The 25th Budapest Nephrology School

Nephrology, Hypertension, Dialysis, Transplantation, Nephropathology

Under the Auspices of
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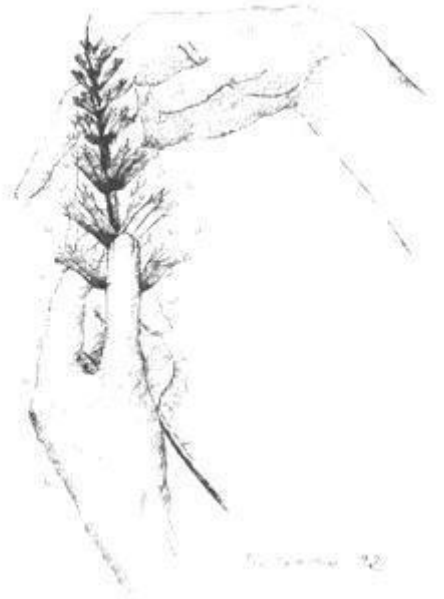

What Should be the Optimal Blood Pressure for CKD Patients after the SPRINT Study and Publication of ACC/AHA Guidelines?

Prof. Andrzej Wiecek

Department of Nephrology, Transplantation and Internal Medicine
Medical University of Silesia, Katowice, Poland

e-mail: awiecek@sum.edu.pl

I would like to thank ERA-EDTA for selecting me as an „ambasador” during this course

Andrzej Wiecek

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- Clinica trials:

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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*

ABSTRACT

BACKGROUND

The most appropriate targets for systolic blood pressure to reduce cardiovascular morbidity and mortality among persons without diabetes remain uncertain.

METHODS

We randomly assigned 9361 persons with a systolic blood pressure of 130 mm Hg or higher and an increased cardiovascular risk, but without diabetes, to a systolic blood-pressure target of less than 120 mm Hg (intensive treatment) or a target of less than 140 mm Hg (standard treatment). The primary composite outcome was myocardial infarction, other acute coronary syndromes, stroke, heart failure, or death from cardiovascular causes.

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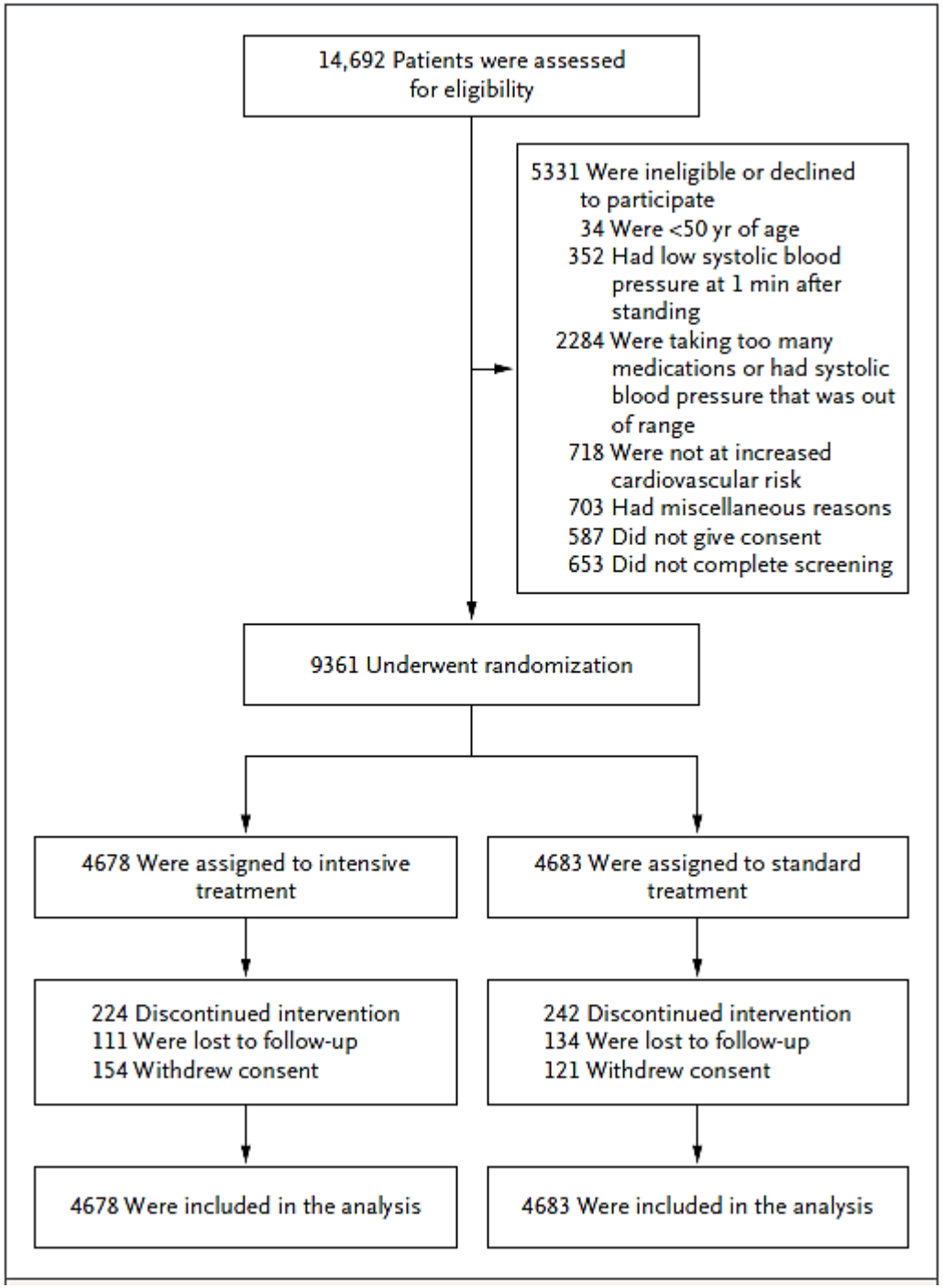
Recruitment procedure

- SPRINT recruited subject in 102 sites in USA and Puerto Rico from Nov. 2010 to March 2013
- The Trial intended to recruit one third of its subjects with CKD
- Patients with diabetes mellitus, polycystic kidney disease, history of stroke, heavy proteinuria (> 1.0 g/d) and patients with eGFR < 20 ml/min/1.73 m2 were excluded from the study
- Total costs of this trial were 157 mln of US dollars

SPRINT Trial
Inclusion criteria

- Participants were required to meet the following criteria:
  - Age > 50 years
  - Systolic BP > 130 mmHg < 180 mmHg
  - Increased risk of cardiovascular events:
    cardiovascular disease other than stroke,
    chronic kidney disease other than ADPKD,
    eGFR 20-60 ml/min. (28% with eGFR< 60 ml/min),
    10-year risk of cardiovascular disease > 15% on the basis of the Framingham risk score or
    age >75 years (28% were 75 years or older)



SPRINT Trial flowchart:

- eligibility,
- randomization
- and follow-up

N. Engl. J. Med., 2015; 373: 2103-2116

SPRINT Trial

Baseline characteristics of the study participants

Table 1. Baseline Characteristics of the Study Participants.*

Characteristic	Intensive Treatment (N=4678)	Standard Treatment (N=4683)
Criterion for increased cardiovascular risk — no. (%)†		
Age ≥75 yr	1317 (28.2)	1319 (28.2)
Chronic kidney disease‡	1330 (28.4)	1316 (28.1)
Cardiovascular disease	940 (20.1)	937 (20.0)
Clinical	779 (16.7)	783 (16.7)
Subclinical	247 (5.3)	246 (5.3)
Framingham 10-yr cardiovascular disease risk score ≥15%	2870 (61.4)	2867 (61.2)
Female sex — no. (%)	1684 (36.0)	1648 (35.2)
Age — yr		
Overall	67.9±9.4	67.9±9.5
Among those ≥75 yr of age	79.8±3.9	79.9±4.1

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Overall	67.9±9.4	67.9±9.5
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Chronic Kidney Disease was defined as an estimated GFR less than 60 ml/ml/1.73 m2 of BSA

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SPRINT Trial

Baseline characteristics of the study participants (cont.)

Table 1. Baseline Characteristics of the Study Participants.*

Characteristic	Intensive Treatment (N = 4678)	Standard Treatment (N = 4683)
Baseline blood pressure — mm Hg		
Systolic	139.7±15.8	139.7±15.4
Diastolic	78.2±11.9	78.0±12.0
Distribution of systolic blood pressure — no. (%)		
≤132 mm Hg	1583 (33.8)	1553 (33.2)
>132 mm Hg to <145 mm Hg	1489 (31.8)	1549 (33.1)
≥145 mm Hg	1606 (34.3)	1581 (33.8)
Serum creatinine — mg/dl	1.07±0.34	1.08±0.34
Estimated GFR — ml/min/1.73 m^2		
Among all participants	71.8±20.7	71.7±20.5
Among those with estimated GFR ≥60 ml/min/1.73 m^2	81.3±15.5	81.1±15.5
Among those with estimated GFR <60 ml/min/1.73 m^2	47.8±9.5	47.9±9.5
Ratio of urinary albumin (mg) to creatinine (g)	44.1±178.7	41.1±152.9

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SPRINT Trial

Baseline characteristics of the study participants (cont.)

Table 1. Baseline Characteristics of the Study Participants.*		
Characteristic	**Intensive Treatment (N = 4678)**	**Standard Treatment (N = 4683)**
Body-mass index‖	29.9±5.8	29.8±5.7
Antihypertensive agents — no./patient	1.8±1.0	1.8±1.0
Not using antihypertensive agents — no. (%)	432 (9.2)	450 (9.6)
Statin use (%)	**42.6 %**	**44.7 %**
Aspirin use (%)	**51.6 %**	**50.4 %**

N. Engl. J. Med., 2015; 373: 2103-2116

Antihypertensive medication used in the SPRINT Trial

TABLE 1

Antihypertensive medications used in SPRINT

Medication class	Intensive therapy (%)	Standard therapy (%)
Angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers	76.7	55.2
Thiazide-type diuretics	54.9	33.3
Dihydropyridine calcium channel blockers	52.8	31.3
Beta-blockers	41.1	30.8
Aldosterone antagonists	8.7	4.0
Other potassium-sparing diuretics	3.1	2.5
Nondihydropyridine calcium channel blockers	4.7	4.3
Direct vasodilators	7.3	2.4

Information from SPRINT Research Group; Wright JT Jr, Williamson JD, Whelton PK, et al. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med 2015; 373:2103–2116.

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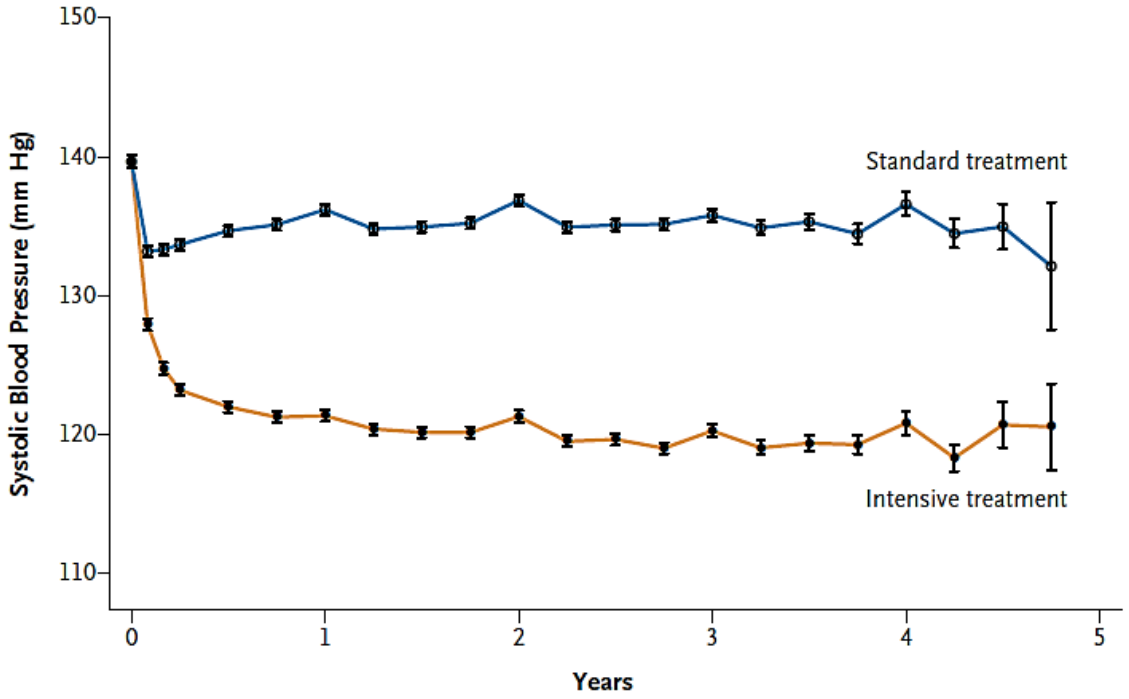
Mean number of antihypertensive tables: 3.0 1.9

Antihypertensive medication used in the SPRINT Trial

- Medications from all major classes of antihypertensive agents were provided by SPRINT at no costs to the participants
- There was no restriction on using any antihypertensive medications and this was at the discretion of individual investigators
- Thiazide-type diuretics were encouraged as first – line agents (with chlorthalidone as the primary thiazide-type diuretic)

SPRINT Trial

Systolic blood pressure in the two treatment arms



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

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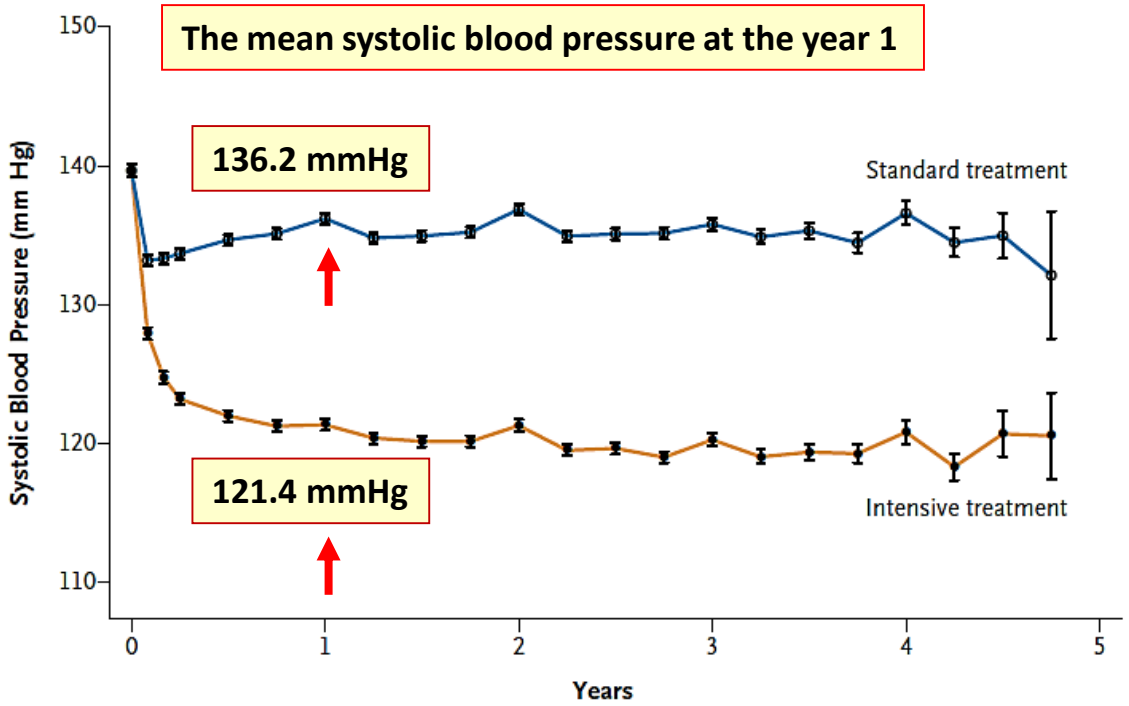

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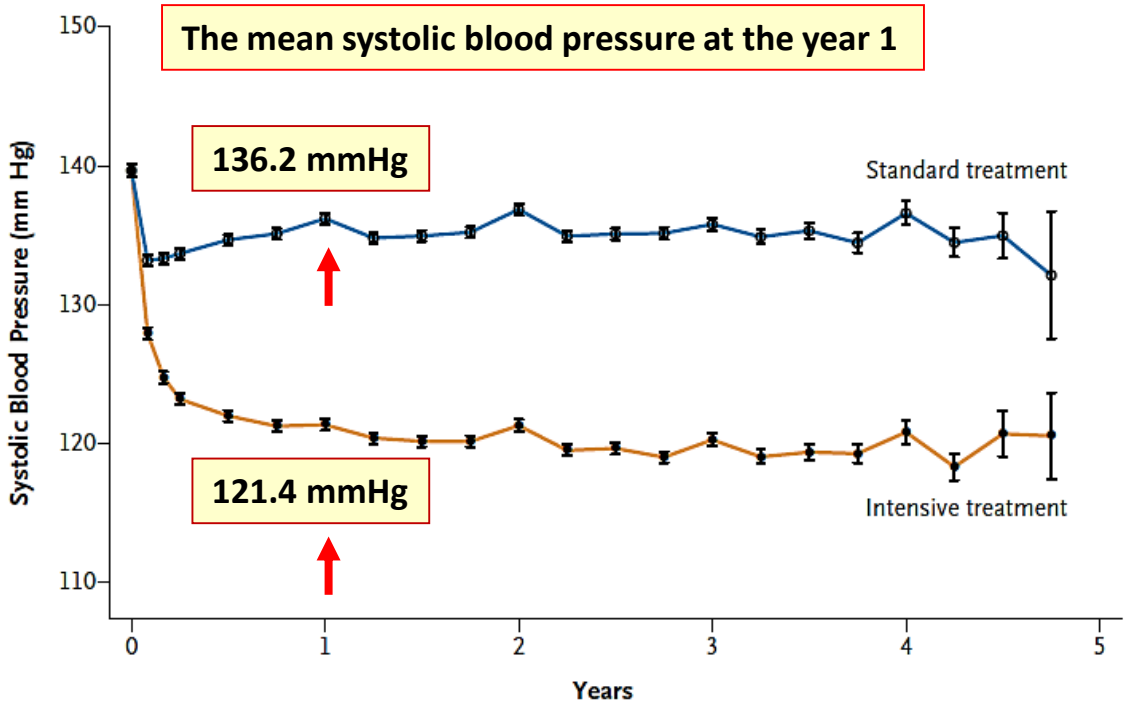

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SPRINT Trial

Primary Outcome

- **Definition of Primary Outcome:**

the rate of composite outcome of myocardial infarction, acute coronary syndrome not resulting in myocardial infarction, stroke, acute decompensated heart failure or death from cardiovascular causes

N. Engl. J. Med., 2015; 373: 2103-2116

SPRINT Trial

Primary Outcome

- Definition of Secondary Outcomes:

individual components of the primary composite outcome plus death from any cause

and

the composite of the primary outcome or death from any case

N. Engl. J. Med., 2015; 373: 2103-2116

SPRINT Trial

Renal outcomes – different definitions

- For patients with chronic kidney disease (eGFR<60 ml/min/1.73 m2) at baseline - renal outcome was defined by:

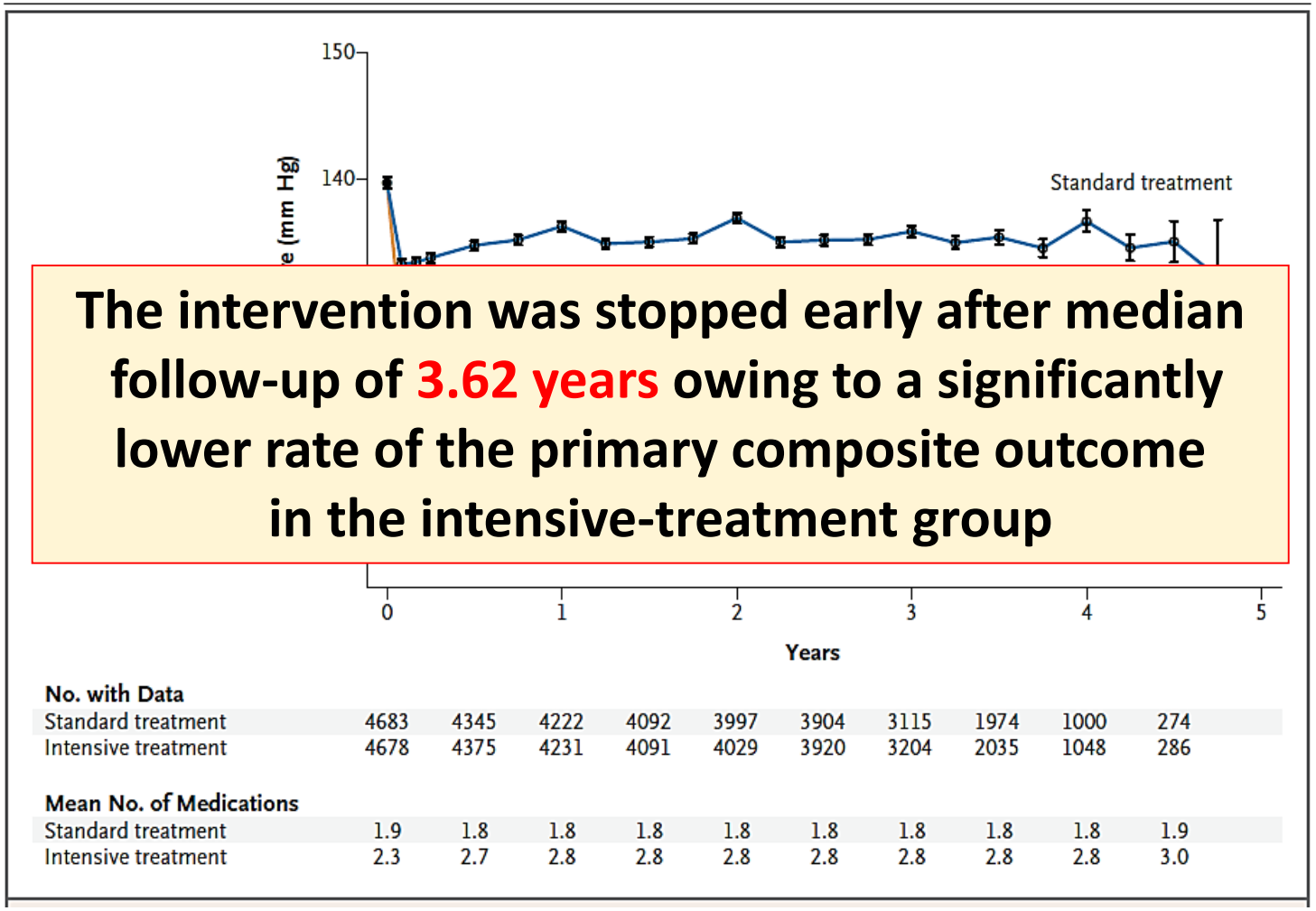
composite of decrease in the eGFR of 50% or more, or development of ESRD requiring long-term dialysis or kidney transplantation

- For participants without chronic kidney disease at baseline - renal outcome was defined by:

a decrease in the eGFR of 30% or more to a value of less than 60 ml/min/1.73 m2

SPRINT Trial

Systolic blood pressure in the two treatment arms



The intervention was stopped early after median follow-up of 3.62 years owing to a significantly lower rate of the primary composite outcome in the intensive-treatment group

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N. Engl. J. Med., 2015; 373: 2103-2116

SPRINT Trial

Primary and secondary outcomes and renal outcomes

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

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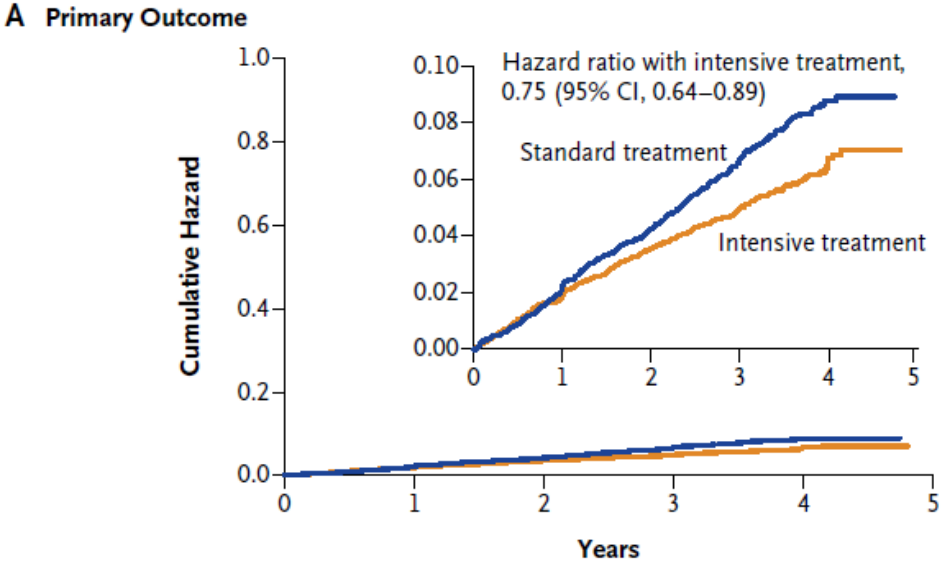
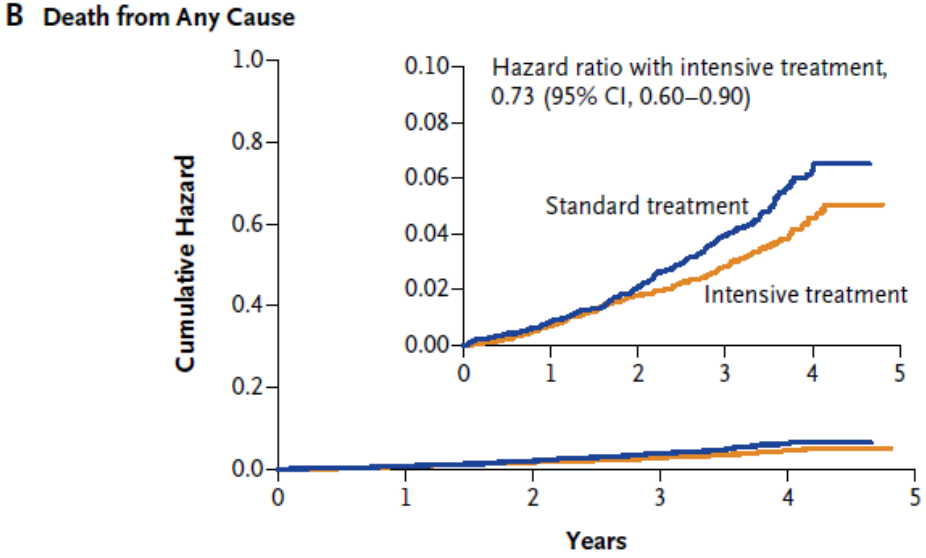
SPRINT Trial

Primary outcome and death from any cause



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



No. at Risk					
Standard treatment	4683	4528	4383	2998	789
Intensive treatment	4678	4516	4390	3016	807

N. Engl. J. Med., 2015; 373: 2103-2116

SPRINT Trial

Primary and secondary outcomes and renal outcomes

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

N. Engl. J. Med., 2015; 373: 2103-2116

SPRINT Trial

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N. Engl. J. Med., 2015; 373: 2103-2116

SPRINT Trial

Serious adverse events

Table 3. Serious Adverse Events, Conditions of Interest, and Monitored Clinical Events.

Variable	Intensive Treatment (N=4678)	Standard Treatment (N=4683)	Hazard Ratio	P Value
	no. of patients (%)			
Serious adverse event*	1793 (38.3)	1736 (37.1)	1.04	0.25
Conditions of interest				
Serious adverse event only				
Hypotension	110 (2.4)	66 (1.4)	1.67	0.001
Syncope	107 (2.3)	80 (1.7)	1.33	0.05
Bradycardia	87 (1.9)	73 (1.6)	1.19	0.28
Electrolyte abnormality	144 (3.1)	107 (2.3)	1.35	0.02
Injurious fall†	105 (2.2)	110 (2.3)	0.95	0.71
Acute kidney injury or acute renal failure‡	193 (4.1)	117 (2.5)	1.66	<0.001

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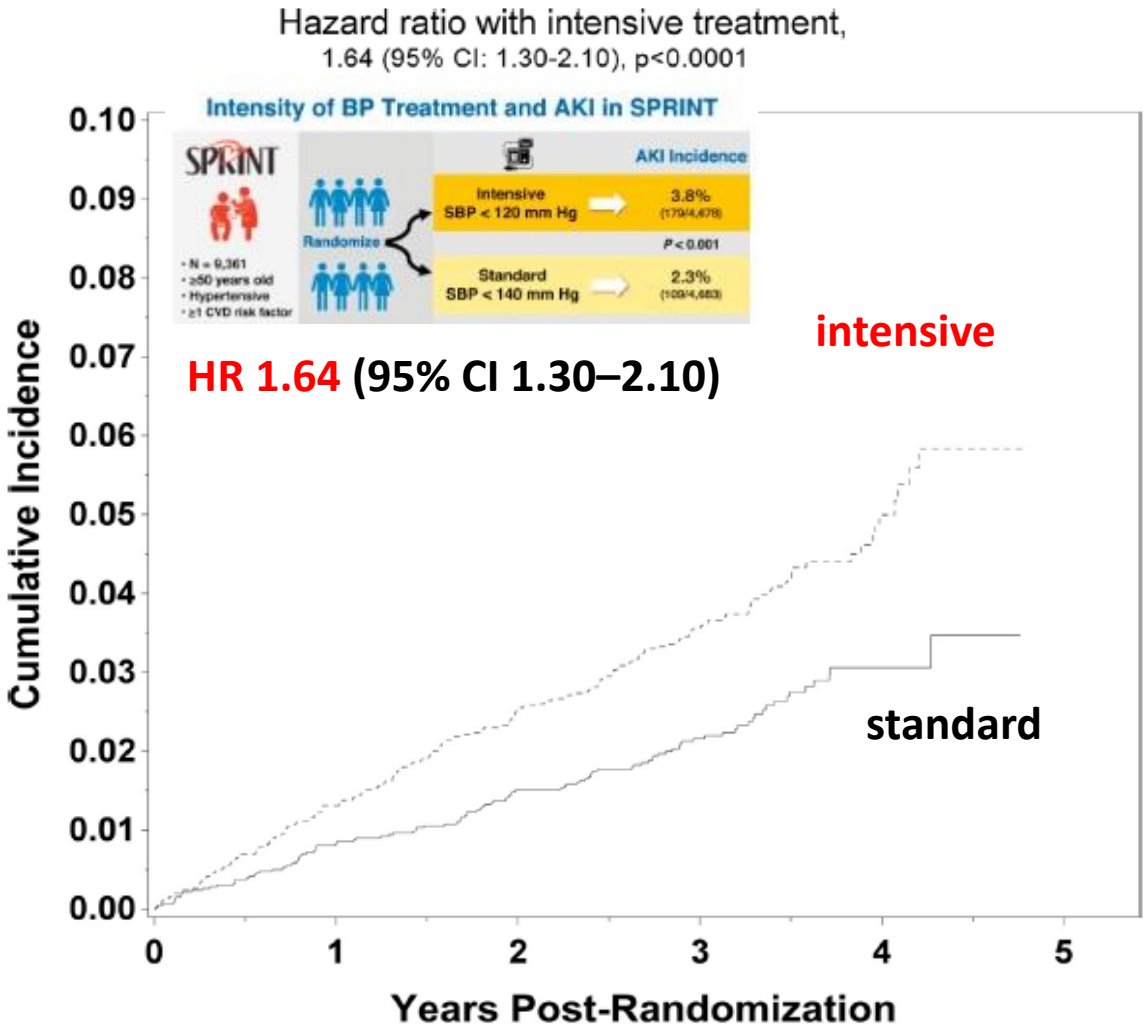
N. Engl. J. Med., 2015; 373: 2103-2116

Acute Kidney Injury in SPRINT



Rocco M.V. et al. Am. J. Kidney Dis. 2018, 71, 352 - 361

Acute Kidney Injury in SPRINT

	AKI	AKI 1 (1.5 – 2.0 x s-creatinine increase)	AKI 2 (2.0 – 3.0 x s-creatinine increase)	AKI 3 (>3.0 x s-creatinine increase)
Intensive	**212**	**128**	**42**	**42**
Standard	**124**	**81**	**18**	**25**

Dialysis treatment 8 vs. 6 patients

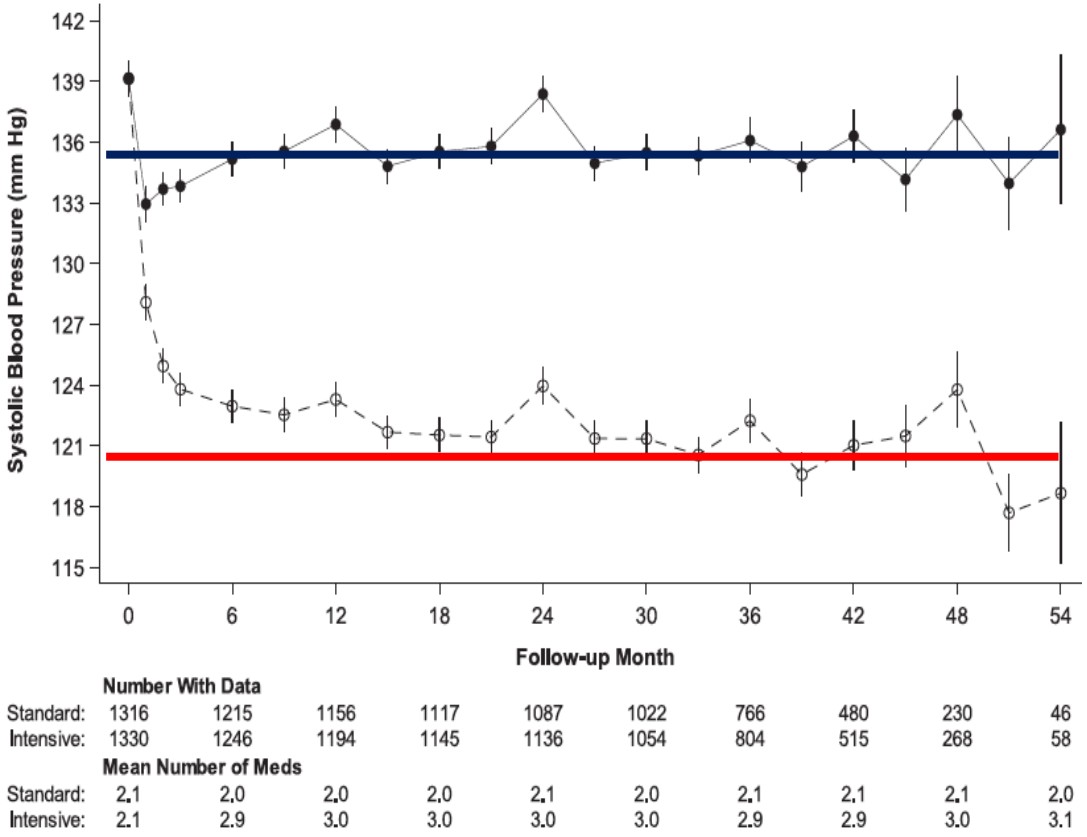
Rocco M.V. et al. Am. J. Kidney Dis. 2018, 71, 352 - 361

Intensive vs. standard BP in CKD patients

Inclusion criteria:

- Hypertension
- High CV risk
- CKD 3-5 (no HD)
- Proteinuria <1g/day
- No diabetes (but IGT)

Total of 2,646 patients

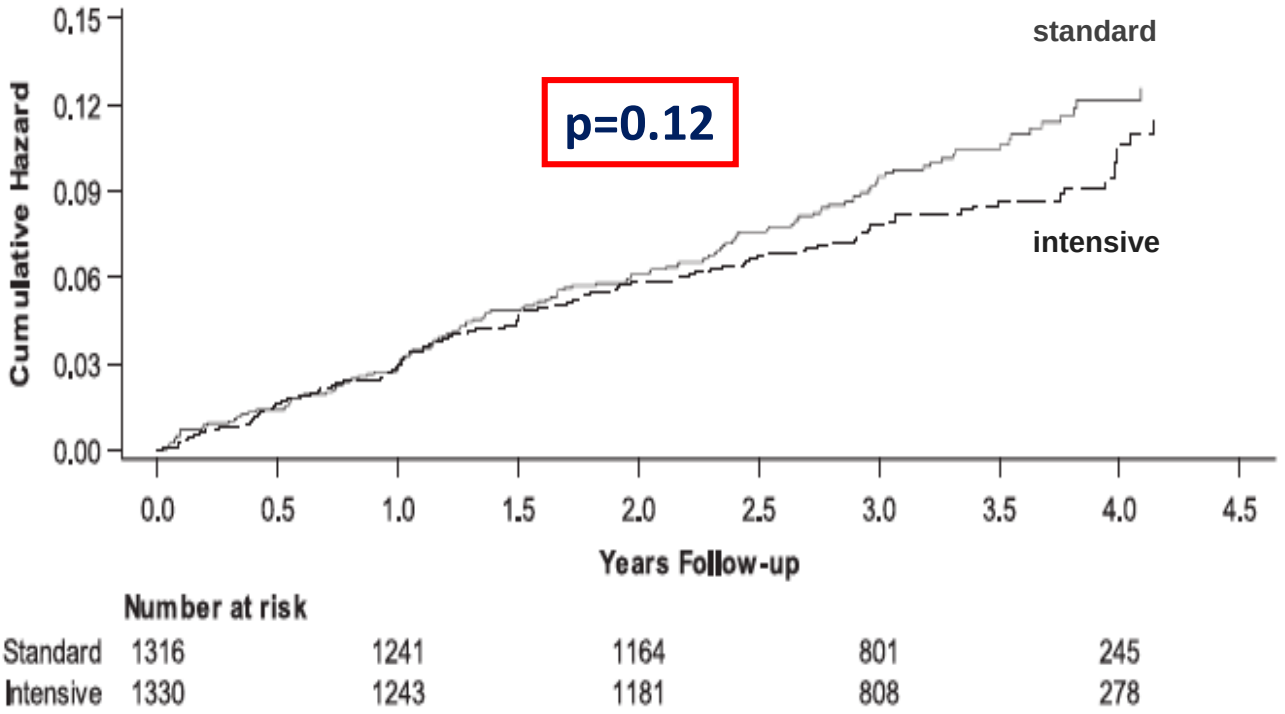


	Number With Data									
Standard:	1316	1215	1156	1117	1087	1022	766	480	230	46
Intensive:	1330	1246	1194	1145	1136	1054	804	515	268	58
	Mean Number of Meds									
Standard:	2.1	2.0	2.0	2.0	2.1	2.0	2.1	2.1	2.1	2.0
Intensive:	2.1	2.9	3.0	3.0	3.0	3.0	2.9	2.9	3.0	3.1

Cheung A.K., et al. J. Am. Soc. Nephrol., 2017, 28, 2812 - 2823

Intensive vs. standard BP in CKD patients

Primary CV Outcome
HR 0.81 (0.63-1.05)

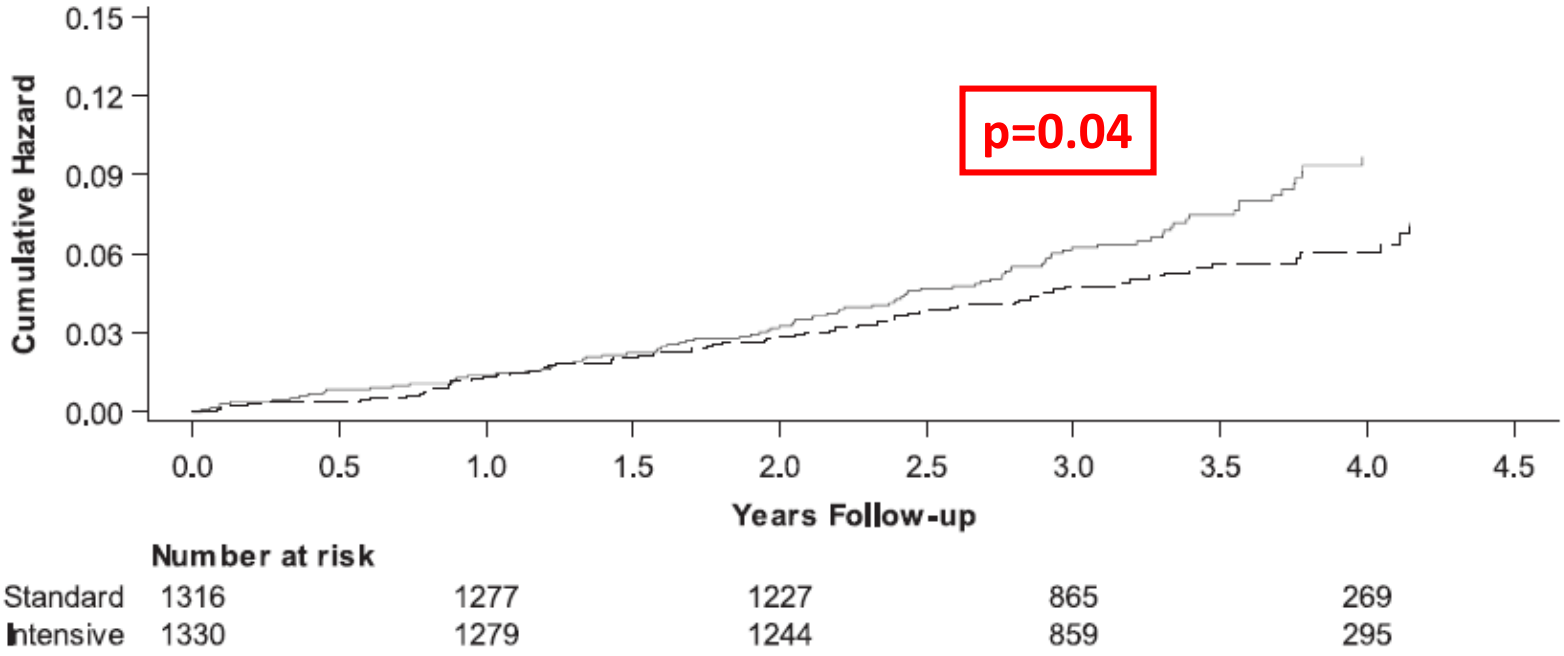


2,646 patients

Cheung A.K., et al. J. Am. Soc. Nephrol., 2017, 28, 2812 - 2823

Intensive vs. standard BP in CKD patients

All-cause death Outcome
HR 0.72 (0.53-0.99)

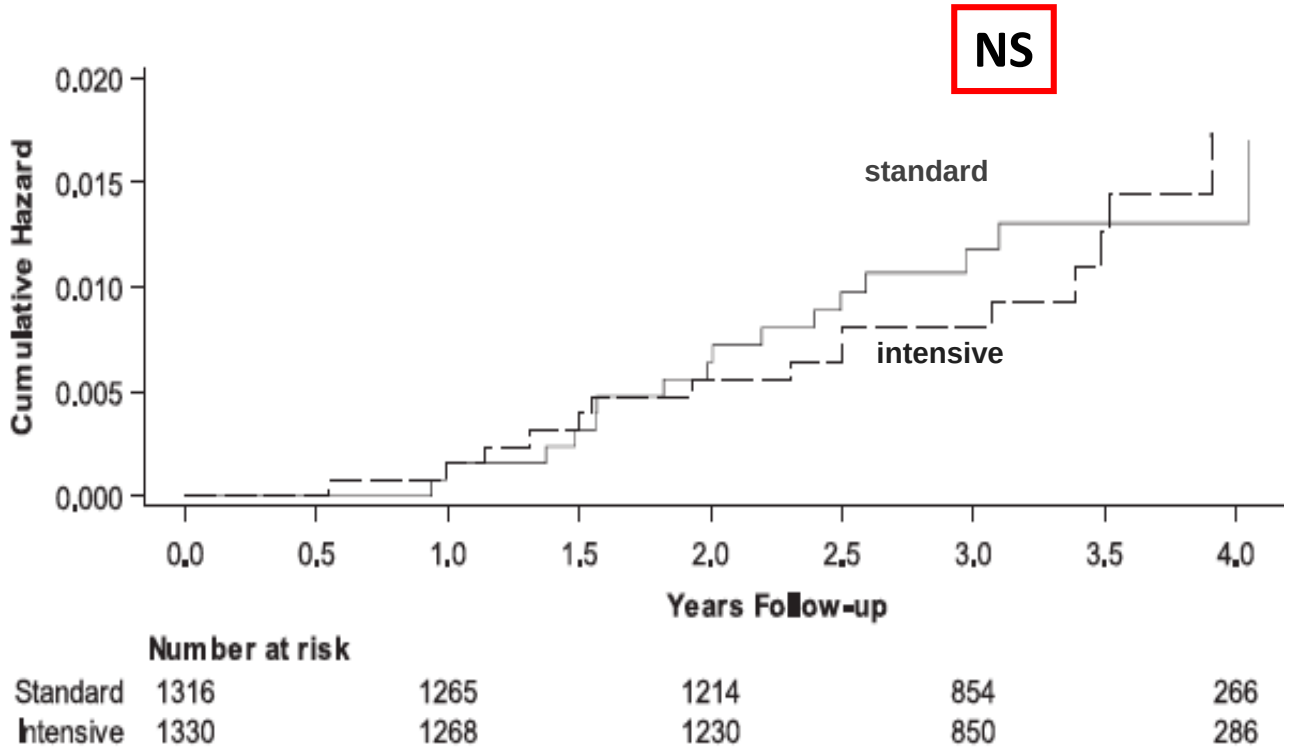


2,646 patients

Cheung A.K., et al. J. Am. Soc. Nephrol., 2017, 28, 2812 - 2823

Intensive vs. standard BP in CKD patients

End-stage renal disease or 50% eGFR decrease
HR 0.90 (0.44-1.83)

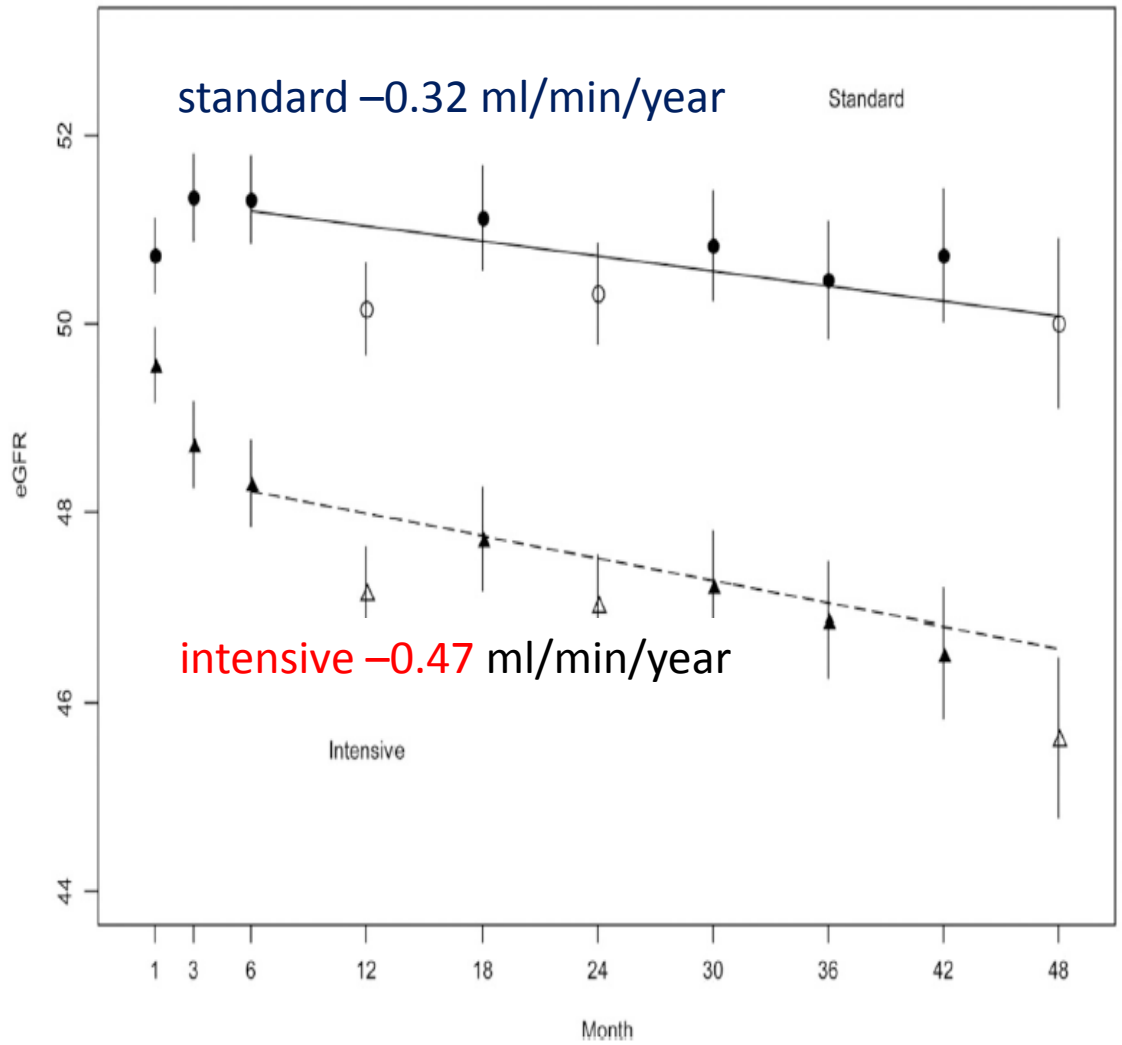


2,646 patients

Cheung A.K., et al. J. Am. Soc. Nephrol., 2017, 28, 2812 - 2823

Intensive vs. standard BP in CKD patients

Change in eGFR



2,646 patients

Cheung A.K., et al. J. Am. Soc. Nephrol., 2017, 28, 2812 - 2823

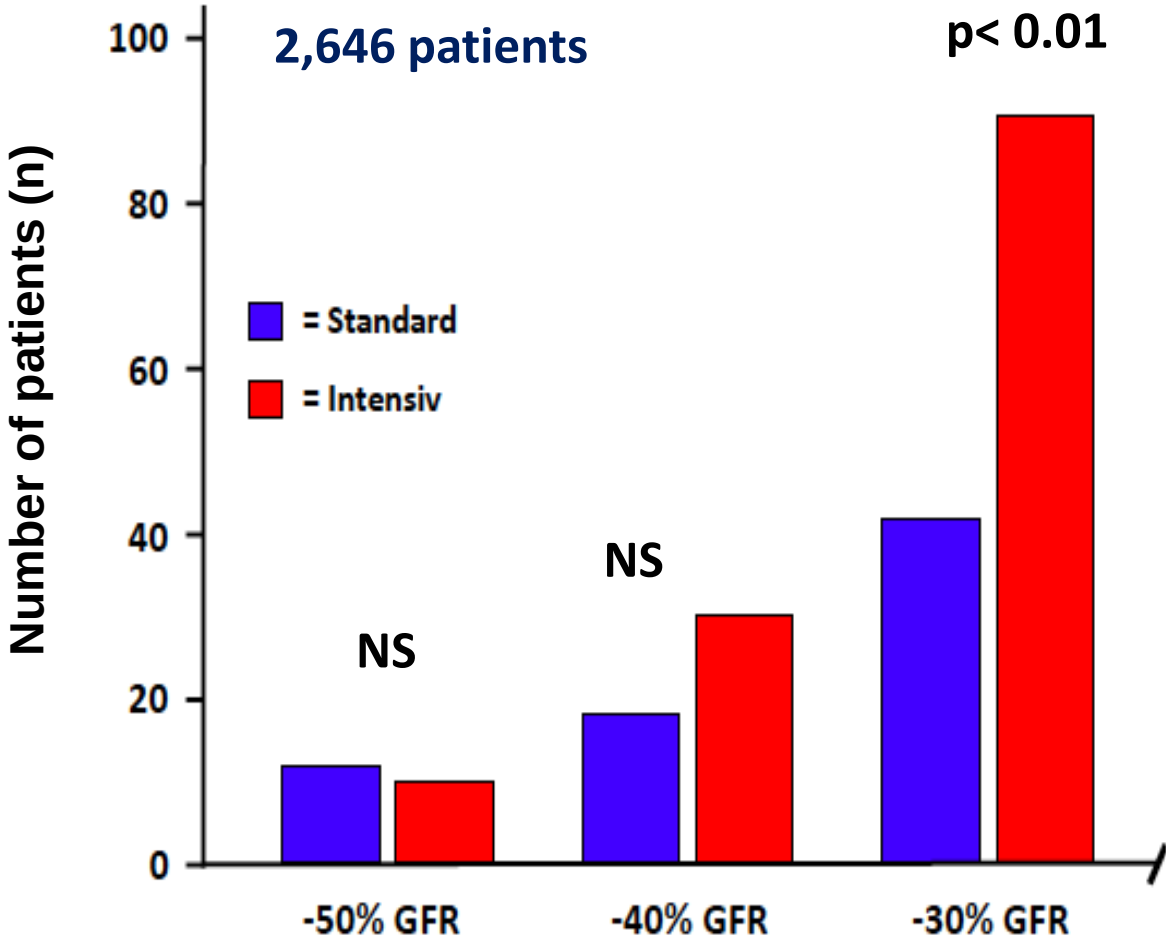
Intensive vs. standard BP in CKD

Adverse effects with lower BP

- Hyperkalemia 36% increased
- Hypokaliemia 87% increased
- Acute kidney injury 46% increased

Cheung A.K., et al. J. Am. Soc. Nephrol., 2017, 28, 2812 - 2823

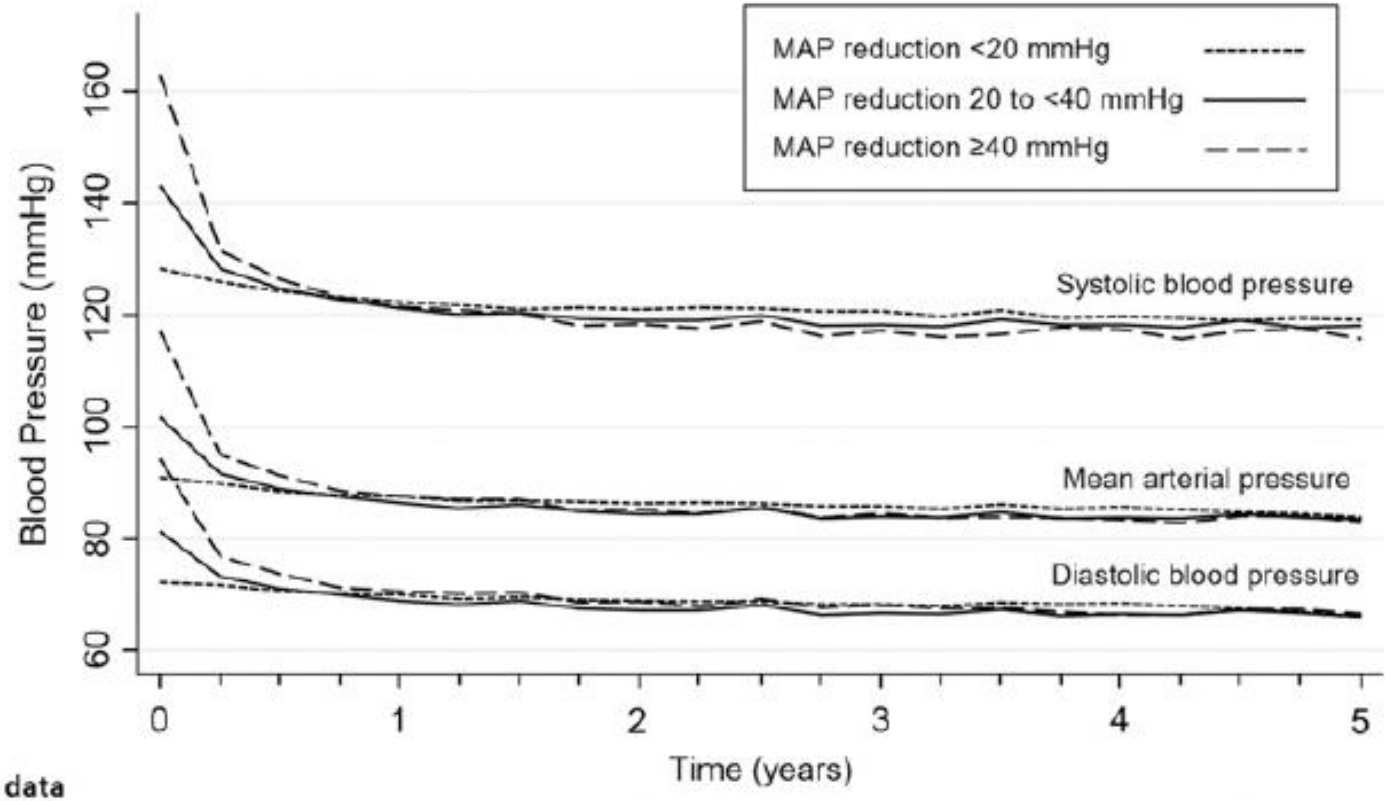
Intensive vs. standard BP in CKD



Cheung A.K., et al. J. Am. Soc. Nephrol., 2017, 28, 2812 - 2823

Kidney function decline in SPRINT Trial (in patients without CKD at baseline)

Patients without CKD (eGFR >60 ml/min/m²)

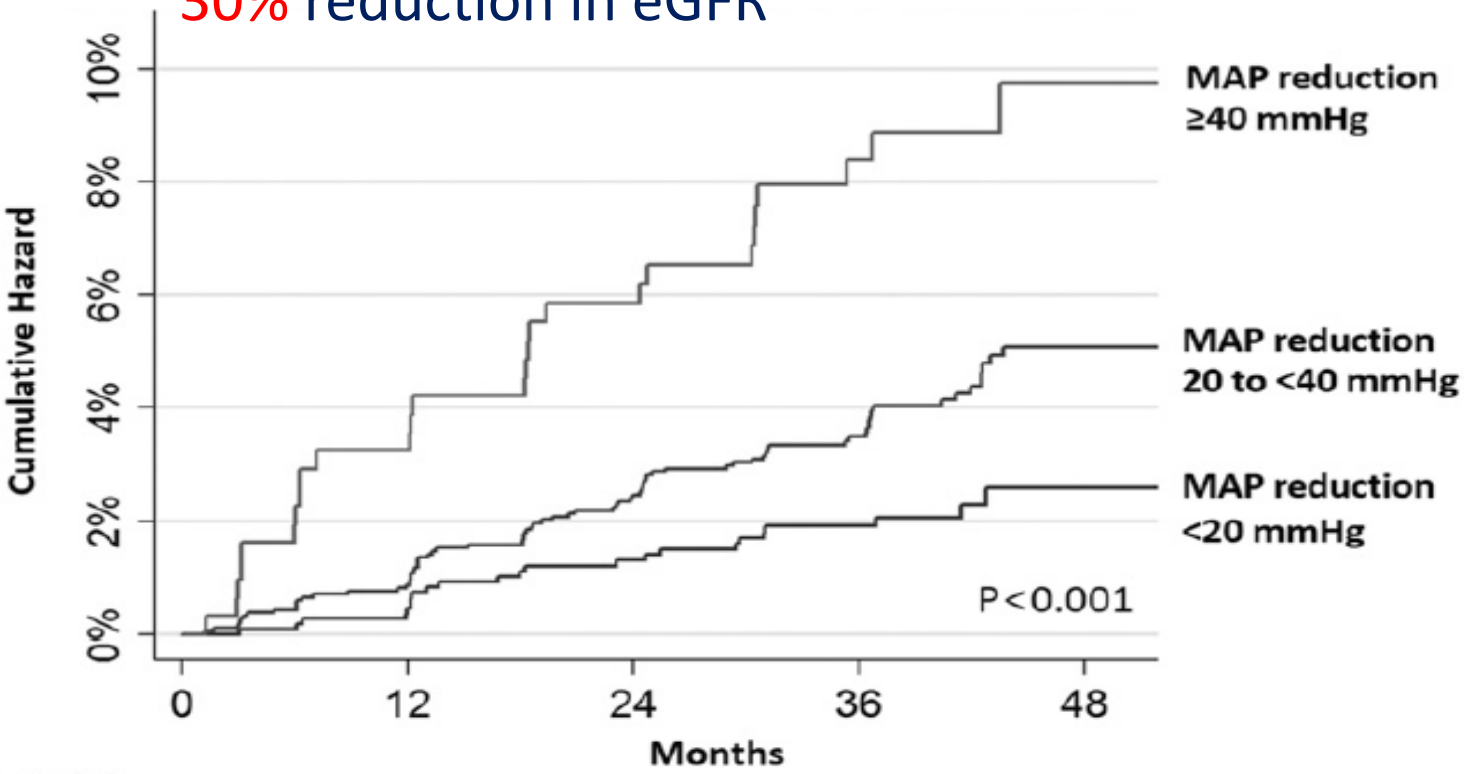


Number with data										
MAP reduction <20 mmHg	1136	1028	967	932	902	851	640	346	136	61
MAP reduction 20 to <40 mmHg	1857	1795	1763	1714	1698	1611	1229	739	331	169
MAP reduction ≥40 mmHg	309	303	299	291	284	280	209	129	58	33

Magrico R., et al. Clin. J. Am. Soc. Nephrol., 2018., 13, 73 - 80

Kidney function decline in SPRINT Trial (in patients without CKD at baseline)

30% reduction in eGFR



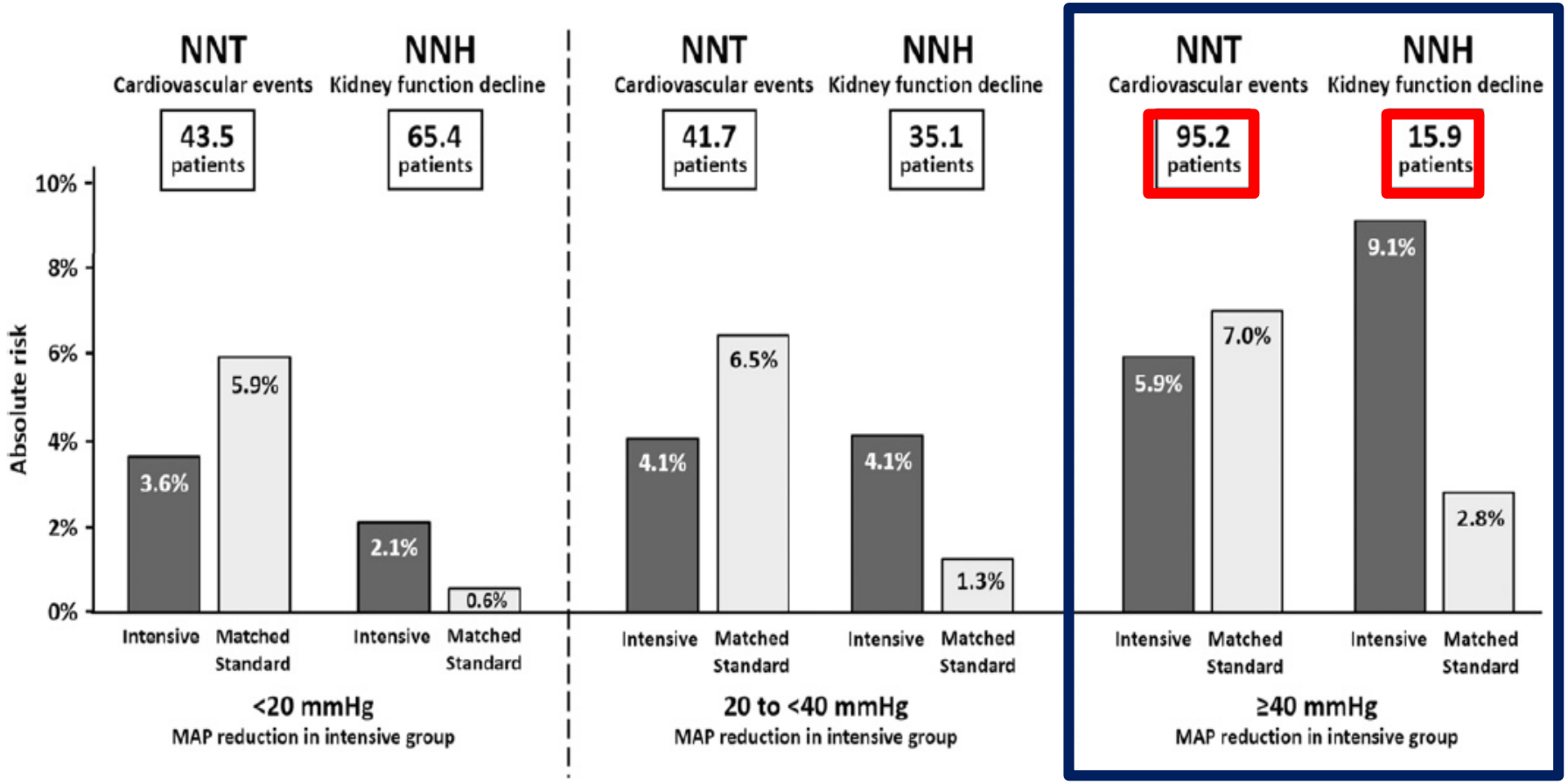
Number at risk					
Less than 20 mmHg	1126	1068	1022	712	170
20 to <40 mmHg	1854	1816	1750	1266	368
40 mmHg or more	309	297	281	204	59

Magrico R., et al. Clin. J. Am. Soc. Nephrol., 2018., 13, 73 - 80

Kidney function decline (a decrease in the eGFR of 30% or more to a value of less than 60 ml/min/1.73 m2) in SPRINT Study

NNT = number needed to treat

NNH = number needed to harm



Magrico R., et al. Clin. J. Am. Soc. Nephrol., 2018., 13, 73 - 80

Why the low BP target did not bring renal benefits in the SPRINT Trial?

- Blood pressure was measured with the use of an automated measurement system (model 907, Omron Healthcare), by patients left alone in the room, which eliminates the „white coat effect" (these values of BP seem to be ca. 10-15 mmHg lower, that obtained with the traditional method, measured in the office by the physician or nurse

Patients' status during the blood pressure measurement reported in different trials

Trial	Device	Status of Observation	References
ACCORD	Model 907, Omron Healthcare, Lake Forest, IL	Attended	The ACCORD Study Group[2]
SPS3	Colin BP-8800C, Press Mate, Meena Medical Inc, Bedford, TX	Attended	The SPS3 Study Group[3]
SPRINT	Model 907, Omron Healthcare, Lake Forest, IL	Unattended	The SPRINT Research Group[7]
HOT	Visomat OZ, D2 International, Hestia Pharma GmbH, Germany	Attended	Hansson et al[9]
TROPHY	HEM-705CP, Omron Healthcare, Lake Forest, IL	Attended	Julius et al[19]
ONTARGET	HEM-757, Omron Corporation, Tokyo, Japan	Attended	Verdecchia et al[20]
TRANSCEND	HEM-757, Omron Corporation, Tokyo, Japan	Attended	Verdecchia et al[20]

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BP was obtained by an automatic device when patient has been resting alone for 5 min.
BP was checked every minute, total 3-5 times and the average value was calculated
The methodology for measuring BP in SPRINT Trial was not the same what is used in most clinical practices and this difference has significant clinical implications

Blood pressure recording in the SPRINT Trial

OMRON

INSTRUCTION MANUAL

OMRON
Digital Automatic Blood Pressure Monitor

Model

HEM-907

Blood pressure recording in the SPRINT Trial

- Targeting the SBP <120 mmHg without using similar BP measurement methods as in the trial may increase the risk of serious adverse events by systematically overshooting the trial-based BP targets and potentially leading to hypotensive complications

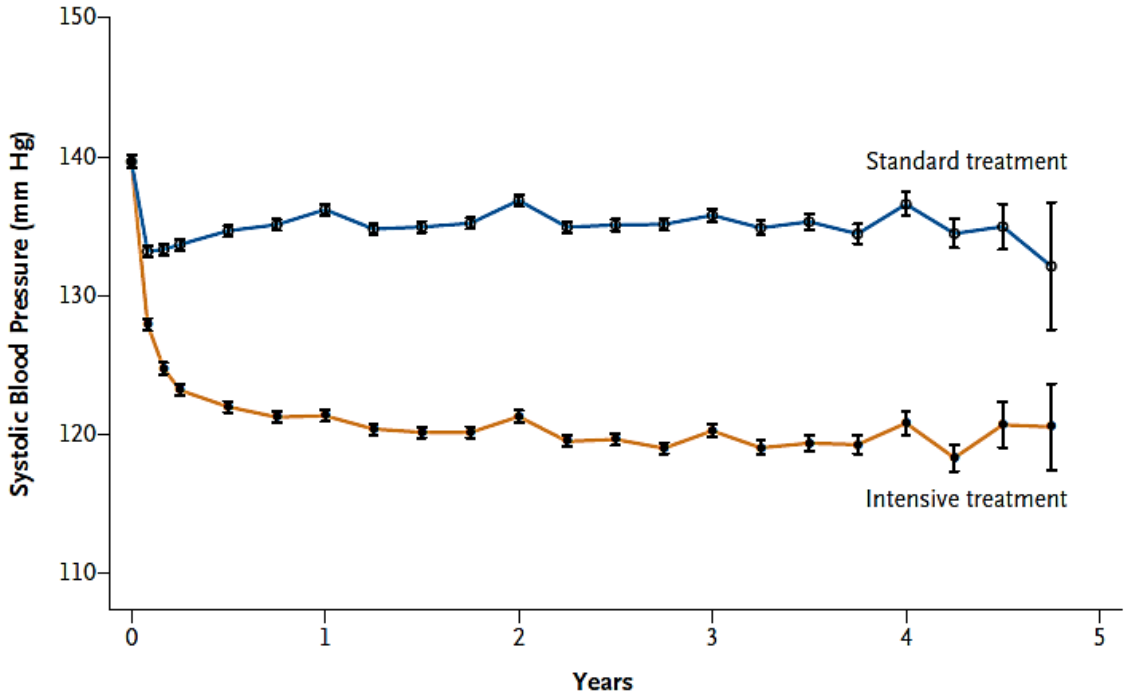
- Thus, applying the SPRINT intensive BP targets based on usual office measurements would correspond to a SBP target range of 125-135 mm Hg

Why it was so many renal outcomes observed in the SPRINT Trial?

- The decline of blood pressure obtained in the high risk population (>50 years of age with cardiovascular risks) was too fast in the intensive-treatment arm!

SPRINT Trial

Systolic blood pressure in the two treatment arms



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

N. Engl. J. Med., 2015; 373: 2103-2116

SPRINT Trial

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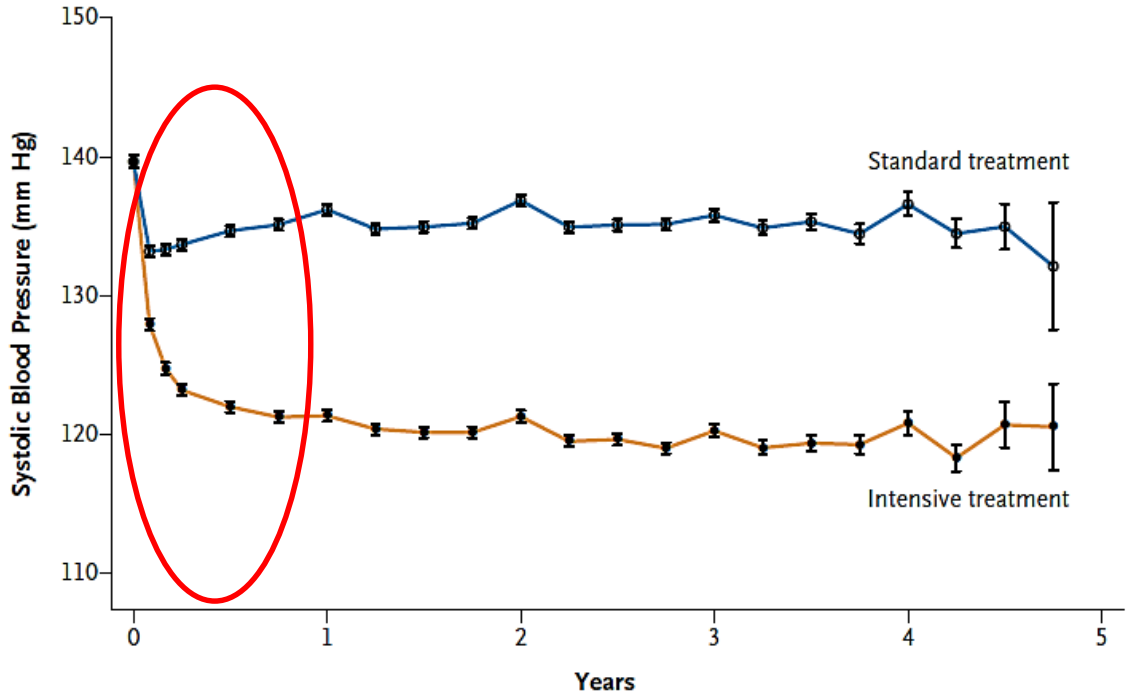

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SPECIAL ARTICLE www.jasn.org

Managing Hypertension in Patients with CKD: A Marathon, Not a SPRINT

Glenn M. Chertow,* Srinivasan Beddhu,† Julia B. Lewis,‡ Robert D. Toto,§ and Alfred K. Cheung†

*Division of Nephrology, Department of Medicine, Stanford University, Stanford, California; †Division of Nephrology, Internal Medicine School of Medicine, University of Utah, Salt Lake City, Utah; ‡Division of Nephrology and Hypertension, Department of Medicine, Vanderbilt University, Nashville, Tennessee; and §Department of Clinical Science, University of Texas Southwestern, Dallas, Texas

ABSTRACT

In this manuscript, nephrologist-investigators from one of five Clinical Center Networks of the Systolic Blood Pressure Intervention Trial (SPRINT) provide background information and context on the intensity of anti-hypertensive therapy in conjunction with the release of detailed results from SPRINT's primary analysis. The authors highlight published evidence on the safety and efficacy of differing intensities of anti-hypertensive therapy in mild to moderate CKD, where SPRINT will help to inform practice, as well as where gaps in evidence will remain. The authors also challenge the nephrology community to renew its attention and efforts on hypertension clinical care and research.

J Am Soc Nephrol 27: 40–43, 2016. doi: 10.1681/ASN.2015101125

were incorrectly relied on to change clinical practice include the provision of antiarrhythmic agents for the treatment of premature ventricular beats after myocardial infarction (a strategy countered by results from the Cardiac Arrhythmia Suppression Trial),[2] the provision of estrogen replacement therapy in postmenopausal women to reduce cardiovascular risk (countered by results from the Heart and Estrogen/Progestin Replacement

J. Am. Soc. Nephrol., 2016, 27, 40-43

SPECIAL ARTICLE www.jasn.org

Managing Hypertension in Patients with CKD: A Marathon, Not a SPRINT

Glenn M. Ch
Alfred K. Ch

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ABSTRACT

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J Am Soc Nephro

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ALERT: SPRINT IS NOT A TYPICAL CKD TRIAL

Clinical trials in nephrology have been few and far between, and we should celebrate SPRINT's success. However, we should recognize what SPRINT is and what it is not. SPRINT is a cardiovascular trial in which a sizeable fraction of patients with mild to moderate CKD was included. SPRINT is not a typical CKD trial. SPRINT is not a trial of CKD progression. SPRINT is a trial comparing the effects of standard versus more intensive antihypertensive therapy in persons with preexisting cardiovascular disease or at high risk for cardiovascular disease, including the elderly and persons with mild to moderate CKD, the

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J. Am. Soc. Nephrol., 2016, 27, 40-43

CLINICAL RESEARCH www.jasn.org

Acute Declines in Renal Function during Intensive BP Lowering: Implications for Future ESRD Risk

Elaine Ku,*† George Bakris,‡ Kirsten L. Johansen,* Feng Lin,§ Mark J. Sarnak,‖ Vito M. Campese,¶ Kenneth Jamerson,** Jennifer J. Gassman,†† Miroslaw Smogorzewski,¶ and Chi-yuan Hsu*

*Division of Nephrology, Department of M*J Am Soc Nephrol* 28: 2794–2801, 2017.cNephrology, Department of Pediatrics, and §Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, California; ‡Department of Medicine, University of Chicago, Chicago, Illinois; ‖Division of Nephrology, Department of Medicine, Tufts University, Boston, Massachusetts; ¶Division of Nephrology, Department of Medicine, University of Southern California, Los Angeles, California; **Division of Cardiovascular Medicine, Department of Medicine, University of Michigan, Ann Arbor, Michigan; and ††Department of Quantitative Health Sciences, Cleveland Clinic, Cleveland, Ohio

J. Am. Soc. Nephrol., 2017, 28, 2794-2801

Association between percentage decline in renal function in the AASK and MDRD studies from time of randomization until month 3 and risk of ESRD

Table 2. Association between percentage decline in renal function in the AASK participants (*n*=899) from time of randomization until month 3 and risk of ESRD

Renal Function Decline, %	Strict BP Arm				Usual BP Arm			
	N	ESRD Incidence[a] (95% CI)	Unadjusted HR (95% CI)	Adjusted HR[b] (95% CI)	*N*	ESRD Incidence[a] (95% CI)	Unadjusted HR (95% CI)	Adjusted HR[b] (95% CI)
AASK	448				451			
<5	271	2.9 (2.4 to 3.6)	1.00 (0.75 to 1.34)	0.94 (0.70 to 1.25)	319	2.9 (2.4 to 3.5)	1.0 (Reference)	1.0 (Reference)
5 to <20	139	3.6 (2.7 to 4.7)	1.26[c] (0.90 to 1.76)	1.19[c] (0.84 to 1.68)	98	6.3 (4.8 to 8.1)	2.22[c] (1.60 to 3.09)	1.83[c] (1.30 to 2.57)
≥20	38	9.8 (6.7 to 14.4)	3.58 (2.32 to 5.52)	3.04 (1.95 to 4.77)	34	10.4 (6.9 to 15.7)	3.83 (2.43 to 6.04)	2.56 (1.60 to 4.11)
MDRD	388				373			
<5	190	7.1 (6.0 to 8.5)	0.93 (0.73 to 1.19)	0.88 (0.68 to 1.13)	182	7.6 (6.4 to 9.0)	1.0 (Reference)	1.0 (Reference)
5 to <20	150	9.7 (8.1 to 11.7)	1.28[c] (0.99 to 1.64)	1.08[c] (0.84 to 1.40)	136	12.6 (10.5 to 15.1)	1.66[c] (1.29 to 2.13)	1.62[c] (1.25 to 2.11)
≥20	48	15.5 (11.5 to 20.9)	2.03 (1.44 to 2.87)	1.57 (1.09 to 2.24)	55	17.3 (13.0 to 23.7)	2.39 (1.71 to 3.35)	1.48 (1.04 to 2.1)

Ku e. et al.,J. Am. Soc. Nephrol., 2017, 28, 2794-2801

CLINICAL RESEARCH www.jasn.org

Acute Declines in Renal Function during Intensive BP Lowering: Implications for Future ESRD Risk

Elaine Ku,*† George Bakris,‡ Kirsten L. Johansen,* Feng Lin,§ Mark J. Sarnak,‖ Vito M. Campese,¶ Kenneth Jamerson,** Jennifer J. Gassman,†† Miroslaw Smogorzewski,¶ and Chi-yuan Hsu*

*Division of Nephrology, Department of M*J Am Soc Nephrol* 28: 2794–2801, 2017.Nephrology, Department of Pediatrics, and §Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, California; ‡Department of Medicine, University of Chicago, Chicago, Illinois; ‖Division of Nephrology, Department of Medicine, Tufts University, Boston, Massachusetts; ¶Division of Nephrology, Department of Medicine, University of Southern California, Los Angeles, California; **Division of Cardiovascular Medicine, Department of Medicine, University of Michigan, Ann Arbor, Michigan; and ††Department of Quantitative Health Sciences, Cleveland Clinic, Cleveland, Ohio

Conclusion:

However, a 5% to <20% eGFR decline in the usual BP arm associated with higher risk of ESRD in AASK (aHR, 1.83; 95% CI, 1.30 to 2.57) and MDRD Trial (aHR, 1.62; 95% CI, 1.25 to 2.11). A ≥20% eGFR decline associated with higher risk of ESRD in both strict and usual BP arms. Thus, acute eGFR declines ≥20% during intensive BP lowering identified a subset of patients at higher risk for adverse outcomes.

Ku e. et al.,J. Am. Soc. Nephrol., 2017, 28, 2794-2801

AJKD

Original Investigation

Blood Pressure Before Initiation of Maintenance Dialysis and Subsequent Mortality

Keiichi Sumida, MD,[1,2,3] Miklos Z. Molnar, MD, PhD,[1,4] Praveen K. Potukuchi, MS,[1] Fridtjof Thomas, PhD,[5] Jun Ling Lu, MD,[1] Vanessa A. Ravel, MPH,[6] Melissa Soohoo, MPH,[6] Connie M. Rhee, MD, MSc,[6] Elani Streja, MPH, PhD,[6] John J. Sim, MD,[7] Kunihiro Yamagata, MD, PhD,[3] Kamyar Kalantar-Zadeh, MD, MPH, PhD,[6] and Csaba P. Kovesdy, MD[1,8]

Background: Mortality is extremely high immediately after the transition to dialysis therapy, but the association of blood pressure (BP) before dialysis therapy initiation with mortality after dialysis therapy initiation remains unknown.

Study Design: Observational study.

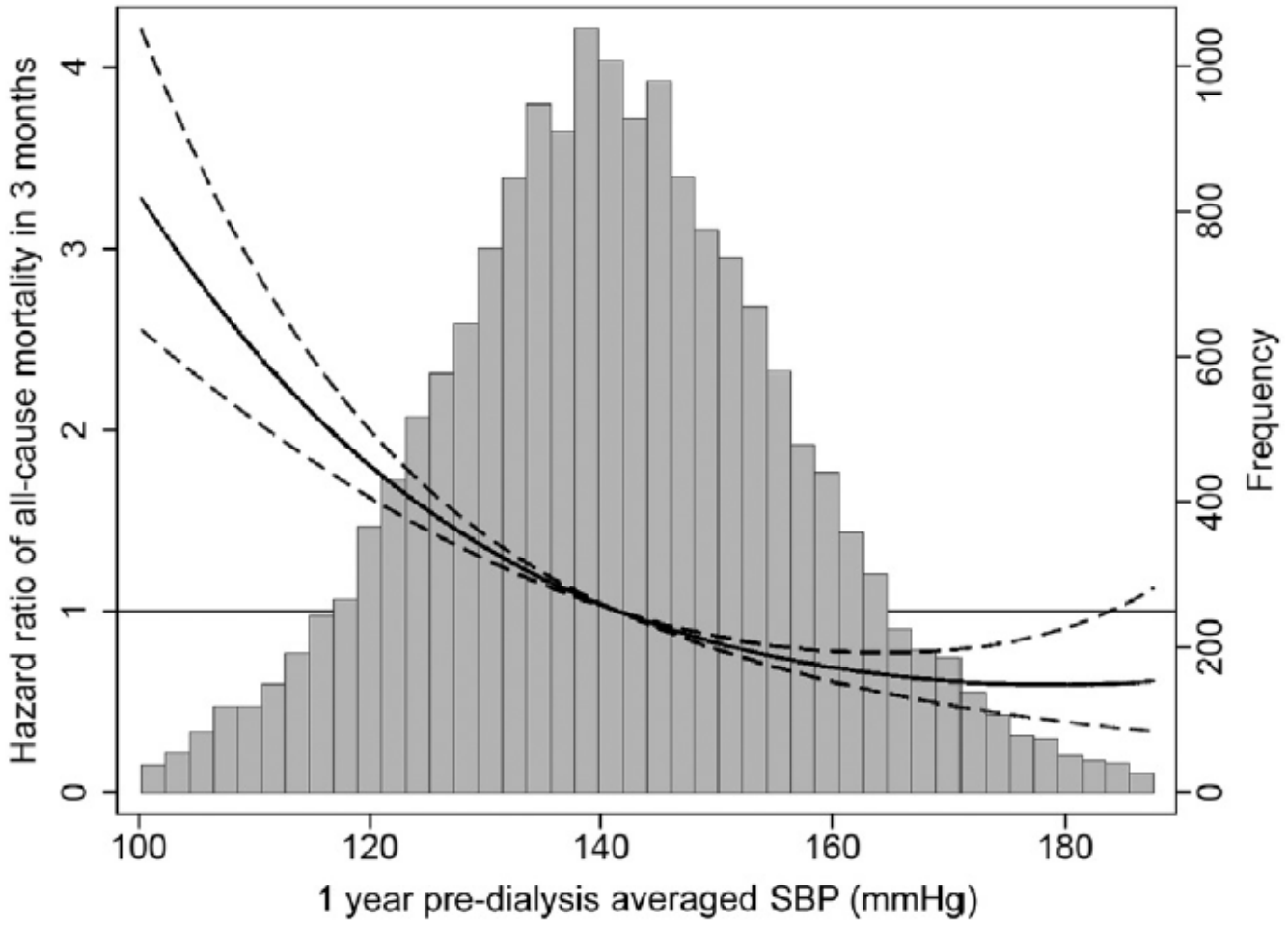
Setting & Participants: 17,729 US veterans transitioning to dialysis therapy in October 2007 to September 2011, with a median follow-up of 2.0 years.

Predictor: Systolic (SBP) and diastolic BP (DBP) averaged over the last 1-year predialysis transition period as 6 (<120 to ≥160 mm Hg in 10−mm Hg increments) and 5 (<60 to ≥90 mm Hg in 10−mm Hg increments) categories, respectively, and as continuous measures.

Outcomes & Measurements: Postdialysis all-cause mortality, assessed over different follow-up periods (ie, <3, 3-<6, 6-<12, and ≥12 months after dialysis therapy initiation) using Cox regressions adjusted for demographics, comorbid conditions, medications, cardiovascular medication adherence, body mass index, estimated glomerular filtration rate, and type of vascular access.

Am. J. Kidney Dis. 2017, 70, 207-217

Association of predialysis systolic blood pressure (SBP) with all-cause mortality in the first 3 months after dialysis initiation



Sumida K. et al., Am. J. Kidney Dis. 2017, 70, 207-217

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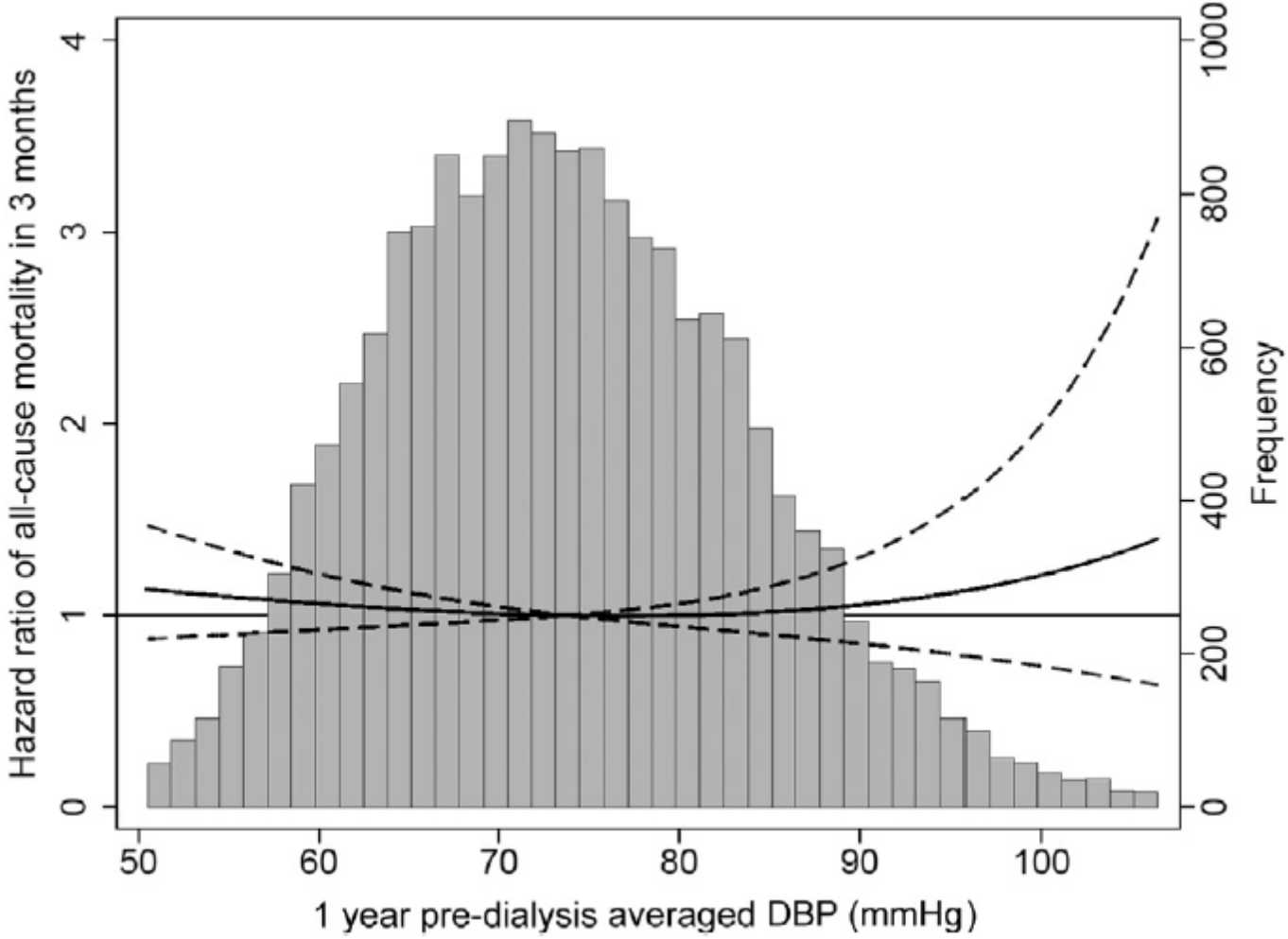


Sumida K. et al., Am. J. Kidney Dis. 2017, 70, 207-217

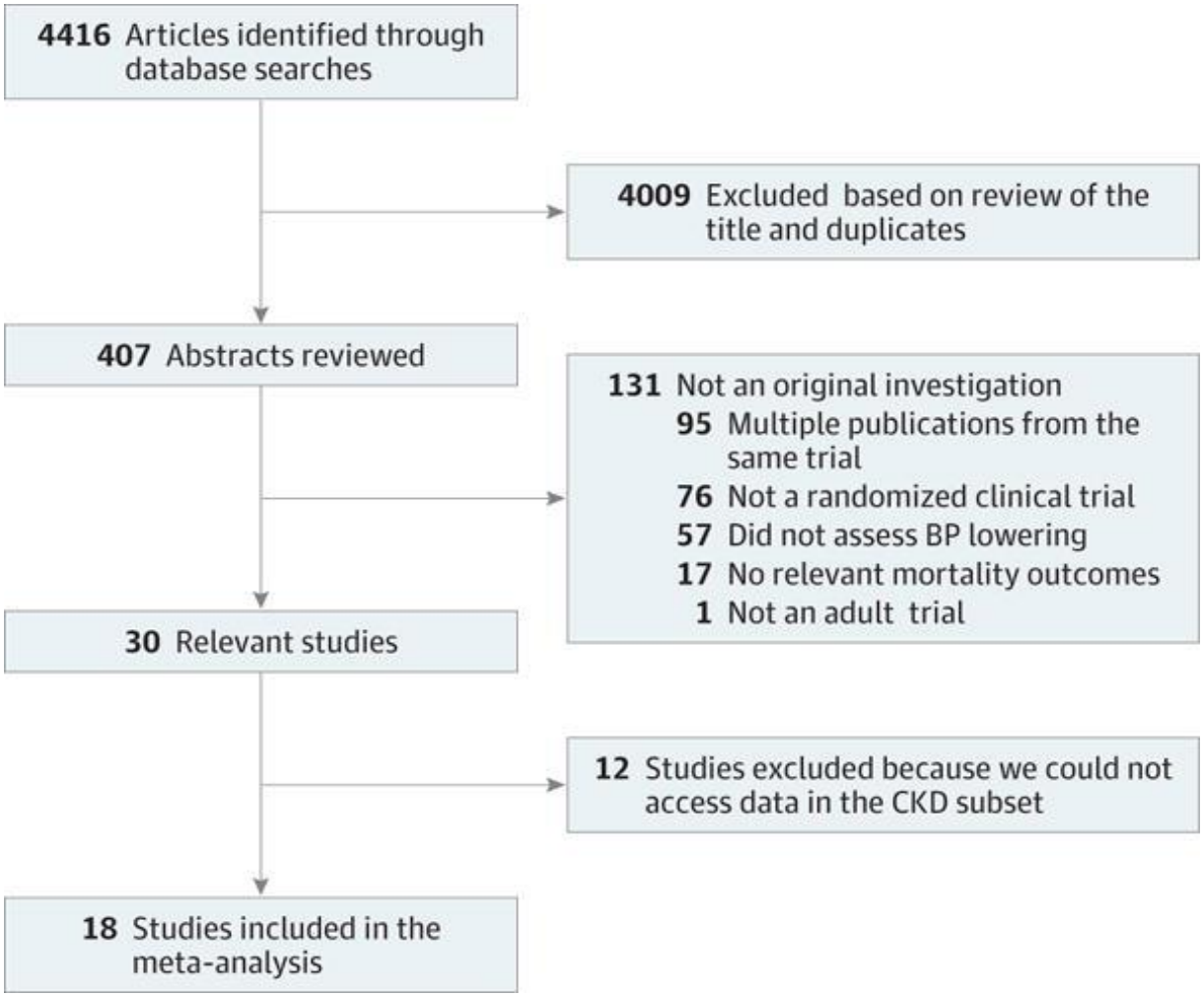
Standard vs. lower target BP in CKD patients (meta-analysis)

Meta-analysis

- All randomized controlled trials until June 2016
- **Comparison of 2 defined blood pressure targets:**
  - **active blood pressure treatment** vs. placebo or no treatment
  - **intensive** vs. less intensive BP control
- Only patients with **CKD stage 3–5 (eGFR < 60 ml/min/1.73m²)** without renal replacement therapy
- Primary outcome: **mortality**
- 18 studies, 15,924 patients, **1,293 deaths**

Malhotra R. et al. JAMA Int. Med., 2017, 177, 1498 - 1505

Standard vs. lower target BP in CKD patients (meta-analysis)

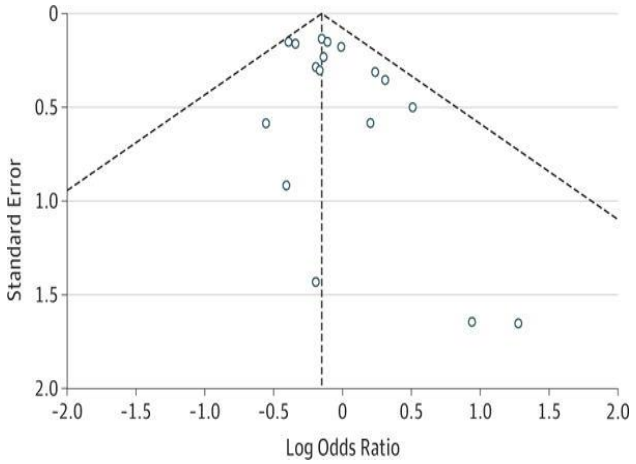


Malhotra R. et al. JAMA Int. Med., 2017, 177, 1498 - 1505

Standard vs. lower target BP in CKD patients (meta-analysis)

Results

- Systolic blood pressure initially **148 mmHg**
- Systolic BP reduction **–8 mmHg** (standard) vs. **–16 mmHg** (lower)
- **Mortality in the "intensively" treated group 14% lower**
- **Without significant heterogeneity across studies**



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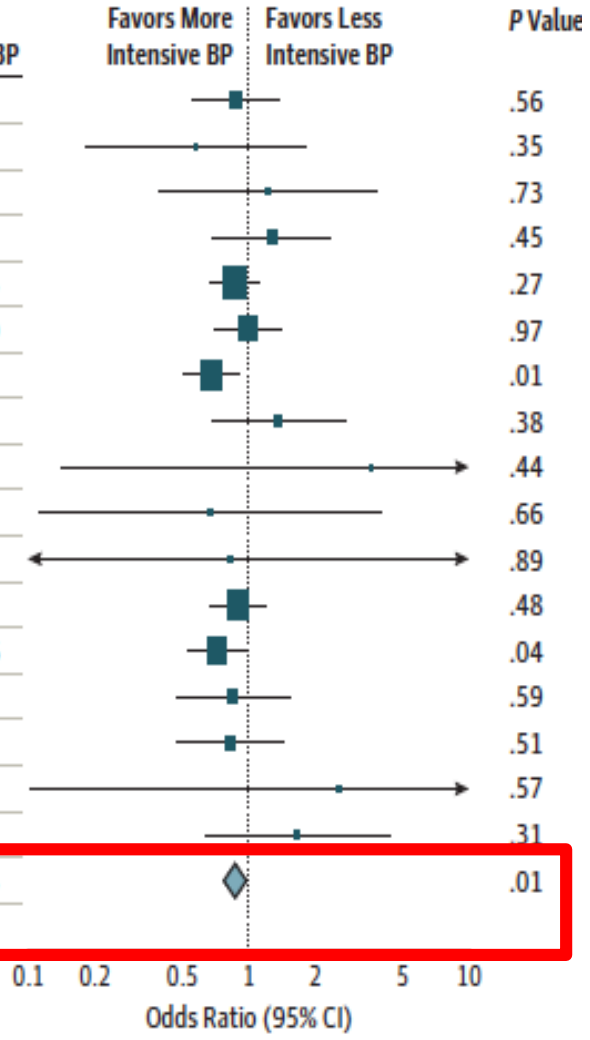
Standard vs. lower target BP in CKD patients (meta-analysis)

Source	Odds Ratio (95% CI)	Score	No. of Deaths/Total No. More Intensive BP	No. of Deaths/Total No. Less Intensive BP	P Value
Wright et al,[14] 2002	0.874 (0.554-1.380)	-0.578	37/540	43/554	.56
Estacio et al,[24] 2000	0.575 (0.182-1.820)	-0.941	5/62	9/68	.35
Schrier et al,[26] 2002	1.227 (0.398-3.865)	0.349	6/57	7/80	.73
Cushman et al,[32] 2010	1.271 (0.685-2.360)	0.761	26/208	20/198	.45
Heerspink et al,[27] 2010	0.862 (0.662-1.123)	-1.102	117/1010	135/1023	.27
Lonn et al,[37] 2016	0.993 (0.699-1.410)	-0.039	49/1220	97/2399	.97
Beckett et al,[30] 2008	0.676 (0.502-0.911)	-2.570	83/788	121/816	.01
Klahr et al,[13] 1994	1.366 (0.681-2.742)	0.878	20/432	14/408	.38
Mant et al,[34] 2016	3.588 (0.140-91.945)	0.772	1/26	0/30	.44
Ruggenenti et al,[22] 2005	0.667 (0.110-4.042)	-0.441	2/167	3/168	.66
Schrier et al,[25] 2002	0.825 (0.050-13.701)	-0.134	1/41	1/34	.89
SHEP Cooperative Research Group,[28] 1991	0.900 (0.670-1.209)	-0.700	96/879	103/859	.48
Wright et al,[17] 2015	0.714 (0.519-0.982)	-2.072	70/1330	95/1316	.04
Benavente et al,[33] 2013	0.850 (0.468-1.544)	-0.534	24/216	25/195	.59
Staessen et al,[29] 1997	0.826 (0.470-1.451)	-0.665	26/242	29/228	.51
Toto et al,[23] 1995	2.566 (0.101-64.993)	0.572	1/42	0/35	.57
UK Prospective Diabetes Study Group,[35] 1998	1.667 (0.626-4.435)	1.023	20/68	7/35	.31
Overall	0.859 (0.764-0.965)	-2.560	584/7451	709/8473	.01
Heterogeneity: $\tau^2 = 0\%$; $P = .77$; $I^2 = 0\%$					



Malhotra et al. JAMA Int Med 2017

Standard vs. lower target BP in CKD patients (meta-analysis)

Summary

- Intensive (systolic) blood pressure control improves CV outcome and mortality in CKD patients
- Progression of CKD is not retarded, with more serious adverse events, particularly hypotension, AKI and worsening of kidney function

Malhotra R. et al. JAMA Int. Med., 2017, 177, 1498 - 1505

Invited Commentary

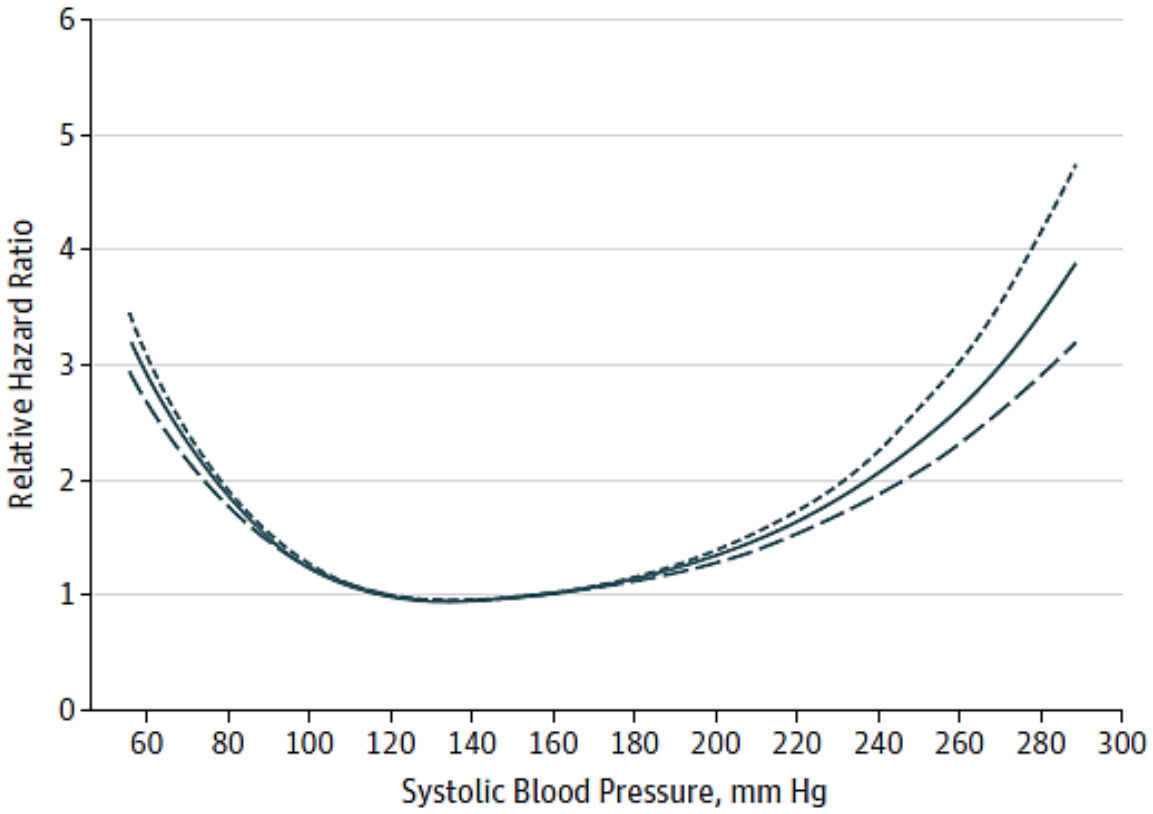
The Ideal Blood Pressure Target for Patients With Chronic Kidney Disease—Searching for the Sweet Spot

Csaba P. Kovesdy, MD

JAMA Internal Medicie, 2017, 177, 1506 - 1507

651.749 US Veterans with estimated GFR lower than 60 ml/min/1.73 m2

Figure. Mortality Hazard Ratios Associated With Various Baseline Systolic Blood Pressures



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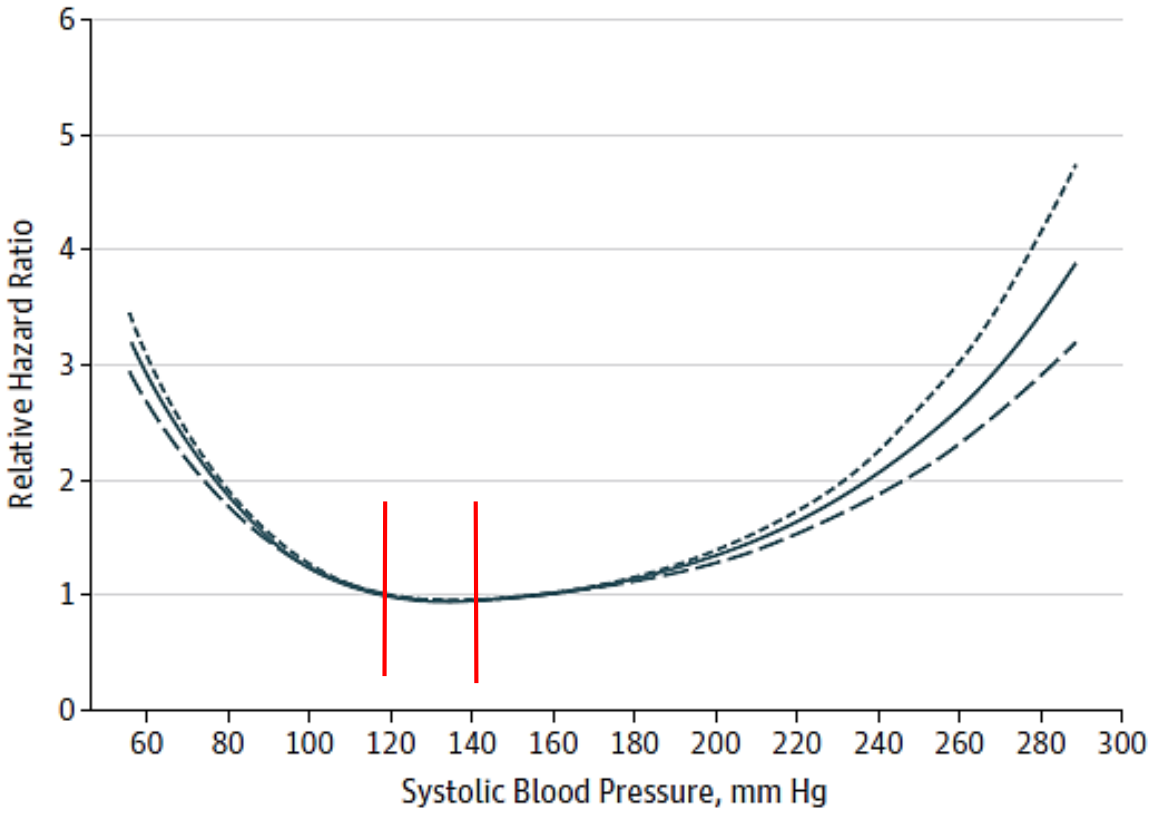

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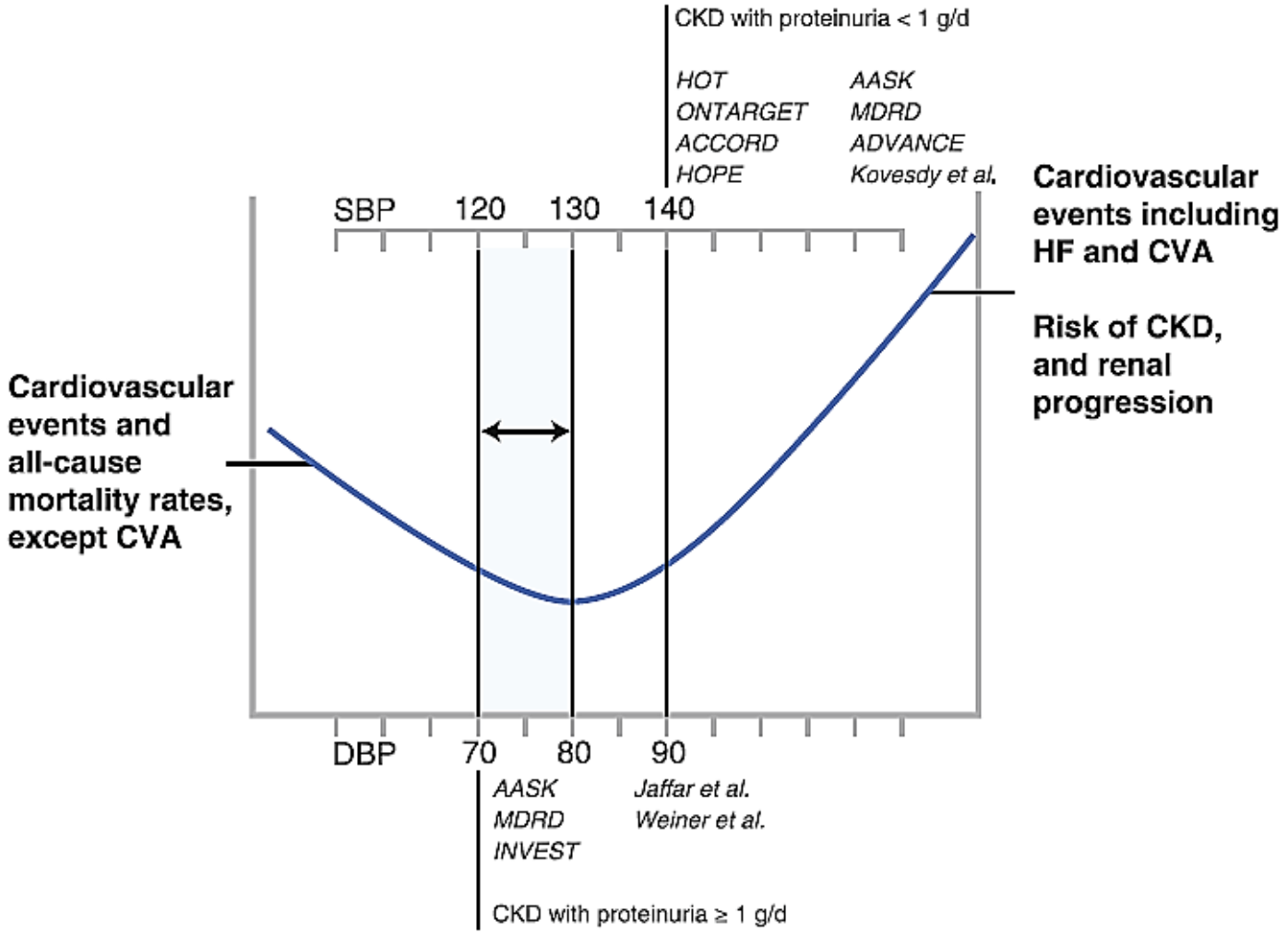
Cardiovascular and renal outcomes according to achieved blood pressure from clinical trials



Khouri Y. et al., Curr. Cardiol. Rep., 2011, 13, 492–501

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

Cost-Effectiveness of Intensive versus Standard Blood-Pressure Control

A.P. Bress, B.K. Bellows, J.B. King, R. Hess, S. Beddhu, Z. Zhang, D.R. Berlowitz, M.B. Conroy, L. Fine, S. Oparil, D.E. Morisky, L.E. Kazis, N. Ruiz-Negrón, J. Powell, L. Tamariz, J. Whittle, J.T. Wright, Jr., M.A. Supiano, A.K. Cheung, W.S. Weintraub, and A.E. Moran, for the SPRINT Research Group*

ABSTRACT

BACKGROUND

In the Systolic Blood Pressure Intervention Trial (SPRINT), adults at high risk for cardiovascular disease who received intensive systolic blood-pressure control (target, <120 mm Hg) had significantly lower rates of death and cardiovascular disease events than did those who received standard control (target, <140 mm Hg). On the basis of these data, we wanted to determine the lifetime health benefits and health care costs associated with intensive control versus standard control.

N. Engl. J. Med. 2017, 377, 745-755

The NEW ENGLAND JOURNAL of MEDICINE

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ABSTRACT

CONCLUSIONS

In this simulation study, intensive systolic blood-pressure control prevented cardiovascular disease events and prolonged life and did so at levels below common willingness-to-pay thresholds per QALY, regardless of whether benefits were reduced after 5 years or persisted for the patient's remaining lifetime. (Funded by the National Heart, Lung, and Blood Institute and others; SPRINT ClinicalTrials.gov number, NCT01206062.)

N. Engl. J. Med. 2017, 377, 745-755

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA 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 Task Force on Clinical Practice Guidelines

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Whelton P. K. et al., J. Am. Coll. Cardiol., 2018, 71: 2199-2269

ACC/AHA 2017 Guidelines

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CLINICAL GUIDELINES | 23 JANUARY 2018

Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Synopsis of the 2017 American College of Cardiology/American Heart Association Hypertension Guideline

FREE

Robert M. Carey, MD; Paul K. Whelton, MB, MD, MSc; for the 2017 ACC/AHA Hypertension Guideline Writing Committee (*)

Carey R.M., Whelton P.K. , Ann. Intern. Med. 2018, 168, 351-358

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VOL. 71, NO. 19, 2018

CLINICAL PRACTICE GUIDELINE

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Writing Committee Members

Paul K. Whelton, MB, MD, MSc, FAHA, *Chair*
Robert M. Carey, MD, FAHA, *Vice Chair*

Wilbert S. Aronow, MD, FACC, FAHA*
Donald E. Casey, Jr, MD, MPH, MBA, FAHA†
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Cheryl Dennison Himmelfarb, RN, ANP, PhD, FAHA§
Sondra M. DePalma, MHS, PA-C, CLS, AACC‖
Samuel Gidding, MD, FAHA¶
Kenneth A. Jamerson, MD#
Daniel W. Jones, MD, FAHA†
Eric J. MacLaughlin, PharmD**
Paul Muntner, PhD, FAHA†
Bruce Ovbiagele, MD, MSc, MAS, MBA, FAHA†
Sidney C. Smith, Jr, MD, MACC, FAHA††
Crystal C. Spencer, JD‡
Randall S. Stafford, MD, PhD‡‡
Sandra J. Taler, MD, FAHA§§
Randal J. Thomas, MD, MS, FACC, FAHA‖‖
Kim A. Williams, Sr, MD, MACC, FAHA†
Jeff D. Williamson, MD, MHS¶¶
Jackson T. Wright, Jr, MD, PhD, FAHA##

*American Society for Preventive Cardiology Representative. †ACC/AHA Representative. ‡Lay Volunteer/Patient Representative. §Preventive Cardiovascular Nurses Association Representative. ‖American Academy of Physician Assistants Representative. ¶Task Force Liaison. #Association of Black Cardiologists Representative. **American Pharmacists Association Representative. ††ACC/AHA Prevention Subcommittee Liaison. ‡‡American College of Preventive Medicine Representative. §§American Society of Hypertension Representative. ‖‖Task Force on Performance Measures Liaison. ¶¶American Geriatrics Society Representative. ##National Medical Association Representative.

Whelton P. K. et al., J. Am. Coll. Cardiol., 2018, 71: 2199-2269

New classification of blood pressure ACC/AHA, 2017

Table 1. Classification of BP*

Category	BP
Normal	<120/80 mm Hg
Elevated	120–129/<80 mm Hg
Stage 1 hypertension	130–139/80–89 mm Hg
Stage 2 hypertension	≥140/90 mm Hg

BP = blood pressure.
* Based on accurate measurements and average of ≥2 readings on ≥2 occasions.

Carey R.M., Whelton P.K. , Ann. Intern. Med. 2018, 168, 351-358

Recommendations for treatment of hypertension in patients with CKD according to the 2017 ACC/AHA Guidelines

9.3. Chronic Kidney Disease

Recommendations for Treatment of Hypertension in Patients With CKD

References that support recommendations are summarized in Online Data Supplements 37 and 38 and Systematic Review Report.

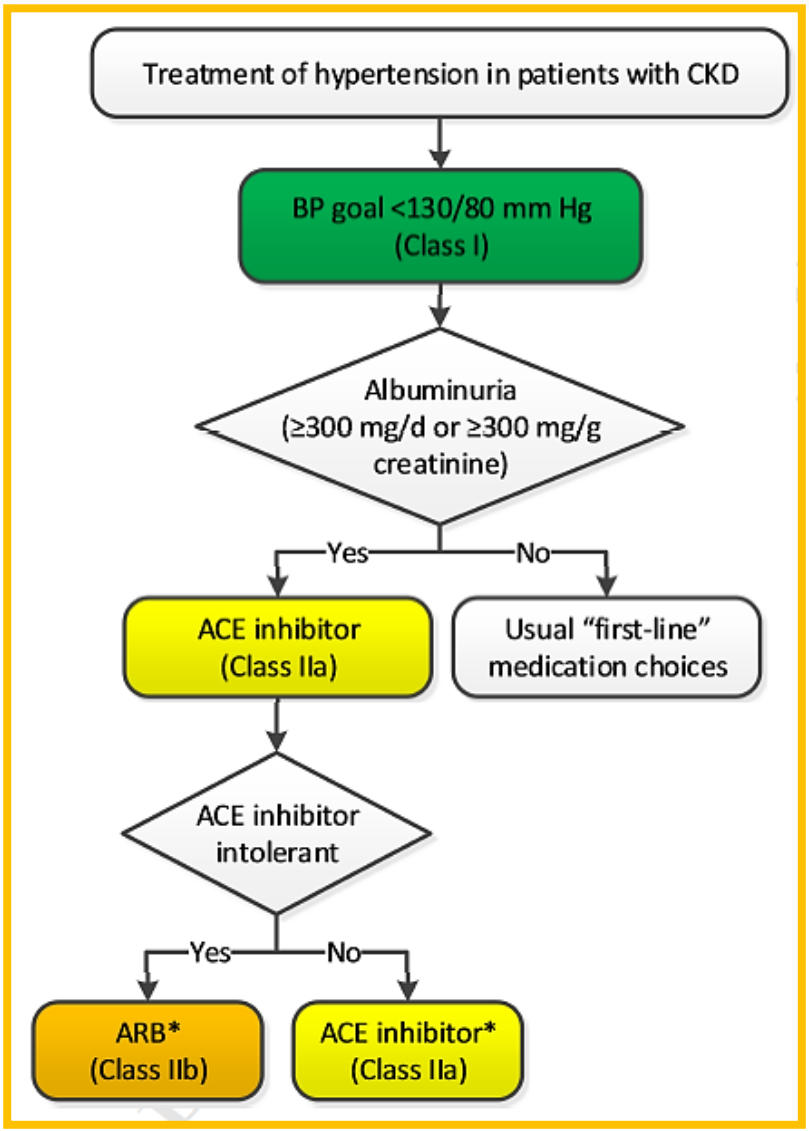
COR	LOE	Recommendations
I	SBP: B-R[SR] DBP: C-EO	1. Adults with hypertension and CKD should be treated to a BP goal of less than 130/80 mm Hg (1-6).
IIa	B-R	2. In adults with hypertension and CKD (stage 3 or higher or stage 1 or 2 with albuminuria [≥300 mg/d, or ≥300 mg/g albumin-to-creatinine ratio or the equivalent in the first morning void]), treatment with an ACE inhibitor is reasonable to slow kidney disease progression (3, 7-12).
IIb	C-EO	3. In adults with hypertension and CKD (stage 3 or higher or stage 1 or 2 with albuminuria [≥300 mg/d, or ≥300 mg/g albumin-to-creatinine ratio in the first morning void]) (7, 8), treatment with an ARB may be reasonable if an ACE inhibitor is not tolerated.

SR indicates systematic review.

COR = Class of Recommendation
LOE = Level of Evidence

Whelton P. K. et al., J. Am. Coll. Cardiol., 2018, 71: 2199-2269

Recommendations for treatment of hypertension in patients with CKD according to the 2017 ACC/AHA Guidelines



Whelton P. K. et al., J. Am. Coll. Cardiol., 2018, 71: 2199-2269

Recommendations for treatment of hypertension in patients after kidney transplantation according to the 2017 ACC/AHA Guidelines

Recommendations for Treatment of Hypertension After Renal Transplantation

References that support recommendations are summarized in Online Data Supplements 39 and 40.

COR	LOE	Recommendations
IIa	SBP: B-NR DBP: C-EO	1. After kidney transplantation, it is reasonable to treat patients with hypertension to a BP goal of less than 130/80 mm Hg (1).
IIa	B-R	2. After kidney transplantation, it is reasonable to treat patients with hypertension with a calcium antagonist on the basis of improved GFR and kidney survival (2).

COR = Class of Recommendation
LOE = Level of Evidence

Whelton P. K. et al., J. Am. Coll. Cardiol., 2018, 71: 2199-2269

Recommendations for treatment of hypertension in patients with stabile ischemic heart disease (SIHD) according to the 2017 ACC/AHA Guidelines

Recommendations for Treatment of Hypertension in Patients With Stable Ischemic Heart Disease (SIHD)

References that support recommendations are summarized in Online Data Supplements 30-32.

COR	LOE	Recommendations
I	SBP: B-R DBP: C-EO	1. In adults with SIHD and hypertension, a BP target of less than 130/80 mm Hg is recommended (1-5).
I	SBP: B-R DBP: C-EO	2. Adults with SIHD and hypertension (BP ≥130/80 mm Hg) should be treated with medications (e.g., GDMT (6) beta blockers, ACE inhibitors, or ARBs) for compelling indications (e.g., previous MI, stable angina) as first-line therapy, with the addition of other drugs (e.g., dihydropyridine CCBs, thiazide diuretics, and/or mineralocorticoid receptor antagonists) as needed to further control hypertension (7-10).
I	B-NR	3. In adults with SIHD with angina and persistent uncontrolled hypertension, the addition of dihydropyridine CCBs to GDMT (6) beta blockers is recommended (8, 11, 12).
IIa	B-NR	4. In adults who have had a MI or acute coronary syndrome, it is reasonable to continue GDMT (6) beta blockers beyond 3 years as long-term therapy for hypertension (13, 14).

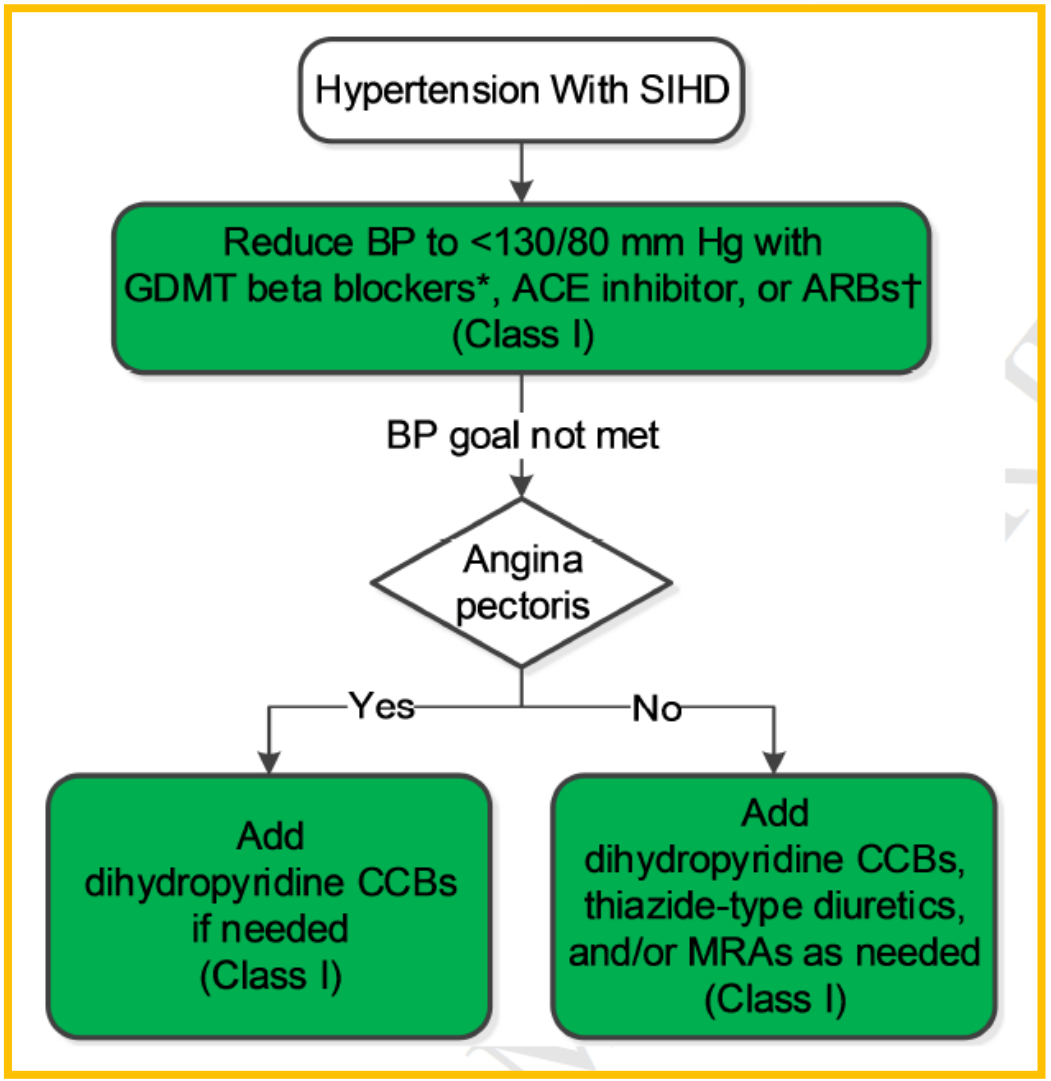
GDMT = Guideline-Directed Management and Therapy

COR = Class of Recommendation
LOE = Level of Evidence

Whelton P. K. et al., J. Am. Coll. Cardiol., 2018, 71: 2199-2269

Recommendations for treatment of hypertension in patients with stabile ischemic heart disease (SIHD) according to the 2017 ACC/AHA Guidelines

GDMT = Guideline-Directed Management and Therapy



Whelton P. K. et al., J. Am. Coll. Cardiol., 2018, 71: 2199-2269

Recommendations for treatment of hypertension in patients with heart failure (HF) according to the 2017 ACC/AHA Guidelines

Recommendation for Prevention of HF in Adults With Hypertension

References that support the recommendation are summarized in Online Data Supplement 33.

COR	LOE	Recommendation
I	SBP: B-R DBP: C-EO	1. In adults at increased risk of HF, the optimal BP in those with hypertension should be less than 130/80 mm Hg (1-3).

COR = Class of Recommendation
LOE = Level of Evidence

Whelton P. K. et al., J. Am. Coll. Cardiol., 2018, 71: 2199-2269

Recommendations for treatment of hypertension in patients with heart failure and reduced EF (HFrEF) according to the 2017 ACC/AHA Guidelines

Recommendations for Treatment of Hypertension in Patients With HF*r*EF

References that support recommendations are summarized in Online Data Supplement 34.

COR	LOE	Recommendation
I	C-EO	1. Adults with HF*r*EF and hypertension should be prescribed GDMT (2) titrated to attain a BP of less than 130/80 mm Hg.
III: No Benefit	B-R	2. Nondihydropyridine CCBs are not recommended in the treatment of hypertension in adults with HF*r*EF (1).

GDMT = Guideline-Directed Management and Therapy

COR = Class of Recommendation
LOE = Level of Evidence

Whelton P. K. et al., J. Am. Coll. Cardiol., 2018, 71: 2199-2269

Recommendations for treatment of hypertension in patients with heart failure and preserved EF (HFpEF) according to the 2017 ACC/AHA Guidelines

Recommendations for Treatment of Hypertension in Patients With HF*p*EF

References that support recommendations are summarized in Online Data Supplements 35 and 36.

COR	LOE	Recommendations
I	C-EO	1. In adults with HF*p*EF who present with symptoms of volume overload, diuretics should be prescribed to control hypertension.
I	C-LD	2. Adults with HF*p*EF and persistent hypertension after management of volume overload should be prescribed ACE inhibitors or ARBs and beta blockers titrated to attain SBP of less than 130 mm Hg (1-6).

COR = Class of Recommendation
LOE = Level of Evidence

Whelton P. K. et al., J. Am. Coll. Cardiol., 2018, 71: 2199-2269

Recommendations for treatment of hypertension in patients with diabetes mellitus according to the 2017 ACC/AHA Guidelines

Recommendations for Treatment of Hypertension in Patients With DM

References that support recommendations are summarized in Online Data Supplements 46 and 47 and Systematic Review Report.

COR	LOE	Recommendations
I	SBP: B-R[SR] DBP: C-EO	1. In adults with DM and hypertension, antihypertensive drug treatment should be initiated at a BP of 130/80 mm Hg or higher with a treatment goal of less than 130/80 mm Hg (1-8).
I	A[SR]	2. In adults with DM and hypertension, all first-line classes of antihypertensive agents (i.e., diuretics, ACE inhibitors, ARBs, and CCBs) are useful and effective (1, 9, 10).
IIb	B-NR	3. In adults with DM and hypertension, ACE inhibitors or ARBs may be considered in the presence of albuminuria (11, 12).

COR = Class of Recommendation
LOE = Level of Evidence

Whelton P. K. et al., J. Am. Coll. Cardiol., 2018, 71: 2199-2269

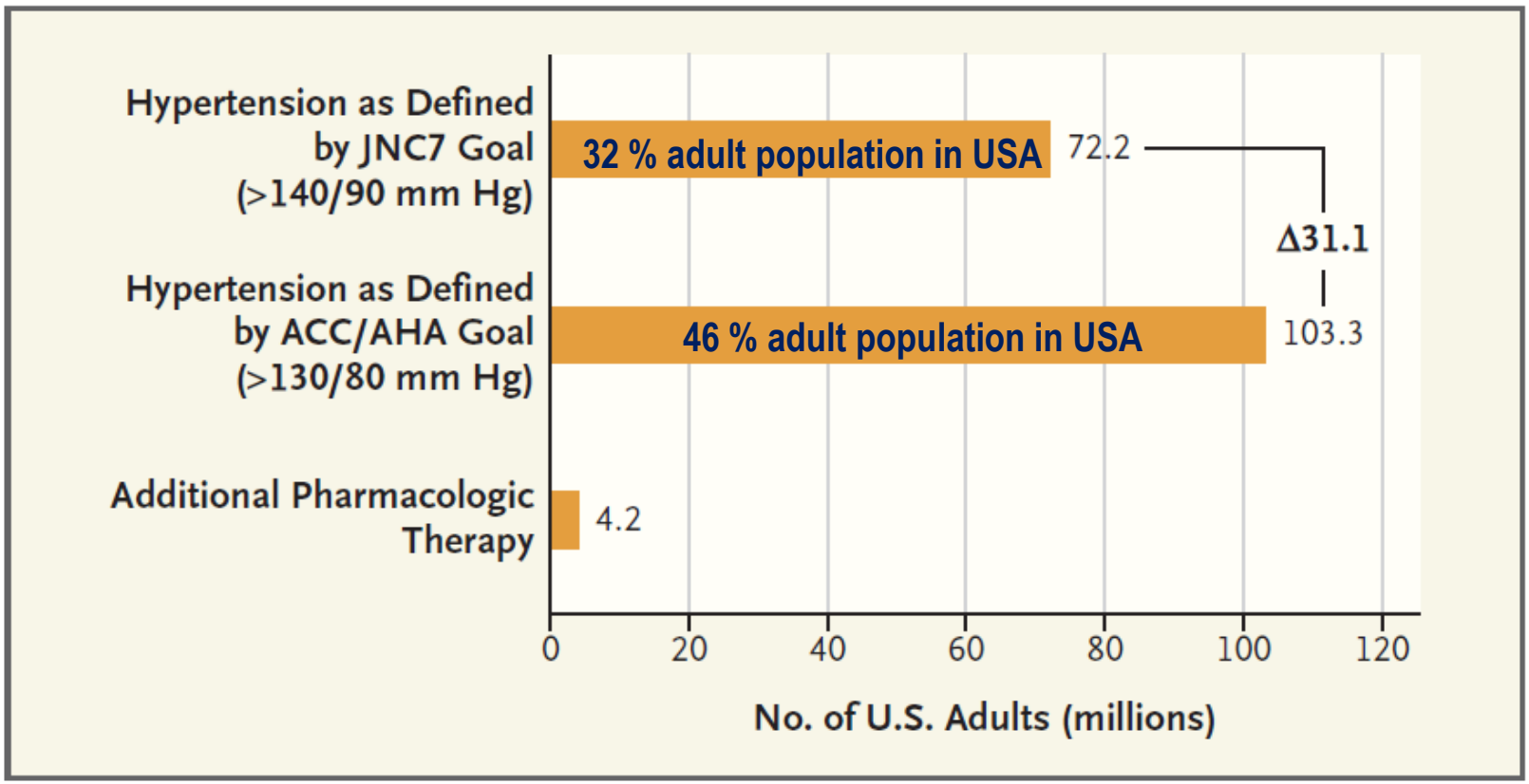
Recommendations for treatment of hypertension in older persons according to the 2017 ACC/AHA Guidelines

Recommendations for Treatment of Hypertension in Older Persons References that support recommendations are summarized in Online Data Supplement 54.		
COR	**LOE**	**Recommendations**
I	A	1. Treatment of hypertension with a SBP treatment goal of less than 130 mm Hg is recommended for noninstitutionalized ambulatory community-dwelling adults (≥65 years of age) with an average SBP of 130 mm Hg or higher (1).
IIa	C-EO	2. For older adults (≥65 years of age) with hypertension and a high burden of comorbidity and limited life expectancy, clinical judgment, patient preference, and a team-based approach to assess risk/benefit is reasonable for decisions regarding intensity of BP lowering and choice of antihypertensive drugs.

COR = Class of Recommendation
LOE = Level of Evidence

Whelton P. K. et al., J. Am. Coll. Cardiol., 2018, 71: 2199-2269

Adults with hypertension as defined by the JNC 7 (2003) and ACC/AHA (2017) Guidelines and effects on the use of pharmacologic therapy



U.S. Adults with Hypertension as Defined by the JNC7 and ACC/AHA Guidelines and Effect on Use of Pharmacologic Therapy.

Bakris G., Sorrentino M., N. Engl. J. Med. , 2018, 378, 497 - 499

Potential U.S. Population Impact of the 2017 ACC/AHA High Blood Pressure Guideline

Paul Muntner, PhD,[a] Robert M. Carey, MD,[b] Samuel Gidding, MD,[c] Daniel W. Jones, MD,[d] Sandra J. Taler, MD,[e] Jackson T. Wright, Jr, MD, PhD,[f] Paul K. Whelton, MB, MD, MSc[g]

ABSTRACT

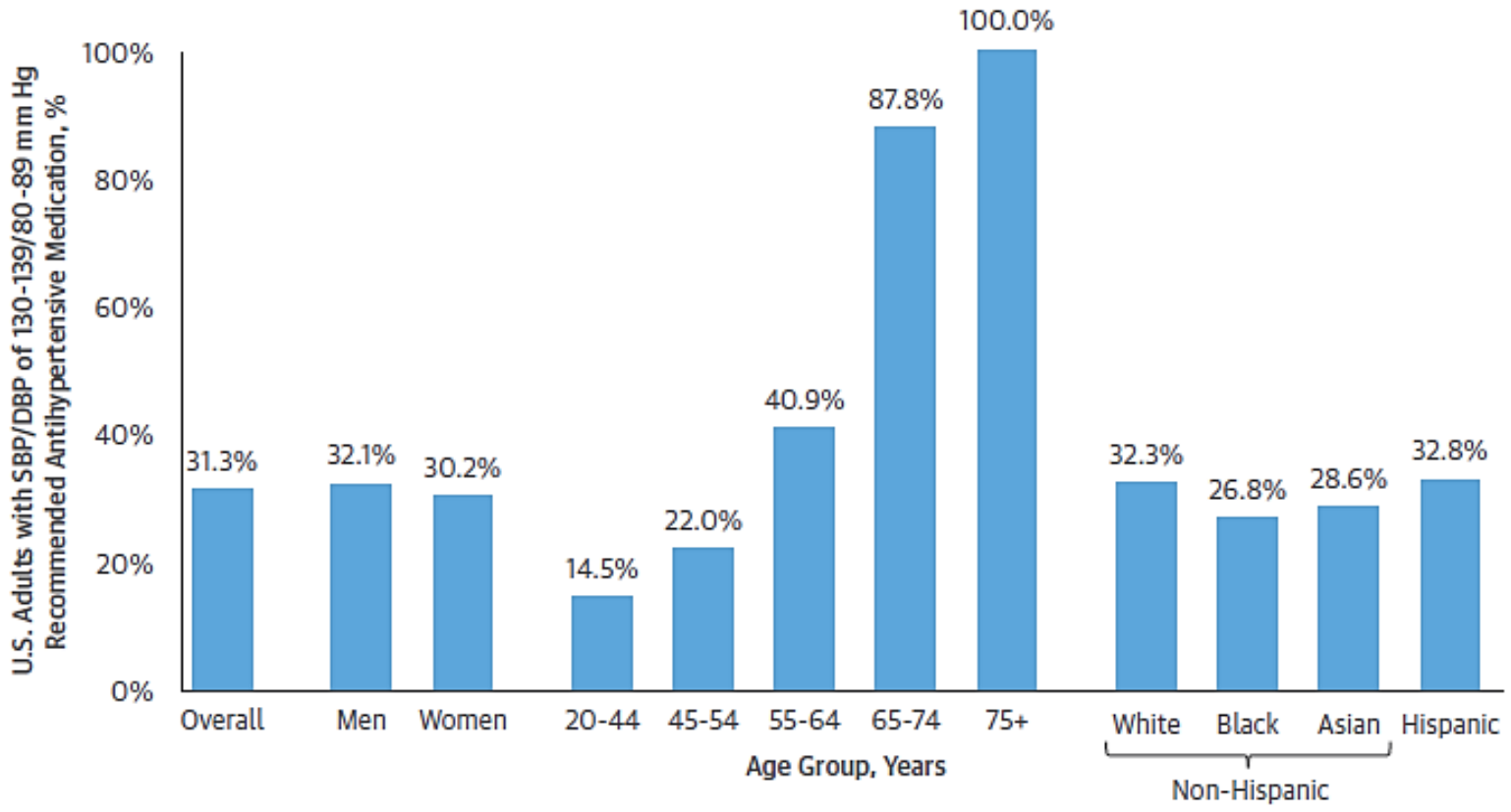
BACKGROUND The 2017 American College of Cardiology/American Heart Association (ACC/AHA) Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults provides recommendations for the definition of hypertension, systolic and diastolic blood pressure (BP) thresholds for initiation of antihypertensive medication, and BP target goals.

OBJECTIVES This study sought to determine the prevalence of hypertension, implications of recommendations for antihypertensive medication, and prevalence of BP above the treatment goal among U.S. adults using criteria from the 2017 ACC/AHA guideline and the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7).

Muntner P. i wsp. J. Am. Coll. Cardiol., 2018, 71, 109 - 118

Percentage of U.S. adults with SBP of 130-139 mmHg or DBP of 80-89 mmHg recommended for antihypertensive medication according to the 2017 ACC/AHA Guideline

FIGURE 1 Percentage of U.S. Adults With SBP of 130 to 139 mm Hg or DBP of 80 to 89 mm Hg Recommended for Antihypertensive Medication According to the 2017 ACC/AHA Guideline



Muntner P. i wsp. J. Am. Coll. Cardiol., 2018, 71, 109 - 118

European Society of Cardiology/European Society of Hypertension

Guidelines 2018

ESC European Society of Cardiology

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

ESC/ESH GUIDELINES

2018 ESC/ESH Guidelines for the management of arterial hypertension

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

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

European Heart Journal, 2018, 00, 1–98, published on-line August 25th

European Society of Cardiology/European Society of Hypertension Guidelines 2018

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

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

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

Williams B. et al., European Heart Journal, 2018, 00, 1–98, published on-line August 25th

European Society of Cardiology/European Society of Hypertension
Guidelines 2018

3.2 Classification of blood pressure

Classification of BP

Recommendation	Class[a]	Level[b]
It is recommended that BP be classified as optimal, normal, high–normal, or grades 1–3 hypertension, according to office BP.	I	C

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BP = blood pressure.
[a]Class of recommendation
[b]Level of evidence.

Williams B. et al.,
European Heart Journal,
2018, 00, 1–98
(published on-line August 25th)

Table 2 ESC Levels of evidence

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

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Table 1 ESC Classes of recommendations

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy.*	Should be considered
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

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Table 9 Definitions of hypertension according to office, ambulatory, and home blood pressure levels

Category	SBP (mmHg)		DBP (mmHg)
Office BP[a]	≥140	and/or	≥90
Ambulatory BP			
Daytime (or awake) mean	≥135	and/or	≥85
Night-time (or asleep) mean	≥120	and/or	≥70
24 h mean	≥130	and/or	≥80
Home BP mean	≥135	and/or	≥85

BP = blood pressure; DBP = diastolic blood pressure; SBP = systolic blood pressure.

[a]Refers to conventional office BP rather than unattended office BP.

Williams B. et al., European Heart Journal, 2018, 00, 1 – 98, publisehd on-line August 25th

European Society of Cardiology/European Society of Hypertension Guidelines 2018

Table 19 Summary of office blood pressure thresholds for treatment

Age group	Office SBP treatment threshold (mmHg)					Office DBP treatment threshold (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke/TIA	
18 - 65 years	≥140	≥140	≥140	≥140[a]	≥140[a]	≥90
65 - 79 years	≥140	≥140	≥140	≥140[a]	≥140[a]	≥90
≥80 years	≥160	≥160	≥160	≥160	≥160	≥90
Office DBP treatment threshold (mmHg)	≥90	≥90	≥90	≥90	≥90	

©ESC/ESH 2018

BP = blood pressure; CAD = coronary artery disease; CKD = chronic kidney disease; DBP = diastolic blood pressure; SBP = systolic blood pressure; TIA = transient ischaemic attack.

[a]Treatment may be considered in these very high-risk patients with high–normal SBP (i.e. SBP 130–140 mmHg).

Williams B. et al., European Heart Journal, 2018, 00, 1 – 98, publisehd on-line August 25th

European Society of Cardiology/European Society of Hypertension Guidelines 2018

Table 23 Office blood pressure treatment target range

Age group	Office SBP treatment target ranges (mmHg)					Office DBP treatment target range (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke[a]/TIA	
18 - 65 years	**Target to 130** *or lower if tolerated* Not <120	**Target to 130** *or lower if tolerated* Not <120	**Target to <140 to 130** *if tolerated*	**Target to 130** *or lower if tolerated* Not <120	**Target to 130** *or lower if tolerated* Not <120	70–79
65 - 79 years[b]	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	70–79
≥80 years[b]	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	70–79
Office DBP treatment target range (mmHg)	70–79	70–79	70–79	70–79	70–79	

CAD = coronary artery disease; CKD = chronic kidney disease (includes diabetic and non-diabetic CKD); DBP = diastolic blood pressure; SBP = systolic blood pressure; TIA = transient ischaemic attack.

[a]Refers to patients with previous stroke and does not refer to blood pressure targets immediately after acute stroke.

[b]Treatment decisions and blood pressure targets may need to be modified in older patients who are frail and independent.

Williams B. et al., European Heart Journal, 2018, 00, 1 – 98, publisehd on-line August 25th

Treatment of BP in CKD patients acc. to the ESC/ESH Guidelines

Therapeutic strategies for treatment of hypertension in CKD

Recommendations	Class[a]	Level[b]
In patients with diabetic or non-diabetic CKD, it is recommended that an office BP of ≥140/90 mmHg be treated with lifestyle advice and BP-lowering medication.[9,203,485]	I	A
In patients with diabetic or non-diabetic CKD: • It is recommended to lower SBP to a range of 130–139 mmHg.[9,487,489]	I	A
• Individualized treatment should be considered according to its tolerability and impact on renal function and electrolytes.	IIa	C
RAS blockers are more effective at reducing albuminuria than other antihypertensive agents, and are recommended as part of the treatment strategy in hypertensive patients in the presence of microalbuminuria or proteinuria.[487,489]	I	A
A combination of a RAS blocker with a CCB or a diuretic[c] is recommended as initial therapy.[175]	I	A
A combination of two RAS blockers is not recommended.[298]	III	A

Williams B. et al.,
European Heart Journal,
2018, 00, 1–98
(published on-line August 25th)

KDIGO guidelines before SPRINT

3.1: We recommend that non-diabetic adults with CKD ND and urine albumin excretion <30 mg per 24h whose office BP is consistently >140 mmHg systolic or >90 mmHg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently <140 mmHg systolic and <90 mmHg diastolic (1B)

3.2: We suggest that non-diabetic adults with CKD ND and urine albumin excretion 30–300 mg per 24h whose office BP is consistently >130 mmHg systolic or >80 mmHg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently <130 mmHg systolic and <80 mmHg diastolic (2D)

3.3: We suggest that non-diabetic adults with CKD ND and urine albumin excretion >300 mg per 24h whose office BP is consistently >130 mmHg systolic or <80 mmHg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently <130 mmHg systolic and <80 mmHg diastolic (2C)

Kidney Int., 2012, 2, suppl., 337-414

KDIGO guidelines before SPRINT

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3.3: We suggest that non-diabetic adults with CKD ND and urine albumin excretion >300 mg per 24h whose office BP is consistently >130 mmHg systolic or <80 mmHg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently <130 mmHg systolic and <80 mmHg diastolic (2C)

Kidney Int., 2012, 2, suppl., 337-414

Old and new classification of blood pressure

Blood Pressure Classification by JNC7 and 2017 ACC/AHA Hypertension Guidelines + ESC/ESH 2018 Guidelines

Systolic, Diastolic Blood Pressure (mm Hg)	JNC7	2017 ACC/AHA	ESC/ESH 2018 (acc SBP only)
<120 and <80	Normal BP	Normal BP	Optimal BP
120–129 and <80	Prehypertension	Elevated BP	Normal BP
130–139 or 80–89	Prehypertension	Stage 1 hypertension	High normal BP
140–159 or 90–99	Stage 1 hypertension	Stage 2 hypertension	Grade 1 Hypertension
≥ 160 or ≥100	Stage 2 hypertension	Stage 2 hypertension	Grade 2 Hypertension

Wiecek A., 2018

SPRINT study vs General CKD Population

Table 1. Considerations regarding external validity of SPRINT in the general CKD population

Characteristic	SPRINT CKD subgroup	General CKD population[a]	Comment
Mean age	71.9 years	74 years	
Comorbidities	No DM, excluded severe or symptomatic CHF, excluded eGFR <20 mL/min/1.73 m^2	44% diabetic, 15% CHF	SPRINT excluded diabetic patients and those with proteinuria >1 g/day
Mortality	6.2% overall (rate of ~2%/year based on average duration of follow-up)	37% overall (rate of 7.4%/year)	
Causes of death	35% attributed to CV causes	Unknown	Highest impact of strict SBP lowering in SPRINT seen for CHD deaths and for sudden cardiac deaths
BP measurement method	Standardized and automated, with evaluator not present	Varies by clinical practice, typically using automated device, with evaluator present	SBP difference between methods with and without evaluator present is estimated at 5–20 mmHg [35]

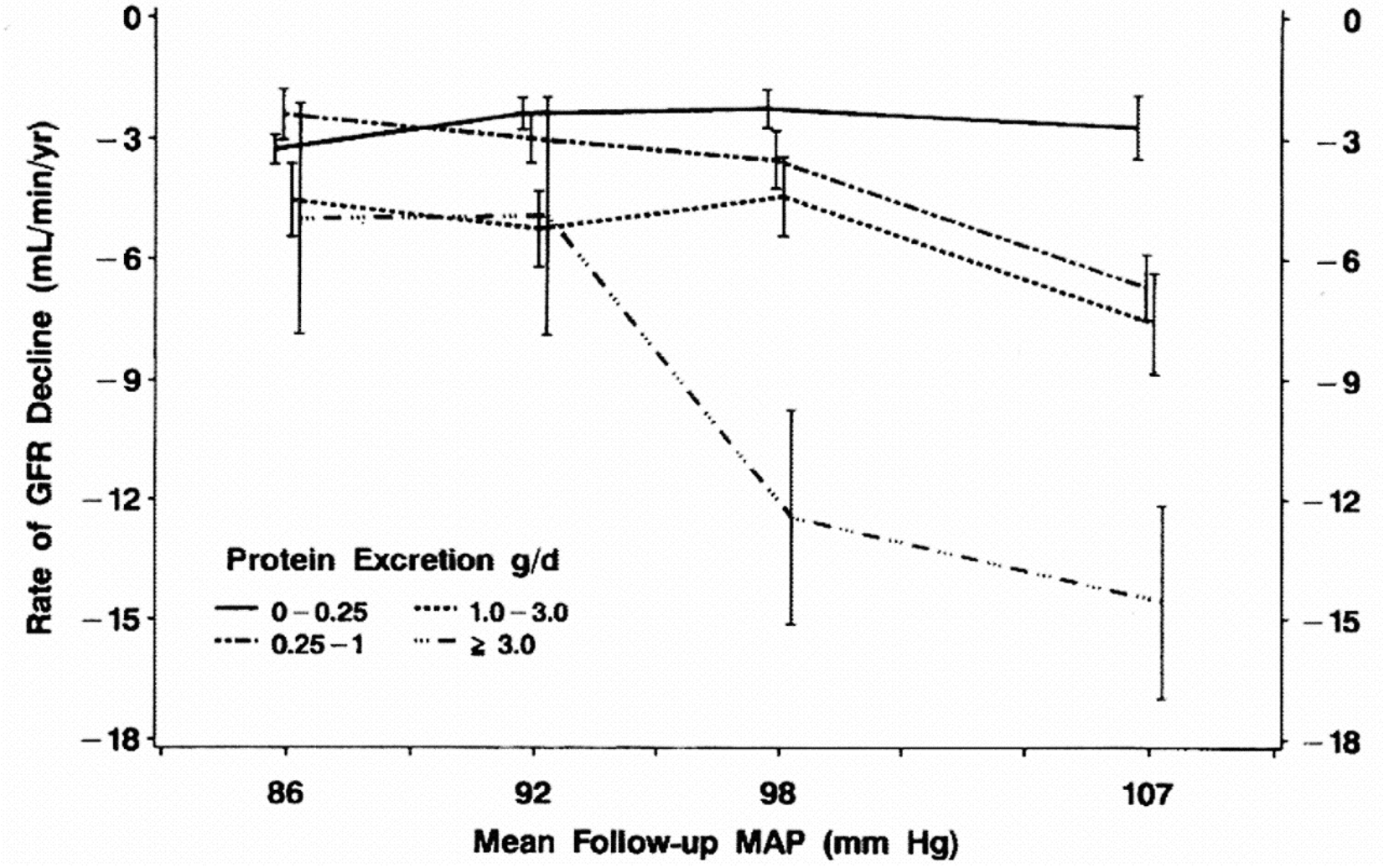
AHD, antihypertensive drug.

[a]Based on baseline characteristics of 651 749 patients included in a large prevalent CKD cohort (Kovesdy *et al.* [6]).

Kovesdy C. P., Nephrol. Dial. Transplant., 2017, 32, ii219 – ii223

Progression of CKD in relation to proteinuria and blood pressure - MDRD Study

(Baseline GFR 25-55 ml/min)



Peterson J.C. et al., Ann Intern Med 1995; 123: 754-762

Event rates for all-cause mortality, incydent coronary heart disease, stroke and end-stage renal disease associated with various systolic blood pressure

n = 339 887 patients with incident CKD

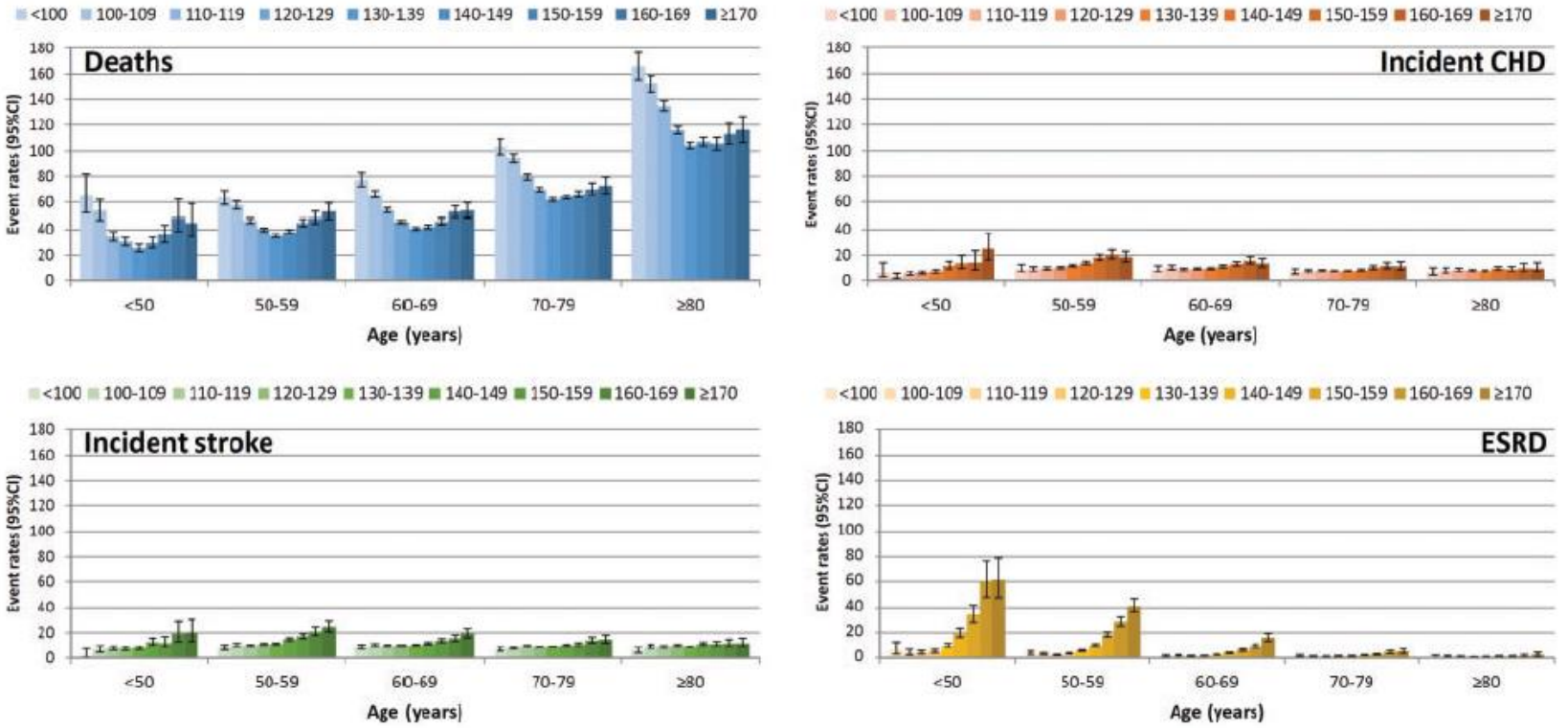


FIGURE 1: Event rates (95% CIs) for all-cause mortality, incident coronary heart disease, incident ischemic stroke and end-stage renal disease associated with various SBP levels in individuals of various age among a cohort of 339 887 patients with incident CKD. Event rates are expressed as event/1000 patient-years. (Based on reanalyzed data from Kovesdy *et al.* [26].)

Kovesdy C. P., Nephrol. Dial. Transplant., 2017, 32, ii219 – ii223

Summary

- Based on the SPRINT Study, ACC/AHA/ASH and many others accepted in 2107 a new classification of blood pressure and the target values for treatment in general population and in CKD patients
- Adopting the new 2017 ACC/AHA/AHA Guidelines would be associated with a substantial increase in the prevalence of hypertension
- This would be accompanied by a marked increase in the recommendation to start and intensify treatment in several million of patients
- The new BP recommendation may increase the risk of AKI and hypotension but in general significantly reduce the death rate

Summary

- ESH/ESC recently published the European Guidelines and did not accept the new classification and new recommendations for treatment for both general population and in CKD patients

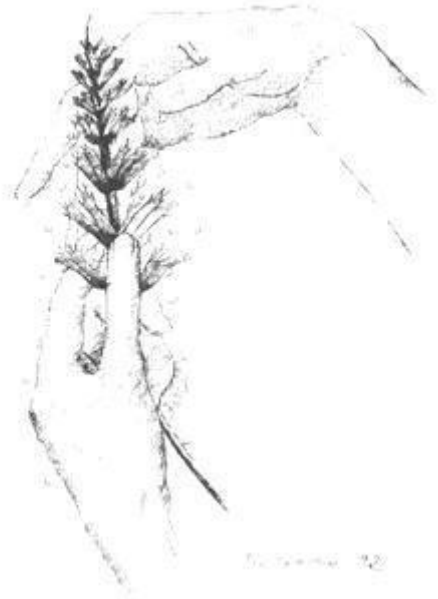
- Optimal (recommended) BP for CKD patients (with proteinuria <1,0 per d) is different in USA (<130/80 mmHg) and in Europe (<140/90 mmHg)

The 25th Budapest Nephrology School

Nephrology, Hypertension, Dialysis, Transplantation, Nephropathology

Under the Auspices of
ISN, ERA-EDTA, RPS, IFKF and ISP

26 - 31 August, 2018



Thank you very much for your attention !!!

Prof. Andrzej Wiecek

Department of Nephrology, Transplantation and Internal Medicine
Medical University of Silesia, Katowice, Poland

e-mail: awiecek@sum.edu.pl