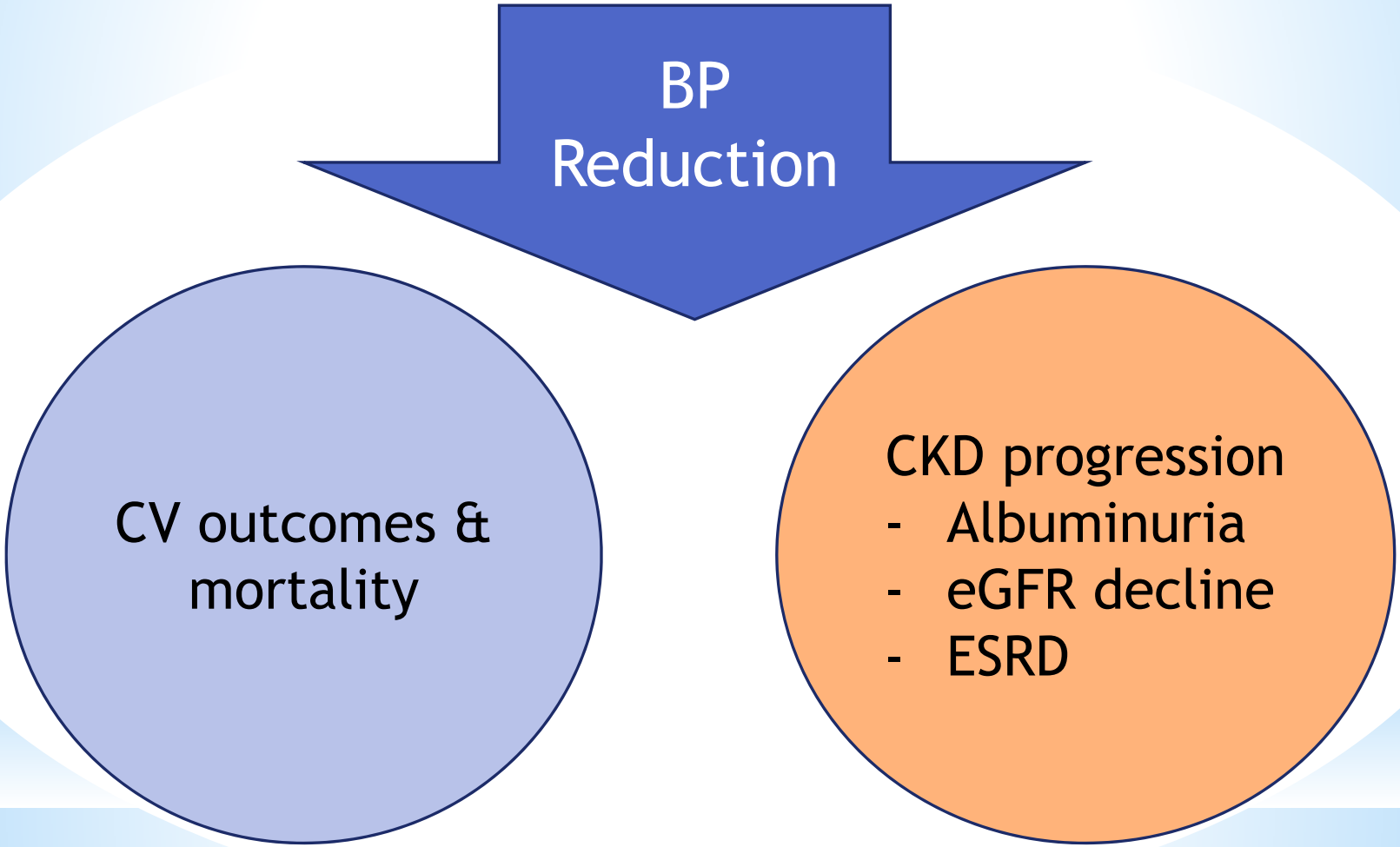
The Optimal Level of BP Control in Patients with CKD

Seung Hyeok Han, MD, PhD

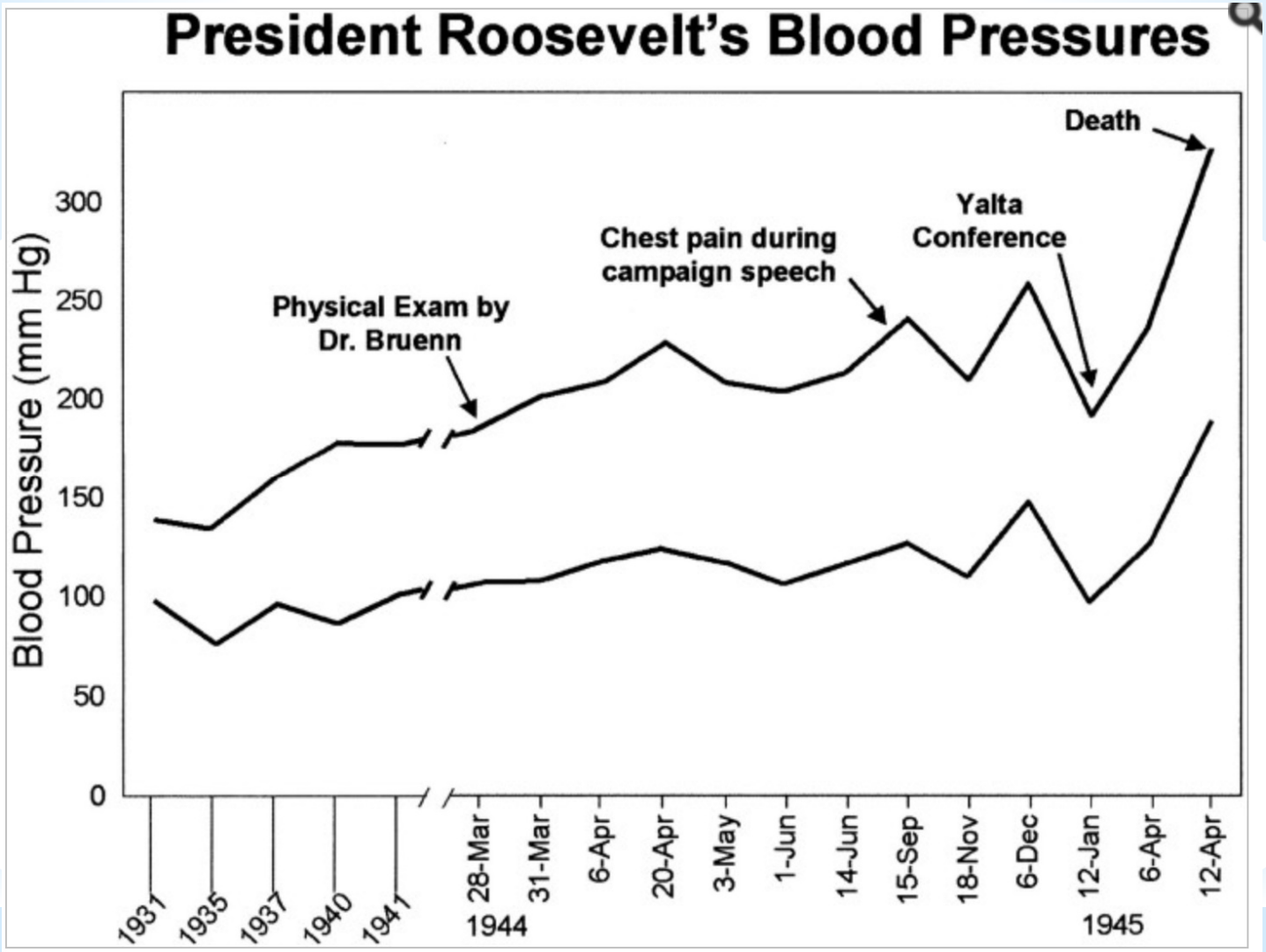
Department of Internal Medicine

Yonsei University College of Medicine

The Scope of 'Optimal' BP



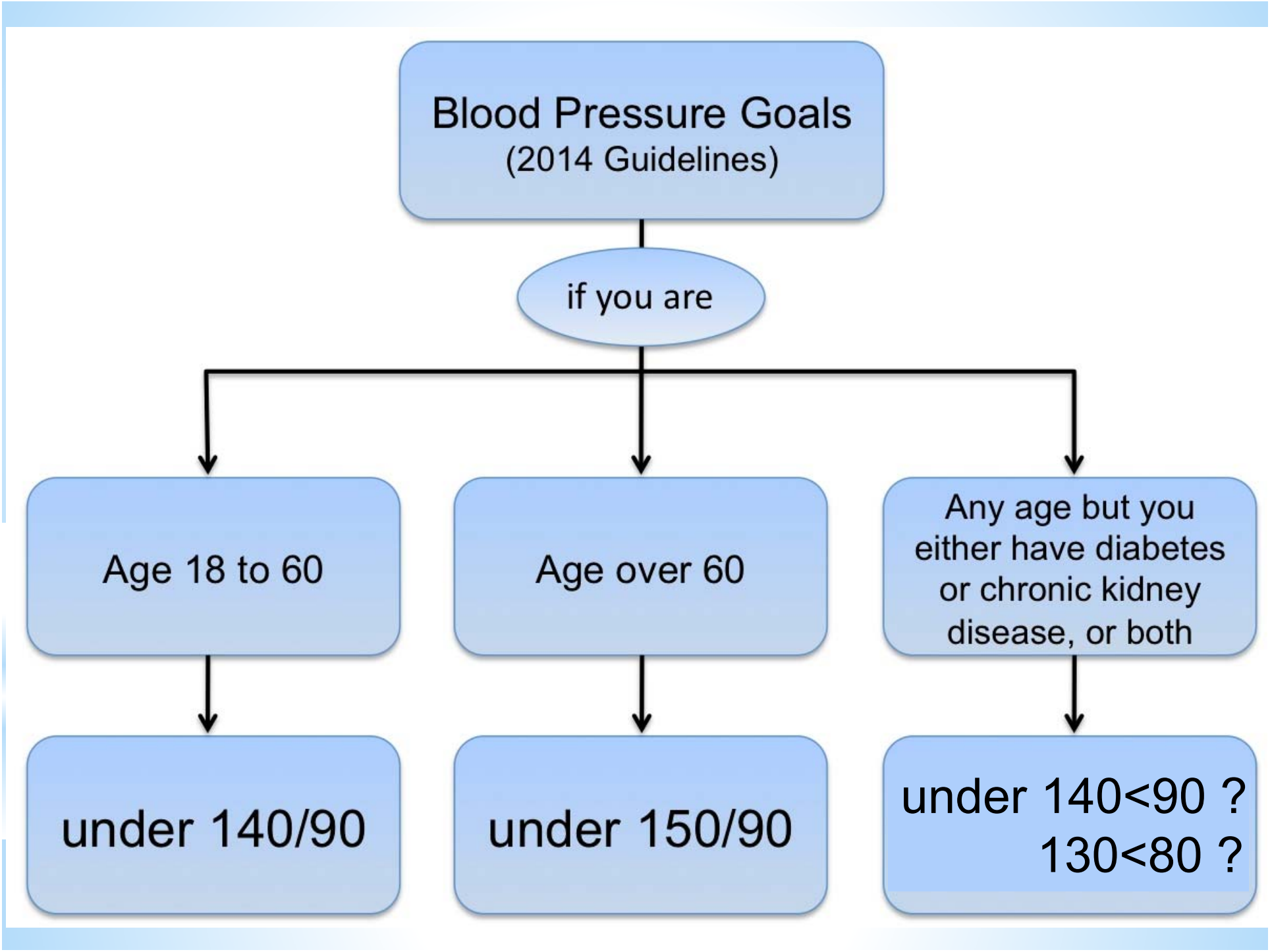
When to Treat?



When to Treat?

When to Treat?

There is a general consensus on the treatment threshold of BP → Initiate to treat HTN when BP > 140/90 mmHg.


Blood Pressure Goals
(2014 Guidelines)
if you are
Age 18 to 60
Age over 60
Any age but you either have diabetes or chronic kidney disease, or both
under 140/90
under 150/90
under 140<90 ?
130<80 ?

Target BP – The Current Guidelines

Guideline	Blood pressure target in CKD without proteinuria*	Blood pressure target in CKD with proteinuria	Recommended first line medication
USA JNC8[91]	<140/<90 mmHg	<140/<90 mmHg	ACEI or ARB
KDIGO[76]	<140/<90 mmHg	<130/<80 mmHg	ACEI or ARB
NICE[80]	<140/<90 mmHg	<130/<80 mmHg	ACEI or ARB‡
CHEP[78]	<140/<90 mmHg	<140/<90 mmHg	ACEI; ARB if ACEI intolerant
ESC/ESH[79]	<140 mmHg	<130 mmHg	ACEI or ARB
ASH/ISH[123]	<140/<90 mmHg	<140/<90 mmHg§	ARB or ACEI
ISHIB[124]	<130/<80 mmHg	<130/<80 mmHg	Diuretic or CCB

Townsend and Taler, Nat Rev Nephrol 2015

Clinical Review & Education

Special Communication

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults

Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

Paul A. James, MD; Suzanne Oparil, MD; Barry L. Carter, PharmD; William C. Cushman, MD; Cheryl Dennison-Himmelfarb, RN, ANP, PhD; Joel Handler, MD; Daniel T. Lackland, DrPH; Michael L. LeFevre, MD, MSPH; Thomas D. MacKenzie, MD, MSPH; Olugbenga Ogedegbe, MD, MPH, MS; Sidney C. Smith Jr, MD; Laura P. Svetkey, MD, MHS; Sandra J. Taler, MD; Raymond R. Townsend, MD; Jackson T. Wright Jr, MD, PhD; Andrew S. Narva, MD; Eduardo Ortiz, MD, MPH

Box. Recommendations for Management of Hypertension

Recommendation 1

In the general population aged ≥60 years, initiate pharmacologic treatment to lower blood pressure (BP) at systolic blood pressure (SBP) ≥150 mm Hg or diastolic blood pressure (DBP) ≥90 mm Hg and treat to a goal SBP <150 mm Hg and goal DBP <90 mm Hg. (Strong Recommendation – Grade A)

Corollary Recommendation

In the general population aged ≥60 years, if pharmacologic treatment for

Recommendation 4

In the population aged ≥18 years with chronic kidney disease (CKD), initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg or DBP ≥90 mm Hg and treat to goal SBP <140 mm Hg and goal DBP <90 mm Hg. (Expert Opinion – Grade E)

Opinion – Grade E)

Recommendation 4

In the population aged ≥18 years with chronic kidney disease (CKD), initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg or DBP ≥90 mm Hg and treat to goal SBP <140 mm Hg and goal DBP <90 mm Hg. (Expert Opinion – Grade E)

Recommendation 5

In the population aged ≥18 years with diabetes, initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg or DBP ≥90 mm Hg and treat to a goal SBP <140 mm Hg and goal DBP <90 mm Hg. (Expert Opinion – Grade E)

Recommendation 6

In the general nonblack population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic, calcium channel blocker (CCB), angiotensin-converting enzyme inhibitor (ACEI), or angiotensin receptor blocker (ARB). (Moderate Recommendation – Grade B)

Recommendation 7

In the general black population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic or CCB. (For

continue to assess BP and adjust the treatment regimen until goal BP is reached. If goal BP cannot be reached with 2 drugs, add and titrate a third drug from the list provided. Do not use an ACEI and an ARB together in the same patient. If goal BP cannot be reached using only the drugs in recommendation 6 because of a contraindication or the need to use more than 3 drugs to reach goal BP, antihypertensive drugs from other classes can be used. Referral to a hypertension specialist may be indicated for patients in whom goal BP cannot be attained using the above strategy or for the management of complicated patients for whom additional clinical consultation is needed. (Expert Opinion – Grade E)

KDIGO 2012

albuminuria	<30 mg/g	30-300 mg/g	>300 mg/g
Diabetes (-)	≤140/90 mmHg (1B)	≤130/80 mmHg (2D)	≤130/80 mmHg (2C)
		ARB or ACE-I (2D)	ARB or ACE-I (1B)
Diabetes (+)	≤140/90 mmHg (1B)	≤130/80 mmHg (2D)	
		ARB or ACE-I (2D)	ARB or ACE-I (1B)

2012 KDIGO BP guideline

Shortcomings

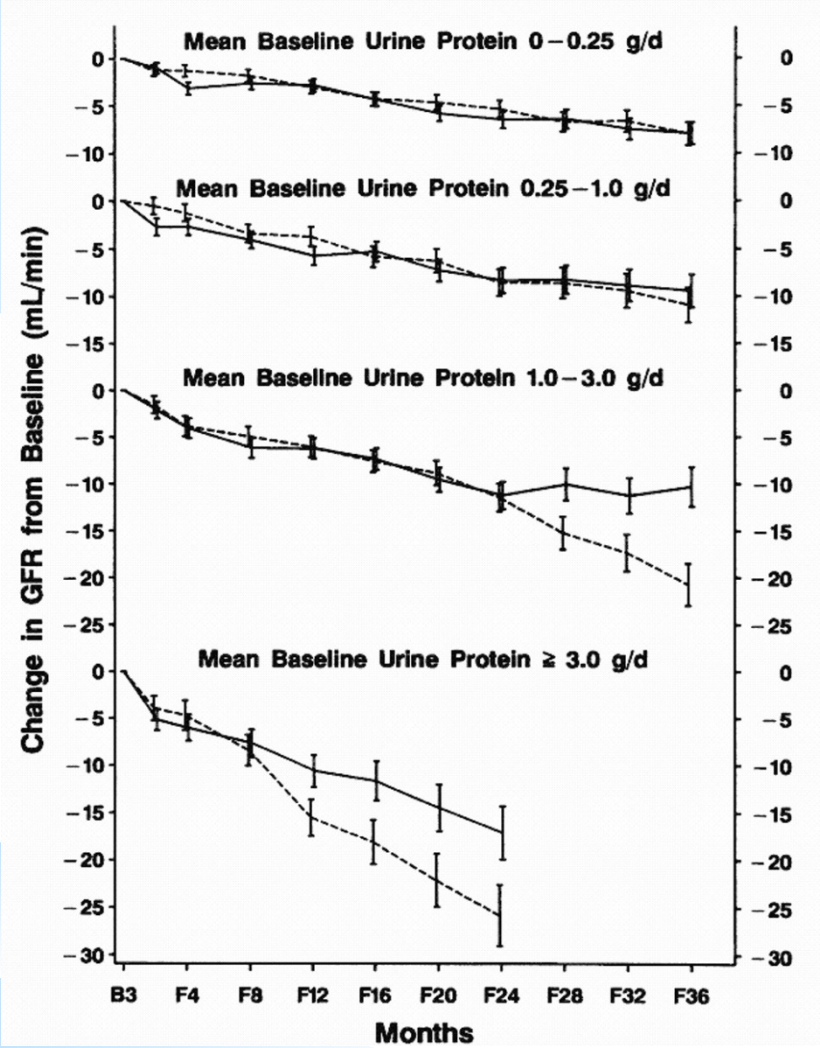
- Most large RCTs (Intensified vs. Conventional BP) : Composite outcomes of death, CV deaths or CV outcomes
  → Renal outcomes?

- Most studies in CKD patients: RAS blockers vs. placebo or CCBs with equally controlled BP
  → Is RAS inhibition more important than BP control?

- Patients with well-controlled BP were excluded from the RCTs and included in the observational studies.

→ Then what is the target BP ?

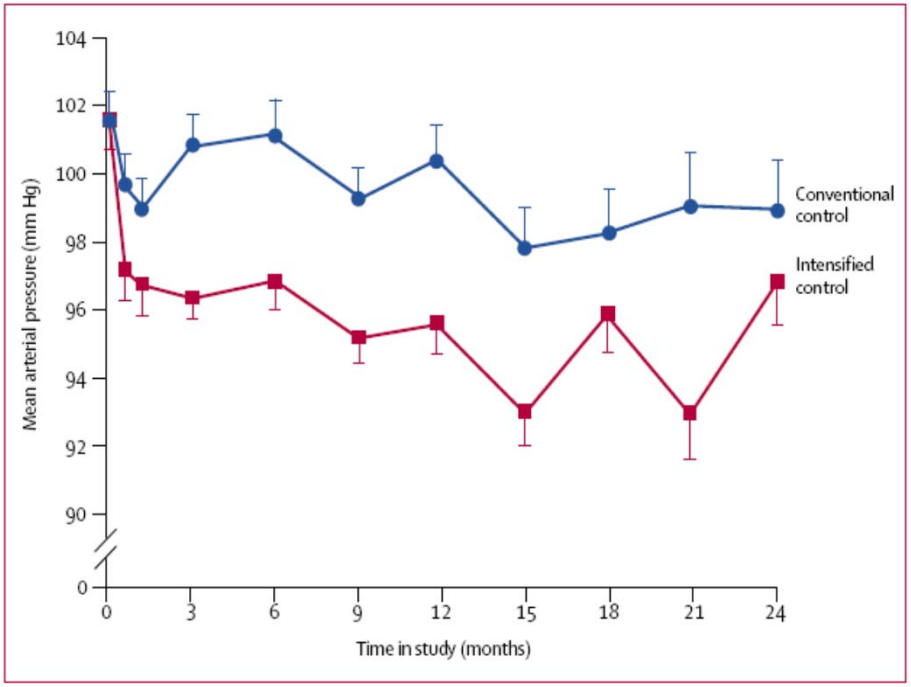
Blood Pressure Control, Proteinuria, and the Progression of Renal Disease (MDRD Study)

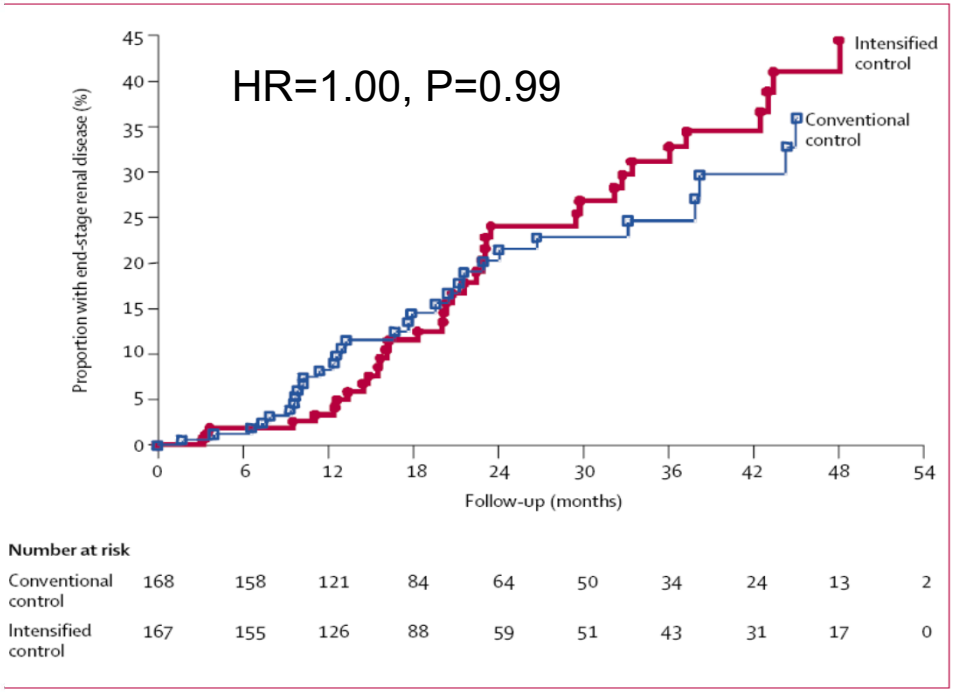


For patients with urinary protein excretion > 1 g/d, target BP should be a mean arterial pressure of < or = 92 mm Hg, equivalent to 125/75 mm Hg

NEJM 1994

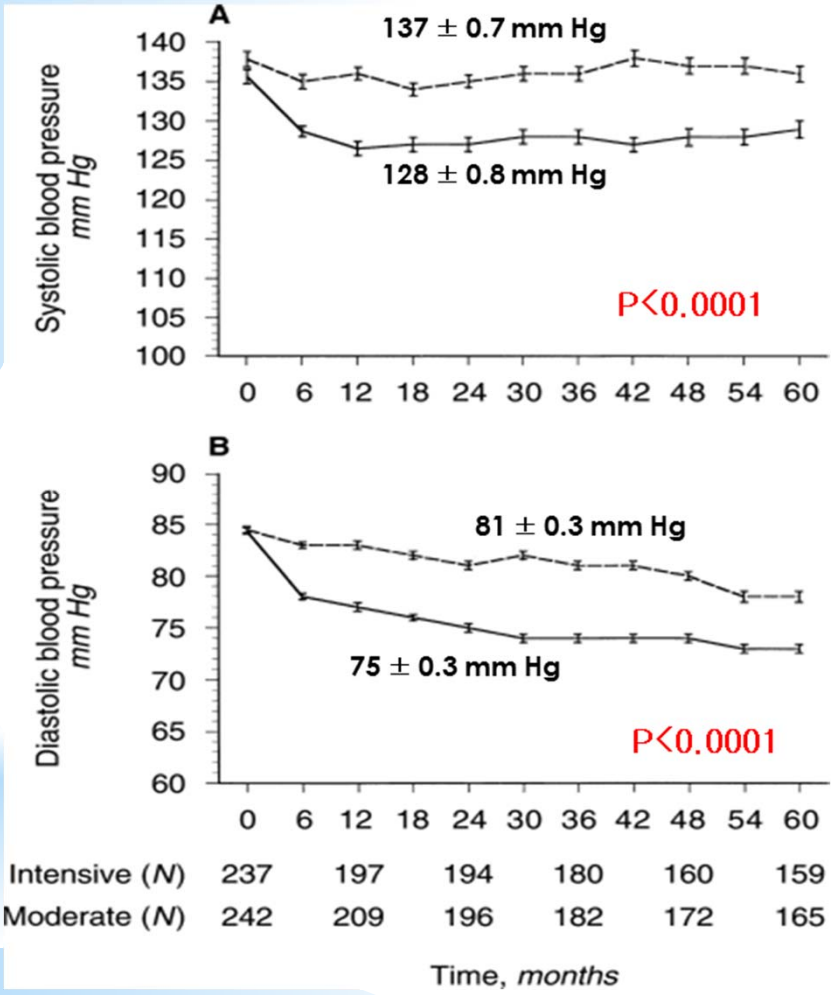
REIN II (2005)

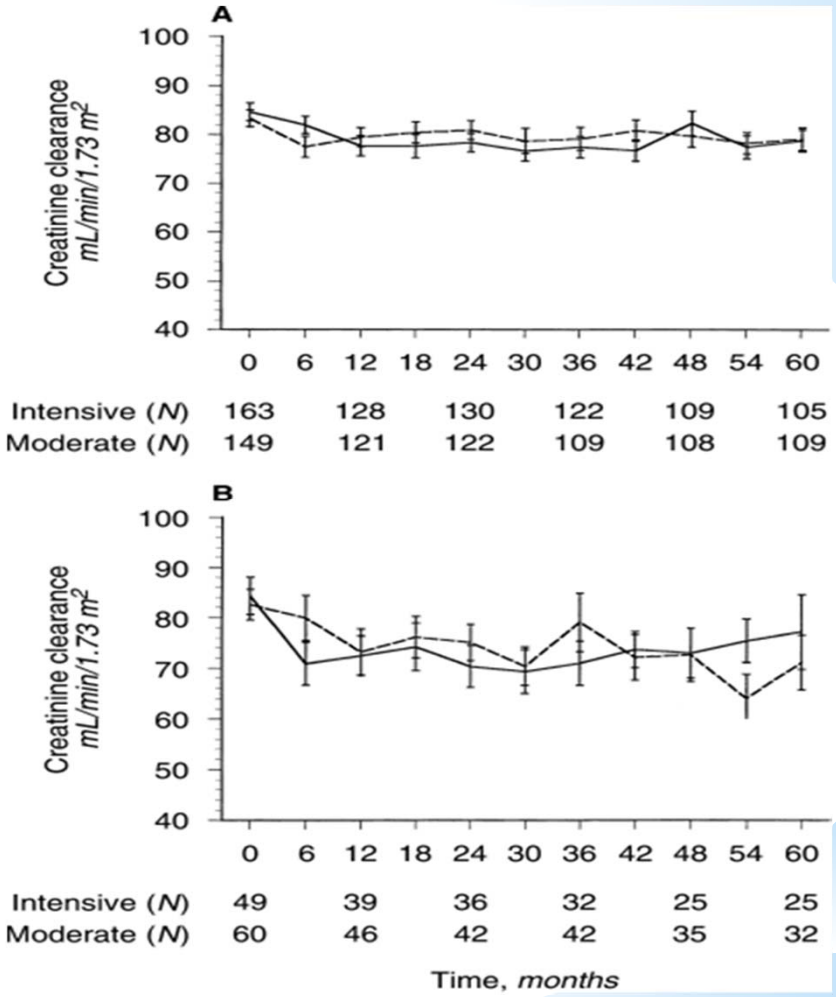




Lancet 2005

ABCD (2002)
(The Appropriate Blood Control in Diabetes Study)

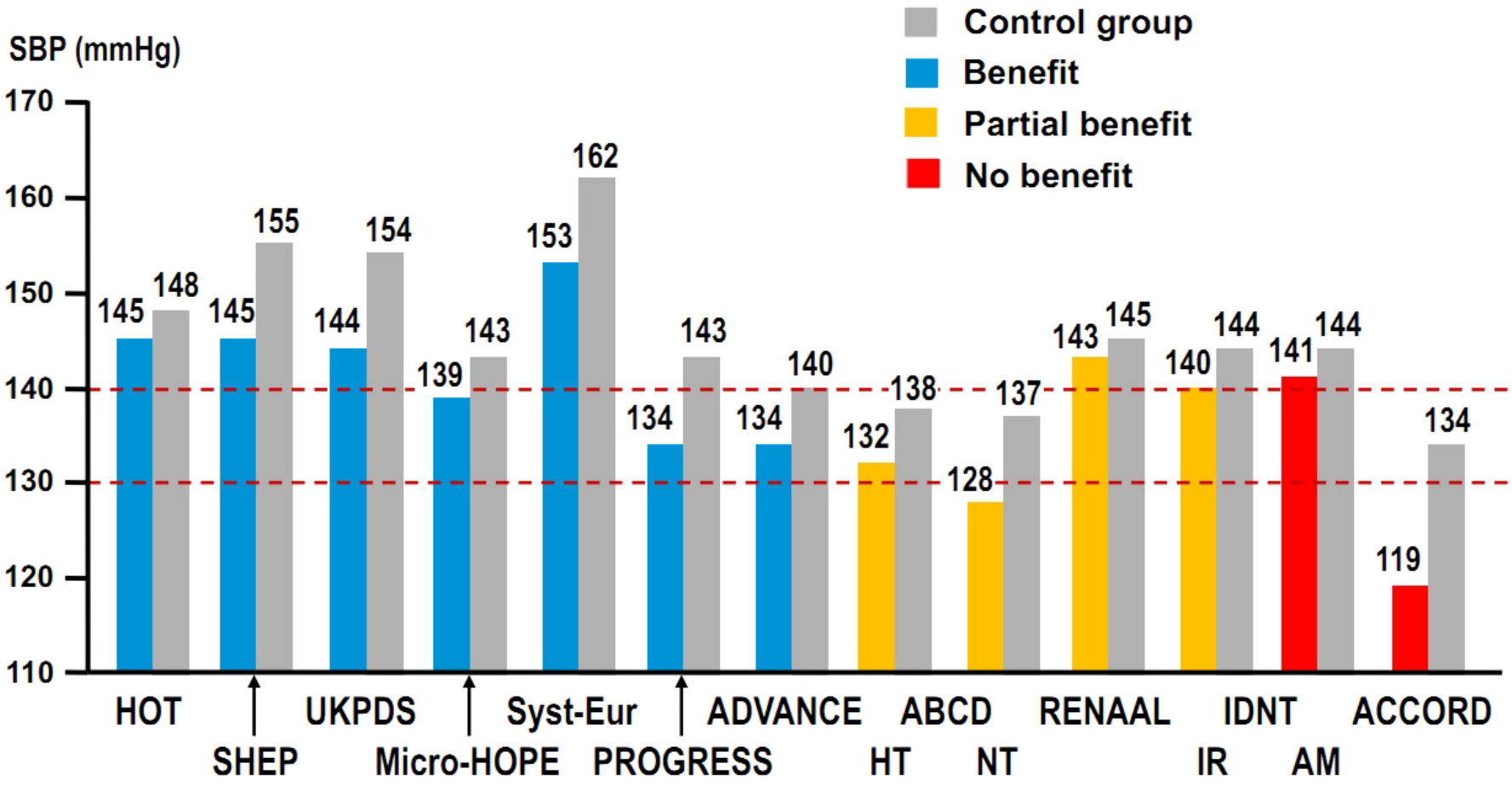




Caveats on the Current Guidelines

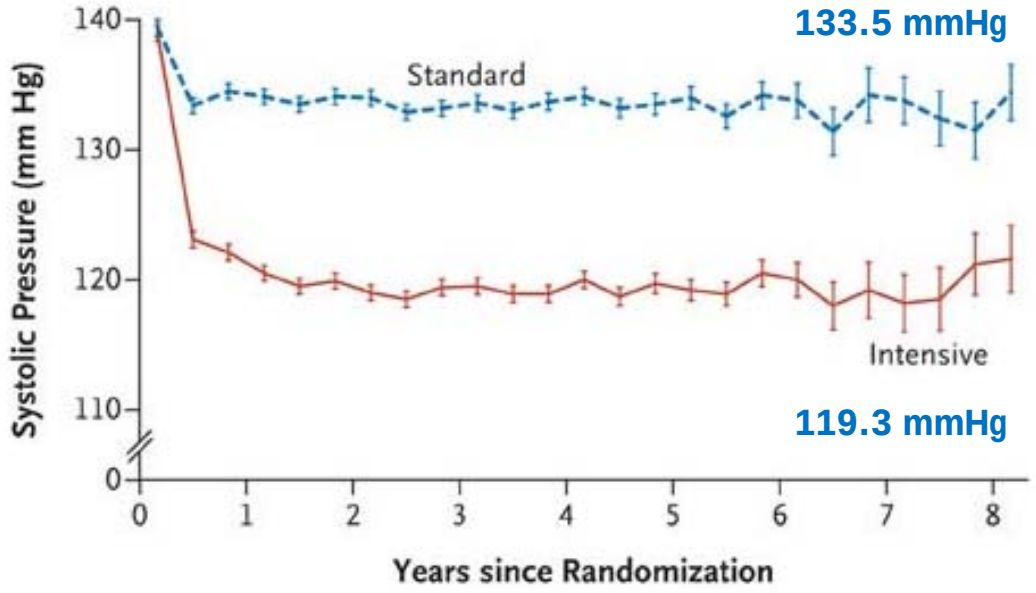
1) Many RCTs failed to find the beneficial effects of lowering BP <130/80 mmHg as compared to <140/90 mmHg in reducing cardiovascular events, renal outcomes, or mortality.
2) The KDIGO panel acknowledged that this decision was **based solely on expert opinion**.

Achieved BP Levels in RCTs



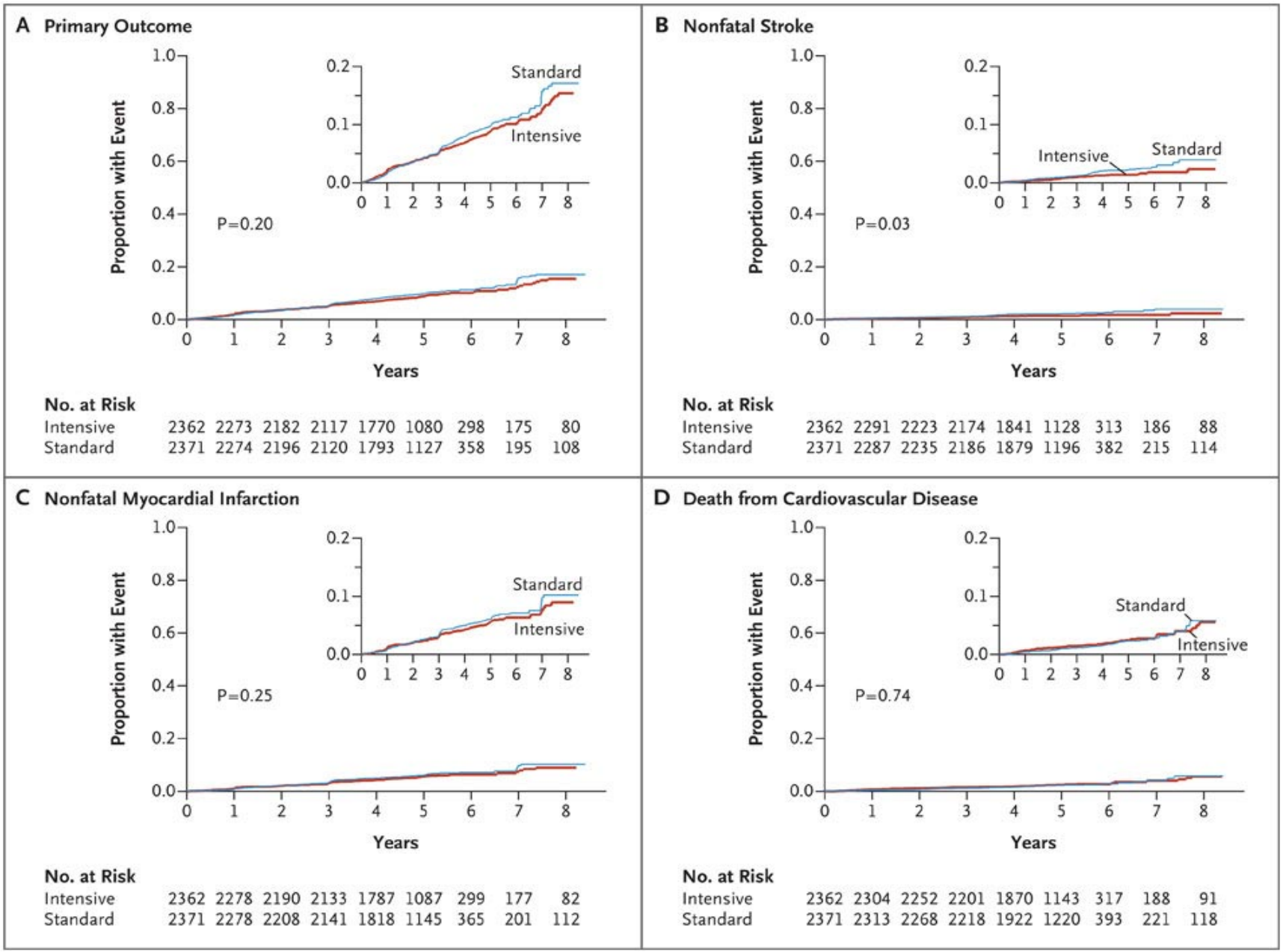
Adapted from Mancia et al. *J Hypertens* 2009; 27: 2121-2158.

Effects of Intensive BP Control in Type 2 DM – The ACCORD Study



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

The ACCORD Investigators - NEJM 2010



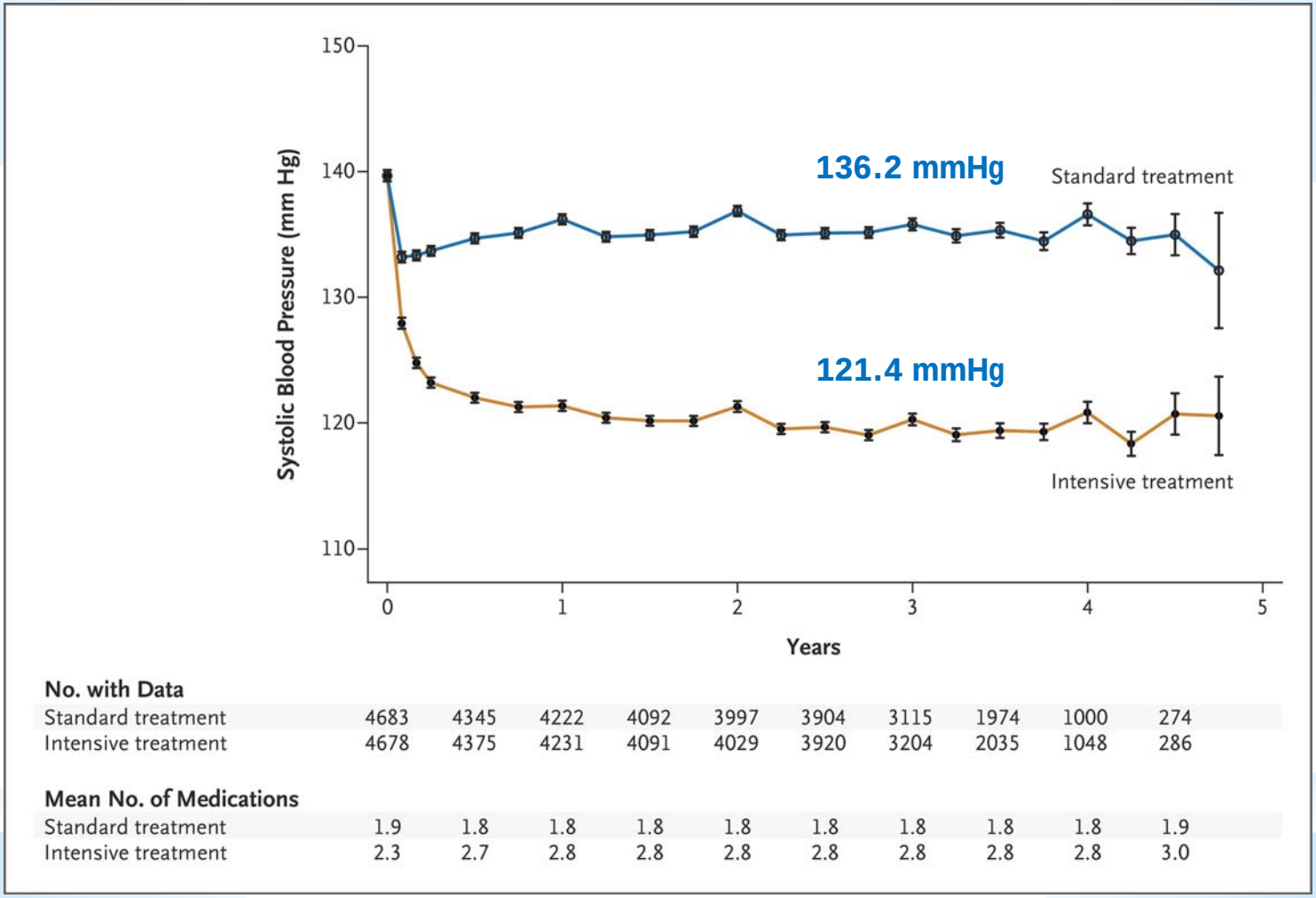
The ACCORD Investigators - NEJM 2010

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

Variable	Intensive Therapy (N=2362)	Standard Therapy (N=2371)	P Value
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 m^2	99 (4.2)	52 (2.2)	<0.001
End-stage renal disease or need for dialysis	59 (2.5)	58 (2.4)	0.93
Serum creatinine — mg/dl	1.1±0.4	1.0±0.5	<0.001
Estimated GFR — ml/min/1.73 m^2	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

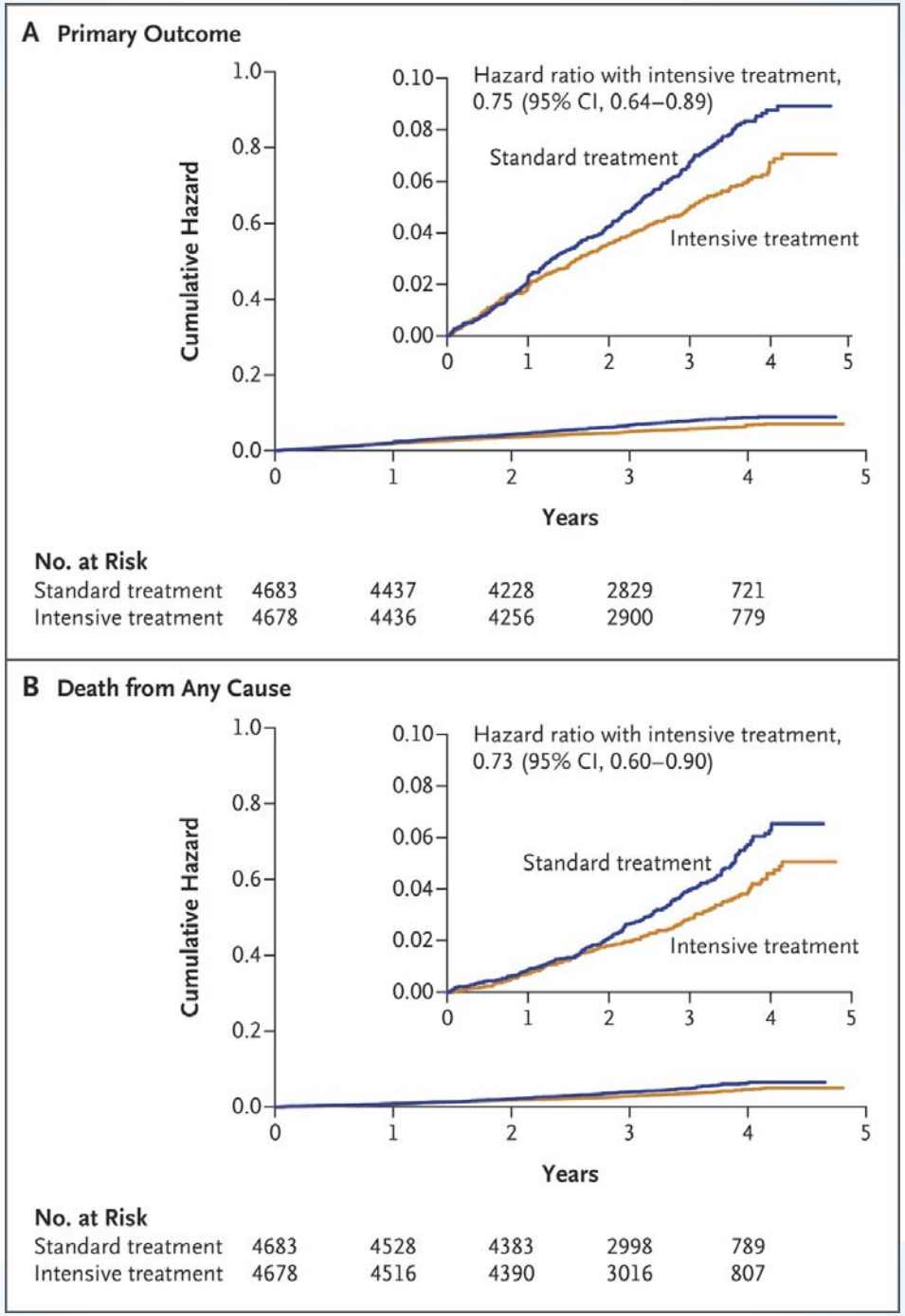
The ACCORD Investigators - NEJM 2010

An RCT of Intensive vs. Standard BP – The SPRINT Research Group



No. with Data										
Standard treatment	4683	4345	4222	4092	3997	3904	3115	1974	1000	274
Intensive treatment	4678	4375	4231	4091	4029	3920	3204	2035	1048	286
Mean No. of Medications										
Standard treatment	1.9	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9
Intensive treatment	2.3	2.7	2.8	2.8	2.8	2.8	2.8	2.8	2.8	3.0

The SPRINT Research Group, NEJM **2015**


A Primary Outcome
Cumulative Hazard
1.0
0.8
0.6
0.4
0.2
0.0
0.10
0.08
0.06
0.04
0.02
0.00
0
1
2
3
4
5
Hazard ratio with intensive treatment,
0.75 (95% CI, 0.64–0.89)
Standard treatment
Intensive treatment
Years
No. at Risk
Standard treatment 4683 4437 4228 2829 721
Intensive treatment 4678 4436 4256 2900 779
B Death from Any Cause
Cumulative Hazard
Hazard ratio with intensive treatment,
0.73 (95% CI, 0.60–0.90)
Standard treatment
Intensive treatment
Years
No. at Risk
Standard treatment 4683 4528 4383 2998 789
Intensive treatment 4678 4516 4390 3016 807

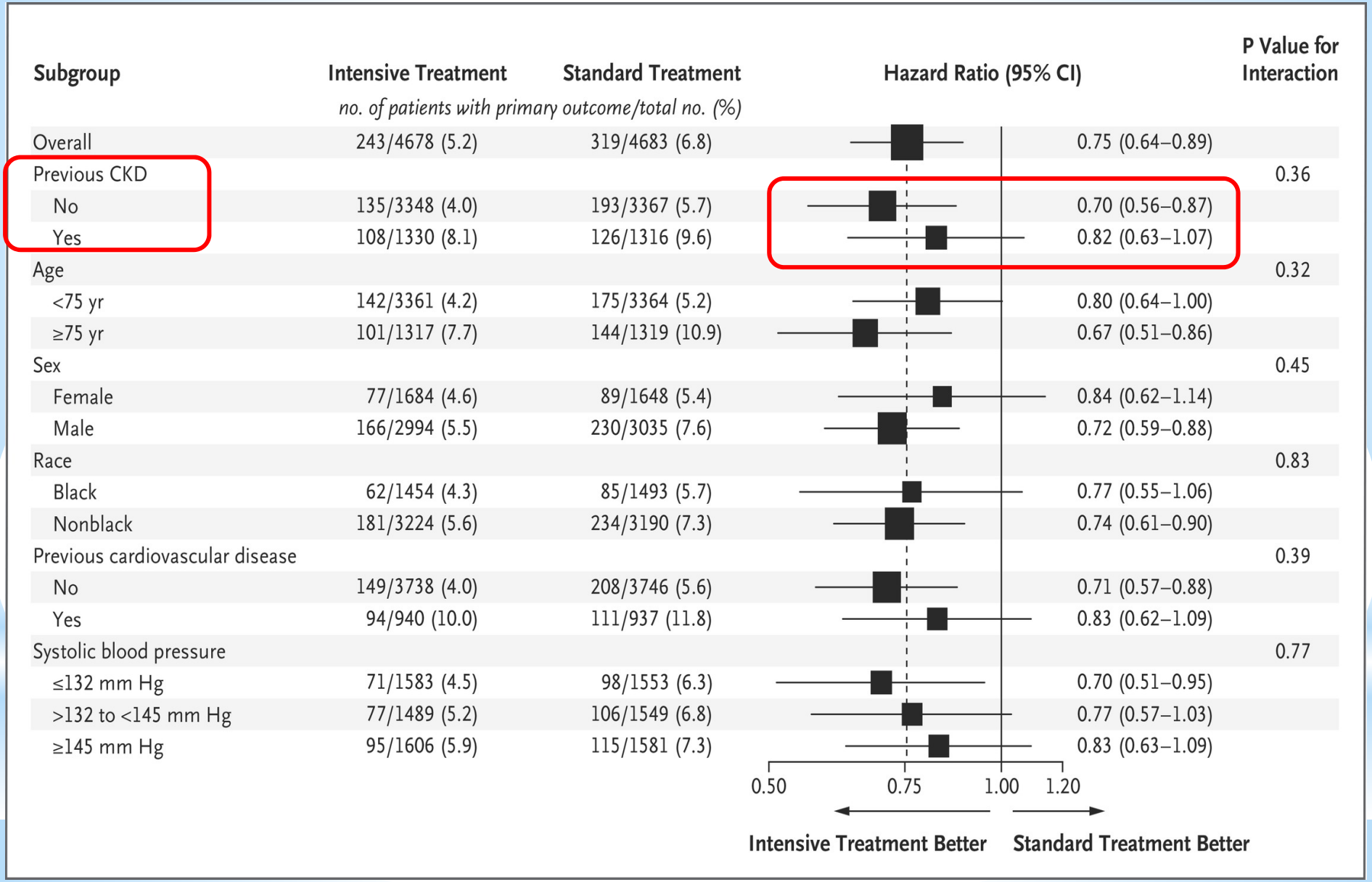
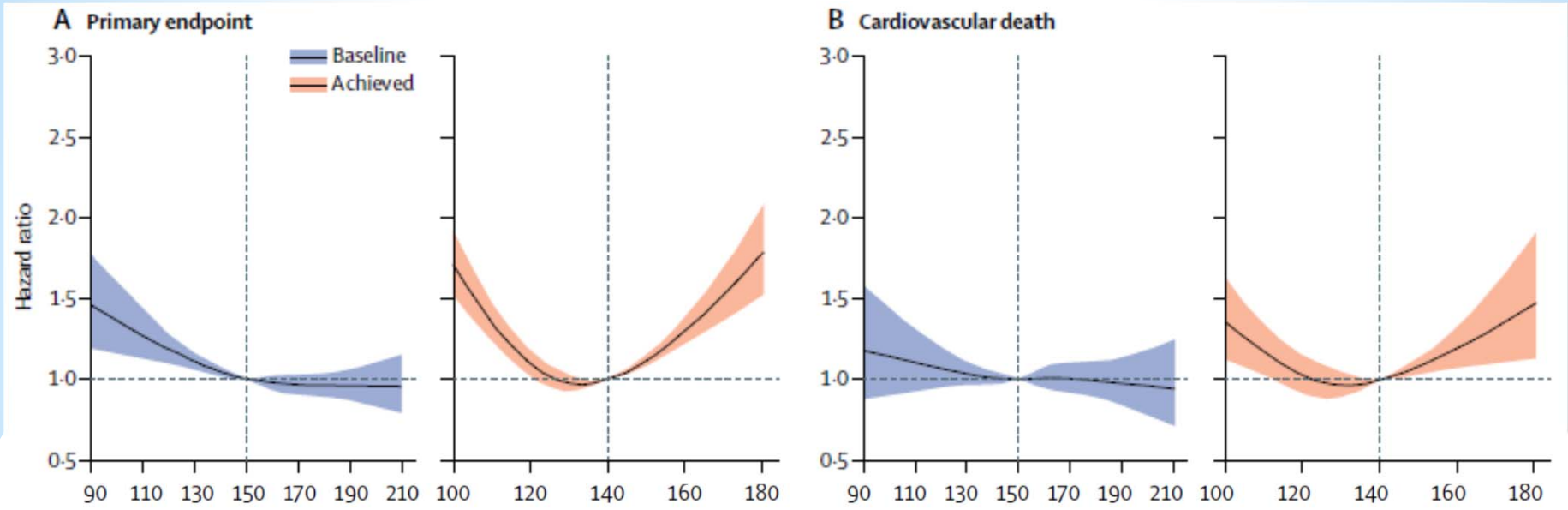

Subgroup
Intensive Treatment
Standard Treatment
Hazard Ratio (95% CI)
P Value for Interaction
no. of patients with primary outcome/total no. (%)
Overall 243/4678 (5.2) 319/4683 (6.8) 0.75 (0.64–0.89)
Previous CKD 0.36
No 135/3348 (4.0) 193/3367 (5.7) 0.70 (0.56–0.87)
Yes 108/1330 (8.1) 126/1316 (9.6) 0.82 (0.63–1.07)
Age 0.32
<75 yr 142/3361 (4.2) 175/3364 (5.2) 0.80 (0.64–1.00)
≥75 yr 101/1317 (7.7) 144/1319 (10.9) 0.67 (0.51–0.86)
Sex 0.45
Female 77/1684 (4.6) 89/1648 (5.4) 0.84 (0.62–1.14)
Male 166/2994 (5.5) 230/3035 (7.6) 0.72 (0.59–0.88)
Race 0.83
Black 62/1454 (4.3) 85/1493 (5.7) 0.77 (0.55–1.06)
Nonblack 181/3224 (5.6) 234/3190 (7.3) 0.74 (0.61–0.90)
Previous cardiovascular disease 0.39
No 149/3738 (4.0) 208/3746 (5.6) 0.71 (0.57–0.88)
Yes 94/940 (10.0) 111/937 (11.8) 0.83 (0.62–1.09)
Systolic blood pressure 0.77
≤132 mm Hg 71/1583 (4.5) 98/1553 (6.3) 0.70 (0.51–0.95)
>132 to <145 mm Hg 77/1489 (5.2) 106/1549 (6.8) 0.77 (0.57–1.03)
≥145 mm Hg 95/1606 (5.9) 115/1581 (7.3) 0.83 (0.63–1.09)
0.50
0.75
1.00
1.20
Intensive Treatment Better
Standard Treatment Better

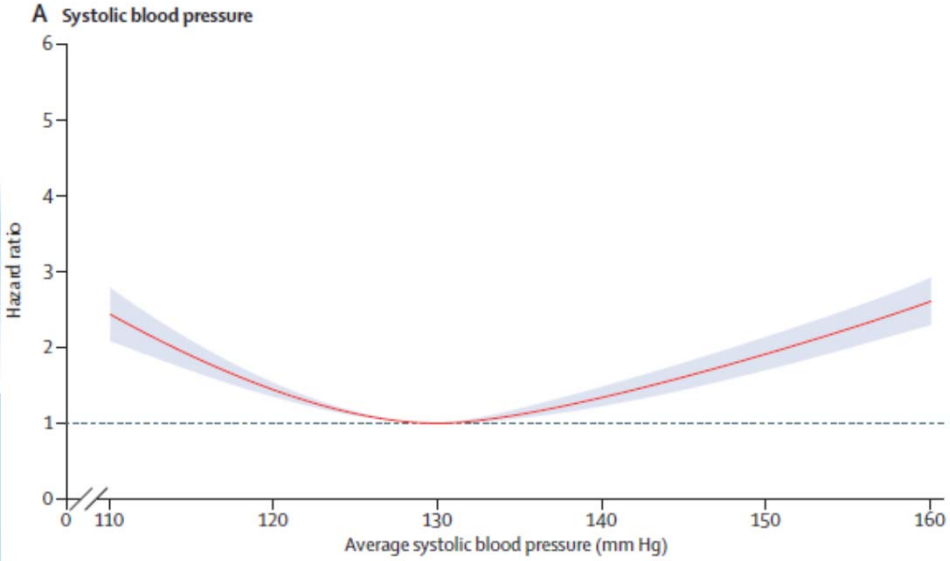
Table 2. Primary and Secondary Outcomes and Renal Outcomes.*

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 m^2§	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

Achieved BP and CV Outcomes

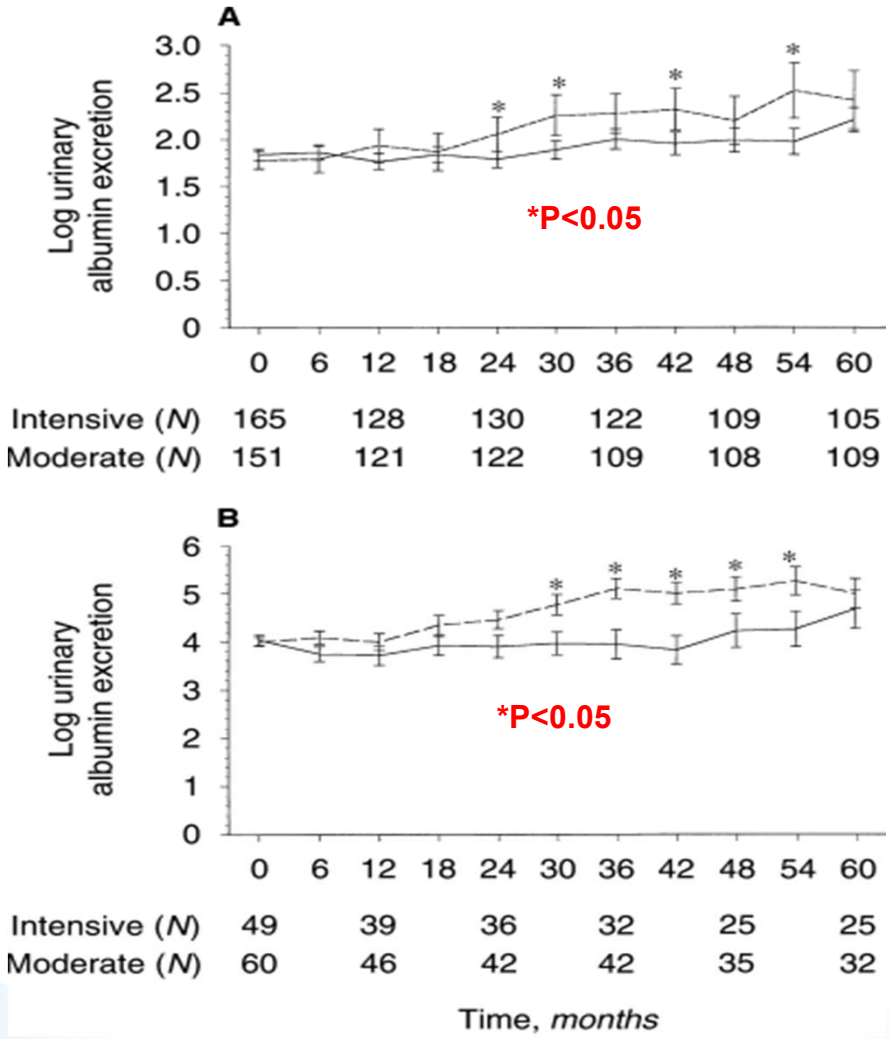


ONTARGET/TRASCENT investigators, Lancet 2017

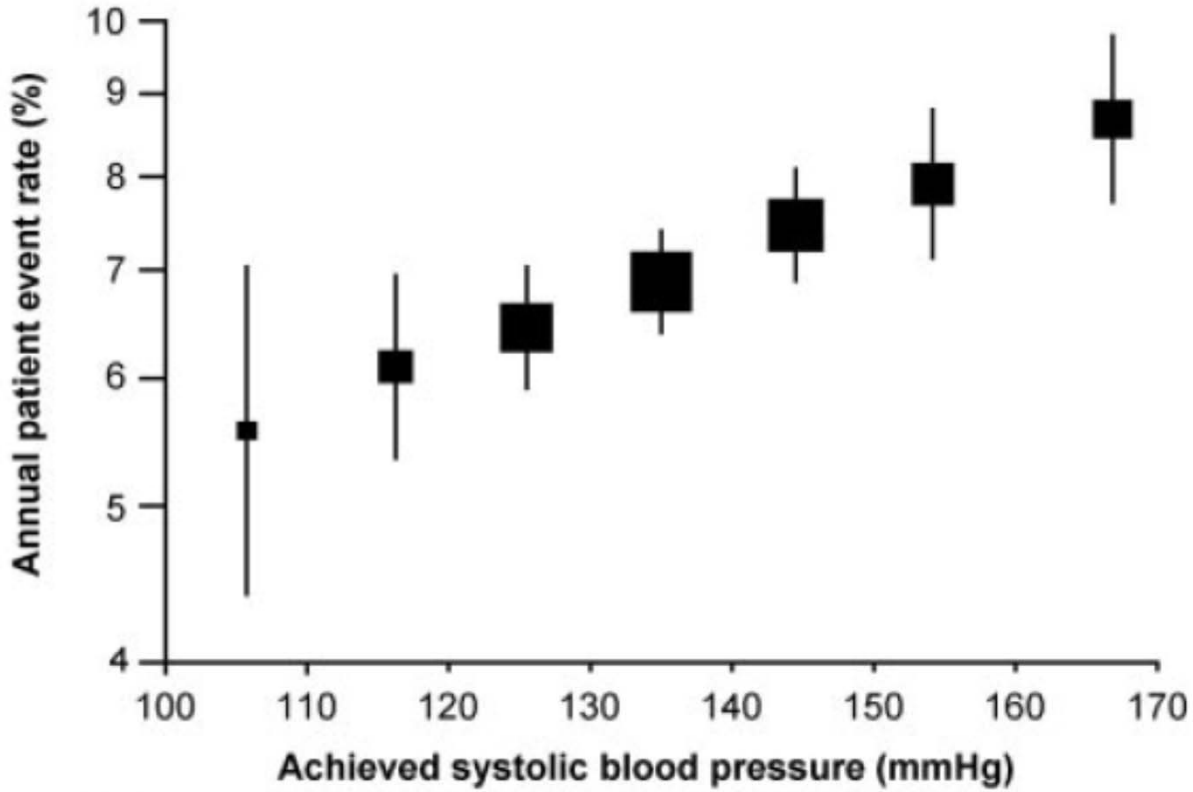


CLARIFY investigators, Lancet 2016

ABCD (2002)
(The Appropriate Blood Control in Diabetes Study)



The ADVANCE Study



Median systolic blood pressure (mmHg)	106	116	125	135	144	154	168
No. of person-years	1431	4266	8974	11983	9138	4942	3470

The ADVANCE Investigators - Lancet 2007; *JASN* 2009

The ACCORD Study

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Ratio of urinary albumin (mg) to creatinine (g)			<0.001
Median	12.6	14.9	
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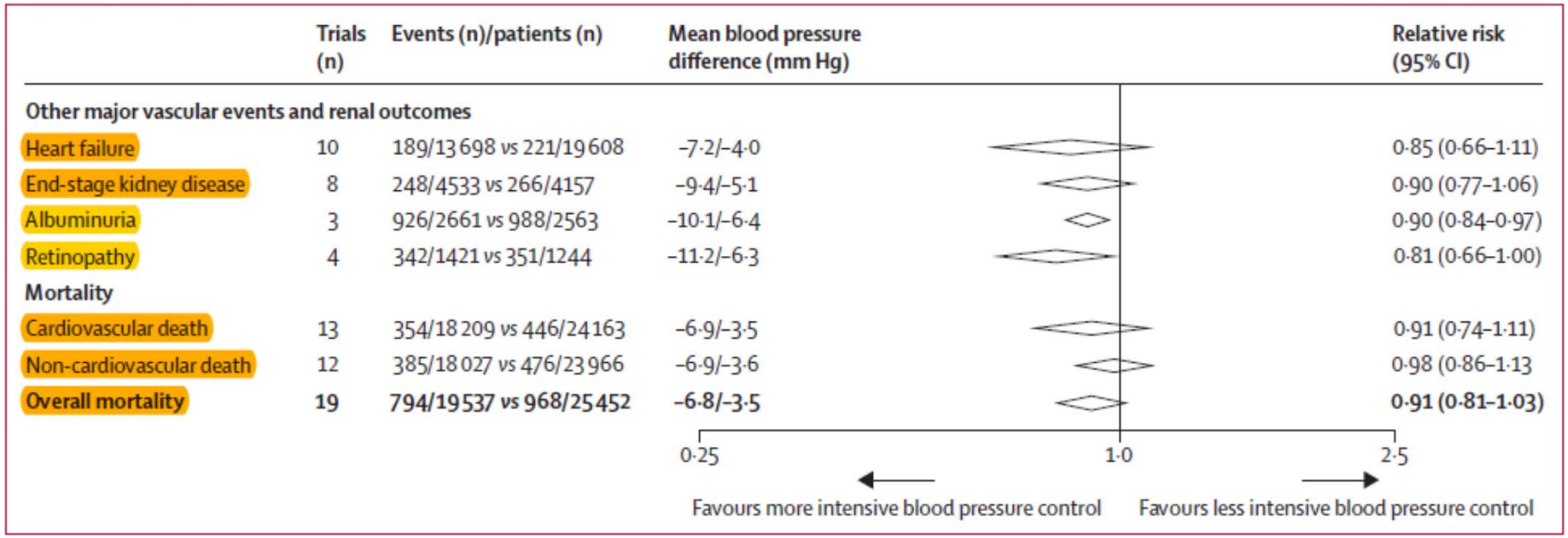
Macroalbuminuria — no. /total no. (%)	143/2174 (6.6)	192/2205 (8.7)	0.009

The ACCORD Investigators - NEJM 2010

BP and Outcomes in CKD - RCTs (Meta-Analysis)



Xie et al, Lancet 2016

JAMA Internal Medicine | Original Investigation

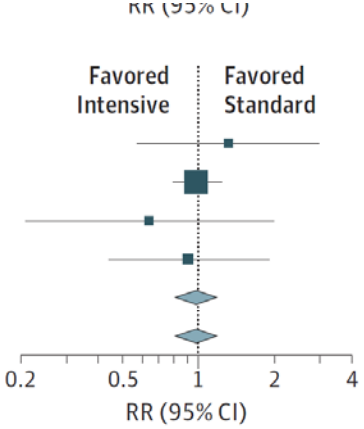
Association of Intensive Blood Pressure Control and Kidney Disease Progression in Nondiabetic Patients With Chronic Kidney Disease

A Systematic Review and Meta-analysis

Tsai et al, 2017

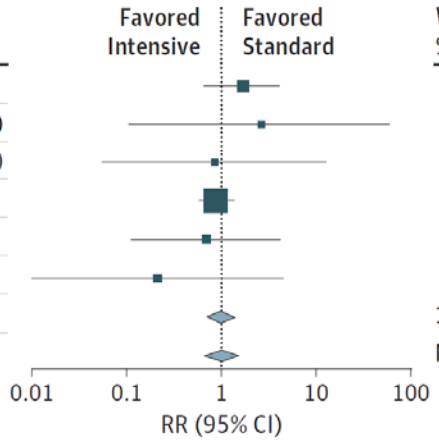
D Composite renal outcome

Study	Intensive Events	Intensive Total	Standard Events	Standard Total	RR (95% CI)	W (Fixed), %	W (Random), %
Toto et al,[28] 1995	11	42	7	35	1.31 (0.57 to 3.02)	5.0	5.8
Wright et al,[16] 2002	121	540	125	554	0.99 (0.80 to 1.24)	80.1	83.3
Hayashi et al,[30] 2010	5	1230	8	1269	0.64 (0.21 to 1.97)	5.1	3.2
Wright et al,[21] 2015	14	1330	15	1316	0.92 (0.45 to 1.91)	9.8	7.7
Fixed-effect model		**3142**		**3174**	**0.98 (0.80 to 1.20)**	**100**	**NA**
Random-effects model					**0.99 (0.81 to 1.21)**	**NA**	**100**

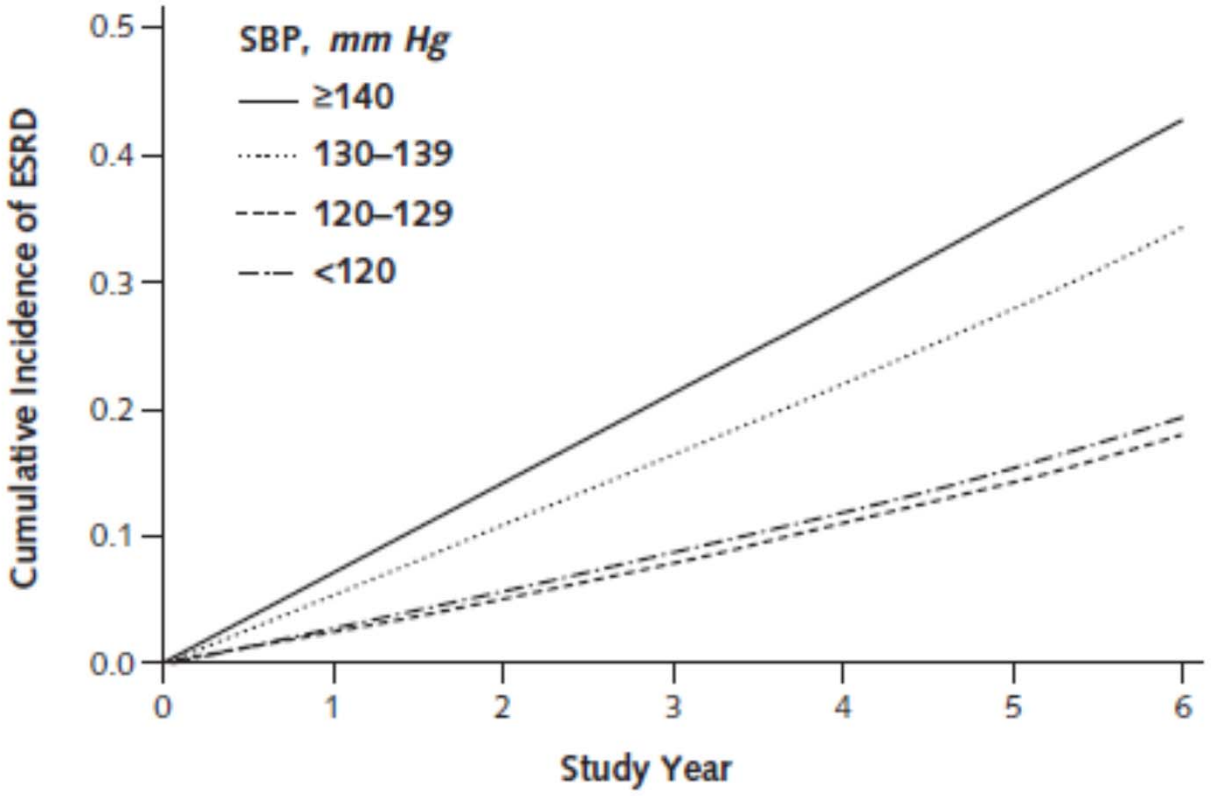


E All-cause mortality

Study	Intensive Events	Intensive Total	Standard Events	Standard Total	RR (95% CI)	W (Fixed), %	W (Random), %
Klahr et al,[15] 1994	12	432	7	408	1.62 (0.64 to 4.07)	12.5	15.5
Toto et al,[28] 1995	1	42	0	35	2.51 (0.11 to 59.62)	0.9	1.3
Schrier et al,[29] 2002	1	41	1	34	0.83 (0.05 to 12.77)	1.9	1.8
Wright et al,[16] 2002	38	540	44	554	0.89 (0.58 to 1.35)	75.2	75.8
Ruggenenti et al,[17] 2005	2	169	3	169	0.67 (0.11 to 3.94)	5.2	4.2
Schrier et al,[31] 2014	0	274	2	284	0.21 (0.01 to 4.30)	4.3	1.4
Fixed-effect model		**1498**		**1484**	**0.95 (0.66 to 1.36)**	**100.0**	**NA**
Random-effects model					**0.95 (0.66 to 1.37)**	**NA**	**100.0**



BP and CKD Progression - Observational Studies



The CRIC Study Investigators, Ann Intern Med 2015

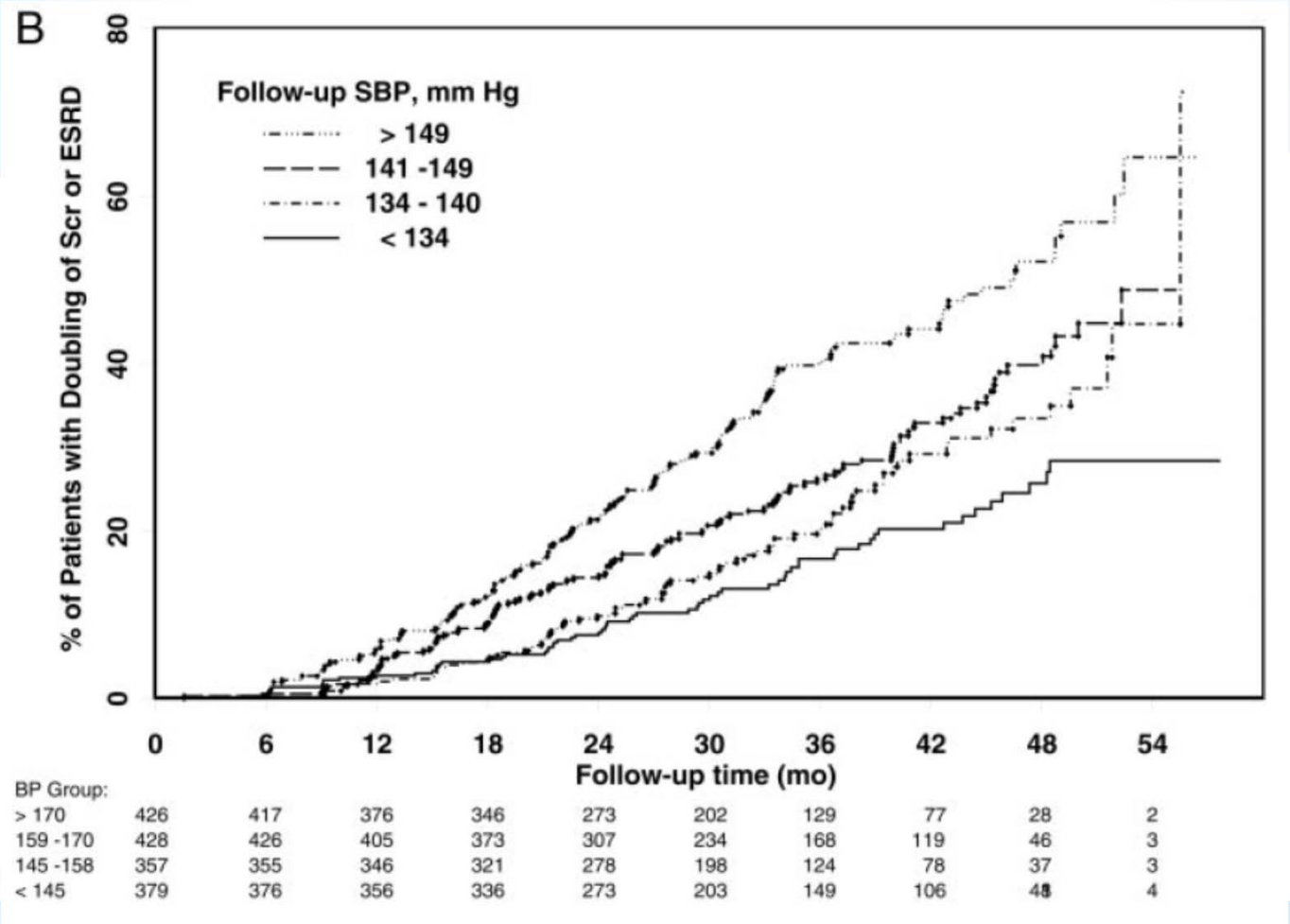
BP and CKD Progression
- Post-hoc Analysis of the RENAAL Study

Table 6. Outcomes Based on Baseline and Last SBP Prior to End Points for Pooled Treatment Groups*

	Event Rate Based on Baseline SBP				Event Rate Based on Last SBP Prior to End Points			
End Point	No. of Patients	Event, No. (%)	HR (95% CI)†	*P* Value	No. of Patients	Event, No. (%)	HR (95% CI)†	*P* Value
Primary: SBP, mm Hg								
<130	169	60 (35.5)	1.00 (Reference)	. . .	278	94 (33.8)	1.00 (Reference)	. . .
130-139	209	66 (31.6)	0.84 (0.59-1.20)	.34	401	141 (35.2)	1.08 (0.83-1.40)	.56
140-159	610	267 (43.8)	1.28 (0.97-1.69)	.08	522	241 (46.2)	1.49 (1.18-1.90)	.001
160-179	373	206 (55.2)	1.82 (1.36-2.42)	<.001	241	158 (65.6)	2.74 (2.12-3.54)	<.001
≥180	152	87 (57.2)	1.85 (1.33-2.57)	<.001	71	52 (73.2)	3.51 (2.50-4.93)	<.001
ESRD: SBP, mm Hg								
<130	169	26 (15.4)	1.00 (Reference)	. . .	286	44 (15.4)	1.00 (Reference)	. . .
130-139	209	33 (15.8)	0.97 (0.58-1.63)	.92	392	55 (14.0)	0.93 (0.62-1.38)	.70
140-159	610	127 (20.8)	1.37 (0.90-2.10)	.14	518	115 (22.2)	1.52 (1.07-2.15)	.02
160-179	373	112 (30.0)	2.13 (1.39-3.27)	<.001	243	89 (36.6)	3.01 (2.10-4.32)	<.001
≥180	152	43 (28.3)	2.02 (1.24-3.29)	.005	74	38 (51.4)	4.63 (3.00-7.15)	<.001
ESRD or death: SBP, mm Hg								
<130	169	43 (25.4)	1.00 (Reference)	. . .	286	82 (28.7)	1.00 (Reference)	. . .
130-139	209	56 (26.8)	1.00 (0.67-1.49)	.99	392	101 (25.8)	0.91 (0.68-1.22)	.54
140-159	610	211 (34.6)	1.38 (0.99-1.91)	.06	518	188 (36.3)	1.33 (1.02-1.72)	.03
160-179	373	171 (45.8)	1.96 (1.40-2.74)	<.001	243	134 (55.1)	2.41 (1.83-3.17)	<.001
≥180	152	74 (48.7)	2.10 (1.44-3.06)	<.001	74	50 (67.6)	3.23 (2.27-4.59)	<.001

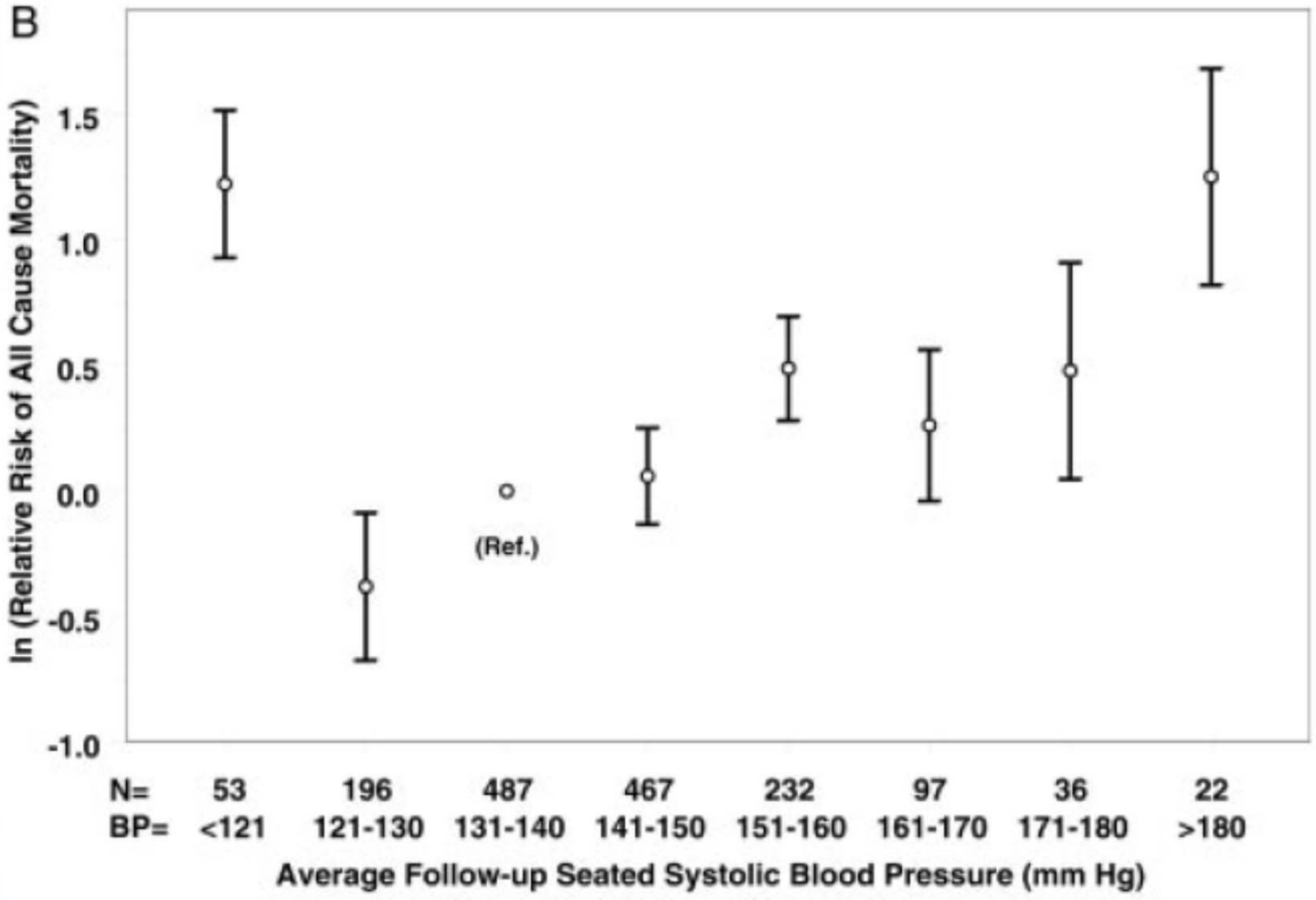
Bakris et al, Arch Intern Med 2003

BP and CKD Progression
- Post-hoc Analysis of the IDNT Study



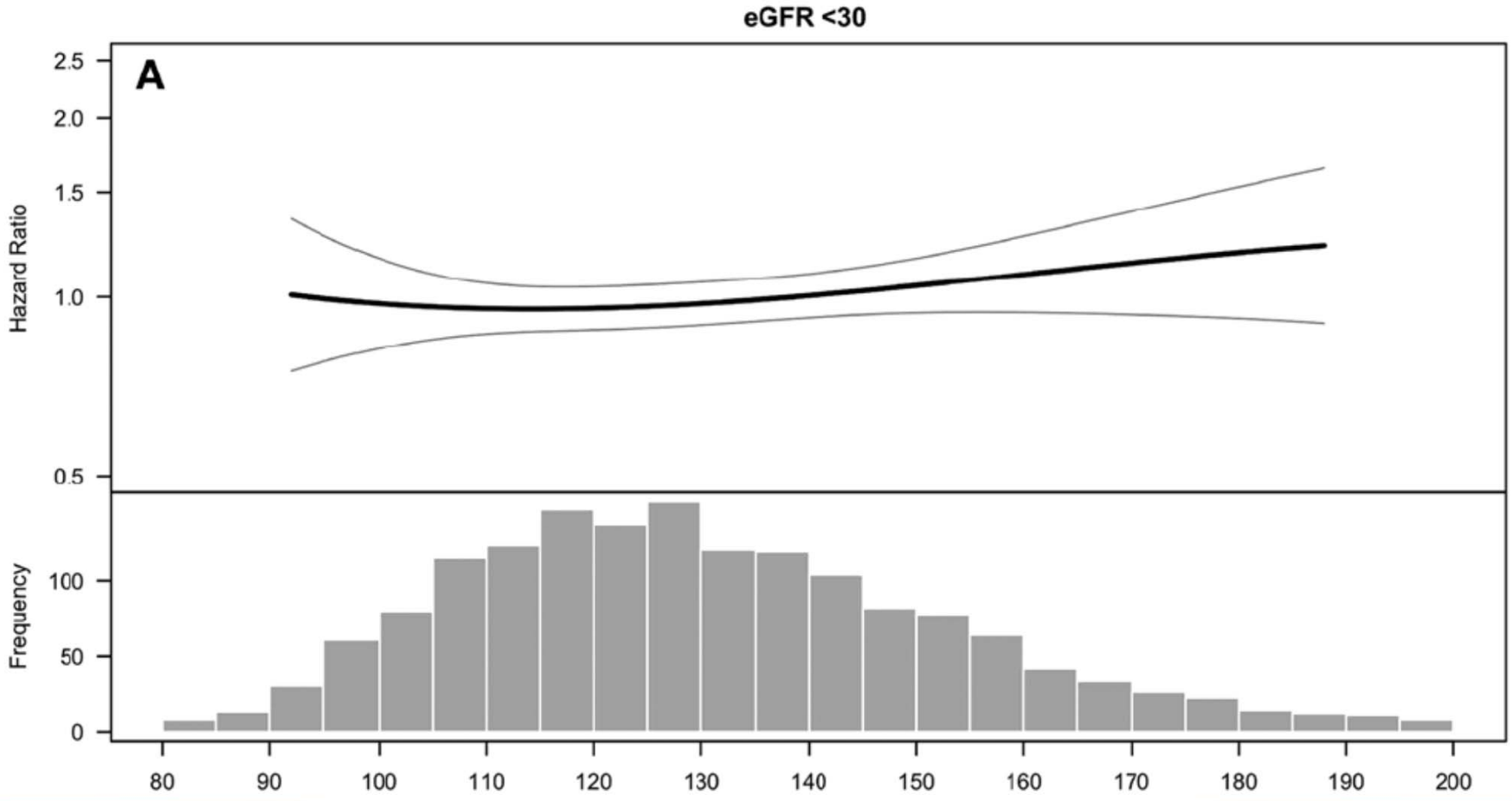
Pohl et al, JASN 2005

BP and Mortality
- Post-hoc Analysis of the IDNT Study



Pohl et al, JASN 2005

BP and Mortality
- CRIC Cohort Study



Bansal et al, Hypertension 2015

Oh et al. BMC Nephrology 2014, 15:80
http://www.biomedcentral.com/1471-2369/15/80

BMC Nephrology

STUDY PROTOCOL Open Access

KNOW-CKD (KoreaN cohort study for Outcome in patients With Chronic Kidney Disease): design and methods

Kook-Hwan Oh[1†], Sue Kyung Park[2†], Hayne Cho Park[1], Ho Jun Chin[1], Dong Wan Chae[1], Kyu Hun Choi[3], Seung Hyeok Han[3], Tae Hyun Yoo[3], Kyubeck Lee[4], Yong-Soo Kim[5], Wookyung Chung[6], Young-Hwan Hwang[7], Soo Wan Kim[8], Yeong Hoon Kim[9], Sun Woo Kang[9], Byung-Joo Park[2], Joongyub Lee[10], Curie Ahn[1*] and Representing KNOW-CKD Study Group

BP and CKD Outcomes in Korean Population

KSN-17-O024

Optimal Target for Blood Pressure Control in Patients with Chronic Kidney Disease: The results from the KNOW-CKD study

Jong Hyun Jhee M.D.[1], Seohyun Park M.D.[1], Hyoungnae Kim M.D.[1], Hae-Ryong Yun M.D.[1], Youn Kyung Kee M.D.[1], Tae-Hyun Yoo M.D., Ph.D.[1], Curie Ahn[2], Kyu Hun Choi[1], and Seung Hyeok Han M.D., Ph.D.[1]

[1]Department of Internal Medicine, College of Medicine, Institute of Kidney Disease Research, Yonsei University College of Medicine, Seoul, Republic of Korea
[2]Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea

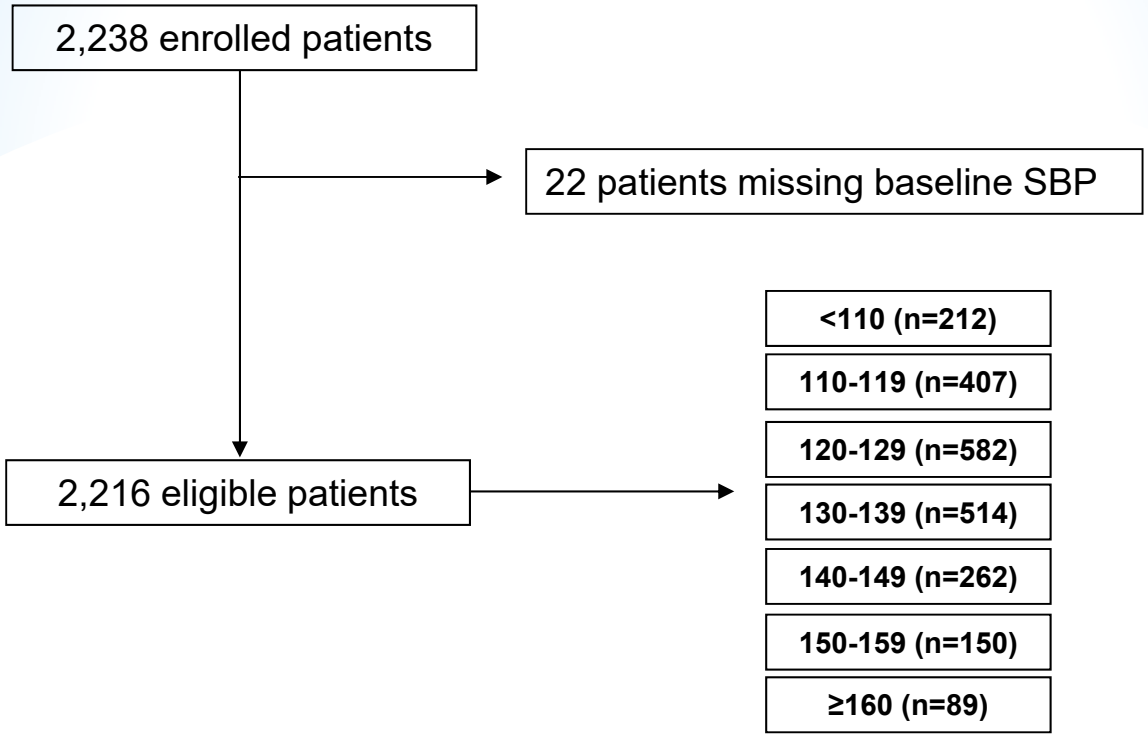
KSN-17-O064

Association between Time-updated Systolic Blood Pressure and the Incident Chronic Kidney Disease: A Nationwide Cohort Study

Tae Ik Chang, MD, PhD [1]; Ea Wha Kang, MD, PhD [1]; Jung Tak Park, MD, PhD[2]; Tae-Hyun Yoo, MD, PhD[2]; Shin-Wook Kang, MD, PhD[2]; and Seung Hyeok Han, MD, PhD [2]

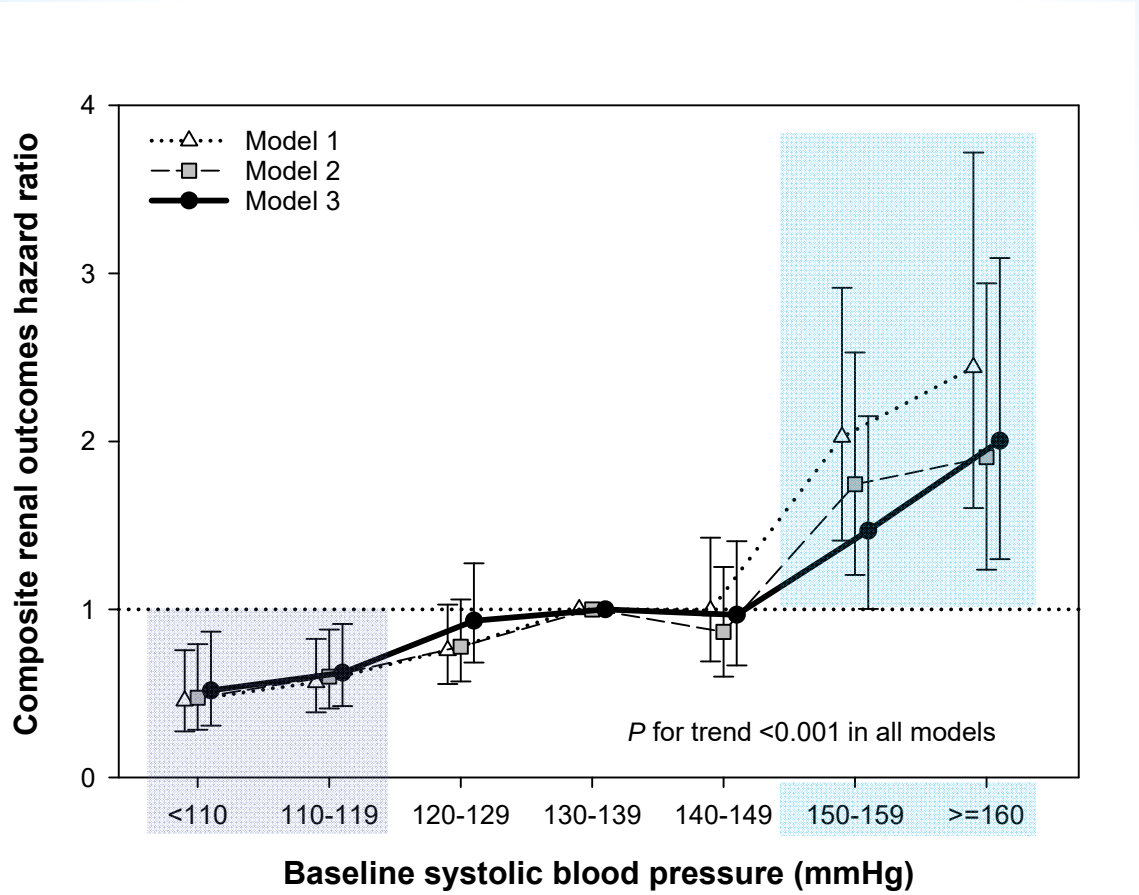
[1]Department of Internal Medicine, NHIS Medical Center, Ilsan Hospital, Goyangshi, Gyeonggi-do, Republic of Korea; [2]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea;

BP and CKD Outcomes in the KNOW-CKD



- Study outcome: composite renal outcome
  - 50% decline in estimated glomerular filtration rate (eGFR)
  - Dialysis initiation
  - Kidney transplantation

BP and CKD Outcomes in the KNOW-CKD



HR (and 95% CI) of primary outcome for baseline SBP categories

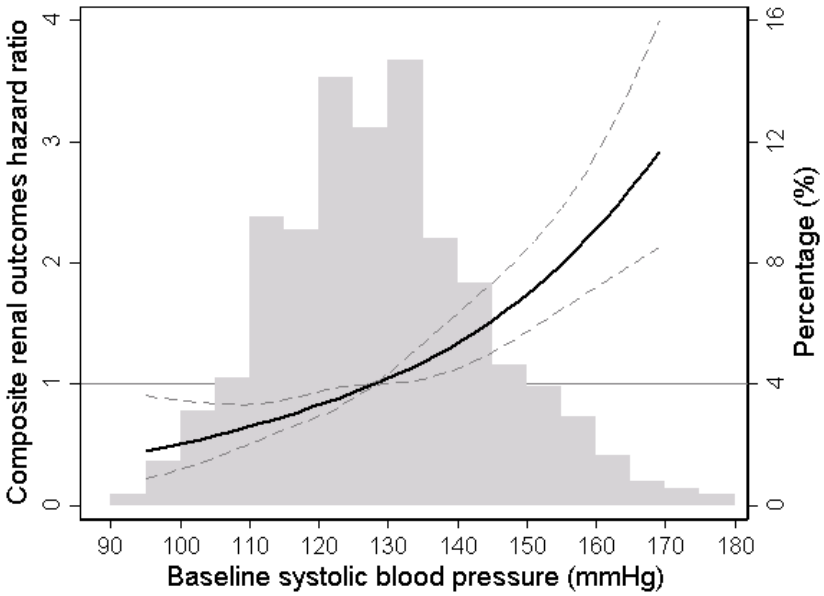
Model 1: unadjusted

Model 2: age, sex, comorbidities, smoking history, cause of CKD, and use of RASB

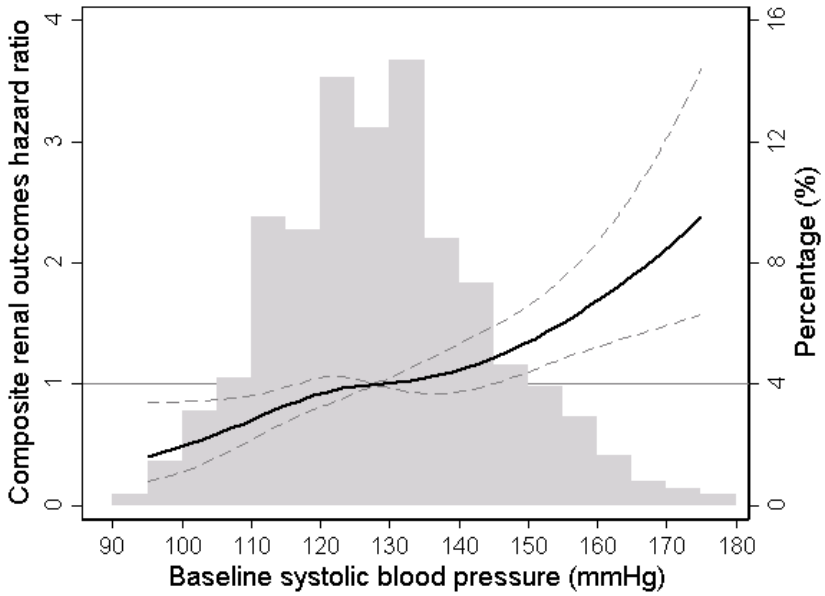
Model 3: model 2 + body mass index, overt proteinuria, and eGFR.

BP and CKD Outcomes in the KNOW-CKD

(A) Unadjusted

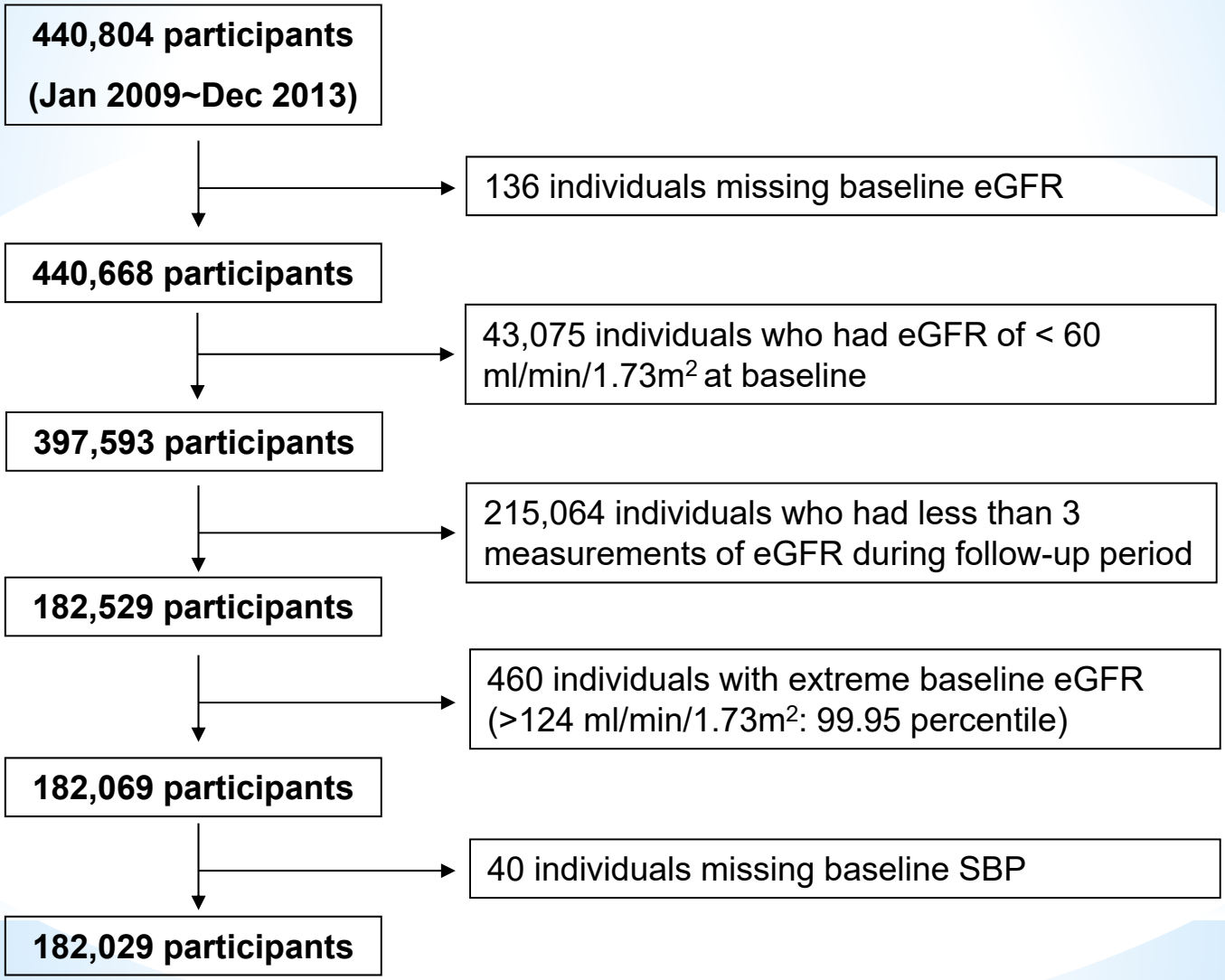


(B) Fully adjusted



Association of baseline SBP with composite outcomes in unadjusted (A) and fully-adjusted (B) HRs of composite renal outcomes in Cox model using restricted cubic spines. Fully-adjusted model was adjusted for age, sex, comorbidities, smoking history, cause of CKD, antihypertensive medications (ACEi or ARB), body mass index, overt proteinuria, and eGFR.

BP and the Incident CKD



BP and the Incident CKD

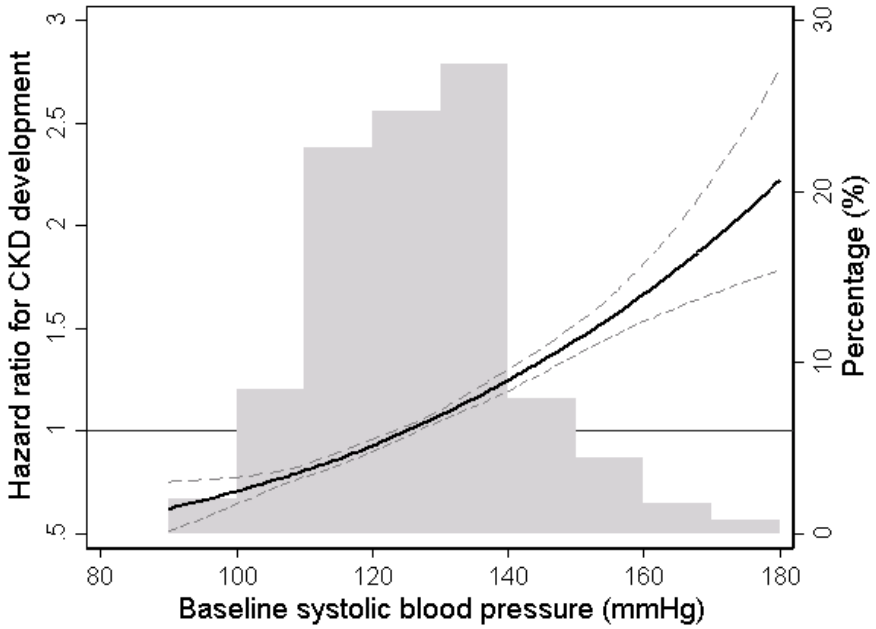
- Exposure: Baseline and time-varying SBP level categorized into 7 groups (<110, 110-<120, 120-<130 [reference: Median=124], 130-<140, 140-<150, 150-<160, and ≥160 mmHg)
- Primary outcome: Development of CKD (≥ 30% decline from baseline eGFR or <60 ml/min/1.73m^2 of eGFR)

- Statistical analyses: Baseline and time-varying Cox proportional hazard regression models with 3 incremental levels of adjustments based on *a priori* considerations:

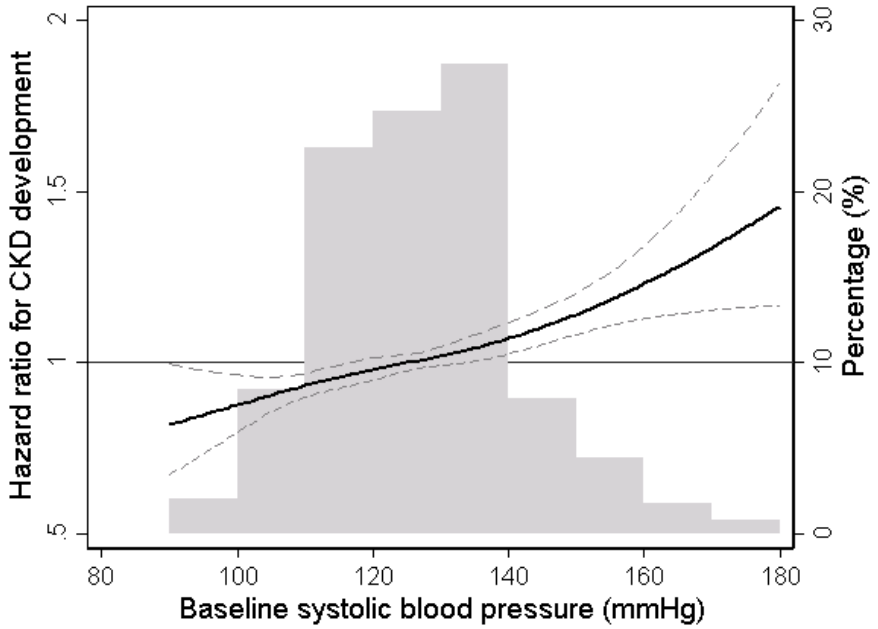
Models	Covariates
Model 1	Unadjusted
Model 2	Age, sex, comorbidities as defined by ICD-10 (DM, IHD, CHF, PAOD, CVD, COPD, CTD, liver disease, and malignancy)
Model 3	SBP and laboratory parameters (total cholesterol, Hb, presence of proteinuria, and eGFR)

BP and the Incident CKD

(A: Model 1-unadjusted)

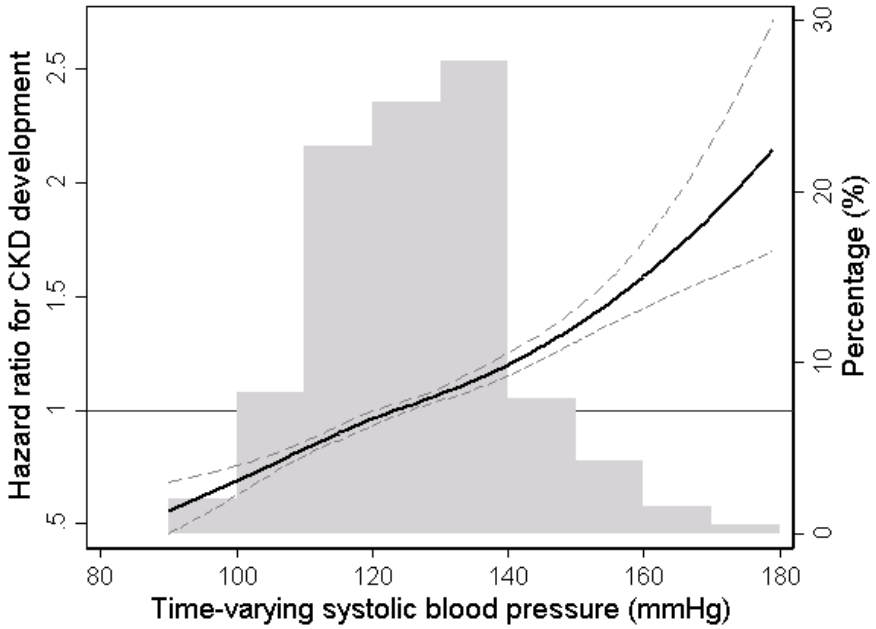


(B: Model 3-fully adjusted)

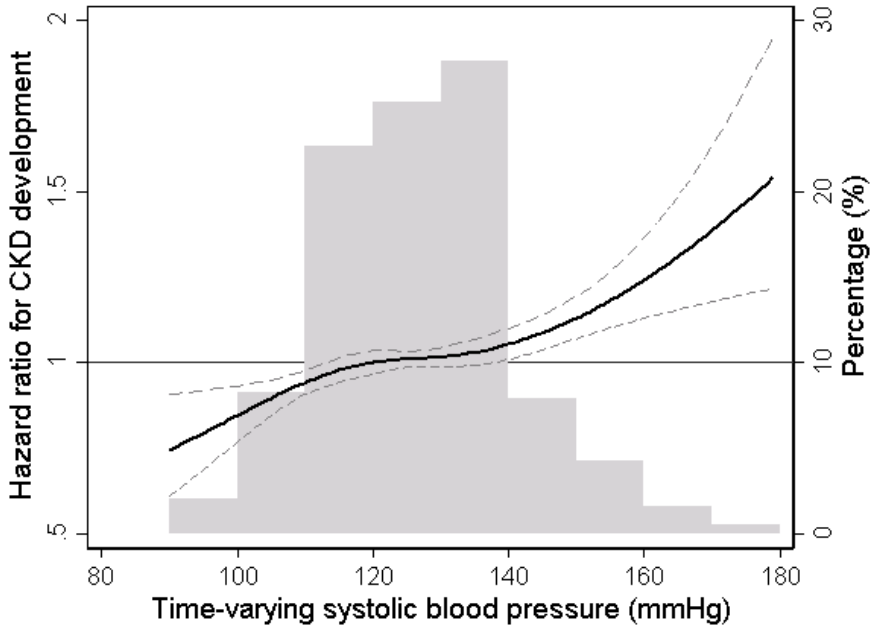


BP and the Incident CKD

(A: Model 1-unadjusted)



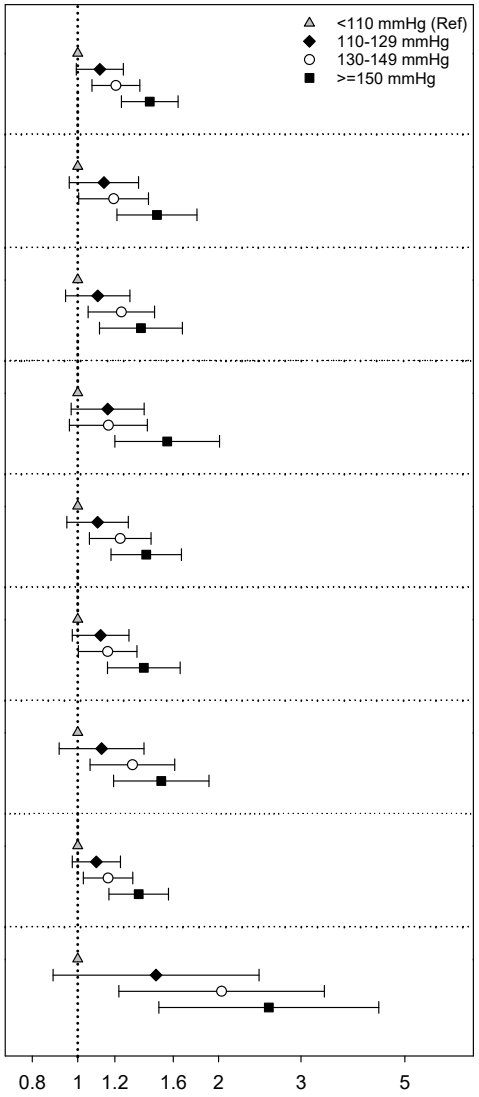
(B: Model 3-fully adjusted)



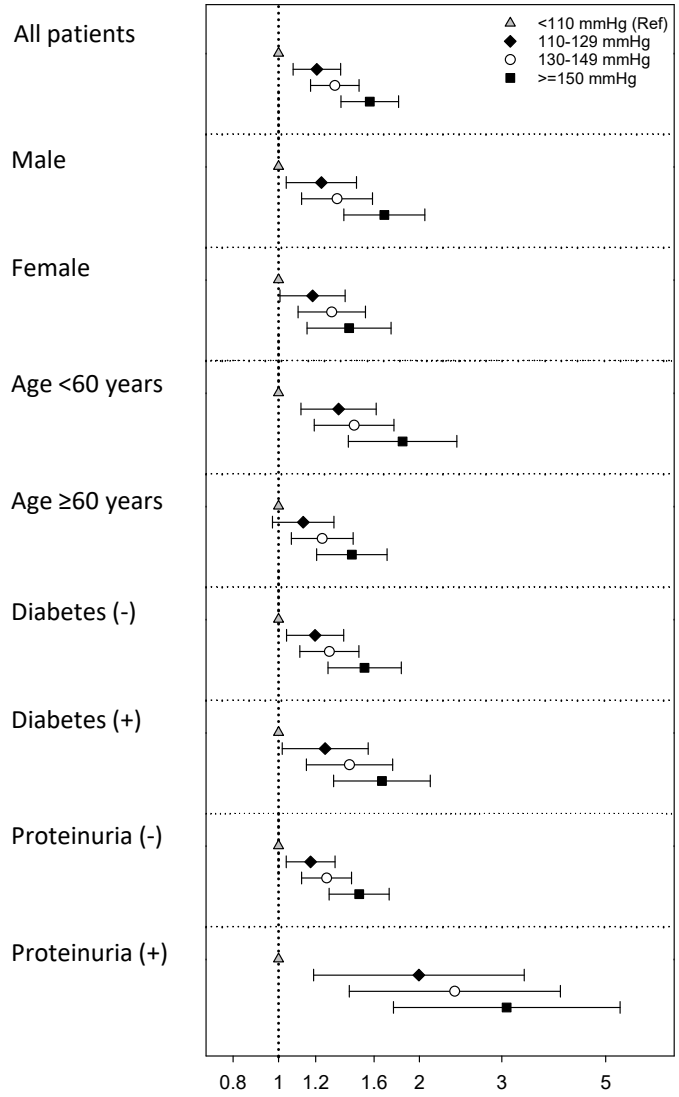
Subgroup analyses

(A)

	Patient, N	CKD, N (%)
All patients	182,029	4,786 (2.63%)
Male	105,205	2,720 (2.59%)
Female	76,824	2,066 (2,69%)
Age <60 years	94,006	1,410 (1.52%)
Age ≥60 years	89,023	3,376 (3.79%)
Diabetes (-)	131,246	2,854 (2.17%)
Diabetes (+)	50,783	1,932 (3.80%)
Proteinuria (-)	173,466	4,349 (2.51%)
Proteinuria (+)	8,135	413 (5.08%)



(B)



Multivariate adjusted hazard ratios of chronic kidney disease (CKD) development associated with baseline (A) and time-varying (B) systolic blood pressure, stratified by gender, age, diabetes, and proteinuria

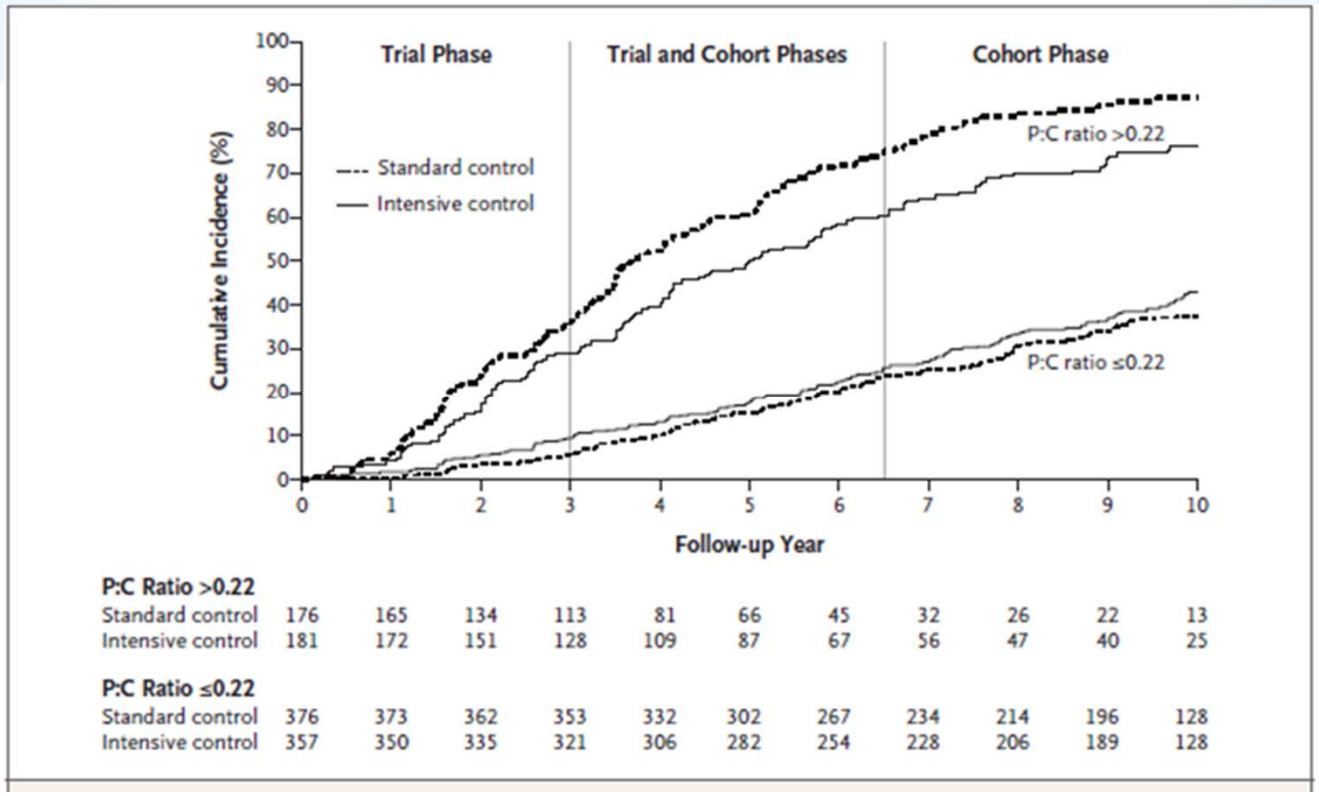

Bias
biased
statistics
tendency
information
behavior
psychology
cognitive
perspective
hypothesis
significance
statistical
test
true
beliefs
describe
others
level
edit
part
prior
tend
explain
term
error
null
terms
ability
one's
need
used
One
group
study
attitude
scientific
based
may
exhibit
factors
accuracy
model
members
type
towards
exceeds
appears
area
unbiased
incorrect
estimator's
whereas
ideology
someone
Main
interferes
includes
extreme
interpret
correspondence
systemic
influenced
greater
unconscious
difference
person
generally
diagnostic
assumed
people
context
processor
parameters
expectation
external
conscious
specificity
personality
rejecting
consists
evaluating
influences
estimator
individuals
Labeling
sampling
parameter
less
take
regression
refers
preference
estimates
new
normal
also
value
even
comes seen
fundamental
way
data
brain
independent
Data-snooping
Systematic
misuse
probability
development
Omitted-variable
overestimate
omits
impartial
one-sided
several
confirms
regard
leads
related
groups
equal
patients
conflicts
ignoring
unprejudiced
estimated
analysis
testing
judged
result
awareness
objective
particular
confirmation
measurements
specification
types
likely
deeply
attribution
Selection
words
prejudice
known
situation
example
mining
affect
techniques
sensitivity
choosing
consider
flexible
implies
Spectrum
judgment
denial
alternative
variable
article
included

Observational Studies vs. RCTs

Observational studies	RCTs
1) Do not see the effect of BP reduction on clinical outcomes 2) Do not reflect dynamic changes of BP during the whole period. 3) Effect of chronically elevated BP before the study is not well captured in time varying model or MSM.	1) Ideal, but relatively short-follow up duration, mostly 3-4 years 2) Initial decline in BP can impair kidney function, but its long-term effect is unknown.

AASK trial

- Randomized trials in 1094 black patients with hypertensive CKD
- Target BP : ≤ **130/80 mmHg** vs. ≤ **140/80 mmHg**



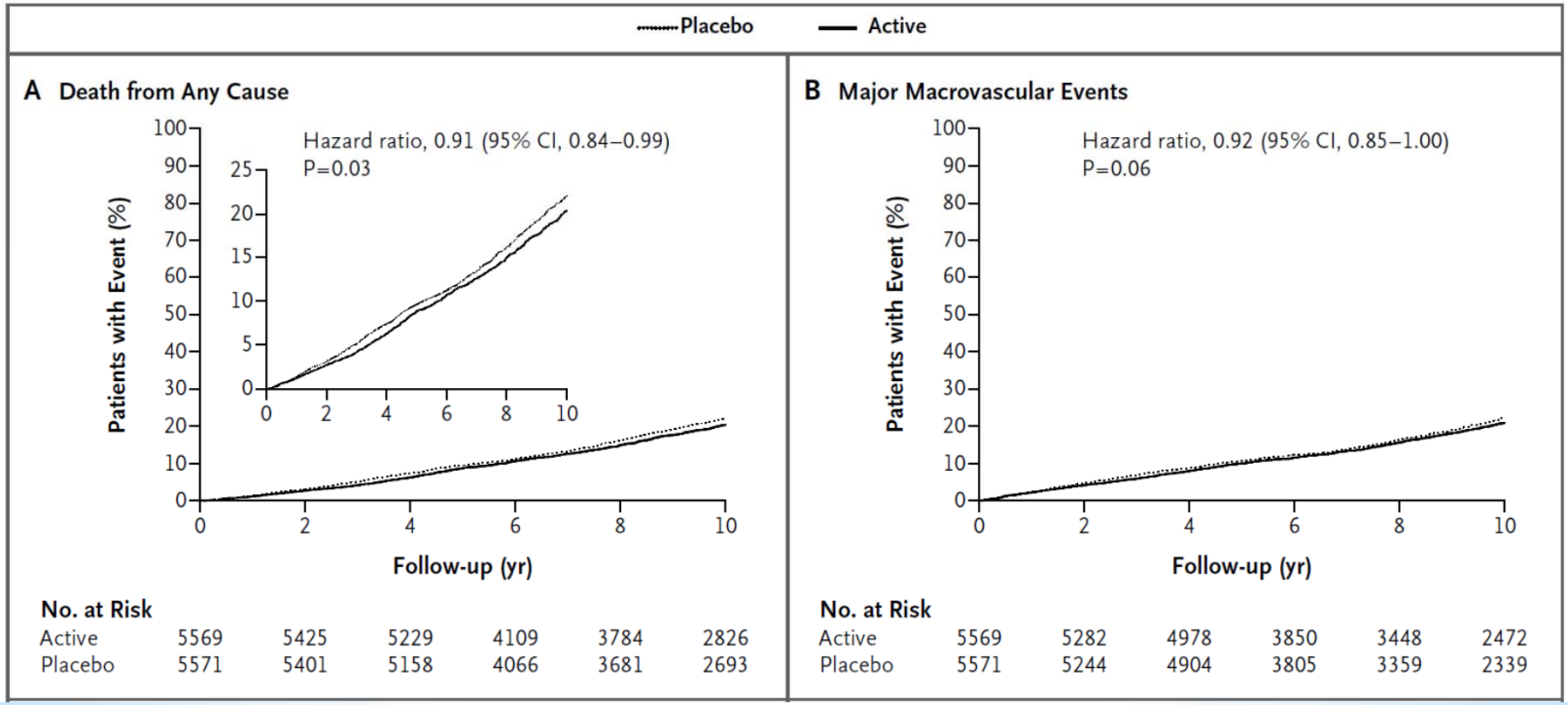
N Engl J Med. 363(10):918-929, 2010.

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*



Summary and Conclusion

1) The optimal target of BP reduction to improve renal and CV outcomes, and mortality has not yet been determined.
2) Although some guidelines suggest a BP target of < 130/80 mmHg, clinical evidence supporting this is lacking.
3) The lower target of SBP is beneficial for the reduction of albuminuria, but not harder outcomes.
4) The beneficial effects of lower BP levels in observational studies should be cautiously interpreted due to many confounding factors.
5) More well-designed RCTs regarding this issue are warranted in diverse groups; presence of diabetes, CV risk, or proteinuria, early vs. late stages of CKD etc.

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Tae Ik Chang
Hyunsun Lim

The KNOW-CKD Investigators

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Dong Wan Chae
Kyu Hun Choi
Curie Ahn

Yonsei University

Jong Hyun Jhee
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Seohyun Park
Su-Young Jung
Youn Kyung Kee
Min Wook Cha
Mi-Sol Lee
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Ki Heon Nam
Chang-Yun Yoon
Jung Tak Park
Tae-Hyun Yoo
Shin-Wook Kang