

## SUPPLEMENTARY DATA

### **Association between early hypertension control and cardiovascular disease incidence in Veterans with diabetes**

Sridharan Raghavan, Yuk-Lam Ho, Vinay Kini, Mary Rhee, Jason L. Vassy, David R. Gagnon, Kelly Cho, Peter W. F. Wilson, Lawrence S. Phillips

#### **Online-only Supplement**

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**Supplementary Table S1. Study participant characteristics across on-treatment systolic blood pressure achieved.**

	On-treatment Systolic Blood Pressure (SBP)					p-value
	SBP 100-119 mmHg N=2966	SBP 120-129 mmHg N=9186	SBP 130-139 mmHg N=15,638	SBP 140-159 mmHg N=14,435	SBP ≥160 mmHg N=1761	
Age, mean ± SD (years)	61.5 ± 10.8	60.3 ± 10.3	61.1 ± 10.4	62.4 ± 10.2	64.3 ± 10.3	<0.001
Male, n (%)	2879 (97.1)	8919 (97.1)	15,277 (97.7)	14,099 (97.7)	1732 (98.4)	0.003
Race, n (%)						
<i>Black or African American</i>	411 (13.9)	1367 (14.9)	2434 (15.6)	2562 (17.7)	387 (22)	
<i>White</i>	2462 (83)	7508 (81.7)	12,697 (81.2)	11,411 (79.1)	1323 (75.1)	<0.001
<i>Other</i>	93 (3.1)	311 (3.4)	507 (3.2)	462 (3.2)	51 (2.9)	
Ethnicity, n (%)						
<i>Hispanic or Latino</i>	186 (6.3)	676 (7.4)	1219 (7.8)	988 (6.8)	114 (6.5)	0.002
<i>Not Hispanic or Unknown</i>	2780 (93.7)	8510 (92.6)	14,419 (92.2)	13,447 (93.2)	1647 (93.5)	
CVD at baseline, n (%)	730 (24.6)	1983 (21.6)	3242 (20.7)	3359 (23.3)	483 (27.4)	<0.001
Cancer at baseline, n (%)	758 (25.6)	2320 (25.3)	3654 (23.4)	2984 (20.7)	285 (16.2)	<0.001
Mental Health Disease at baseline, n (%)	497 (16.8)	1669 (18.2)	2605 (16.7)	1910 (13.2)	146 (8.3)	<0.001
Kidney Disease at baseline, n (%)	27 (0.9)	56 (0.6)	89 (0.6)	127 (0.9)	40 (2.3)	<0.001
Smoking Status, n (%)						
<i>Current</i>	590 (19.9)	1816 (19.8)	2883 (18.4)	2460 (17)	242 (13.7)	
<i>Former</i>	1802 (60.8)	5532 (60.2)	9639 (61.6)	9074 (62.9)	1114 (63.3)	<0.001
<i>Never</i>	574 (19.4)	1838 (20)	3116 (19.9)	2901 (20.1)	405 (23)	
BMI, mean ± SD (kg/m <sup>2</sup> )	31.4 ± 6	31.8 ± 5.9	31.9 ± 6	31.8 ± 6.1	31.1 ± 6.3	<0.001
Hemoglobin A1c, mean ± SD (% [mmol/mol])	7.4 ± 1.7 [57 ± 13]	7.5 ± 1.7 [58 ± 13]	7.5 ± 1.7 [58 ± 13]	7.6 ± 1.8 [60 ± 14]	7.9 ± 2.0 [63 ± 16]	<0.001
Glucose, mean ± SD (mg/dL)	154.9 ± 65.7	155.8 ± 62.5	156.9 ± 64.1	161 ± 67.3	165.6 ± 69.8	<0.001
Diabetes medications, n (%)						
<i>None</i>	521 (17.6)	1569 (17.1)	2642 (16.9)	2524 (17.5)	367 (20.8)	
<i>Regimens with insulin</i>	527 (17.8)	1792 (19.5)	3163 (20.2)	3134 (21.7)	375 (21.3)	<0.001
<i>Regimens without insulin</i>	1918 (64.7)	5825 (63.4)	9833 (62.9)	8777 (60.8)	1019 (57.9)	
Total Cholesterol, mean ± SD (mg/dL)	184.9 ± 44	185.2 ± 43.7	186.2 ± 43.5	188 ± 44.6	189.9 ± 43.9	<0.001
HDL Cholesterol, mean ± SD (mg/dL)	41.2 ± 11.8	41 ± 11.6	41.2 ± 11.4	42 ± 11.6	42.5 ± 12.2	<0.001
LDL Cholesterol, mean ± SD (mg/dL)	108.4 ± 35.2	108.4 ± 35.3	109.6 ± 35	111 ± 36.4	113.6 ± 37.4	<0.001
Triglyceride, mean ± SD (mg/dL)	192.2 ± 155.2	196 ± 184.4	194.7 ± 197.7	189 ± 157.2	181.9 ± 132.5	0.001
Lipid medications, n (%)	2205 (74.3)	6696 (72.9)	11,156 (71.3)	9724 (67.4)	1066 (60.5)	<0.001
eGFR, mean ± SD (ml/min/1.73m <sup>2</sup> )	80.8 ± 19	82.5 ± 18.3	82.1 ± 18.2	80.3 ± 19.3	75.9 ± 21	<0.001
Elixhauser score, mean ± SD	-2.7 ± 6.2	-3 ± 6.2	-3 ± 5.9	-2.6 ± 5.6	-1.9 ± 5	<0.001
Systolic Blood Pressure, mean ± SD (mmHg)	141.5 ± 9.8	142.1 ± 9.6	144.6 ± 10.3	150.3 ± 12.6	160.3 ± 16	<0.001
Diastolic Blood Pressure, mean ± SD (mmHg)	79.5 ± 8.1	80.2 ± 7.9	80.2 ± 8.1	81.2 ± 8.8	83.7 ± 10.6	<0.001
Number of blood pressure medications, mean ± SD	1 (1, 2)	1 (1, 2)	1 (1, 2)	1 (1, 2)	2 (1, 3)	<0.001
Anti-hypertensive class, n (%)						
<i>ACE-inhibitor/ARB</i>	1874 (63.2)	5747 (62.6)	9547 (61.1)	8882 (61.5)	1076 (61.1)	0.06
<i>Calcium channel blocker</i>	231 (7.8)	823 (9)	1989 (12.7)	3065 (21.2)	560 (31.8)	<0.001
<i>Beta-blocker</i>	736 (24.8)	1979 (21.5)	3110 (19.9)	3749 (26)	687 (39)	<0.001
<i>Diuretic</i>	576 (19.4)	1750 (19.1)	3436 (22)	4541 (31.5)	710 (40.3)	<0.001
Follow-up time, mean ± SD (years)	9.1 ± 2.0	9.4 ± 1.9	9.3 ± 1.9	9.4 ± 2.0	9.1 ± 2.3	<0.001

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Abbreviations: **CVD**, Cardiovascular disease; **SBP**, Systolic blood pressure; **BMI**, Body mass index; **HDL**, High density lipoprotein; **LDL**, Low density lipoprotein; **eGFR**, Estimated glomerular filtration rate; **ACE**, Angiotensin converting enzyme; **ARB**, Angiotensin receptor blocker

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**Supplementary Table S2. ICD-10 diagnosis codes used to classify causes of death in the National Death Index.**

Causes of death	ICD-10 codes
Abnormal/Accident <i>Homicide</i> <i>Exposure</i> <i>Collision</i> <i>Terror</i>	X85 or Y00-Y09 X00-X59, Y10-Y90 except Y87 Vx Ux
Cancer	D00-D48,9, all of C, K31.7, K635, Q850
Cardiovascular diseases	I10-I16, I20-I25, I27-I28, I34-I37, I42, I44-I51, I60-I75, I77-I78, I97, I99, R00, R58, G45
Cirrhosis	K70.2, K70.3, K74.0, K74.6, K74.3, K74.4, K74.5
COPD	J44
Chronic Kidney Disease	B52.0, C68.9, D59.3, I12.0, I13.1, I13.2, I70.1, I72.2, I77.3, K76.7, M05x, M06x, M08x, M10.3, M12.0, N00x, N01x, N02x, N03x, N04x, N05x, N06x, N07x, N13.1, N13.2, N14x, N17x, N18x, N19x, Q61, Q62.0, Q62.2, R94.4
Dialysis	Z91.15, Z99.2, Z49, T82.81
Diabetes	E10, E11, E13, E14
Infectious	Ax, Bx, L00-L08, B20
Mental Illness	F20-F439, F601, F940, X60-X84, G301, G300, G308, G309

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**Supplementary Table S3. ICD-9 diagnosis codes used to classify baseline comorbidities.**

Condition	ICD-9 Codes
CVD including MI, TIA, stroke, or peripheral vascular disease	430-438, 410-414, 440.2-440.4, 443.9
Chronic Kidney Disease (CKD) or End Stage Renal Disease (ESRD)	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93; 585.5, 585.6, 585.3, 585.4
Liver Disease	571.0, 571.1, 571.3, 571.4, 571.8, 571.9
Hepatitis	573.3, 070.1, 070.2, 070.3, 070.4, 070.5, 070.6, 070.7, 070.8, 070.9
Dialysis	V45.1, V56.xx, 996.73, procedure code 38.95
Cancer, other than non-melanoma skin cancer	140.00-239.00, <b>except</b> 173.2, 173.4 and 173.9
Major mental health disorder: schizophrenia	295, 301.2, 313.2
Alzheimer's Disease	331.0
Dementia	290.x, 291.2, 294.1, 331.x (exclude 331.83), 333.0, 333.4, 797.x, 332.0, 294.8, 046.1, 046.3
Cirrhosis	571.2, 571.5, 571.6
Anemia	280-285
Arthritis	274, 446.5, 710.9, 714.0-714.2, 714.4, 714.89-715, 716.1-716.39, 716.5-716.9, 725
Fatigue	780.71, 780.79
Gait Abnormality or difficulty walking	719.7, 781.2-781.4
Depression/anxiety	296, 300.0-300.9, 309.0-309.1, 311
Hyperlipidemia	272.4
Hypertension	401-105, 437.2
Atrial Fibrillation	427.31
Sleep Apnea	327.2, 780.53, 780.57
COPD	490-491, 492.0, 492.8, 493.2, 496
Schizophrenia	295
Substance	304, 305.2-305.9
Diabetes	250 - at least 1 PCP code OR [2 codes elsewhere AND use of diabetes specific medications (see list below)]
Amputation	Procedure code: V49.7x;
CABG/PCI	CPT codes: 24900, 24920, 24930, 27025, 27027, 27122, 27215-27218, 27226-27228, 27235, 27236, 27244, 27245, 27248, 27254, 27590, 27594, 27880, 27881, 27886, 27888, 28805; VA rated disability condition ('Amputation', 'Prosthetic') Procedure codes: V45.28, 00.66, 0.66, 36.01-36.02, 36.05, 36.10-36.17, 36.19 CPT codes: 33510-33514, 33516-33523, 33533-33536, 33572, 92920-92921, 92924-92925, 92933-92934, 92937-92938, 92941, 92943-92944, 92982, 92984, 92995-92996, 93540, 93564, 93570, C9602-C9608, S2205-S2209
Medications	
Diabetes medications	Exenatide, Insulin, Acetohexamide, Alogliptin, Canagliflozin, Chlorpropamide, Dapagliflozin, Empagliflozin, Glimepiride, Glipizide, Glyburide, Linagliptin, Metformin, Nateglinide, Pioglitazone, Repaglinide, Rosiglitazone, Saxagliptin, Sitagliptin, Tolazamide, Tolbutamide, Troglitazone, Albiglutide, Dulaglutide, Liraglutide, Lixisenatide, Pramlintide
Statin	Atorvastatin, Cerivastatin, Fluvastatin, Lovastatin, Pitavastatin, Pravastatin, Rosuvastatin, Simvastatin

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**Supplementary Table S4. Frequency of each component of the ASCVD composite outcome across eight participant groups defined by pre- and on-treatment systolic blood pressure.**

SBP at treatment initiation (mmHg)	On-treatment SBP	<u>Myocardial infarction</u>	
		Non-fatal	Fatal
130-139	100-119 (N= 658)	35 (5.3%)	9 (1.4%)
	120-129 (N= 2158)	98 (4.5%)	22 (1.0%)
	130-139 (N= 2966)	129 (4.3%)	28 (0.9%)
	140-159 (N= 1859)	102 (5.5%)	32 (1.7%)
≥140	100-119 (N= 1689)	82 (4.9%)	25 (1.5%)
	120-129 (N= 5548)	282 (5.1%)	63 (1.1%)
	130-139 (N= 10,888)	500 (4.6%)	145 (1.3%)
	140-159 (N= 11,663)	584 (5.0%)	221 (1.9%)
SBP at treatment initiation (mmHg)	On-treatment SBP	<u>Stroke</u>	
		Non-fatal	Fatal
130-139	100-119 (N= 658)	17 (2.6%)	0 (0.0%)
	120-129 (N= 2158)	71 (3.3%)	1 (0.0%)
	130-139 (N= 2966)	125 (4.2%)	0 (0.0%)
	140-159 (N= 1859)	105 (5.6%)	1 (0.1%)
≥140	100-119 (N= 1689)	61 (3.6%)	1 (0.1%)
	120-129 (N= 5548)	229 (4.1%)	1 (0.0%)
	130-139 (N= 10,888)	464 (4.3%)	6 (0.1%)
	140-159 (N= 11,663)	713 (6.1%)	10 (0.1%)

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**Supplementary Table S5. Association of pre-treatment systolic blood pressure with ASCVD events, all-cause mortality, and cardiovascular disease mortality.**

Pre-treatment SBP (mmHg)	<u>ASCVD events</u>		<u>CVD mortality</u>		<u>All-cause mortality</u>	
	Hazard Ratio (95% CI)	p-value	Hazard Ratio (95% CI)	p-value	Hazard Ratio (95% CI)	p-value
<b>130-139</b>	Ref	-	Ref	-	Ref	-
<b>≥140</b>	1.10 (1.02, 1.19)	0.02	1.25 (1.10, 1.43)	0.0007	1.15 (1.08, 1.23)	<0.0001

Abbreviations: **ASCVD**, Atherosclerotic cardiovascular disease; **CVD**, Cardiovascular disease; **SBP**, Systolic blood pressure

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**Supplementary Table S6. Association of on-treatment systolic blood pressure with ASCVD events, all-cause mortality, and cardiovascular disease mortality.**

On-treatment SBP (mmHg)	ASCVD events		CVD mortality		All-cause mortality	
	Hazard Ratio (95% CI)	p-value	Hazard Ratio (95% CI)	p-value	Hazard Ratio (95% CI)	p-value
<b>100-119</b>	0.90 (0.76, 1.06)	0.2	1.19 (0.93, 1.51)	0.16	1.16 (1.02, 1.31)	0.02
<b>120-129</b>	Ref	-	Ref	-	Ref	-
<b>130-139</b>	1.03 (0.93, 1.14)	0.5	1.02 (0.87, 1.20)	0.8	0.91 (0.83, 0.98)	0.02
<b>140-159</b>	1.24 (1.13, 1.37)	<0.0001	1.14 (0.98, 1.34)	0.1	0.98 (0.90, 1.06)	0.6
<b>≥160</b>	1.57 (1.34, 1.85)	<0.0001	1.90 (1.53, 2.36)	<0.0001	1.38 (1.22, 1.57)	<0.0001

Abbreviations: **ASCVD**, Atherosclerotic cardiovascular disease; **CVD**, Cardiovascular disease; **SBP**, Systolic blood pressure



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**Supplementary Table S7. Association of pre-treatment systolic blood pressure with ASCVD events among individuals aged 55-65 years at baseline.**

Pre-treatment SBP (mmHg)	ASCVD events	
	Hazard Ratio (95% CI)	p-value
130-139	Ref	-
≥140	1.08 (0.96, 1.21)	0.2

Abbreviations: **ASCVD**, Atherosclerotic cardiovascular disease

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**Supplementary Table S8. Association of on-treatment systolic blood pressure with ASCVD events among individuals aged 55-65 years at baseline.**

On-treatment SBP (mmHg)	ASCVD events	
	Hazard Ratio (95% CI)	p-value
<b>100-119</b>	0.95 (0.73, 1.23)	0.7
<b>120-129</b>	Ref	-
<b>130-139</b>	1.04 (0.90, 1.21)	0.6
<b>140-159</b>	1.19 (1.02, 1.38)	0.02
<b>≥160</b>	1.55 (1.20, 2.00)	0.0007

Abbreviations: **ASCVD**, Atherosclerotic cardiovascular disease

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**Supplementary Table S9. Causes of death among study participants with diabetes and hypertension.**

Causes of death *	All participants n (%)	On-treatment systolic blood pressure (mm Hg)				
		100-119 n (%)	120-129 n (%)	130-139 n (%)	140-159 n (%)	≥160 n (%)
Cardiovascular diseases	1559 (29.0%)	108 (26.7%)	239 (24.7%)	463 (28.6%)	599 (30.5%)	150 (35.9%)
Cancer	1261 (23.5%)	109 (27.0%)	256 (26.4%)	399 (24.7%)	429 (21.8%)	68 (16.3%)
COPD	269 (5.0%)	28 (6.9%)	57 (5.9%)	66 (4.1%)	101 (5.1%)	17 (4.1%)
Diabetes	494 (9.2%)	31 (7.7%)	76 (7.9%)	144 (8.9%)	187 (9.5%)	56 (13.4%)
Chronic kidney disease	157 (2.9%)	9 (2.2%)	26 (2.7%)	33 (2.0%)	70 (3.6%)	19 (4.5%)
Infection	140 (2.6%)	7 (1.7%)	23 (2.4%)	33 (2.0%)	63 (3.2%)	14 (3.3%)
Mental illness	179 (3.3%)	14 (3.5%)	33 (3.4%)	60 (3.7%)	65 (3.3%)	7 (1.7%)
Abnormal/Accident	96 (1.8%)	9 (2.2%)	21 (2.2%)	33 (2.0%)	26 (1.3%)	7 (1.7%)
Other chronic diseases	3 (0.1%)	0 (0.0%)	2 (0.2%)	1 (0.1%)	0 (0.0%)	0 (0.0%)
All other	1214 (22.6%)	89 (22.0%)	235 (24.3%)	385 (23.8%)	425 (21.6%)	80 (19.1%)

Abbreviations: **COPD**, Chronic obstructive pulmonary disease

\* Causes of death are classified based on the definitions used in the National Death Index using ICD-10 codes listed in Table S2.