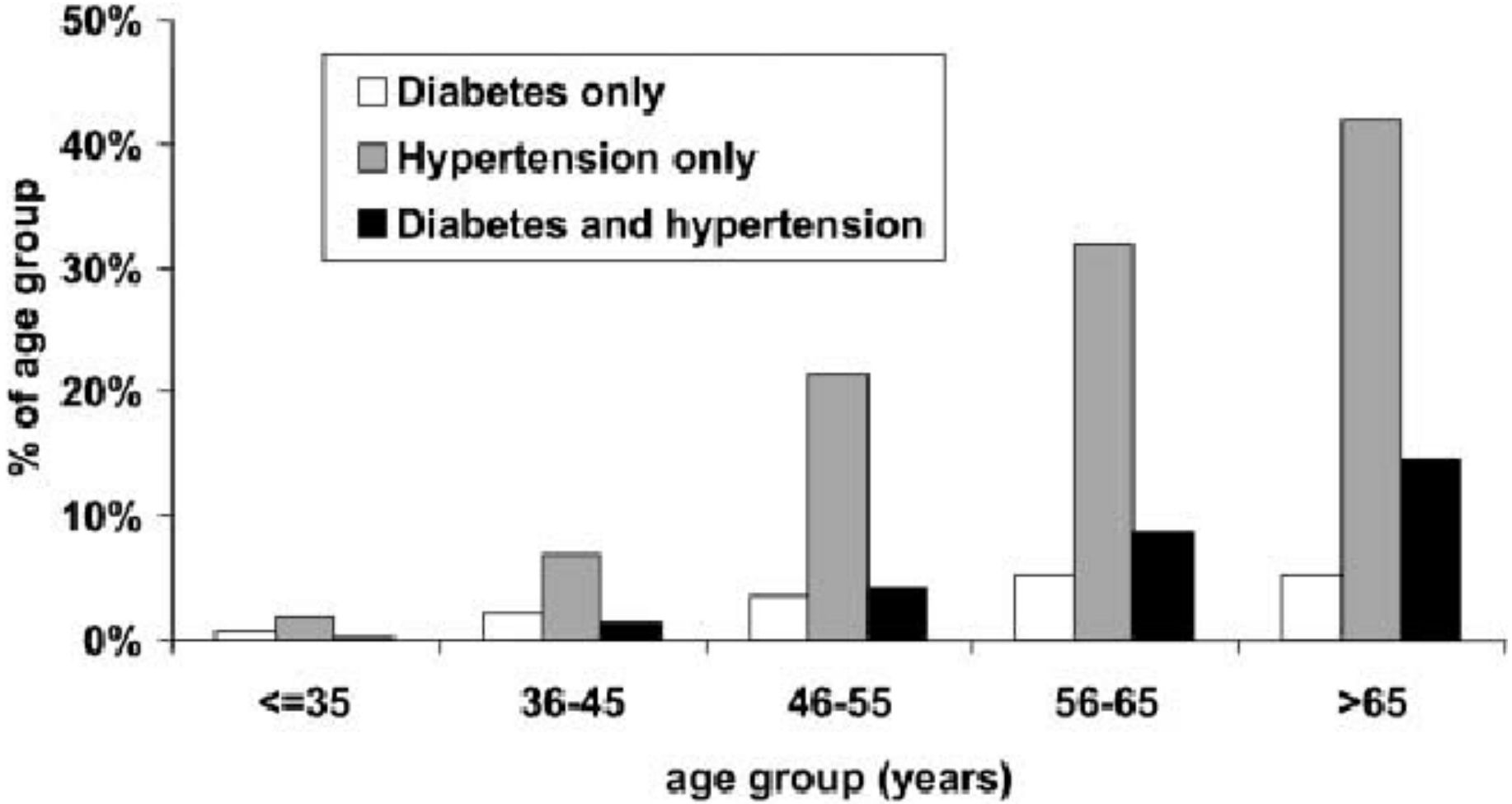
Incidence in T1DM

- 5% @ 10 yrs
- 33% @ 20 yrs
- 70% @ 40 yrs

Incidence in T2DM

- 40% @ the time of Dx
- >80% of adults w/ T2DM

DM & HTN
CV events



T2DM & CVD

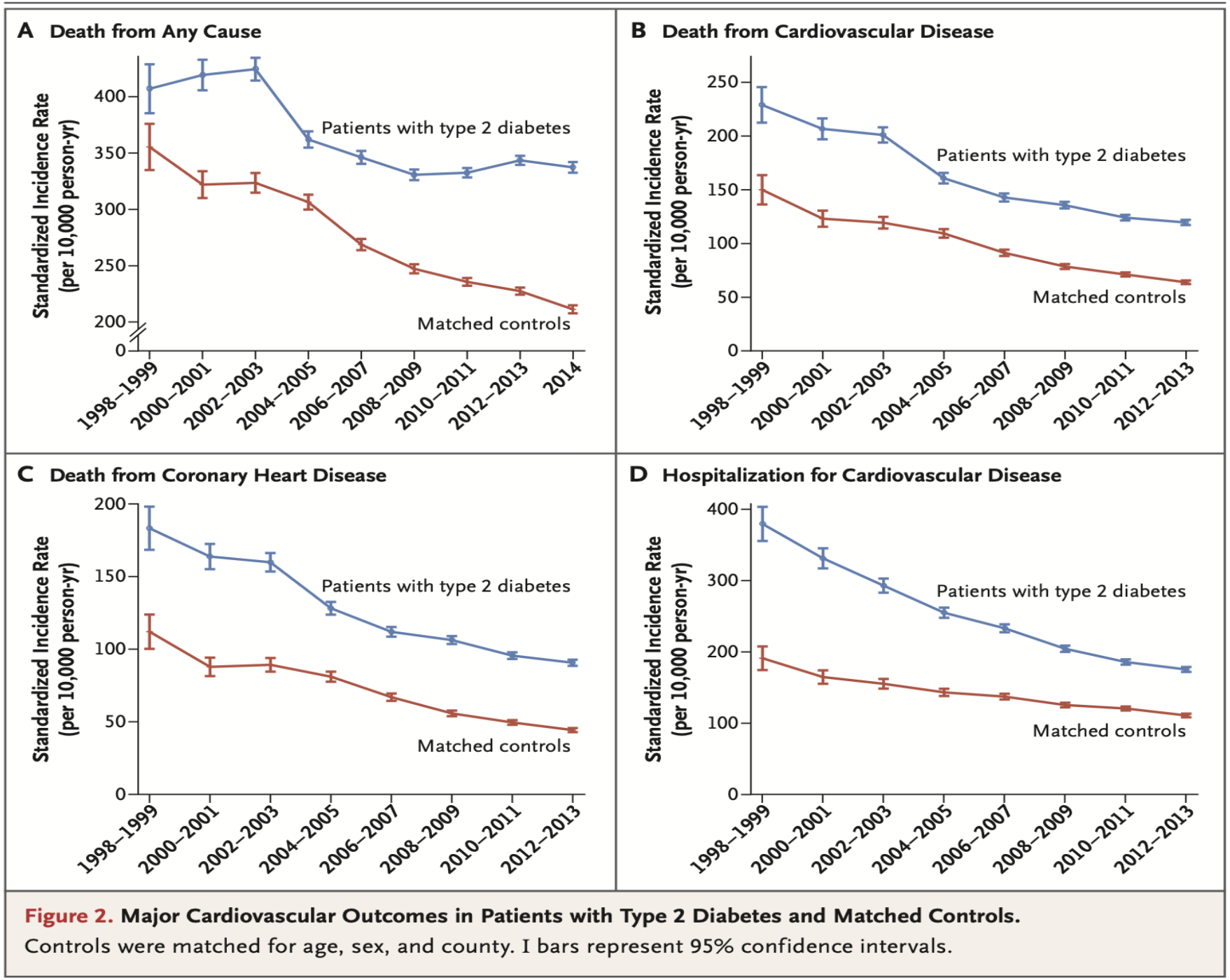
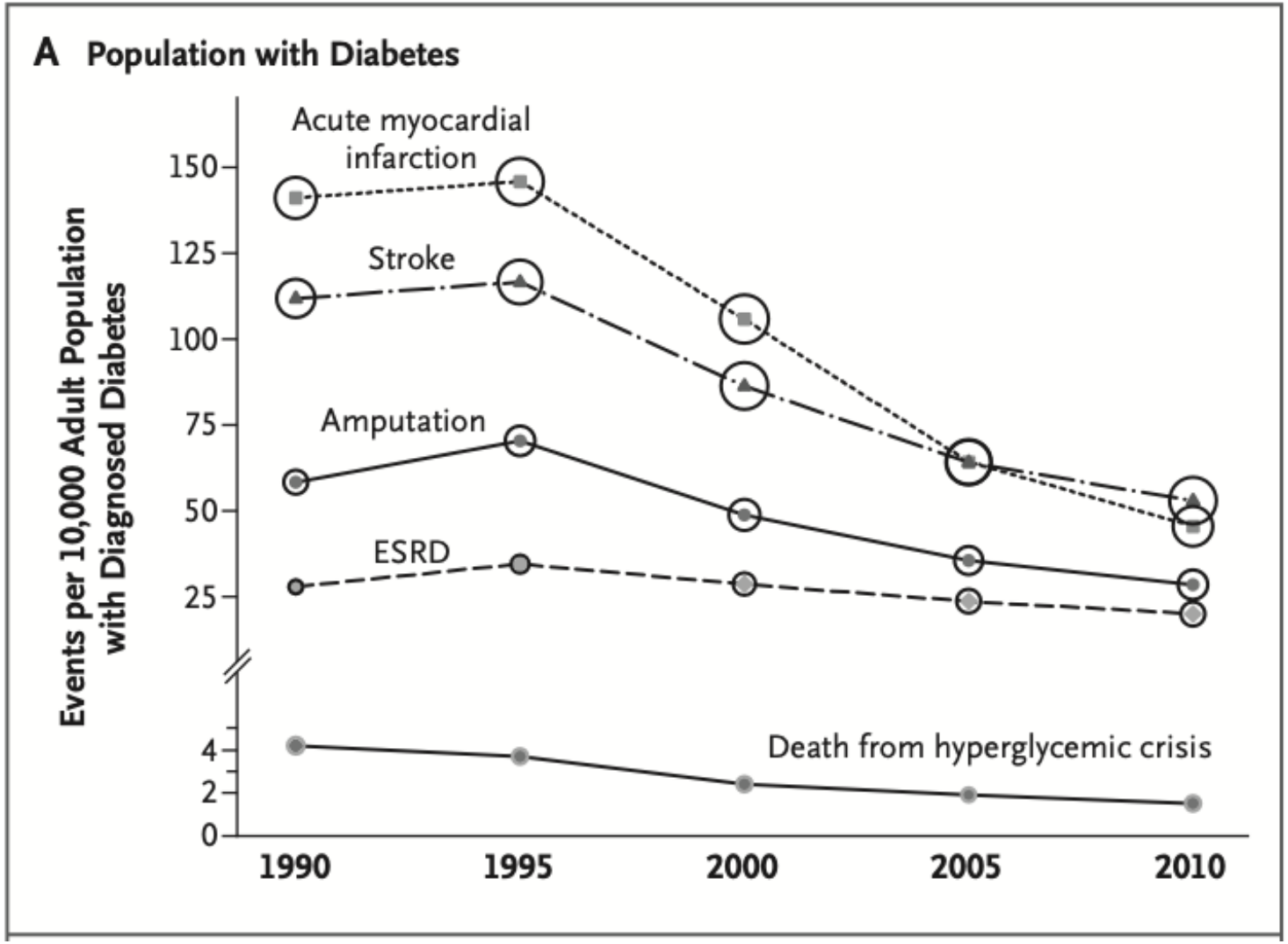
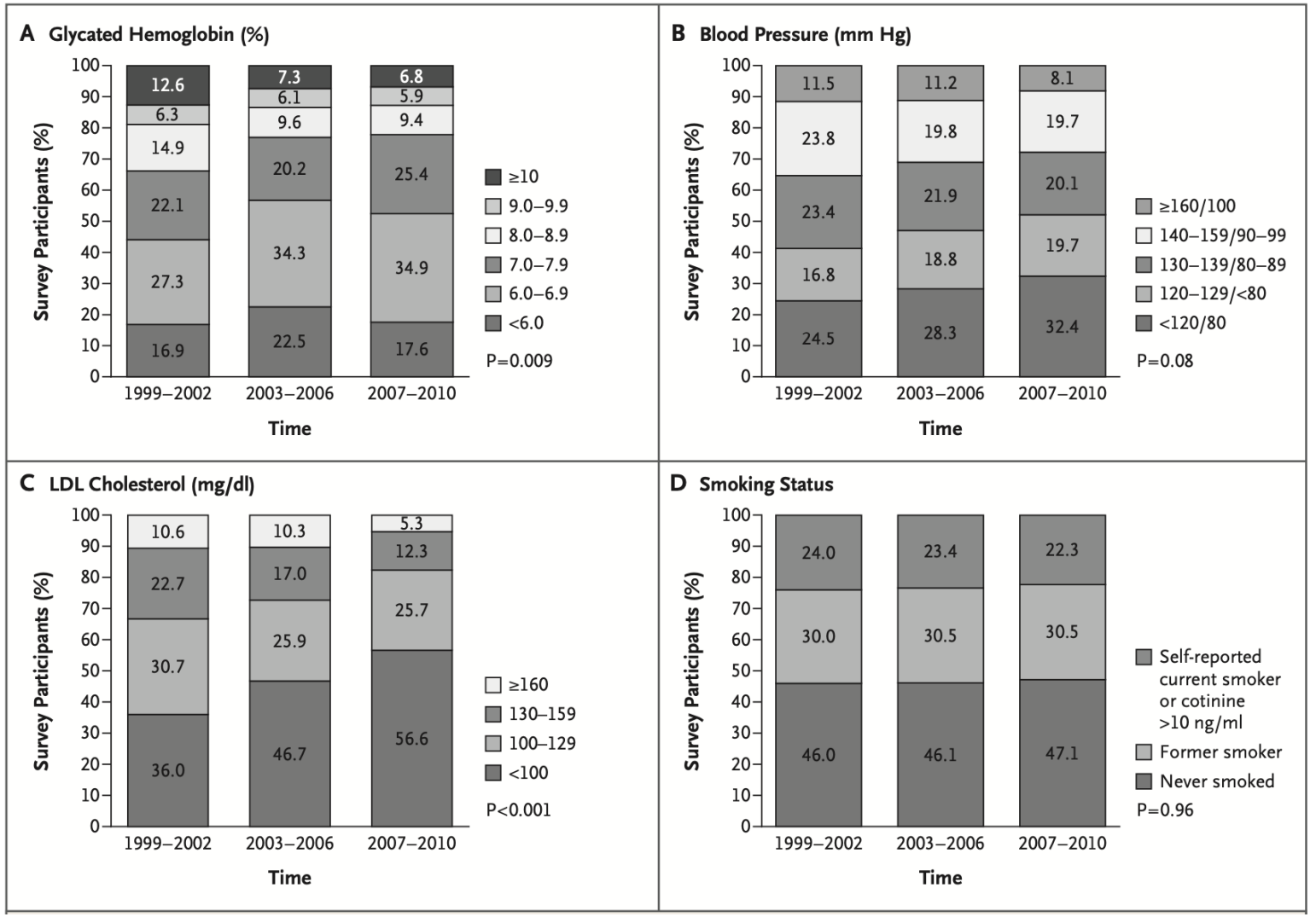


Figure 2. Major Cardiovascular Outcomes in Patients with Type 2 Diabetes and Matched Controls.
Controls were matched for age, sex, and county. I bars represent 95% confidence intervals.

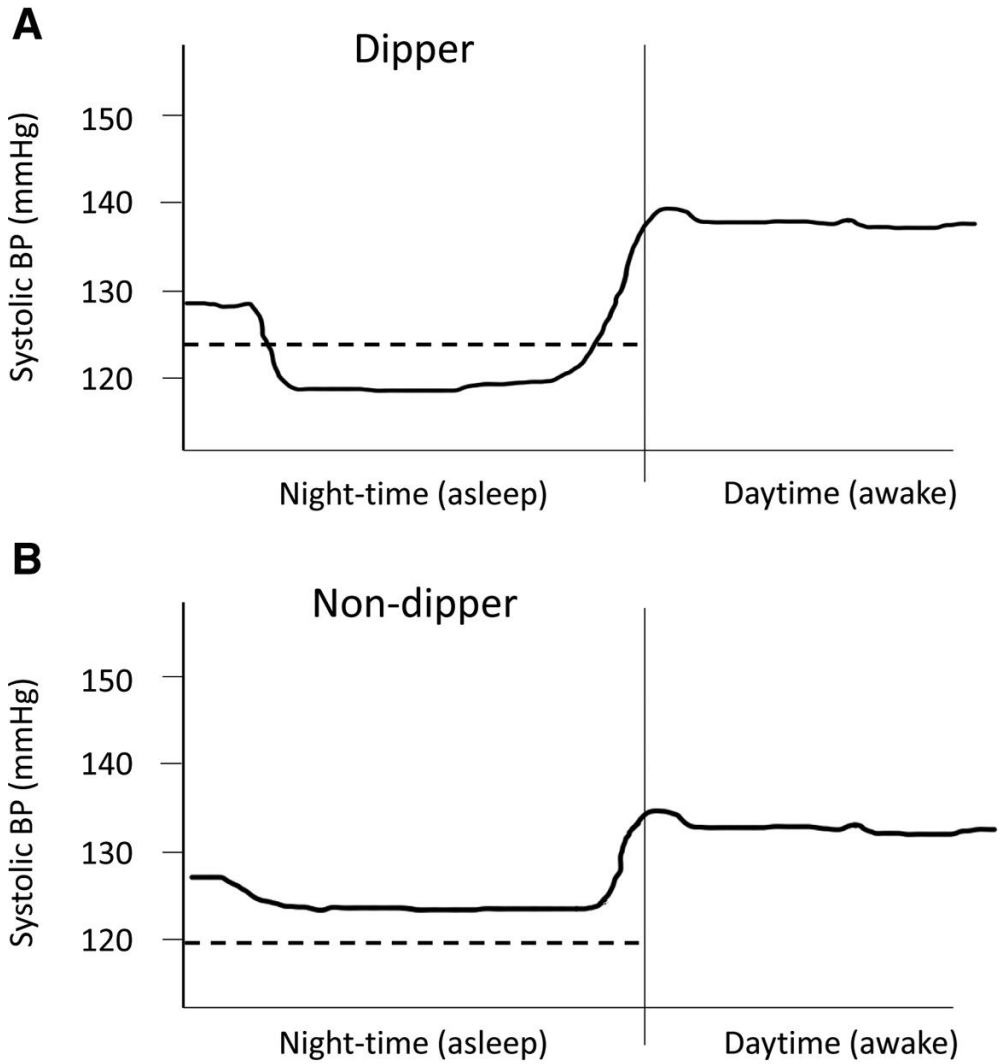
Since 1990s …

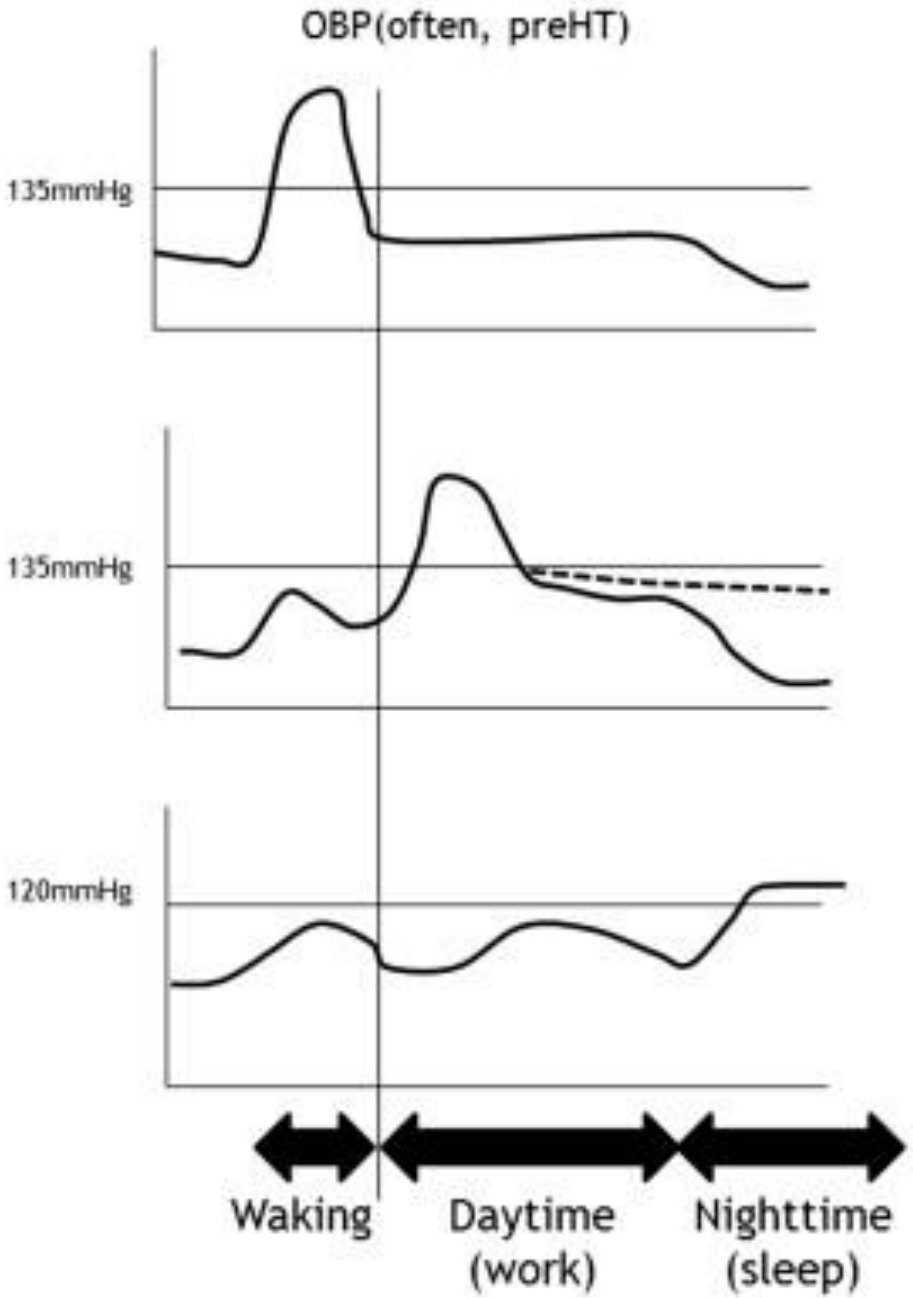

A Population with Diabetes
Events per 10,000 Adult Population with Diagnosed Diabetes
Acute myocardial infarction
Stroke
Amputation
ESRD
Death from hyperglycemic crisis
150
125
100
75
50
25
4
2
0
1990
1995
2000
2005
2010

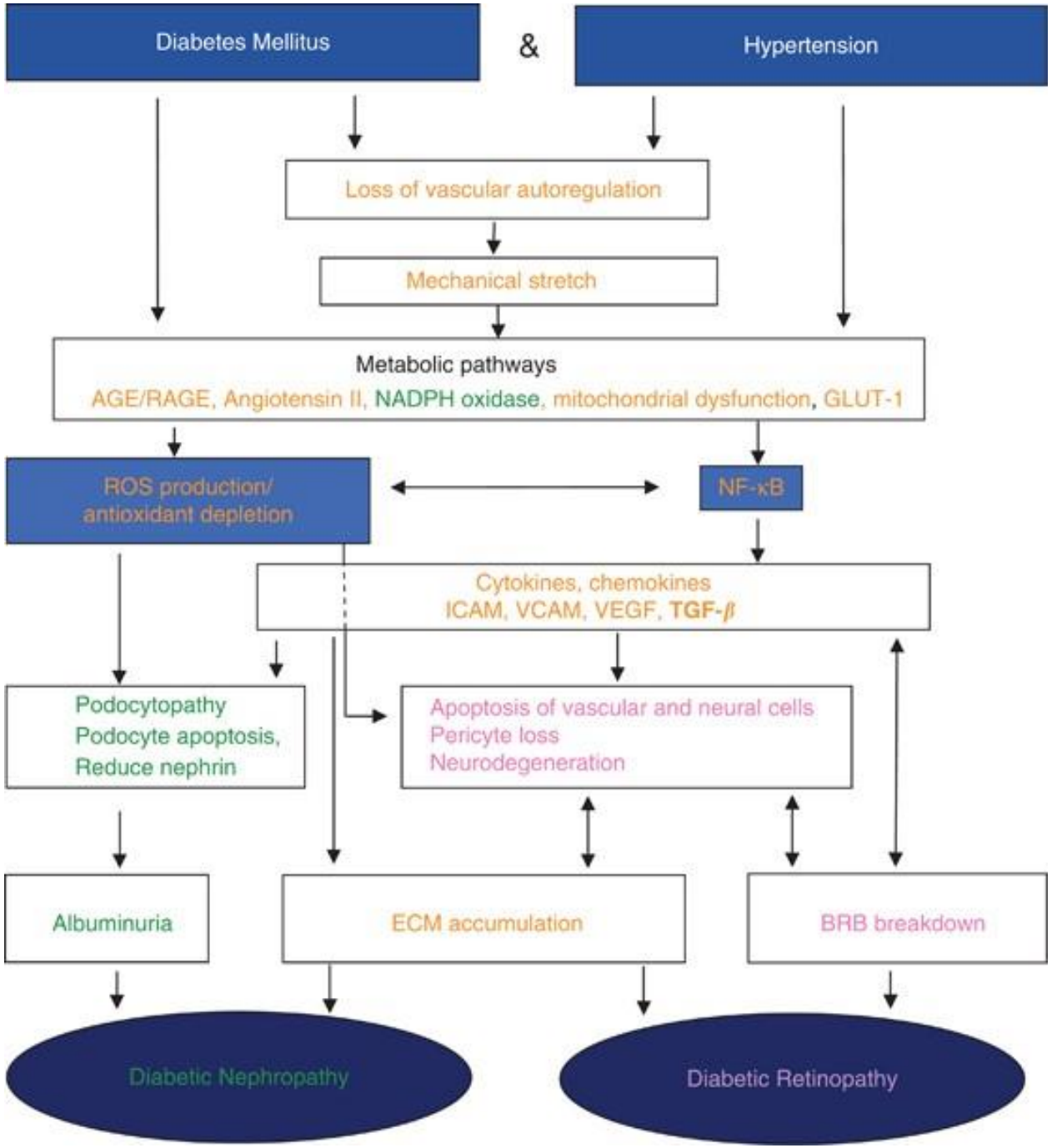
The reasons…


A Glycated Hemoglobin (%)
Survey Participants (%)
100
90
80
70
60
50
40
30
20
10
0
12.6
6.3
14.9
22.1
27.3
16.9
7.3
6.1
9.6
20.2
34.3
22.5
6.8
5.9
9.4
25.4
34.9
17.6
1999–2002
2003–2006
2007–2010
Time
≥10
9.0–9.9
8.0–8.9
7.0–7.9
6.0–6.9
<6.0
P=0.009
B Blood Pressure (mm Hg)
Survey Participants (%)
11.5
23.8
23.4
16.8
24.5
11.2
19.8
21.9
18.8
28.3
8.1
19.7
20.1
19.7
32.4
1999–2002
2003–2006
2007–2010
Time
≥160/100
140–159/90–99
130–139/80–89
120–129/<80
<120/80
P=0.08
C LDL Cholesterol (mg/dl)
Survey Participants (%)
10.6
22.7
30.7
36.0
10.3
17.0
25.9
46.7
5.3
12.3
25.7
56.6
1999–2002
2003–2006
2007–2010
Time
≥160
130–159
100–129
<100
P<0.001
D Smoking Status
Survey Participants (%)
24.0
30.0
46.0
23.4
30.5
46.1
22.3
30.5
47.1
1999–2002
2003–2006
2007–2010
Time
Self-reported current smoker or cotinine >10 ng/ml
Former smoker
Never smoked
P=0.96

HTN in DM


A
Dipper
Systolic BP (mmHg)
150
140
130
120
Night-time (asleep)
Daytime (awake)
B
Non-dipper
Systolic BP (mmHg)
150
140
130
120
Night-time (asleep)
Daytime (awake)


OBP(often, preHT)
135mmHg
135mmHg
120mmHg
Waking
Daytime
(work)
Nighttime
(sleep)


Diabetes Mellitus
&
Hypertension
Loss of vascular autoregulation
Mechanical stretch
Metabolic pathways
AGE/RAGE, Angiotensin II, NADPH oxidase, mitochondrial dysfunction, GLUT-1
ROS production/
antioxidant depletion
NF-κB
Cytokines, chemokines
ICAM, VCAM, VEGF, TGF-β
Podocytopathy
Podocyte apoptosis,
Reduce nephrin
Apoptosis of vascular and neural cells
Pericyte loss
Neurodegeneration
Albuminuria
ECM accumulation
BRB breakdown
Diabetic Nephropathy
Diabetic Retinopathy

Intensity of treatment

UKPDS = std vs intensive control of BP (90s)

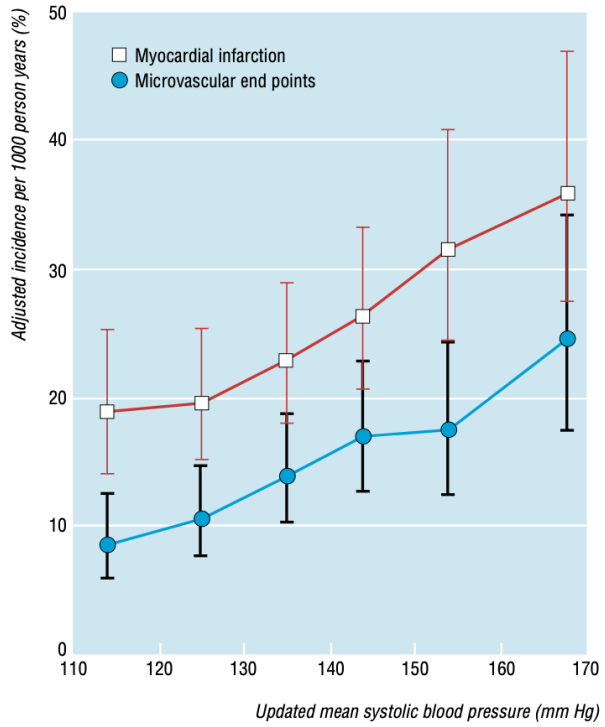
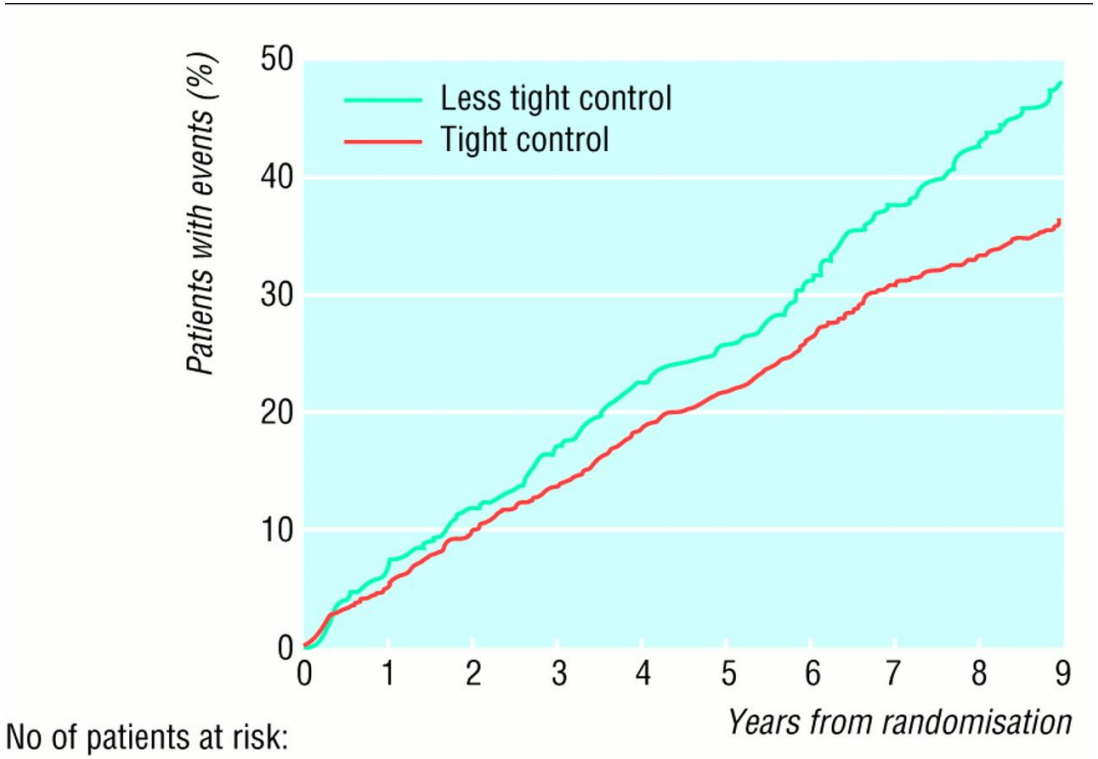


Fig 2 Incidence rates (95% confidence interval) of myocardial infarction and microvascular end points by category of updated mean systolic blood pressure, adjusted for age, sex, and ethnic group expressed for white men aged 50-54 years at diagnosis and mean duration of diabetes of 10 years



No of patients at risk:

Less tight control	390	321	247	106
Tight control	758	640	494	235

Reduction in risk with tight control 24% (95% CI 8% to 38%)(P = 0.0046)

What should be the goals ?

<140, <130, <120,…

The case for 140 (SBP<140)

The NEW ENGLAND JOURNAL of MEDICINE

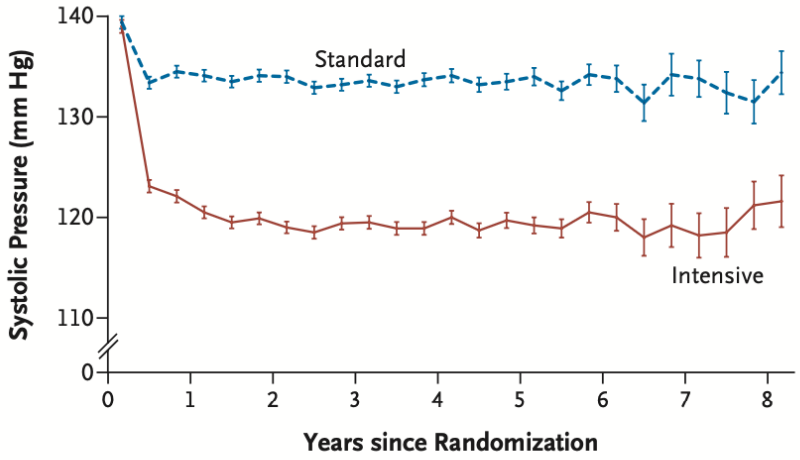
ORIGINAL ARTICLE

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

The ACCORD Study Group*

<120 vs <140 = no difference in CV events

except for preventing Stroke



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

Figure 1. Mean Systolic Blood-Pressure Levels at Each Study Visit.

I bars indicate 95% confidence intervals.

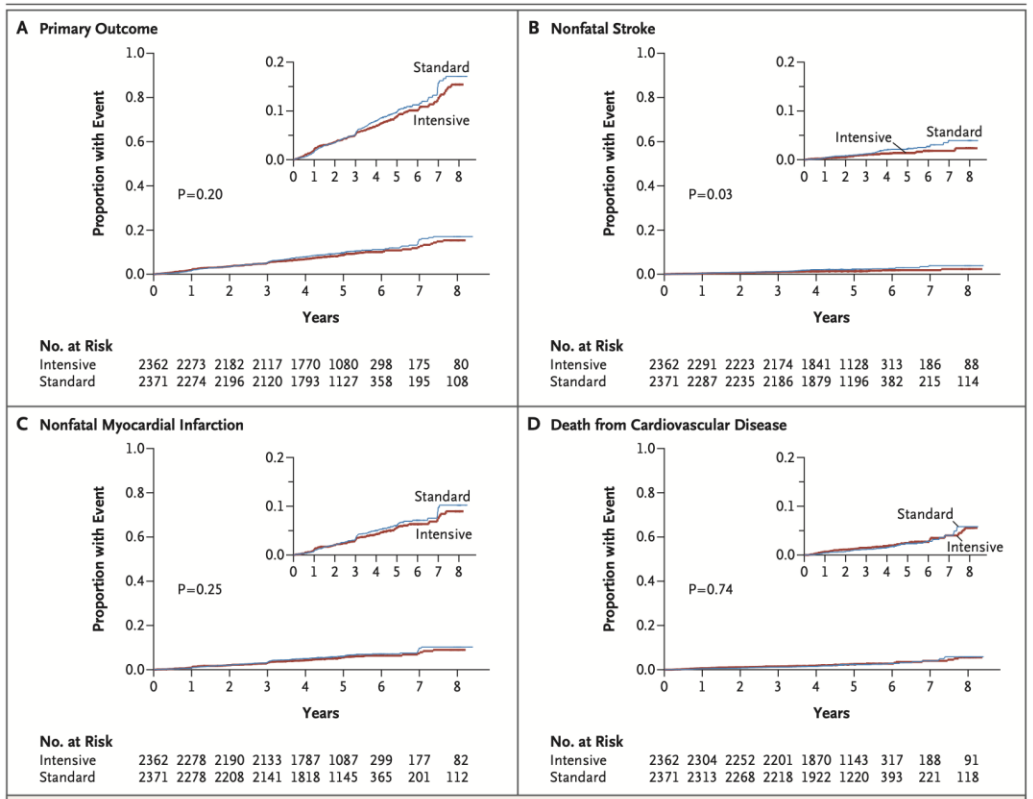


Figure 2. Kaplan–Meier Analyses of Selected Outcomes.

Shown are the proportions of patients with events for the primary composite outcome (Panel A) and for the individual components of the primary outcome (Panels B, C, and D). The insets show close-up versions of the graphs in each panel.

Table 2. Serious Adverse Events and Clinical Measures after Randomization.*

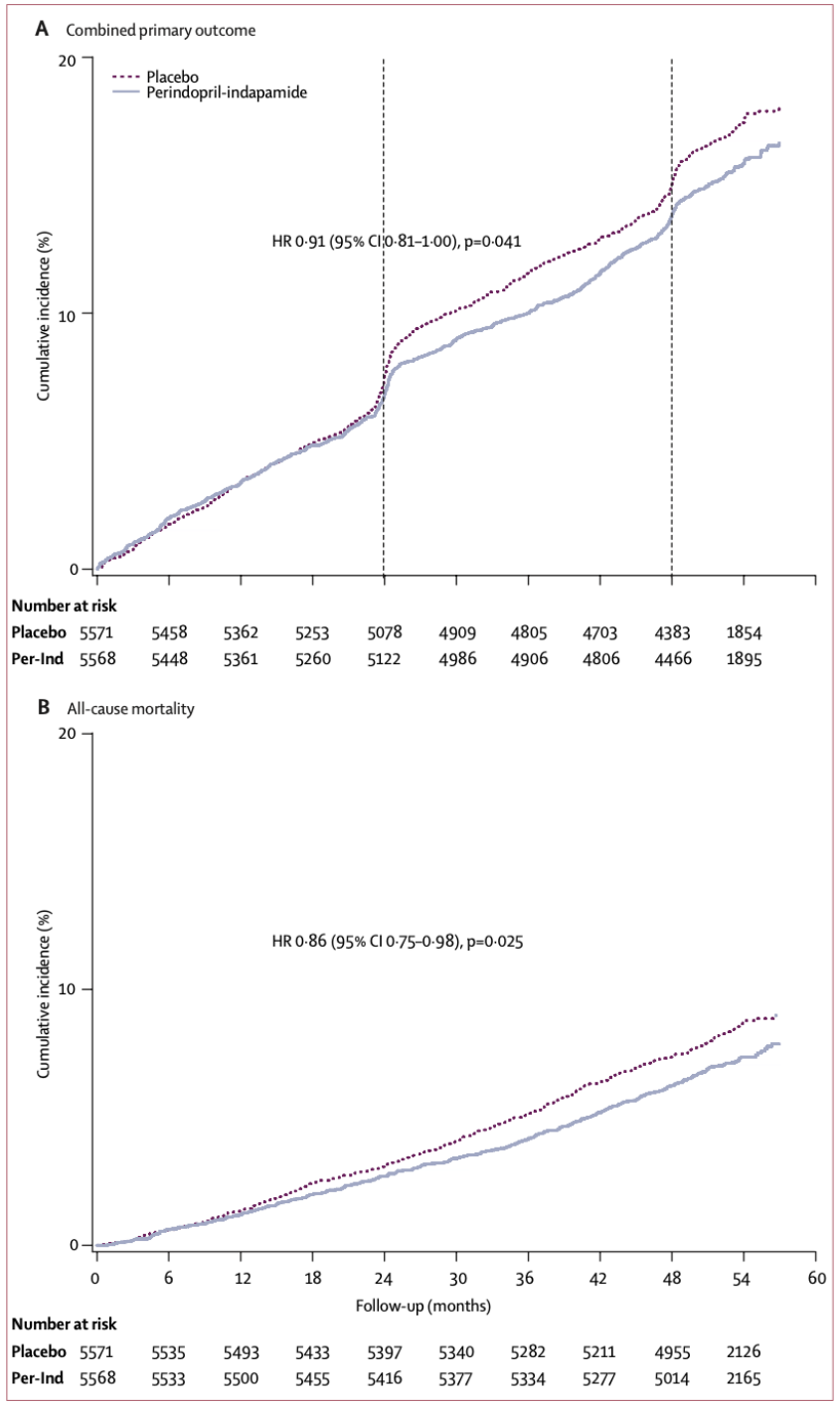
Variable	Intensive Therapy (N=2362)	Standard Therapy (N=2371)	P Value
Serious adverse events — no. (%)†			
Event attributed to blood-pressure medications	77 (3.3)	30 (1.27)	<0.001
Hypotension	17 (0.7)	1 (0.04)	<0.001
Syncope	12 (0.5)	5 (0.21)	0.10
Bradycardia or arrhythmia	12 (0.5)	3 (0.13)	0.02
Hyperkalemia	9 (0.4)	1 (0.04)	0.01
Angioedema	6 (0.3)	4 (0.17)	0.55
Renal failure	5 (0.2)	1 (0.04)	0.12
End-stage renal disease or need for dialysis	59 (2.5)	58 (2.4)	0.93
Symptoms affecting quality of life — no./total no. (%)‡			
Hives or swelling	44/501 (8.8)	41/468 (8.8)	1.00
Dizziness when standing	217/501 (44.3)	188/467 (40.3)	0.36
Adverse laboratory measures — no. (%)			
Potassium <3.2 mmol/liter	49 (2.1)	27 (1.1)	0.01
Potassium >5.9 mmol/liter	73 (3.1)	72 (3.0)	0.93
Elevation in serum creatinine			
>1.5 mg/dl in men	304 (12.9)	199 (8.4)	<0.001
>1.3 mg/dl in women	257 (10.9)	168 (7.1)	<0.001
Estimated GFR <30 ml/min/1.73 m²	99 (4.2)	52 (2.2)	<0.001
Clinical measures§			
Glycated hemoglobin — %	7.6±1.3	7.5±1.2	0.13
Fasting plasma glucose — mg/dl	147.1±56.6	148.1±57.5	0.58
Plasma LDL cholesterol — mg/dl	98.7±40.3	96.8±37.8	0.10
Plasma HDL cholesterol — mg/dl	46.7±14.0	47.8±14.9	0.02
Plasma triglycerides — mg/dl			0.001
Median	138	131	
Interquartile range	97–210	92–197	
Potassium — mg/dl	4.3±0.5	4.4±0.5	0.17
Serum creatinine — mg/dl	1.1±0.4	1.0±0.5	<0.001
Estimated GFR — ml/min/1.73 m²	74.8±25.0	80.6±24.8	<0.001
Ratio of urinary albumin (mg) to creatinine (g)			<0.001
Median	12.6	14.9	
Interquartile range	6.4–41.7	7.0–56.8	
Microalbuminuria — no./total no. (%)	656/2174 (30.2)	712/2205 (32.3)	0.13
Macroalbuminuria — no. /total no. (%)	143/2174 (6.6)	192/2205 (8.7)	0.009
Weight — kg	93.3±21.2	92.5±20.2	0.20

ACCORD

- <120 >>> some good effects BUT more side effects as well !
- More hypotension, increased SCr, lower K+
- 👉 for most pts, may be <140 is good !

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**



- Less macro events by 10%
- less all cause mortality by 14%

☞ <140 was appropriate !

>>> prevent micro and macro events

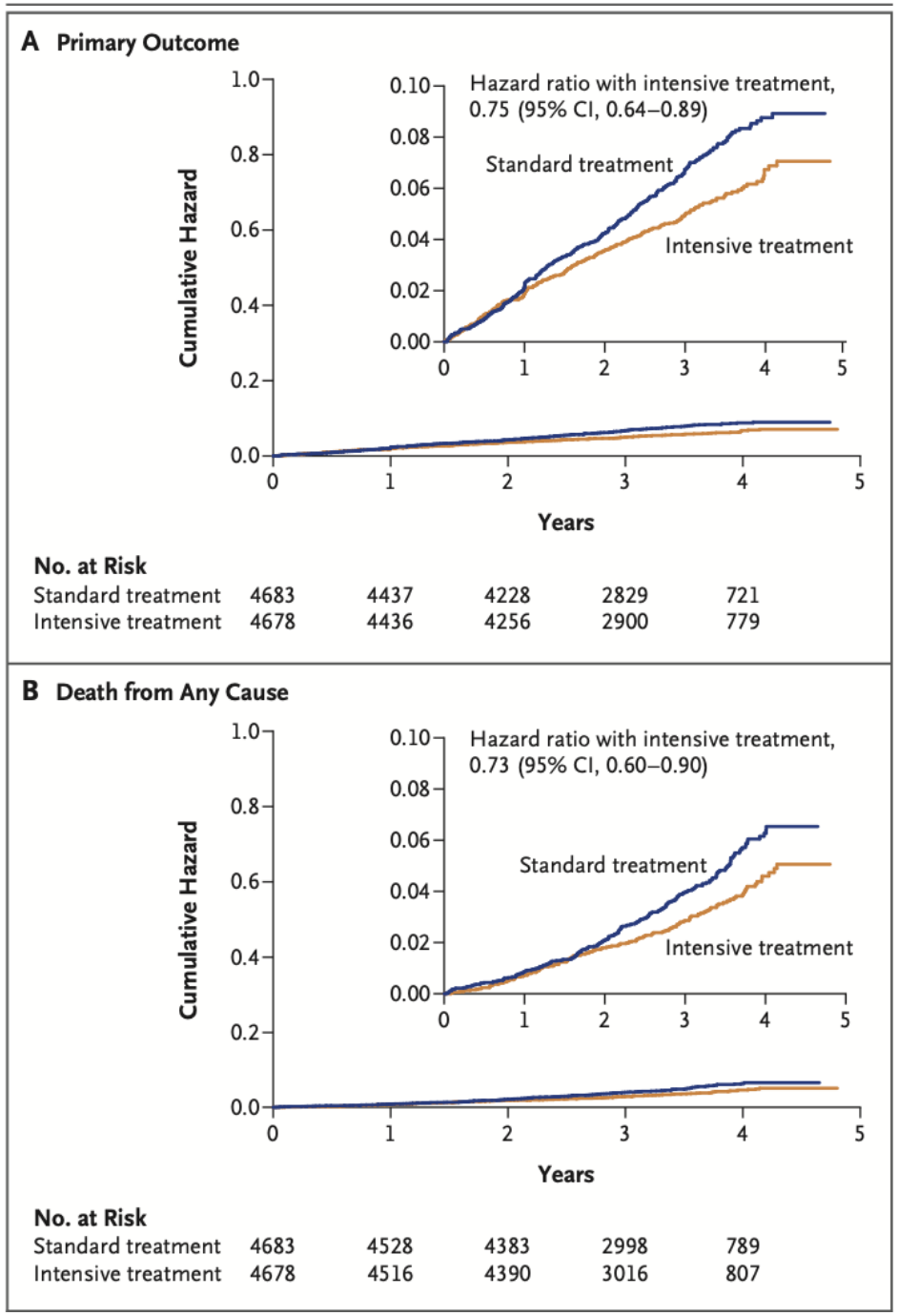
The case for 120 (SBP<120)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 26, 2015 VOL. 373 NO. 22

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group*



SPRINT

- Inclusion: Age>50; BP 130-180; high risk for CV events (>75yr; eGFR 30-60)
- Exclusion: **DM**; prior CV events
- Life expect <3
- Intensive arm= BP<120
- Std arm = BP <140
- Primary outcome= composite of CV mortality stroke, HF, ACS
- in 3 yrs >>> 25% reduction in the INTENSIVE arm
- in 3 yrs >>> 27% decrease in all cause mortality
- So, such good benefit >>> STOP the trial ! (after 3 yr)
- >>> may be <120 for “some” pts

When there is not real good data…

RESEARCH

Effect of antihypertensive treatment at different blood pressure levels in patients with diabetes mellitus: systematic review and meta-analyses

Mattias Brunström, Bo Carlberg

SBP>140

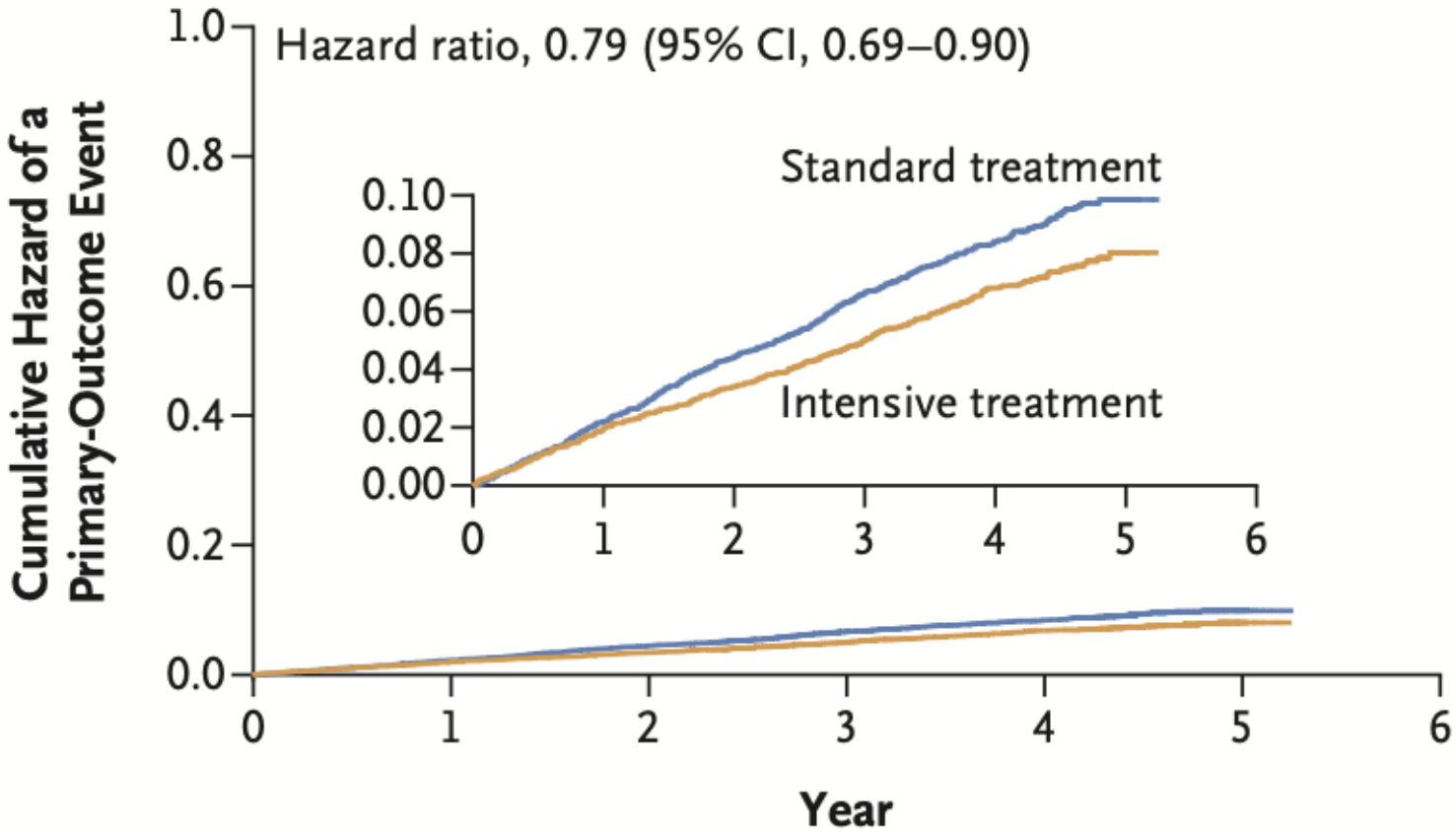
= we need

for all cause Mort >>> achieve 130-140
& <130 make no difference (AE)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 27, 2025 VOL. 392 NO. 12

Intensive Blood-Pressure Control in Patients with Type 2 Diabetes



No. at Risk

Standard treatment	6407	6087	5814	4626	3674	132
Intensive treatment	6414	6092	5871	4692	3738	112

Does Intensive Blood-Pressure Control Benefit in Patients with Type 2 Diabetes? The BPROAD Trial

#NephJC

COHORT

145 sites, China

n=12821

T2DM, elevated SBP, and increased risk of CVD

63.8 yrs mean age

45.3% women

4.2 years follow up

INTERVENTION

INTENSIVE GROUP (SBP <120 mmHg) N=6414

121.6 mmHg

After 1 yr

Mean SBP

STANDARD GROUP (SBP <140 mmHg) N=6407

133.2 mmHg

OUTCOMES

	INTENSIVE GROUP (IR)		STANDARD GROUP (IR)
PRIMARY OUTCOME	1.65	HR 0.79 (95% CI, 0.69- 0.90)	2.09
CKD PROGRESSION	1.61	HR 1.36 (95% CI, 0.70-2.59)	1.11
SERIOUS ADVERSE EVENT	36.5%	HR 1.00 (95% CI, 0.94- 1.06)	36.3%

Composite of nonfatal stroke, nonfatal MI, hospitalization for heart failure, or death from cardiovascular causes

IR- incidence rate, number of events/100 person years

Conclusion: Among patients with type 2 diabetes, the incidence of major cardiovascular events was significantly lower with intensive treatment targeting a systolic blood pressure of less than 120 mm Hg than with standard treatment targeting a systolic blood pressure of less than 140 mm Hg

References: Bi Y et al. BPROAD Research Group. Intensive Blood-Pressure Control in Patients with Type 2 Diabetes. N Engl J Med. 2024 Nov 16.

VA by Kajaree Giri MD, DM X@KajareeG

Table 3. Adverse Events.*

Outcome	Intensive Treatment (N=6414)		Standard Treatment (N=6407)		Hazard Ratio (95% CI)	P Value
	No. of Events	Percentage of Participants	No. of Events	Percentage of Participants		
Serious adverse event†	2340	36.5	2328	36.3	1.00 (0.94–1.06)	0.96
Conditions of interest‡						
Arrhythmia	69	1.1	68	1.1	1.01 (0.72–1.41)	0.95
Electrolyte abnormality	36	0.6	35	0.6	1.03 (0.65–1.64)	0.91
Injurious fall	65	1.0	61	1.0	1.06 (0.75–1.51)	0.74
Symptomatic hypotension	8	0.1	1	<0.1	7.92 (0.99–63.34)	0.05
Syncope	10	0.2	10	0.2	1.00 (0.41–2.39)	0.99
Acute renal failure	4	0.1	5	0.1	0.79 (0.21–2.95)	0.73
Clinical safety alerts§						
Serum sodium <130 mmol/liter	46	0.7	47	0.8	0.97 (0.65–1.46)	0.89
Serum sodium >150 mmol/liter	22	0.4	25	0.4	0.88 (0.49–1.56)	0.65
Serum potassium <3.0 mmol/liter	32	0.5	33	0.5	0.97 (0.60–1.58)	0.90
Serum potassium >5.5 mmol/liter	177	2.8	125	2.0	1.41 (1.12–1.77)	0.003

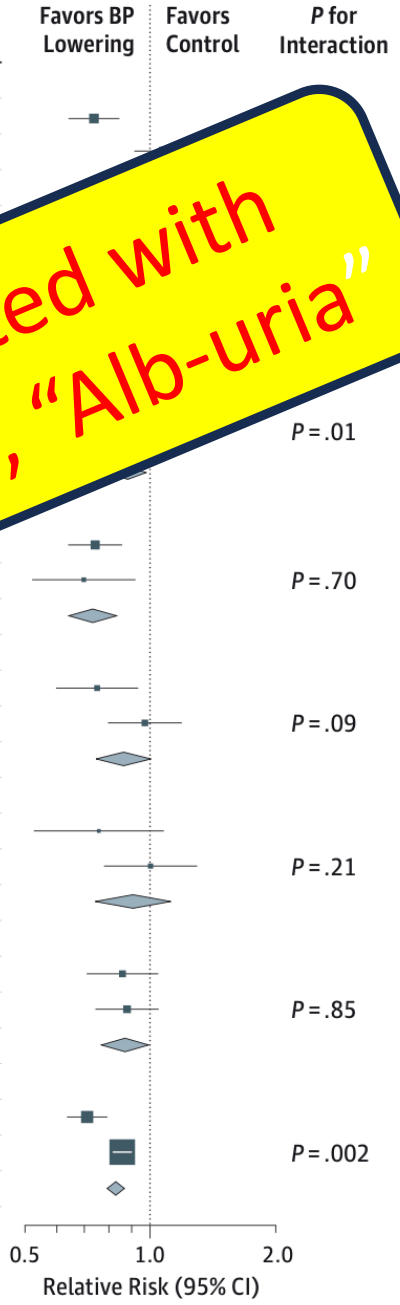
Research

Original Investigation

Blood Pressure Lowering in Type 2 Diabetes
A Systematic Review and Meta-analysis

Connor A. Emdin, HBSc; Kazem Rahimi, DM, MSc; Bruce Neal, PhD; Thomas Callender, MBChB; Vlado Perkovic, PhD; Anushka Patel, PhD

Outcome	No. of Studies	Baseline SBP, Mean, mm Hg	BP Lowering, No. Events	BP Lowering, No. Participants	Control, No. Events	Control, No. Participants	Relative Risk (95% CI)	*P* for Interaction
Mortality, mm Hg								
≥140[16, 18, 19, 27-30, 35, 39-41, 51, 55, 56, 64, 65, 77-80]	13	149	1614	16418	1626	14580	0.73 (0.64-0.84)	
<140[17, 31, 36-38, 58-60, 80, 81]	7	137	720	1275	693	11284	1.07 (0.92-1.26)	
Overall							0.87 (0.78-0.96)	
Cardiovascular disease, mm Hg								
≥140[16, 18, 19, 27-30, 35, 39-41, 46, 47, 51-53]	11	148	1861	14976	1918	14068	0.74 (0	
<140[17, 31, 36-38, 58-60, 80, 81]	6	137	1369	10780	1362	10794		
Overall								
Coronary heart disease, mm Hg								
≥140[16, 18, 27, 29, 30, 35, 39-41, 47, 51, 64, 65]	10	148	858	14875				
<140[17, 31, 36-38, 43, 58-60, 80, 81]	7	137	532					*P* = .01
Overall								
Stroke, mm Hg								
≥140[16, 18, 19, 27, 29, 30, 35, 39-41, 45-47, 51, 55, 56, 63-65]	14						.86)	
<140[31, 36-38, 58-60, 80, 81]							(0.52-0.92)	*P* = .70
Overall							0.73 (0.64-0.83)	
Heart failure, mm Hg								
≥140[16, 18, 29, 30, 35, 39					814	12676	0.75 (0.59-0.94)	
<140[31, 42, 43				092	534	8115	0.97 (0.79-1.19)	*P* = .09
Ove							0.86 (0.74-1.00)	
		147	389	12475	346	11530	0.75 (0.52-1.08)	
	3	138	207	7360	214	7382	1.00 (0.77-1.29)	*P* = .21
							0.91 (0.74-1.12)	
	4	146	564	7946	586	7753	0.86 (0.70-1.04)	
, 81	3	137	280	1835	319	1813	0.88 (0.74-1.05)	*P* = .85
O							0.87 (0.76-0.99)	
Albuminuria, mm Hg								
≥140[16, 28-30, 64, 65]	4	146	1681	8447	1898	7647	0.71 (0.63-0.79)	
<140[17, 36-38, 59, 60]	3	137	1118	5357	1265	5174	0.86 (0.81-0.90)	*P* = .002
Overall							0.83 (0.79-0.87)	



BP reduction <130mmHg is associated with lower risk of "stroke", "retinopathy", "Alb-uria"

Circulation

CLINICAL PRACTICE GUIDELINES

2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

Sept, 16 2025

5.3.1. Diabetes

Recommendations for Diabetes
Referenced studies that support the recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	A	1. In adults with T2D and hypertension, antihypertensive drug treatment should be initiated at an SBP of ≥130 mm Hg with a treatment goal of <130 mm Hg, with encouragement to achieve an SBP <120 mm Hg to reduce CVD morbidity and mortality.[1–5]
1	C-LD	2. In adults with T2D and hypertension, antihypertensive drug treatment should be initiated at a DBP of ≥80 mm Hg with a treatment goal of <80 mm Hg to reduce CVD morbidity and mortality.[6]
1	A	3. In adults with T2D and hypertension, all first-line classes of antihypertensive agents (ie, thiazide-type diuretics, long-acting CCB, ACEi, and ARB) are useful and effective for BP lowering.[1,7–9]
1	A	4. In adults with diabetes and hypertension, ACEi or ARB are recommended in the presence of CKD as identified by eGFR <60 mL/min/1.73 m^2 or albuminuria ≥30 mg/g and should be considered when mild albuminuria (<30 mg/g) is present to delay progression of diabetes-related kidney disease.[10–12]

ESC European Society of Cardiology
European Heart Journal (2024) **00**, 1–107
https://doi.org/10.1093/eurheartj/ehae178

2024 ESC Guidelines for the management of elevated blood pressure and hypertension

9.6.3. Managing blood pressure in diabetes

We recommend that all patients with diabetes are offered pharmacological BP-lowering treatment with a BP target of 120–129/70–79 mmHg, if feasible and tolerated

Recommendation Table 25 — Recommendations for managing hypertension in patients with diabetes

Recommendations	Class[a]	Level[b]
In most adults with elevated BP and diabetes, after a maximum of 3 months of lifestyle intervention, BP lowering with pharmacological treatment is recommended for those with confirmed office BP ≥130/80 mmHg to reduce CVD risk.[445,749]	I	A
BP-lowering drug treatment is recommended for people with pre-diabetes or obesity when confirmed office BP is ≥140/90 mmHg or when office BP is 130–139/80–89 mmHg and the patient is at predicted 10-year risk of CVD ≥10% or with high-risk conditions, despite a maximum of 3 months of lifestyle therapy.[445]	I	A
In persons with diabetes who are receiving BP-lowering drugs, it is recommended to target systolic BP to 120–129 mmHg, if tolerated.[136,146,445,747,749–752]	I	A

Table 5. Summary of Clinical Treatment Guidelines for Hypertension Treatment

Guidelines	Definition	Target blood pressure	First-line agents	Indication for dual antihypertensive therapy
ACC/AHA	130/80	<130/80	Diuretics Angiotensin-converting enzyme inhibitors* Angiotensin receptor blockers* Calcium channel blockers	>140/90
ADA	140/90	<140/90 Or <130/80 with high cardiovascular risk (existing atherosclerotic cardiovascular disease or 10-y risk score ≥15%) provided it can be safely attained	Angiotensin-converting enzyme inhibitors* Angiotensin receptor blockers * Thiazide-like diuretics Dihydropyridine calcium channel blockers	>160/100

Should all DM pts be on ACEi/ARBs ?

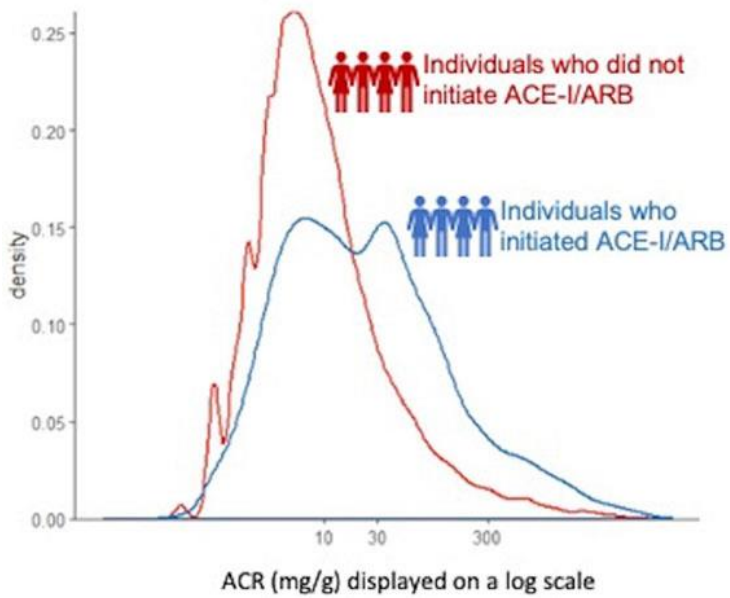
All major antihypertensive drug classes have been shown to reduce CV outcomes in type 2 diabetes

starting with dual combination therapy and using drug combinations in the majority of the patients**, is **even more necessary for diabetic patients

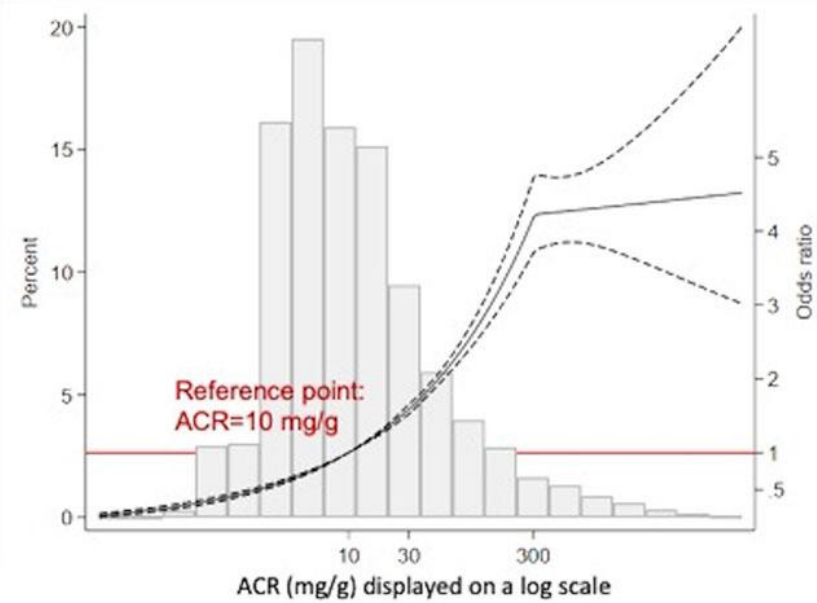
Table S10 Choice of starting blood pressure-lowering treatment, depending on comorbidity

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

Distribution of ACR stratified by ACE-I/ARB initiation



Association between ACR level and ACE-I/ARB initiation



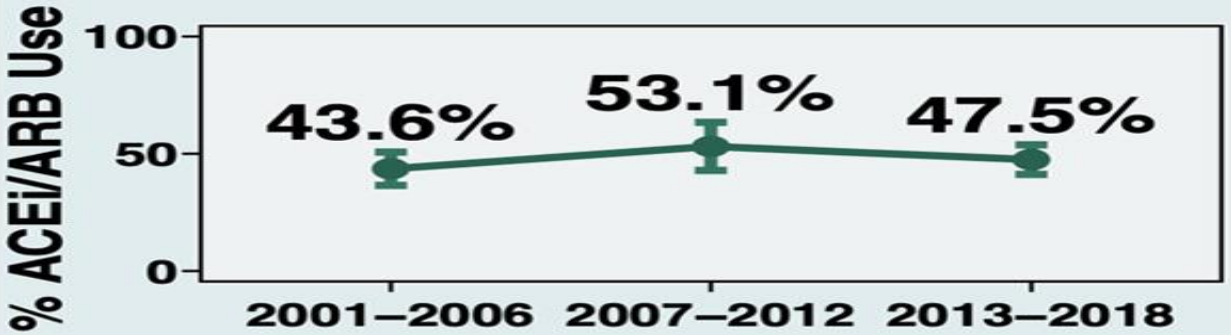
- *Albuminuria test results change patient care*
- *Adherence to albuminuria testing is a key step in optimal medical management*

Angiotensin converting enzyme inhibitor or angiotensin receptor blocker use among hypertensive US adults with albuminuria

National Health and Nutrition Examination Survey 2001-2018

20,538 adults with hypertension

No Significant Trend in ACEi/ARB Usage Among UACR ≥300 mg/g



Estimated US adults with hypertension & UACR ≥300 mg/g *not* taking ACEi/ARB

1.6 million

Adjusted prevalence ratios of ACEi/ARB use by UACR

0-29 mg/g	Ref
30-299 mg/g	1.11
≥300 mg/g	0.95

Conclusion

ACEi/ARB underutilization is a significant gap in care for hypertension with albuminuria.

When we don't have a definite answer…

RESEARCH

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]

If we have DM with normotension
>>> ACEi/ARBs = CCBs = diuretics (in outcomes)

the difference is only if we had Alb-uria !

Conclusions

This analysis of head to head comparison trials of RAS blockers versus other antihypertensive agents in people with diabetes (and largely without microalbuminuria or proteinuria) failed to show a superiority of RAS blockers compared with other antihypertensive agents for the prevention of hard outcomes. The results support the recommendation of both the 2013 European Society of Cardiology/European Society of Hypertension guidelines[5] and the 2014 eighth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure[6] that any class of antihypertensive agents can be used in people with diabetes especially in those without renal impairment.

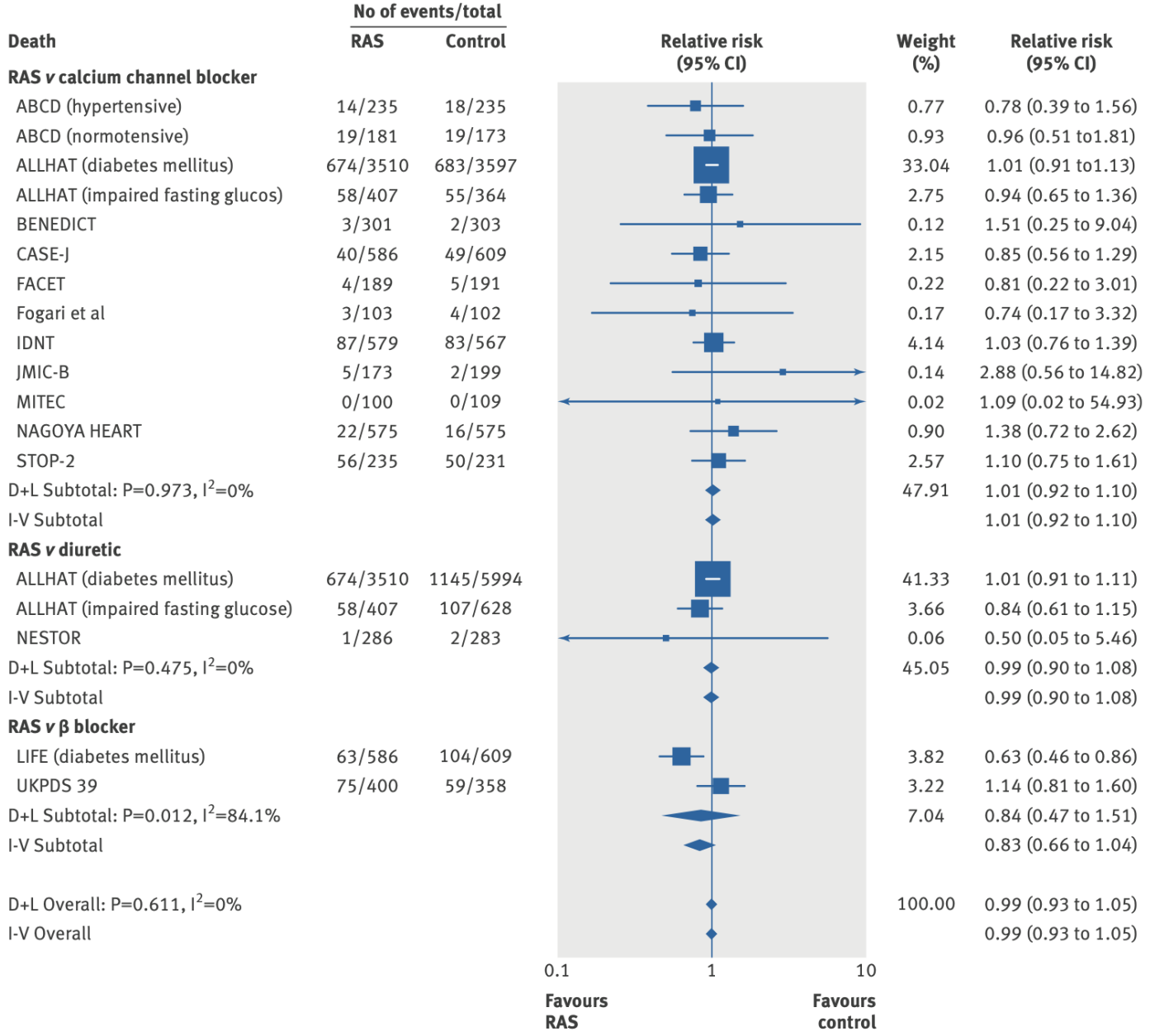
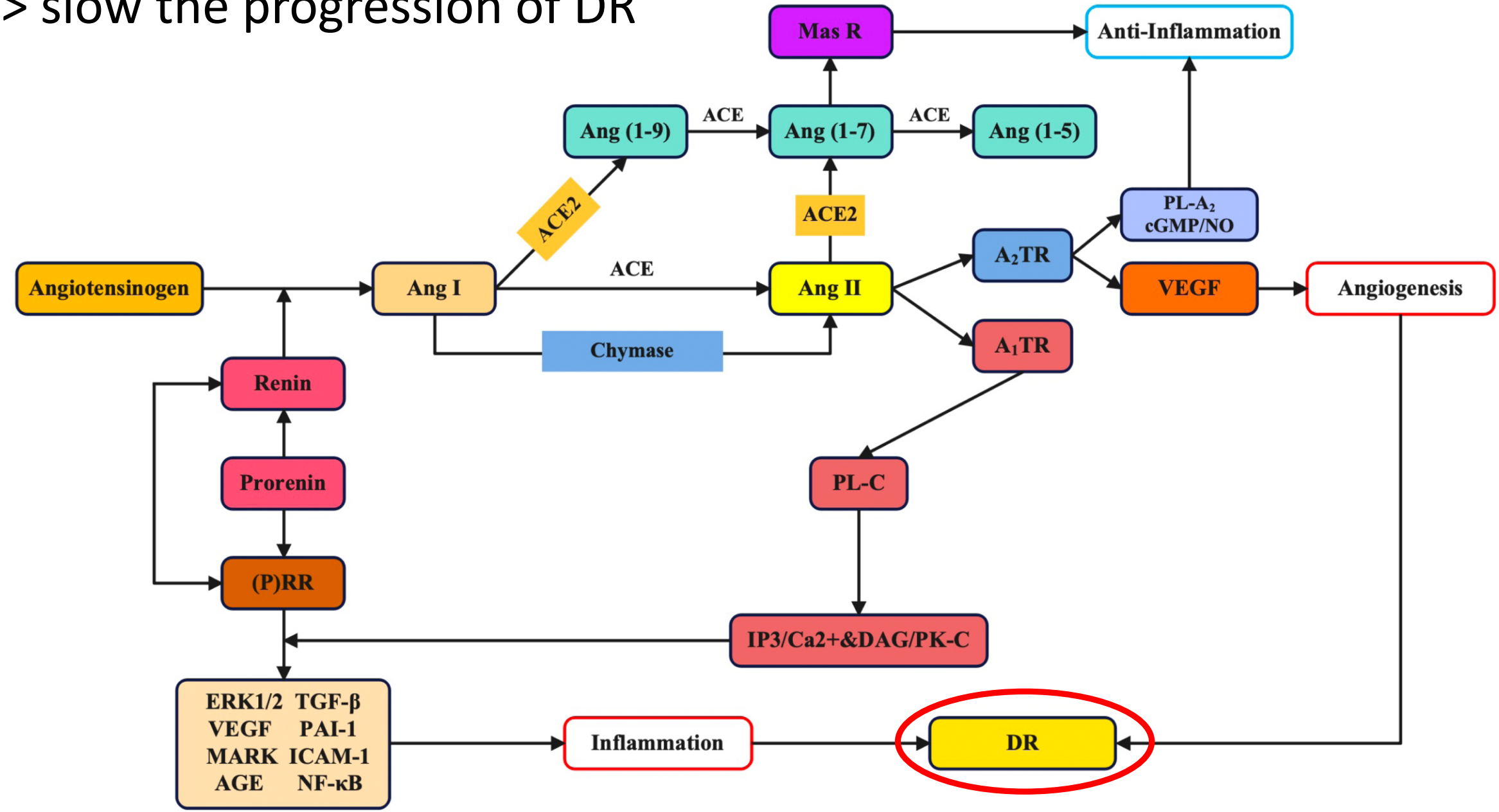


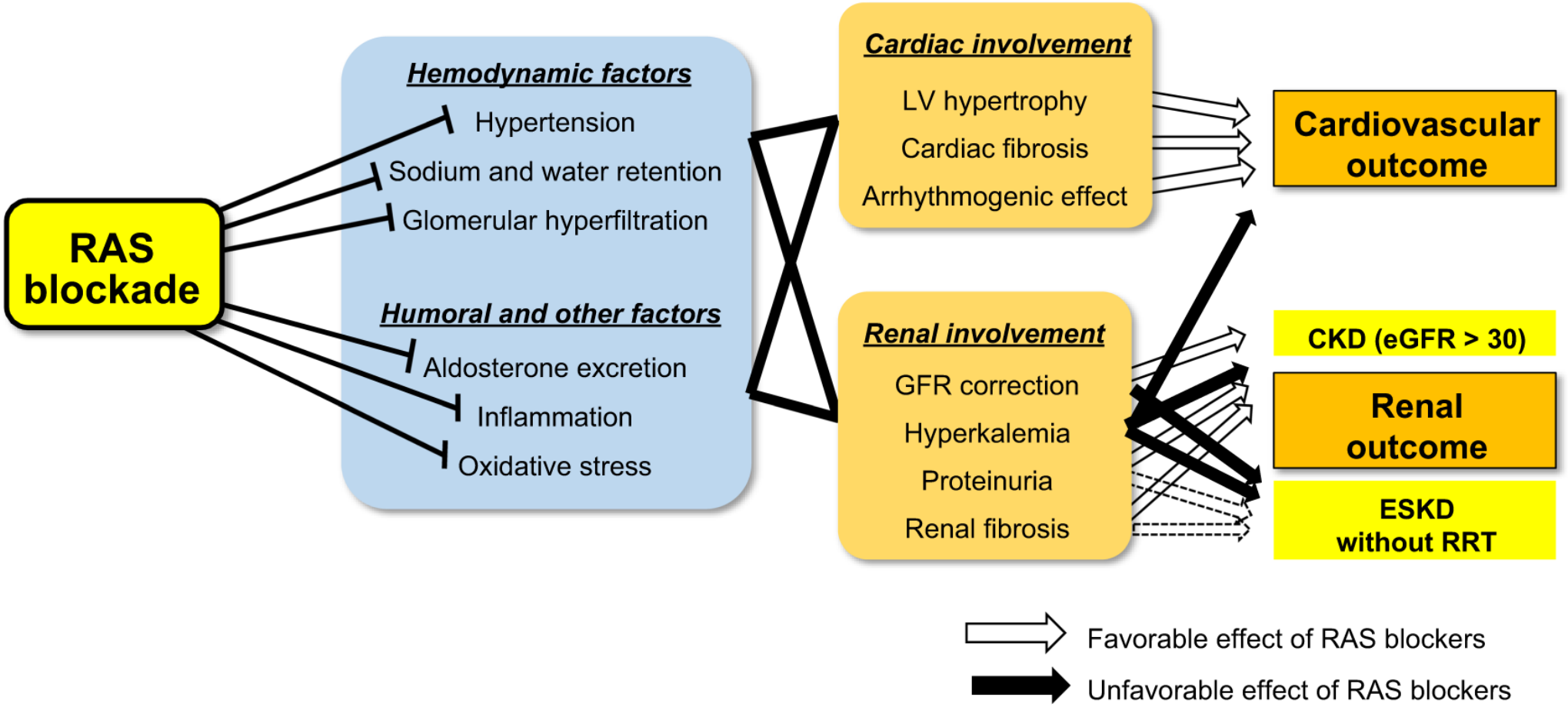
Fig 1 | Outcomes of death with renin angiotensin system (RAS) blockers compared with other antihypertensives in people with diabetes

ACEi/ARB

>>> slow the progression of DR



ACEi/ARB >>> slow the progression of CKD



What is the benefit of RAS inhibition in advanced CKD?

Kidney Medicine

Methods

Chronic Renal Insufficiency Cohort (CRIC)
Observational study

eGFR < 30
N = 678

Grouped by RAS inhibitor use pattern

Associated use patterns with ESKD and mortality

Findings

	57% consistent RAS inhibition	13% intermittent RAS inhibition	7% started RAS inhibition during the year	23% no RAS inhibition
ESKD	**Ref HR** (95% CI)	**1.46** (0.83 - 2.55)	**0.78** (0.33 - 1.84)	**1.09** (0.71 - 1.67)
Mortality	**Ref HR** (95% CI)	**1.23** (0.80 - 1.90)	**1.10** (0.63 - 1.92)	**1.02** (0.74 - 1.40)

Conclusions: In a U.S. CKD population, use of RAS inhibition in eGFR <30 is heterogeneous. There was no difference in risk of progression to ESKD or mortality across patterns of RAS inhibitor use.

Reference: Arora N, Katz R, Bansal N. ACE Inhibitor/Angiotensin Receptor Blocker Use Patterns in Advanced CKD and Risk of Kidney Failure and Death. *Kidney Medicine,* 2020.

Visual Abstract by Anna Gaddy, MD @AnnaGaddy

What is the role of initiation of ACEi or ARB in advanced chronic kidney disease?

#NephJC

Systematic review and meta-analysis

Ovid Medline & CKD EPI Clinical Trials Consortium

1739 participants from 18 trials

Mean eGFR 22.2 ml/min/1.73 m^2

Objective

To compare use of ACEi/ARB Vs. placebo or other antihypertensives in patients with Stage 4 CKD with rates of KFRT and death

Findings

624 (35.9%) developed KFRT

133 (7.6%) died during a median follow-up of 34 months

KFRT- Kidney failure with renal replacement therapy

Outcomes

ACEi/ARB treatment initiation led to lower risk for KFRT HR 0.66 (95% CI, 0.55 to 0.79)

No risk reduction for risk of death HR 0.86 (95 % CI 0.58-1.28)

Conclusion: Initiation of ACEi or ARB therapy protects against KFRT, but not death, in people with advanced CKD

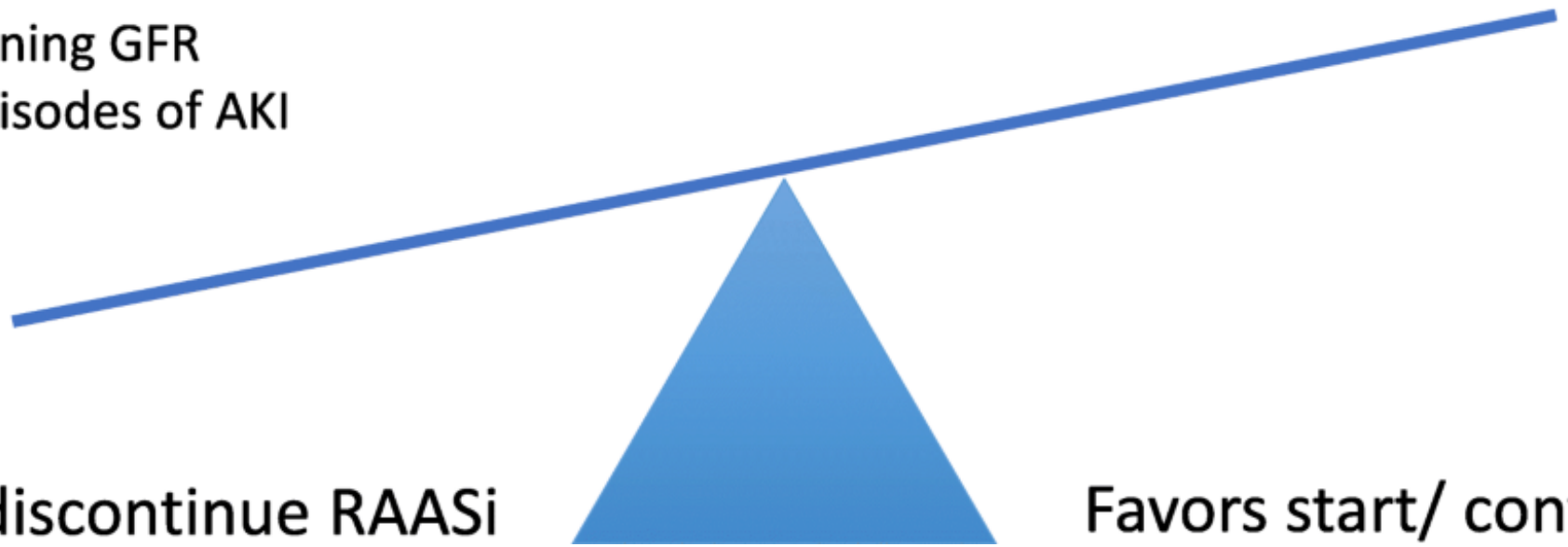
Reference: Ku E et al Ann Intern Med. 2024 Jul;177(7):953-963. doi: 10.7326/M23-3236

VA by Nikhil Elenjickal MD, DNB @DrNikhilJ1

Factors to consider for use of RAASi in advanced CKD

- Elderly
- Minimal baseline proteinuria
- Polycystic kidney disease
- Impaired renal perfusion (e.g. renovascular disease)
- Rapidly declining GFR
- Repeated episodes of AKI
- Hypotension

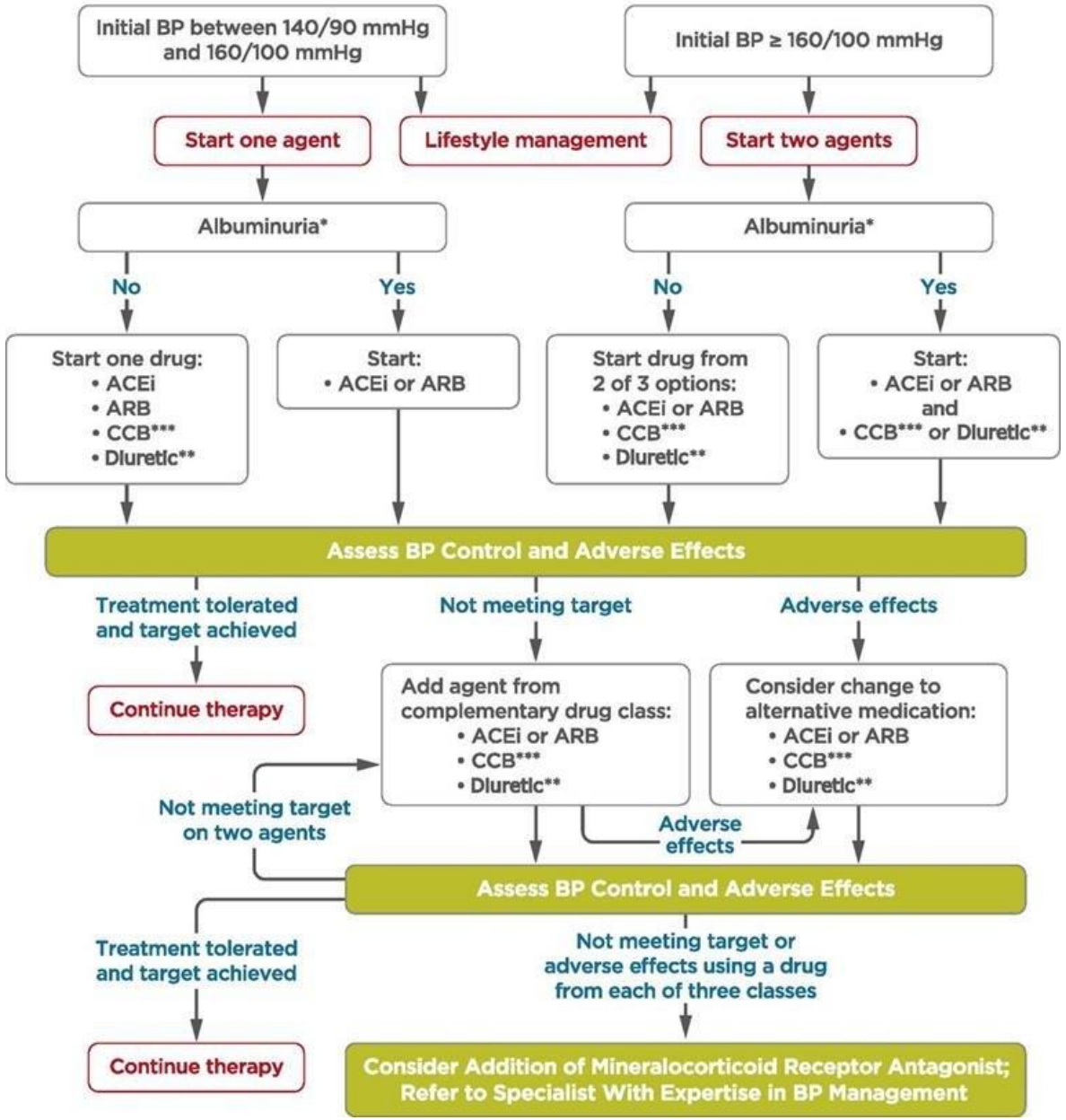
- Young patients
- Higher baseline GFR (e.g. 20-30ml/min)
- Substantial initial reduction in proteinuria
- Tolerable increase in creatinine and K levels
- Significant rebound proteinuria following drug cessation



Favors no/ discontinue RAASi

Favors start/ continue RAASi

Recommendations for the Treatment of Confirmed Hypertension in People With Diabetes



Guideline (year)	Diagnostic / grade threshold	When to **start pharmacologic therapy** in people with diabetes	Usual **BP treatment target** (if tolerated)	First-line agents / renal notes	Monitoring / special remarks
ADA — Standards of Care (2025). Diabetes Journals+1	Uses conventional office BP thresholds; emphasises measurement accuracy and out-of-office BP for confirmation. Diabetes Journals	Start drugs if BP ≥ **130/80 mmHg** in most adults with diabetes and/or when CV or renal risk factors present; individualise for frailty. professional.diabetes.org+1	**Target <130/80 mmHg** for most adults with diabetes if tolerated; relax target in frail/elderly or those at risk of hypotension. Diabetes Journals+1	RAS blockade (ACE-I or ARB) recommended early when albuminuria/CKD or high CV risk; add thiazide-type diuretic or long-acting CCB if needed. professional.diabetes.org+1	Recommends home BP (HBPM) / ambulatory BP monitoring (ABPM) where possible; emphasises lifestyle measures (sodium, weight, exercise). professional.diabetes.org
AHA/ACC (2025 high-BP guideline) — living guideline. AHA Journals+1	Lower diagnostic threshold compared with some European guidelines (stage 1 ≥130/80 mmHg) and risk-based classification. PMC	Recommends initiating pharmacologic therapy at **≥130/80 mmHg** for people with diabetes (especially with additional CVD/CKD/target-organ damage or elevated 10-yr risk). PMC+1	General target **<130/80 mmHg** for most people with diabetes if tolerated. Emphasises individualized therapy and careful monitoring for adverse effects of intensive lowering. PMC+1	Recommends accurate standardized BP measurement, ABPM/HBPM for out-of-office confirmation, and risk-based decision making. Guideline described as a "living" document (updates expected). AHA Journals+1	
ESC/ESH (European) — 2023 guideline. PubMed+1	Uses grades: normal / high-normal / grade-1 (≥140/90 mmHg) etc.; emphasizes clinic and out-of-office measurements. PubMed	For many European recommendations, pharmacologic therapy commonly started at **≥140/90 mmHg** in the general population; in high-risk subgroups (including some with diabetes + risk/target organ damage) earlier treatment is considered — individualisation stressed. For diabetes, consider earlier/lower thresholds depending on overall risk. PubMed+1	ESC/ESH generally recommends **<140/90 mmHg** as an initial objective for most; lower goals (≈130/80) may be reasonable/tolerated in selected high-risk patients but must be balanced against harms. (European guidance therefore is somewhat less uniformly aggressive than AHA/ACC on a population level.) PubMed+1	Recommends ACE-I/ARB as part of combination therapy when albuminuria/CKD present; combination therapy and early combination are encouraged to reach targets. PubMed	Strong emphasis on out-of-office BP (ABPM/HBPM), sodium restriction, and stepwise drug combinations; warns about overtreatment in frail/elderly. Lippincott Journals
IDF — Global Clinical Practice Recommendations (2025). International Diabetes Federation+1	Global recommendations oriented to diabetes care; stresses BP screening in all people with diabetes and adaptation to resource settings. International Diabetes Federation	Recommends initiating therapy earlier in patients with diabetes and additional CV/renal risks; exact numeric thresholds aligned with ADA/AHA for contexts where feasible (risk-based). Emphasises graded approach for low-resource settings. International Diabetes Federation	Recommends ambitious BP control (consistent with cardio-renal protection principles) where safe — typically aiming for **≈130/80 mmHg** when tolerated; pragmatic (less-intensive) targets may be advised where resources or patient factors require. International Diabetes Federation	Recommends RAS blockade for albuminuria/CKD, and local adaptation (medication availability, monitoring capacity). Highlights implementation differences between resource settings. International Diabetes Federation	Strong emphasis on implementability: HBPM/ABPM where available, but pragmatic monitoring algorithms for low-resource settings; lifestyle interventions central

Summary

- Reducing BP reduce CV events (ASCVD)
- BP goals in pts with DM:
- For most <140/90
- For pts @ high risk <130/80 or
- even sometimes if you can tolerate <120/80
- Individualize ttt
- ACEi/ARB >>> if alburia

- Just reduce BP

? Practical Take-Home

- T1DM & T2DM >>> aim for a BP **<130/80 mmHg** if tolerated and no specific contraindication (eg advanced CKD stage with hypotension risk).
- Use RAS-inhibition (ACEi/ARB) early if albuminuria or CKD is present
- If target not reached: escalate with thiazide-type diuretic (or thiazide-like) and a long-acting CCB, in combination with RAS-inhibitor.
- Routinely monitor with home BP or ambulatory BP where possible.
- Lifestyle modification remains imperative — weight loss (if overweight/obese), sodium restriction (especially relevant in CKD), physical activity, dietary quality.
- Individualize: In older, frail, or advanced CKD patients, consider slightly more conservative targets, with frequent monitoring for possible overtreatment or adverse effects (AKI, hypotension).

MERCI