

## DATA SUPPLEMENT

**Supplemental Table 1. International Classifiers of Disease (ICD)-9 and -10 exclusions for resistant hypertensive subjects**

Description	ICD-9-CM codes	ICD-10-CM-codes
<i>Exclusion for Case Type I, Case Type II, and Control if ever present in a patient record</i>		
Malignant neoplasm of unspecified adrenal gland	194.0	C74.9
Benign neoplasm of unspecified adrenal gland	227.0	D35.00
Disorders of the adrenal gland (excluding adrenal insufficiencies)	255.0, 255.1*, 255.2, 255.3, 255.6, 255.8, 255.9	E24.*, E26.*, E25.*, E27.0, E27.5, E27.8, E27.9
Secondary Hypertension	405.*	I15.0, I15.8
Chronic pulmonary heart disease	416.*	I27.*
Nephrotic syndrome	581.*	N04.*, N08
Chronic glomerulonephritis	582.*	N03.*, N08
Bulbus cordis anomalies	745.*	Q20.*, Q21.*
Coarctation of aorta	747.1*	Q25.1, Q25.2
<i>Exclusion for Case Type I and Case Type II if present in a patient record 5 years before or 1 year after identification as a Case</i>		
Thyrotoxicosis	242.*	E05.*
Disorder of thyrocalcitonin secretion	246.0	E07.0
Disorders of the thyroid NEC	246.8	E03.4, E07.89
Disorders of the thyroid NOS	246.9	E07.9
Parathyroid disorder NEC	252.8	E21.4
Parathyroid disorder NOS	252.9	E21.5
Obstructive uropathy	599.6*	N13.9

Abbreviations: NEC, not elsewhere classified; NOS, not otherwise classified

**Supplemental Table 2. International Classifiers of Disease (ICD)-9 and ICD-10****codes used for history of diagnosis**

<b>Diagnosis</b>	<b>ICD-9 codes</b>	<b>ICD-10 codes</b>	<b>Other</b>
Chronic kidney disease stage 3	585.1	N18.1	eGFR > 30 mL/min/1.73 m <sup>2</sup>
	585.2	N18.2	but < 60 mL/min/1.73 m <sup>2</sup>
Ischemic heart disease	410.*	I20.*	
	411.*	I22.*	
	413.*	I24.*	
	414.*	I25.*	
Type 2 diabetes mellitus	250	E11	
	250.*	E11.*	
	327.2*	G47.3*	
Smoking	305.1	F17.*	
	V15.82	Z87.891	

Abbreviations: eGFR, estimated glomerular filtration rate

**Supplemental Table 3. The daily dose and frequency of thiazide diuretic and dihydropyridine calcium channel blocker prescription in patients with apparent treatment-resistant hypertension prior to spironolactone prescription**

Medication	Daily dose	Patients prescribed, n (%)*
Thiazide diuretic		884
	12.5 mg	86 (9.7)
	25 mg	566 (64.0)
	50 mg	78 (8.8)
	unknown	154 (17.4)
Dihydropyridine calcium channel blocker		980
Amlodipine		
	2.5 mg	8 (0.8)
	5 mg	99 (10.1)
	7.5 mg	3 (0.3)
	10 mg	312 (31.8)
	unknown	52 (5.3)
Nifedipine		
	30 mg	38 (3.9)
	60 mg	100 (10.2)
	90 mg	110 (11.2)
	120 mg	25 (2.6)
	unknown	233 (23.8)

\*The frequency of medication dose based on medication type, e.g. thiazide diuretic or dihydropyridine calcium channel blocker.

**Supplemental Table 4. Characteristics of spironolactone responders and nonresponders in European Americans.**

Variable	N	Nonresponders (n=343)	Responders (n=771)	p-value*
Age, years	1,114	65.66 ± 13.09	66.21 ± 12.04	0.50
Female, n (%)	1,114	151 (44.0%)	368 (47.7%)	0.25
BMI, kg/m <sup>2</sup>	1,023	31.3 ± 7.2	32.5 ± 7.7	0.01
Diagnostic History				
T2DM, n (%)	1,114	173 (50.4%)	393 (51.0%)	0.87
CKD3, n (%)	1,114	124 (36.2%)	296 (38.4%)	0.48
IHD, n (%)	1,114	149 (43.4%)	280 (36.3%)	0.02
Smoking, n (%)	1,114	75 (21.9%)	157 (20.4%)	0.57
Baseline measures				
SBP, mmHg	1,114	131.37 ± 16.99	145.91 ± 18.52	< 0.001
DBP, mmHg	1,114	69.46 ± 10.88	76.78 ± 12.52	< 0.001
Serum sodium, mmol/L	872	138.45 ± 3.26	139.04 ± 3.00	0.01
Serum potassium, mmol/L	871	3.99 ± 0.46	3.93 ± 0.43	0.07
Creatinine, mg/dL	878	1.11 ± 0.37	1.07 ± 0.37	0.11
eGFR, mL/min/1.73m <sup>2</sup>	1,029	75.16 ± 24.47	75.23 ± 19.83	0.96
Glucose, mg/dL	875	124.46 ± 56.69	126.59 ± 48.81	0.57
HbA1c, %	383	6.76 ± 1.67	7.24 ± 3.54	0.10
HDL cholesterol, mg/dL	420	46.96 ± 18.89	44.11 ± 14.83	0.10
LDL cholesterol, mg/dL	390	92.09 ± 37.86	95.30 ± 34.75	0.43
Triglycerides, mg/dL	426	167.8 ± 117.0	182.5 ± 129.4	0.27
Difference from baseline following initial spironolactone prescription				
Serum sodium, mmol/L	810	-0.70 ± 2.63	-1.12 ± 2.71	0.04

Serum potassium, mmol/L	812	0.12 ± 0.48	0.27 ± 0.43	< 0.001
Creatinine, mg/dL	816	0.01 ± 0.23	0.13 ± 0.32	< 0.001
eGFR, mL/min/1.73m <sup>2</sup>	924	-4.82 ± 15.68	-8.76 ± 14.51	< 0.001
Glucose, mg/dL	810	1.44 ± 47.52	0.01 ± 39.03	0.65
HbA1c, %	181	-0.13 ± 1.31	-0.05 ± 0.92	0.63
HDL cholesterol, mg/dL	156	0.03 ± 9.35	-0.94 ± 8.62	0.54
LDL cholesterol, mg/dL	142	-7.29 ± 35.21	-8.63 ± 35.09	0.86
Triglycerides, mg/dL	162	-11.99 ± 107.79	-22.93 ± 121.66	0.59

Abbreviations: BMI, body mass index; CKD 3, chronic kidney disease stage three; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; IHD, ischemic heart disease; LDL, low-density lipoprotein; N, number of individuals with the specific measure; SBP, systolic blood pressure.

Data are presented as mean ± standard deviation for continuous variables and count (%) for categorical variables.

\* P-values from the multivariable regression model are provided for all variables except HbA1c, HDL cholesterol, LDL cholesterol, and triglycerides. Univariate p-values are provided for these variables.

**Supplemental Table 5. Characteristics of spironolactone responders and nonresponders in African Americans.**

Variable	N	Nonresponders (n=106)	Responders (n=263)	p-value*
Age, years	369	57.23 ± 11.30	58.65 ± 12.64	0.32
Female, n (%)	369	64 (60.3%)	164 (62.4%)	0.72
BMI, kg/m <sup>2</sup>	335	35.3 ± 9.7	37.3 ± 9.2	0.40
Diagnostic History				
T2DM, n (%)	369	63 (59.4%)	173 (65.7%)	0.25
CKD3, n (%)	369	39 (36.8%)	102 (38.8%)	0.72
IHD, n (%)	369	30 (28.3%)	71 (27.0%)	0.80
Smoking, n (%)	369	21 (19.8%)	211 (20.5%)	0.87
Baseline measures				
SBP, mmHg	369	139.15 ± 17.46	152.51 ± 18.40	< 0.001
DBP, mmHg	369	78.78 ± 11.67	85.50 ± 12.53	< 0.001
Serum sodium, mmol/L	304	139.37 ± 3.00	139.81 ± 2.85	0.23
Serum potassium, mmol/L	304	3.81 ± 0.50	3.84 ± 0.44	0.58
Creatinine, mg/dL	306	1.14 ± 0.33	1.16 ± 0.54	0.73
eGFR, mL/min/1.73m <sup>2</sup>	353	81.69 ± 20.78	83.42 ± 22.80	0.51
Glucose, mg/dL	304	129.05 ± 64.32	128.05 ± 55.37	0.89
HbA1c, %	155	7.45 ± 2.17	7.22 ± 1.65	0.50
HDL cholesterol, mg/dL	155	49.07 ± 14.93	49.21 ± 15.95	0.56
LDL cholesterol, mg/dL	147	106.51 ± 43.81	106.70 ± 33.43	0.98

Triglycerides, mg/dL	152	151.35 ± 92.16	135.01 ± 88.22	0.34
Difference from baseline following initial spironolactone prescription				
Serum sodium, mmol/L	291	0.17 ± 2.52	-0.52 ± 2.63	0.05
Serum potassium, mmol/L	292	0.16 ± 0.50	0.19 ± 0.39	0.57
Creatinine, mg/dL	292	0.06 ± 0.23	0.14 ± 0.26	0.01
eGFR, mL/min/1.73m <sup>2</sup>	330	-6.50 ± 15.89	-9.99 ± 16.61	0.09
Glucose, mg/dL	291	-5.56 ± 48.63	-1.37 ± 44.65	0.48
HbA1c, %	103	-0.54 ± 0.97	0.02 ± 1.23	0.09
HDL cholesterol, mg/dL	58	3.17 ± 17.66	-1.67 ± 10.92	0.24
LDL cholesterol, mg/dL	55	0.04 ± 19.86	-4.82 ± 34.85	0.65
Triglycerides, mg/dL	58	-43.47 ± 109.99	-11.64 ± 61.01	0.21

Abbreviations: BMI, body mass index; CKD 3, chronic kidney disease stage three; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; IHD, ischemic heart disease; LDL, low-density lipoprotein; N, number of individuals with the specific measure; SBP, systolic blood pressure.

Data are presented as mean ± standard deviation for continuous variables and count (%) for categorical variables.

\* P-values from the multivariable regression model are provided for all variables except HbA1c, HDL cholesterol, LDL cholesterol, and triglycerides. Univariate p-values are provided for these variables.