



99^η Επιστημονική Συνάντηση ΕΝΕ
Θεσσαλονίκη, 19-23 Οκτωβρίου 2023



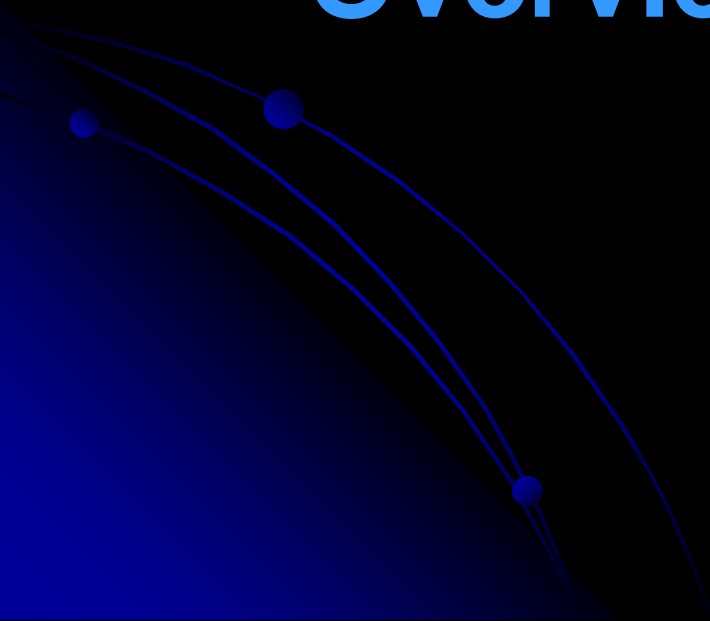
Θεραπευτικοί στόχοι υπέρτασης σε ασθενείς με ΣΔ

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Overview of guidelines



Target BP for patients with DM in international guidelines since 1997

Organization	Year	Systolic BP (mmHg)	Diastolic BP (mmHg)
JNC VI	1997	<130	<85
WHO/ISH	1999	<130	<85
British Hypertension Society	1999	<140	<80
Canadian Hypertension Society	1999	<130	<80
National Kidney Foundation	2000	<130	<80
ADA	2001–2012	<130	<80
ESH/ESC	2003	<130	<80
JNC VII	2003	<130	<80
British Hypertension Society	2004	<130	<80
ESH/ESC	2007	<130	<80
NICE	2008	<130	<80
KDIGO	2012	≤140	≤90
ADA	2013	<140	<80
ESH/ESC	2013	<140	<85
JNC VIII	2014	<140	<90

RCTs of intensive vs. standard treatment strategies

Clinical trial	Population	Intensive	Standard	Outcomes
ACCORD BP (35)	4,733 participants with T2D aged 40–79 years with prior evidence of CVD or multiple cardiovascular risk factors	SBP target: <120 mmHg Achieved (mean) SBP/DBP: 119.3/64.4 mmHg	SBP target: 130–140 mmHg Achieved (mean) SBP/DBP: 135/70.5 mmHg	<ul style="list-style-type: none"> • No benefit in primary end point: composite of nonfatal MI, nonfatal stroke, and CVD death • Stroke risk reduced 41% with intensive control, not sustained through follow-up beyond the period of active treatment • Adverse events more common in intensive group, particularly elevated serum creatinine and electrolyte abnormalities
ADVANCE (36)	11,140 participants with T2D aged ≥55 years with prior evidence of CVD or multiple cardiovascular risk factors	Intervention: a single-pill, fixed-dose combination of perindopril and indapamide Achieved (mean) SBP/DBP: 136/73 mmHg	Control: placebo Achieved (mean) SBP/DBP: 141.6/75.2 mmHg	<ul style="list-style-type: none"> • Intervention reduced risk of primary composite end point of major macrovascular and microvascular events (9%), death from any cause (14%), and death from CVD (18%) • 6-year observational follow-up found reduction in risk of death in intervention group attenuated but still significant (242)
HOT (37)	18,790 participants, including 1,501 with diabetes	DBP target: ≤80 mmHg Achieved (mean): 81.1 mmHg, ≤80 group; 85.2 mmHg, ≤90 group	DBP target: ≤90 mmHg	<ul style="list-style-type: none"> • In the overall trial, there was no cardiovascular benefit with more intensive targets • In the subpopulation with diabetes, an intensive DBP target was associated with a significantly reduced risk (51%) of CVD events
SPRINT (43)	9,361 participants without diabetes	SBP target: <120 mmHg Achieved (mean): 121.4 mmHg	SBP target: <140 mmHg Achieved (mean): 136.2 mmHg	<ul style="list-style-type: none"> • Intensive SBP target lowered risk of the primary composite outcome 25% (MI, ACS, stroke, heart failure, and death due to CVD) • Intensive target reduced risk of death 27% • Intensive therapy increased risks of electrolyte abnormalities and AKI

10. Cardiovascular Disease and Risk Management: *Standards of Care in Diabetes—2023*

- For people with diabetes and hypertension, blood pressure targets should be individualized through a shared decision-making process that addresses cardiovascular risk, potential adverse effects of antihypertensive medications, and patient preferences. (B)
- People with diabetes and hypertension qualify for antihypertensive drug therapy when the blood pressure is persistently elevated $\geq 130/80$ mmHg. The on-treatment target blood pressure goal is $< 130/80$ mmHg, if it can be safely attained. (B)

2023 ESH Guidelines for the management of arterial hypertension

Recommendations and statements	CoR	LoE
BP should be monitored to detect hypertension in all patients with diabetes, because it is a frequent comorbidity associated with an increase CV risk and risk for kidney events.	I	A
Non-dipping or elevated night-time BP are frequent in type 2 diabetes and should be monitored by ABPM or HBPM.	I	B
Antihypertensive treatment in type 2 diabetes is recommended to protect against macrovascular and microvascular complications.	I	A
Immediate lifestyle interventions and antihypertensive drug treatment are recommended for people with type 2 diabetes when office SBP is ≥ 140 mmHg and DBP is ≥ 90 mmHg.	I	A
Drug treatment strategies in patients with type 2 diabetes should be the same as for patients without diabetes but the primary aim is to lower BP below $<130/80$ mmHg	I	A
BP control is difficult in diabetes and combination treatment is almost always necessary.	I	B



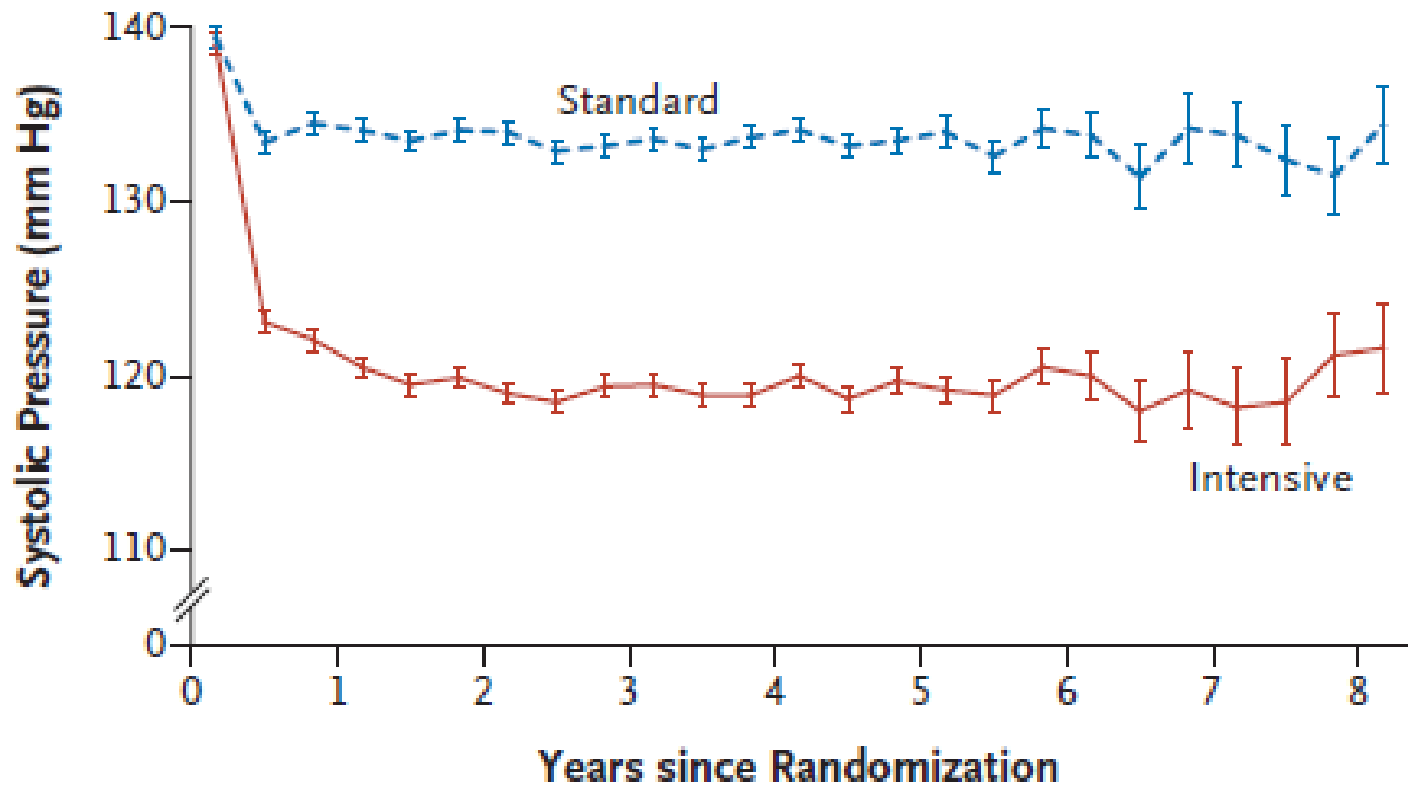
RCTs

ACCORD-BP/SPRINT

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

Characteristic	Overall (N=4733)	Intensive Therapy (N=2362)	Standard Therapy (N=2371)	P Value
Age — yr	62.2±6.9	62.2±6.8	62.2±6.9	0.82
Female sex — no. (%)	2258 (47.7)	1128 (47.8)	1130 (47.7)	0.95
Race or ethnic group — no. (%)†				
Non-Hispanic white	2864 (60.5)	1455 (61.6)	1409 (59.4)	0.13
Black	1142 (24.1)	561 (23.8)	581 (24.5)	0.56
Hispanic	330 (7.0)	159 (6.7)	171 (7.2)	0.53
Education — no./total no. (%)				0.18
Less than high school	771/4729 (16.3)	404/2359 (17.1)	367/2370 (15.5)	
High-school graduate or GED	1271/4729 (26.9)	606/2359 (25.7)	665/2370 (28.1)	
Some college	1530/4729 (32.4)	776/2359 (32.9)	754/2370 (31.8)	
College degree or higher	1157/4729 (24.5)	573/2359 (24.3)	584/2370 (24.6)	
Previous cardiovascular event — no. (%)	1593 (33.7)	804 (34.0)	789 (33.3)	0.58
Previous heart failure — no./total no. (%)	203/4683 (4.3)	109/2338 (4.7)	94/2345 (4.0)	0.28
Cigarette-smoking status — no./total no. (%)				0.94
Current	626/4728 (13.2)	314/2358 (13.3)	312/2370 (13.2)	
Former	1981/4728 (41.9)	992/2358 (42.1)	989/2370 (41.7)	
Never	2121/4728 (44.9)	1052/2358 (44.6)	1069/2370 (45.1)	
Weight — kg	92.0±18.6	92.1±19.4	91.8±17.7	0.57
Body-mass index	32.1±5.6	32.2±5.7	32.1±5.4	0.58
Blood pressure — mm Hg‡				
All participants				
Systolic	139.2±15.8	139.0±16.1	139.4±15.5	0.47
Diastolic	76.0±10.4	75.9±10.6	76.0±10.2	0.87

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



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

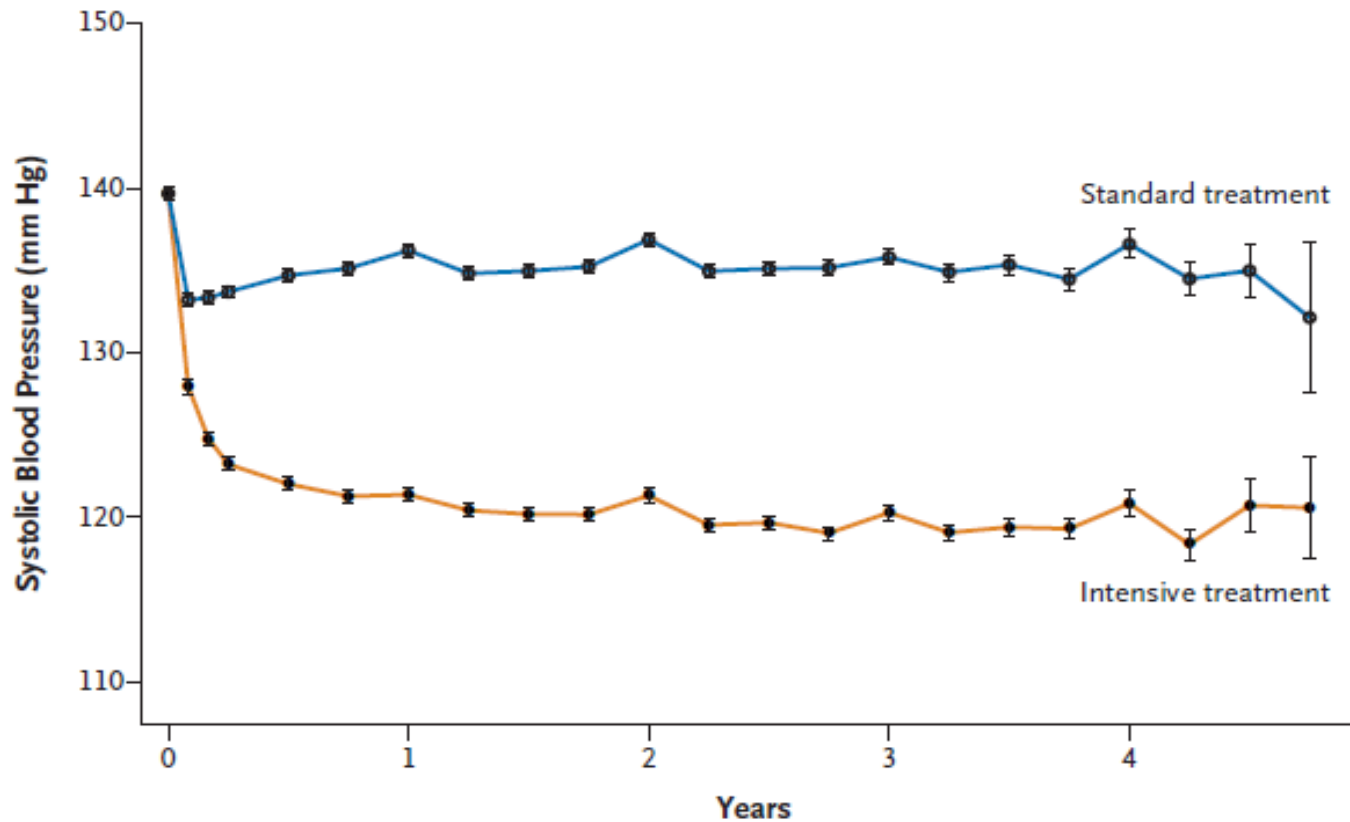
Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus

Outcome	Intensive Therapy (N=2363)		Standard Therapy (N=2371)		Hazard Ratio (95% CI)	P Value
	no. of events	%/yr	no. of events	%/yr		
Primary outcome*	208	1.87	237	2.09	0.88 (0.73–1.06)	0.20
Prespecified secondary outcomes						
Nonfatal myocardial infarction	126	1.13	146	1.28	0.87 (0.68–1.10)	0.25
Stroke						
Any	36	0.32	62	0.53	0.59 (0.39–0.89)	0.01
Nonfatal	34	0.30	55	0.47	0.63 (0.41–0.96)	0.03
Death						
From any cause	150	1.28	144	1.19	1.07 (0.85–1.35)	0.55
From cardiovascular cause	60	0.52	58	0.49	1.06 (0.74–1.52)	0.74
Primary outcome plus revascularization or nonfatal heart failure	521	5.10	551	5.31	0.95 (0.84–1.07)	0.40
Major coronary disease event†	253	2.31	270	2.41	0.94 (0.79–1.12)	0.50
Fatal or nonfatal heart failure	83	0.73	90	0.78	0.94 (0.70–1.26)	0.67

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

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%	3556 (76.0)	3547 (75.7)
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
Race or ethnic group — no. (%) [§]		
Non-Hispanic black	1379 (29.5)	1423 (30.4)
Hispanic	503 (10.8)	481 (10.3)
Non-Hispanic white	2698 (57.7)	2701 (57.7)
Other	98 (2.1)	78 (1.7)
Black race [¶]	1454 (31.1)	1493 (31.9)
Baseline blood pressure — mm Hg		
Systolic	139.7±15.8	139.7±15.4
Diastolic	78.2±11.9	78.0±12.0

A Randomized Trial of Intensive versus Standard Blood-Pressure Control



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

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

Outcome	Intensive Treatment		Standard Treatment		Hazard Ratio (95% CI)	P Value
	<i>no. of patients (%)</i>	<i>% per year</i>	<i>no. of patients (%)</i>	<i>% per year</i>		
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

Post-hoc analyses



Outcomes of Combined CV Risk Factor Management in T2D: the ACCORD trial

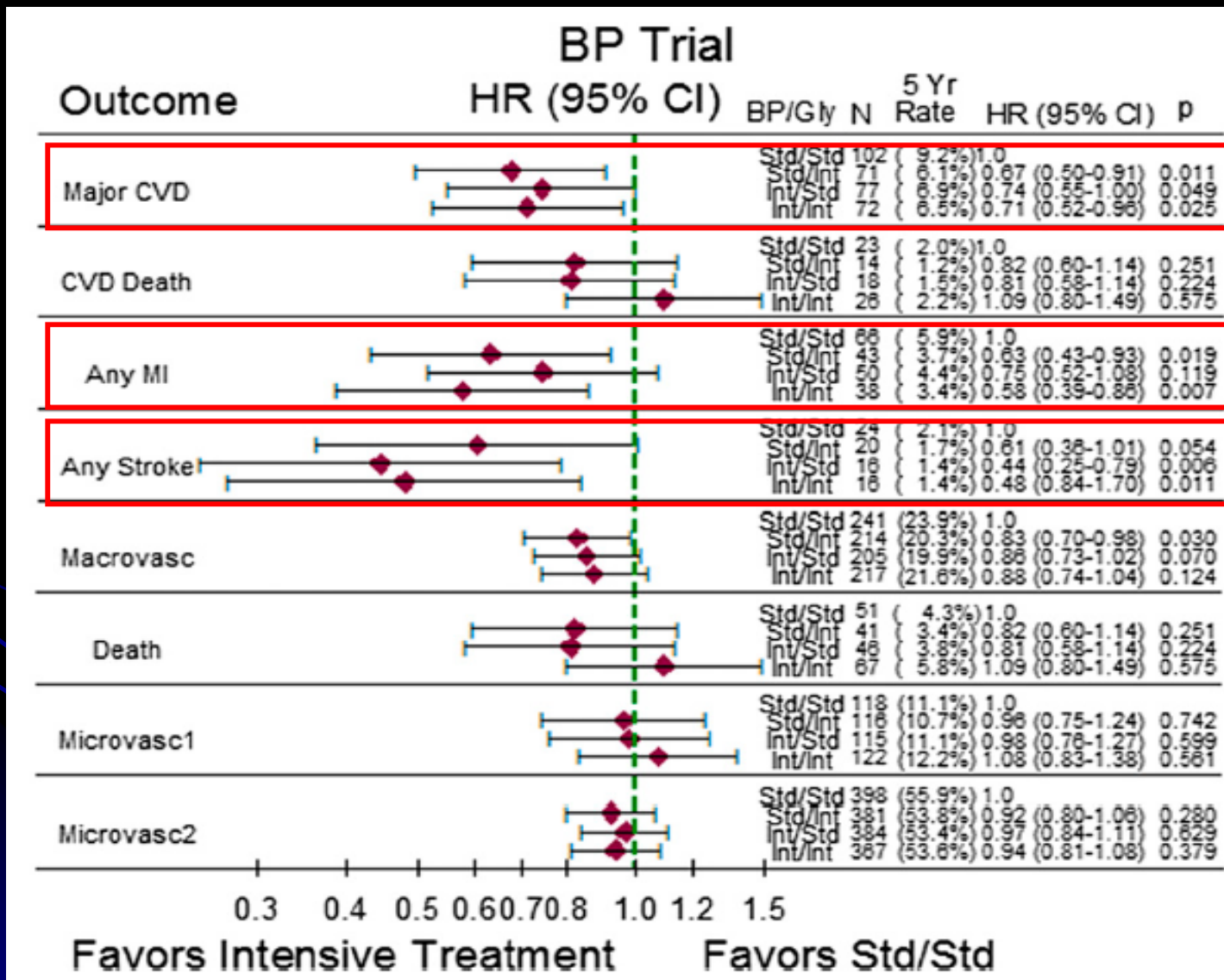
Table 1—Baseline characteristics of ACCORD trial participants

Baseline characteristic	BP trial (n = 4,733)	Lipid trial (n = 5,518)	Glycemia trial (n = 10,251)
Age (years)	62.2 (6.8)	62.3 (6.8)	62.2 (6.8)
Women	47.7	30.7	38.5
Ethnicity			
White	60.5	68.4	64.8
Black	24.1	15.1	19.3
Hispanic	7.0	7.4	7.2
Other	15.8	17.2	16.6
Median duration of diabetes (years)	10 (10)	9 (10)	10 (10)
Previous CVD event	33.7	36.5	35.2
Smoking status			
Current smoker	13.2	14.6	14.0
Former smoker	41.9	46.2	44.2
BMI (kg/m ²)	32.1 (5.6)	32.3 (5.4)	32.2 (5.5)
Systolic BP (mmHg)	139.2 (15.8)	133.9 (17.8)	136.4 (17.1)
Diastolic BP (mmHg)	76.0 (10.4)	74.0 (10.8)	74.9 (10.7)
Median HbA _{1c} (%)	8.3 (1.1)	8.3 (1.0)	8.3 (1.1)
Median HbA _{1c} (mmol/mol)	67.0 (12.0)	67.0 (10.9)	67.0 (12.0)
Total cholesterol (mg/dL)	192.8 (44.8)	175.2 (37.3)	183.3 (41.8)
LDL cholesterol (mg/dL)	110.0 (36.7)	100.6 (30.7)	104.9 (33.9)
HDL cholesterol in women (mg/dL)	51.3 (13.8)	41.4 (7.8)	47.0 (12.6)
HDL cholesterol in men (mg/dL)	41.7 (11.8)	36.6 (7.3)	38.6 (9.6)
Median triglyceride (mg/dL)	147 (128)	162 (116)	155 (122)
Serum creatinine (mg/dL)	0.9 (0.2)	0.9 (0.2)	0.9 (0.2)

Outcomes of Combined CV Risk Factor Management in T2D: the ACCORD trial

Measure	BP trial			
	Standard BP		Intensive BP	
	Standard glycemia	Intensive glycemia	Standard glycemia	Intensive glycemia
Median HbA _{1c} (%)	7.5 (1.1)	6.5 (1.1)	7.5 (1.2)	6.4 (1.2)
Median HbA _{1c} (mmol/mol)	58.0 (12.0)	48.0 (12.0)	58.0 (13.1)	46.0 (13.1)
Mean systolic BP (mmHg)	134.7 (15.6)	133.3 (14.9)	120.2 (14.6)	120.5 (15.0)
Mean diastolic BP (mmHg)	70.9 (10.5)	69.7 (10.7)	64.4 (10.2)	64.3 (9.9)
Mean LDL cholesterol (mg/dL)	100.4 (39.5)	100.2 (38.8)	102.8 (41.4)	102.1 (41.2)
Mean HDL cholesterol (mg/dL)	46.8 (14.9)	47.6 (14.4)	46.1 (14.4)	45.6 (13.6)
Median triglycerides (mg/dL)	141.0 (120.0)	127.0 (99.0)	142.5 (119.0)	140.0 (119.0)

Outcomes of Combined CV Risk Factor Management in T2D: the ACCORD trial



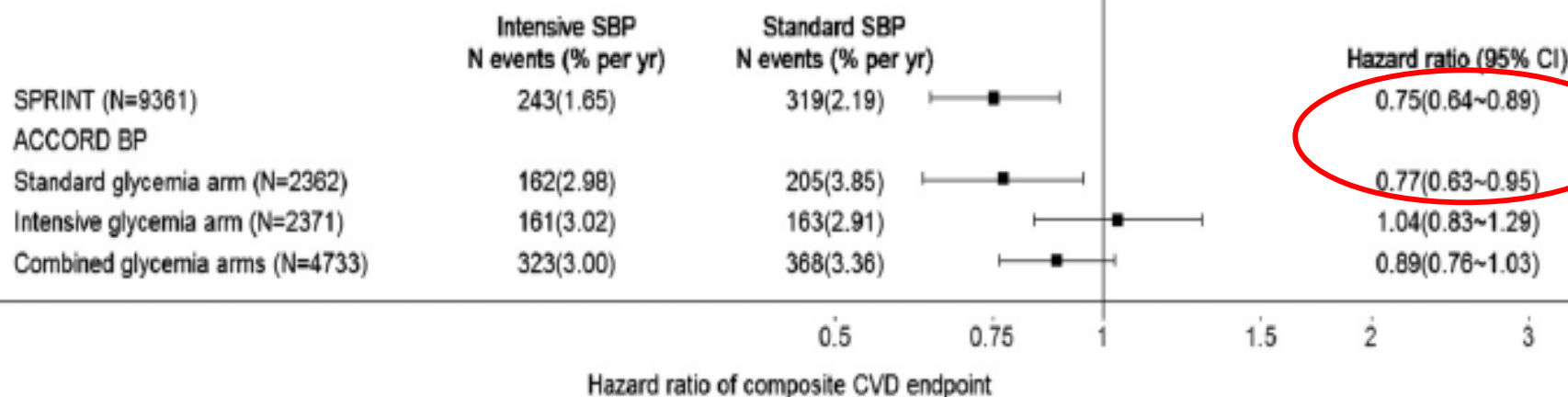
Effects of Intensive Systolic Blood Pressure Lowering on Cardiovascular Events and Mortality in Patients With Type 2 Diabetes Mellitus on Standard Glycemic Control and in Those Without Diabetes Mellitus: Reconciling Results From ACCORD BP and SPRINT

	SPRINT		ACCORD-BP			
	Standard SBP	Intensive SBP	Standard Glycemia		Intensive Glycemia	
			Standard SBP	Intensive SBP	Standard SBP	Intensive SBP
	n=4683	n=4678	n=1178	n=1184	n=1193	n=1178
Age, y	67.9±9.5	67.9±9.4	62.7±6.7	62.8±6.8	62.8±6.8	62.6±6.4
Female sex, %	35.2	36.0	47.1	46.9	48.2	48.6
White race, %	57.7	57.7	59.5	58.7	55.9	61.0
Never smoked, %	44.2	43.8	45.4	45.9	44.8	43.4
SBP, mm Hg	140±15	140±16	140±15	138±16	139±15	139±16
DBP, mm Hg	78±12	78±12	76±10	76±10	76±10	76±10
Clinical atherosclerotic disease, % [†]	20.0	20.0	33.3	33.0	33.4	35.1
Antihypertensive agents (no./patient)	1.8±1.0	1.8±1.0	1.7±1.1	1.7±1.2	1.6±1.1	1.7±1.1
Duration of diabetes mellitus	NA	NA	9.0 (5.0, 15.0)	9.0 (5.0, 15.0)	10.0 (5.0, 16.0)	9.0 (5.0, 15.0)
Glycated hemoglobin%	Not reported	Not reported	8.3±1.0	8.3±1.0	8.3±1.0	8.3±1.0
Fasting plasma glucose, mg/dL	99±13	99±14	173±55	175±55	172±54	175±55
BMI, kg/m ²	29.8±5.7	29.9±5.8	32.1±5.2	32.3±5.6	32.1±5.5	32.1±5.6
Estimated MDRD GFR, mL/min/1.73 m ²	72±21	72±21	91±23	91±23	91±24	90±24
Urine albumin creatinine ratio, mg/g	9.4 (5.6, 21.8)	9.6 (5.7, 21.1)	16.0 (7.0, 56.0)	15.0 (7.0, 45.0)	14.0 (7.0, 42.0)	15.0 (7.0, 46.0)

Effects of Intensive Systolic Blood Pressure Lowering on Cardiovascular Events and Mortality in Patients With Type 2 Diabetes Mellitus on Standard Glycemic Control and in Those Without Diabetes Mellitus: Reconciling Results From ACCORD BP and SPRINT

A

Composite CVD endpoint



Interaction p-values for comparisons of the effects of intensive SBP versus standard SBP

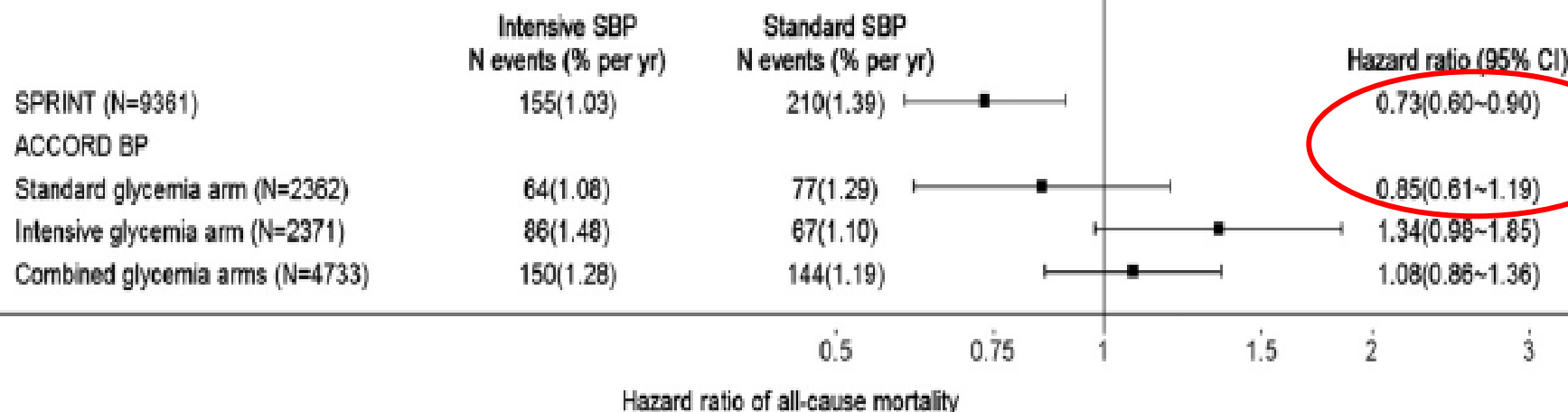
For composite CVD endpoint

SPRINT vs. ACCORD BP standard glycemia arm	0.87
SPRINT vs. ACCORD BP intensive glycemia arm	0.023
ACCORD BP intensive vs. standard glycemia arm	0.053
SPRINT vs. ACCORD BP combined glycemia arms	0.16

Effects of Intensive Systolic Blood Pressure Lowering on Cardiovascular Events and Mortality in Patients With Type 2 Diabetes Mellitus on Standard Glycemic Control and in Those Without Diabetes Mellitus: Reconciling Results From ACCORD BP and SPRINT

B

All-cause mortality



Interaction p-values for comparisons of the effects of intensive SBP versus standard SBP

	For composite CVD endpoint	For all-cause mortality
SPRINT vs. ACCORD BP standard glycemia arm	0.87	0.46
SPRINT vs. ACCORD BP intensive glycemia arm	0.023	0.002
ACCORD BP intensive vs. standard glycemia arm	0.053	0.051
SPRINT vs. ACCORD BP combined glycemia arms	0.16	0.015

A pooled individual patient-level data analysis of the ACCORD-BP and SPRINT trials

	Baseline by study		Baseline by randomization		
	ACCORD-BP	SPRINT	Standard	Intensive	<i>P</i>
<i>N</i>	4,733	9,361	7,054	7,040	
Age, years	62.7 (6.7)	67.9 (9.4)	66.2 (9.0)	66.2 (8.9)	0.99
Female, <i>n</i> (%)	2,258 (47.7)	3,332 (35.6)	2,778 (39.4)	2,812 (39.9)	0.51
Race or ethnic group, <i>n</i> (%)					0.585
Non-Hispanic black	1,127 (23.8)	2,802 (29.9)	2,003 (28.4)	1,926 (27.4)	
Hispanic	330 (7.0)	984 (10.5)	651 (9.2)	663 (9.4)	
Other	495 (10.5)	176 (1.9)	331 (4.7)	340 (4.8)	
Non-Hispanic white	2,781 (58.8)	5,399 (57.7)	4,069 (57.7)	4,111 (58.4)	
SBP, mmHg	139.2 (15.8)	139.7 (15.6)	139.56 (15.4)	139.46 (15.9)	0.71
Diastolic blood pressure, mmHg	76.0 (10.4)	78.1 (11.9)	77.35 (11.5)	77.45 (11.5)	0.60
History of CVD, <i>n</i> (%)	1,593 (33.7)	1,877 (20.1)	1,726 (24.5)	1,744 (24.8)	0.69
Framingham 10-year cardiovascular death risk in %*	32 (22, 45)	22 (15, 32)	25 (17, 36)	25 (17, 37)	0.64
Nonsmoker, <i>n</i> (%)	4,107 (86.8)	8,121 (86.8)	6,141 (87.1)	6,087 (86.5)	0.31
BMI	32.2 (5.5)	29.9 (5.8)	30.58 (5.7)	30.67 (5.9)	0.33
Serum creatinine, mg/dL	0.9 (0.2)	1.1 (0.3)	1.0 (0.3)	1.0 (0.3)	0.78
Estimated GFR, mL/min/1.73 m ²	91.6 (28.8)	71.7 (20.6)	78.4 (24.8)	78.4 (26.1)	0.99
Ratio of urinary albumin (mg) to creatinine (g)	15.0 (7.0, 47.0)	9.5 (5.6, 21.4)	10.8 (6.0, 28.2)	11.0 (6.0, 28.0)	0.46

A pooled individual patient-level data analysis of the ACCORD-BP and SPRINT trials

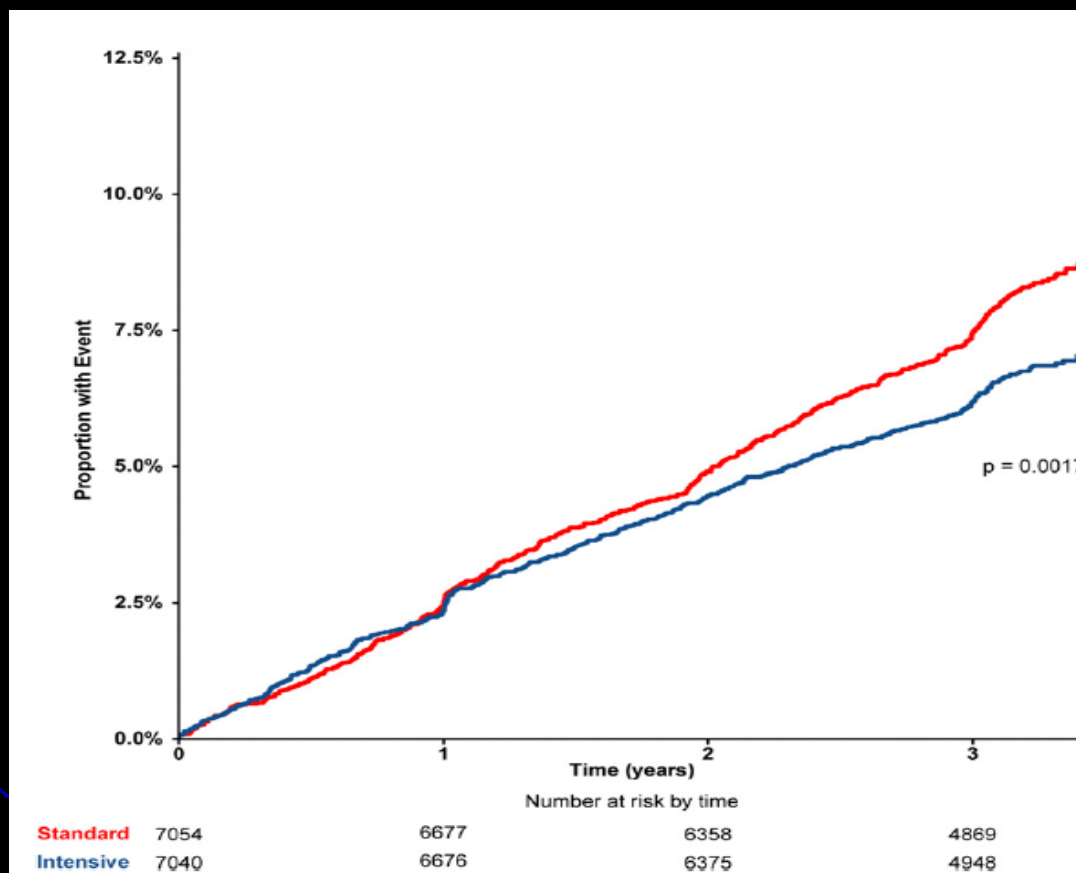


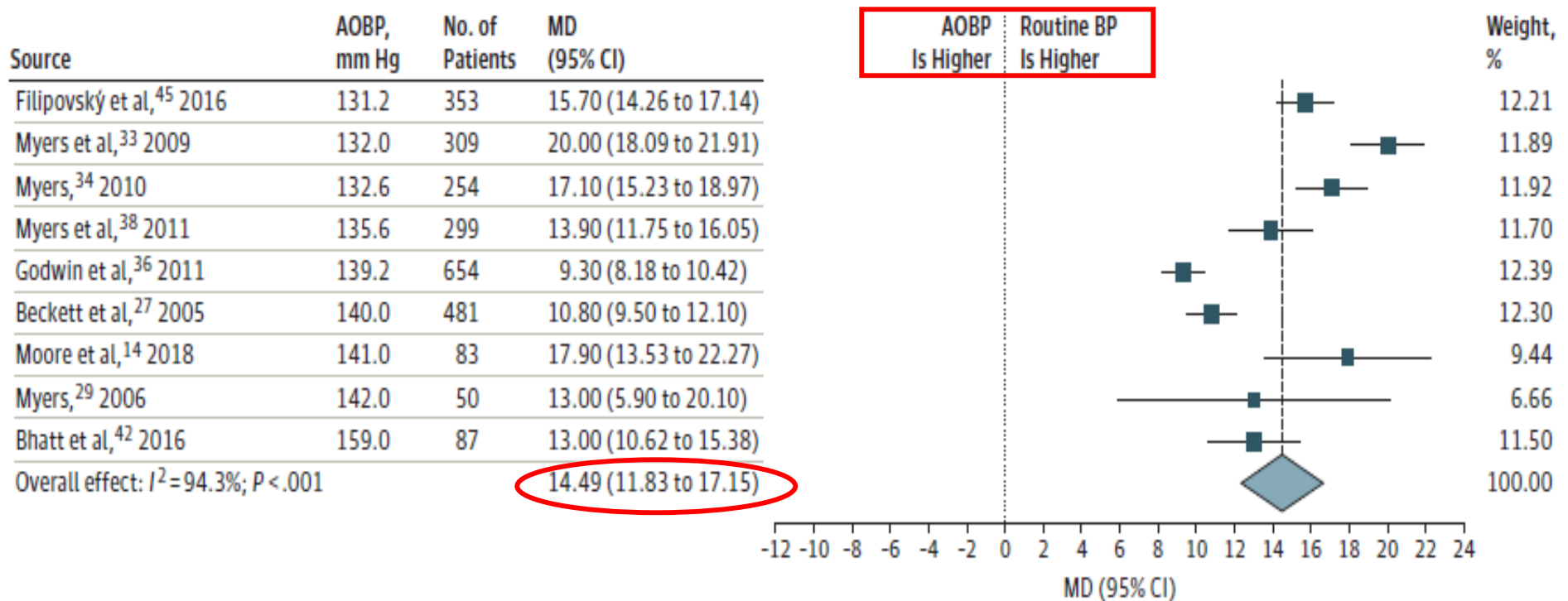
Figure 1—A Kaplan-Meier plot of the composite primary end point in the pooled cohort ($n = 14,094$). Primary composite end point consists of myocardial infarction, stroke, and cardiovascular death plus unstable angina and acute cardiac decompensation. The hazard ratio for primary end point event is 0.82 (95% CI 0.73–0.93), $P = 0.0017$. No significant interaction between T2DM and treatment allocation was observed (P for interaction = 0.13).

**Standardized BP measurements to guide
therapy with intensive BP targets**



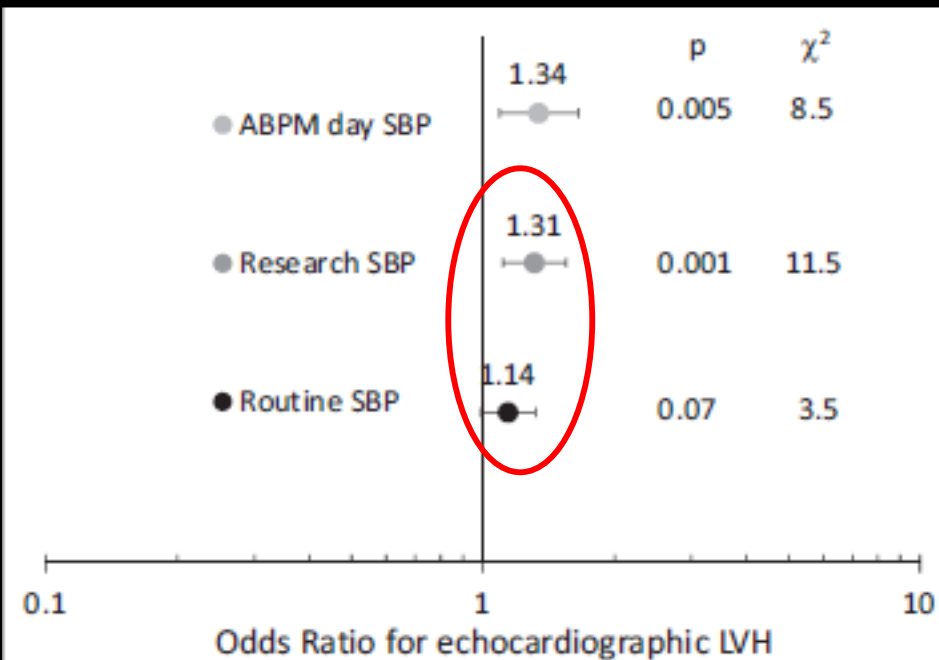
Comparing Automated Office Blood Pressure Readings With Other Methods of Blood Pressure Measurement for Identifying Patients With Possible Hypertension

A Systematic Review and Meta-analysis



Implications of Blood Pressure Measurement Technique for Implementation of Systolic Blood Pressure Intervention Trial (SPRINT)

Variable	Bias (95% CI)	Limits of Agreement
Research grade, routine SBP	-12.7 (-14.7 to -10.7)	-46.1 to 20.7
Research grade, routine DBP	-12.0 (-13.4 to -10.7)	-34.2 to 10.1
Research grade, day ABPM SBP	-7.9 (-9.4 to -6.4)	-33.2 to 17.4
Research grade, day ABPM DBP	-11.7 (-12.7 to -10.8)	-27.8 to 4.3
Routine clinic, day ABPM SBP	4.8 (2.9-6.7)	-26.9 to 36.5
Routine clinic, day ABPM DBP	0.3 (-0.9 to 1.5)	-19.5 to 20.1



ΑΧΕΠΑ

ΠΑΝΕΠΙΣΤΗΜΙΑΚΟ ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ ΘΕΣΣΑΛΟΝΙΚΗΣ ΑΧΕΠΑ