

Outcomes ascertainment

The primary outcome measures for this study included: a) cardiovascular events: (adjudicated heart failure events, atherosclerotic events), b) renal outcomes (50% decrease in eGFR or end-stage renal disease) and c) all-cause mortality. These events were adjudicated from study entry through March 2012. Participants' follow-up was censored at the end of the follow-up time period, loss to follow-up, or death, whichever occurred first. Study personnel identified possible heart failure events by reviewing hospital billing codes. Two independent reviewers adjudicated heart failure events and classified them as probable or definite. Criteria for congestive heart failure events included a combination of symptoms (dyspnea on exertion, paroxysmal nocturnal dyspnea, and orthopnea), accompanied by radiographic changes (pulmonary edema, congestion) or pertinent findings on physical examination (evidence of two or more of the following: pulmonary rales, S3 gallop, jugular venous distension > 5 cm, and peripheral edema). Renal disease progression was defined by a composite of ESRD or halving of eGFR from baseline. ESRD was defined as receipt of chronic dialysis or kidney transplant and was ascertained primarily through self-report. Estimated GFR was calculated from serum creatinine and cystatin C using a CRIC Study equation. Time to eGFR halving was imputed assuming a linear decline in kidney function between in-person annual visit measures.

Other outcomes included mortality and adjudicated atherosclerotic cardiovascular events.

Mortality was ascertained from reports of next of kin, retrieval of death certificates, obituaries, reviews of hospital records, and linkage with the Social Security Death Master File.

Atherosclerotic events included adjudicated myocardial infarction, cerebrovascular accident, or peripheral vascular disease. Criteria for myocardial infarction classified as definite, probable or

possible, included a combination of chest pain, electrocardiographic abnormalities and elevated cardiac biomarkers. Peripheral vascular disease procedures were ascertained using International Classification of Diseases, Ninth Revision codes. Clinical PAD events were defined as occlusive artery disease resulting in amputation, peripheral surgical or percutaneous revascularization procedures, any arterial angioplasty, or any artery-artery bypass graft. Incident PAD was defined as a new onset ABI of <0.9 or clinical PAD during the follow-up period. Two neurologists adjudicated cerebrovascular accidents.

Table S1. Characteristics of patients with and without pulmonary hypertension (PH) measures in the CRIC cohort

Variables	With PH measures (N=2959)	Without PH measures (N=561)	P value
Age	59.6 (10.6)	58.3 (11.6)	0.01
Gender			
Male	1593 (53.8%)	333 (59.4%)	0.01
Race/ethnicity			
Non-Hispanic White	1360 (46.0%)	154 (27.5%)	<.0001
Non-Hispanic Black	1330(44.9%)	131(23.4%)	
Hispanic	142(4.8%)	263(46.9%)	
Other	127(4.3%)	13(2.3%)	
Cardiovascular Disease	1093 (36.9%)	178 (31.7%)	0.01
Stroke	325 (11.0%)	54 (9.6%)	0.34
Congestive heart failure	323 (10.9%)	51 (9.1%)	0.19
Peripheral vascular disease	229 (7.7%)	39 (7.0%)	0.51
Chronic Obstructive Pulmonary Disease	150 (5.1%)	17 (3.0%)	0.03
Systolic BP (mmHg)	126.4 (21.4)	130.4 (23.4)	<0.0001
Diastolic BP (mmHg)	69.7 (12.7)	70.7 (13.9)	0.09
Diabetes	1429 (48.3%)	319 (56.9%)	0.0002
Body Mass Index (kg/m ²)	32.0 (7.7)	32.7 (8.3)	0.05
Current Smoker	373 (12.6%)	55 (9.8%)	0.06
Proteinuria (g/24 hr)	1.0 (2.1)	1.5 (2.8)	<0.001
eGFR	42.7 (17.1)	39.5 (16.8)	<0.001
Serum Urea Nitrogen	30.8 (15.9)	32.9 (16.3)	0.0040
Albuminuria	513.9 (1361.9)	1061.9 (2191.1)	<0.001
Glucose (mg/dL)	115.3 (50.6)	119.0 (52.4)	0.11
Hemoglobin (g/dL)	12.8 (1.8)	12.6 (1.9)	0.0013
Serum Albumin (g/dL)	4.1 (0.4)	3.9 (0.5)	<0.001
Calcium (mg/dL)	9.3 (0.5)	9.3 (0.5)	0.74
Phosphate (mg/dL)	3.7 (0.7)	3.8 (0.7)	0.0062
Bicarbonate (mmol/L)	24.4 (3.2)	23.9 (3.5)	<0.001
Uric Acid (mg/dL)	7.4 (1.9)	7.5 (2.0)	0.14
LDL cholesterol (mg/dL)	99.3 (34.4)	102.4 (38.2)	0.05
Triglycerides (mg/dL)	151.8 (100.8)	172.4 (127.2)	<0.001
HDL (mg/dL)	48.9 (15.8)	45.1 (14.7)	<0.001
HsCRP	5.4 (9.4)	5.3 (8.6)	0.82
Use of ACEI or ARB	2052 (69.3%)	385 (68.6%)	0.73
Use of statins	1767 (59.7%)	315 (56.1%)	0.11
Use of beta-blockers	1512 (51.1%)	292 (52.0%)	0.67
Use of diuretics	1766 (59.7%)	335 (59.7%)	0.98
BNP	88.2(233.7)	107.7(228.3)	0.07

Table S2. Cross sectional association between clinical and demographic factors and prevalent PH in CRIC study participants

Variable	Pulmonary hypertension Odds ratio(95% CI)*
Age (per 5-year increase)	1.30(1.23, 1.39)
Male gender	0.88(0.71, 1.08)
Race	
Non-Hispanic black vs. Non-Hispanic white	1.53(1.23, 1.91)
Hispanic vs. Non-Hispanic white	1.32(0.82, 2.13)
Others vs. Non-Hispanic white	1.14(0.68, 1.92)
eGFR (per SD decrease)	1.19(1.05, 1.34)
Proteinuria (per SD increase)	1.10(0.99, 1.22)
Diabetes	0.99(0.80, 1.23)
Hypertension	1.57(1.03, 2.38)
Hyperlipidemia	0.88(0.63, 1.24)
Chronic obstructive pulmonary disease	1.64(1.09, 2.46)
Smoking	0.74(0.53, 1.02)
BMI (kg/m ²)	
<18.5 vs. 18.5-24.9	1.21(0.37, 3.91)
25-29.9 vs. 18.5-24.9	1.19(0.86, 1.66)
>30 vs. 18.5-24.9	1.01(0.73, 1.38)
Left ventricular ejection fraction (each SD decrease)	1.08(0.98, 1.19)
Diastolic relaxation	
Mild abnormality vs. Normal	0.44(0.35, 0.56)
Moderate abnormality vs. Normal	0.68(0.46, 1.00)
Severe abnormality vs. Normal	0.75(0.30, 1.85)

*Model adjusted for age, gender, race, eGFR, proteinuria, diabetes, hypertension, smoking, COPD, BMI and LVEF; SD- standard deviation;

Table S3. Associations between various categories of Tricuspid regurgitant velocity (TRV) and outcomes

TRV categories (m/sec)	Renal events HR (95% CI)	Mortality HR (95% CI)	CV events (composite) HR (95% CI)
2.6-2.9 vs. <2.5	1.00(0.74 – 1.34)	1.11(0.80 – 1.53)	1.17(0.86 – 1.59)
3.0-3.4 vs. <2.5	1.62(1.09 – 2.43)	1.94(1.28 – 2.95)	1.87(1.22 – 2.84)
>3.4 vs. <2.5	2.71(1.17 – 6.26)	1.73(0.92 – 3.25)	3.50(1.95 – 6.30)

Model adjusted for age, gender, race, clinical center, smoking, diabetes, hypertension, previous cardiovascular disease, COPD, BMI, albumin, BNP, hemoglobin LDL cholesterol, use of RAS blockers, diuretics, statins and beta-blockers, LVEF, LVH, eGFR and Proteinuria

Table S4. Associations between various categories of PASP and outcomes

PASP categories (mm Hg)	Renal events HR (95% CI)	Mortality HR (95% CI)	CV events (composite) HR (95% CI)
36-45 vs. <35	1.21(0.84 – 1.75)	1.55(1.07 – 2.26)	1.19(0.80 – 1.76)
46-55 vs. <35	1.47(0.72 – 3.01)	1.59(0.70 – 3.60)	1.35(0.63 – 2.86)
>55 vs. <35	2.66(0.96 – 7.40)	2.16(1.13 – 4.15)	4.36(2.32 – 8.16)

Model adjusted for age, gender, race, clinical center, smoking, diabetes, hypertension, previous cardiovascular disease, COPD, BMI, albumin, BNP, hemoglobin LDL cholesterol, use of RAS blockers, diuretics, statins and beta-blockers, LVEF, LVH, eGFR and Proteinuria

Table S5. Associations between PH, TRV and PASP and incident CV events (excluding participants with pre-existing CVD-until year 1 CRIC visit)

Outcome	Variable	Unadjusted		Model A*		Model B*		Model C*		Model D*	
		HR(95pct CI)	P-value)	HR(95pct CI)	P-value)	HR(95pnt CI)	P-value)	HR(95pct CI)	P-value)	HR(95pct CI)	P-value)
Cardiovascular events	PH (Yes vs. No)	1.58 (1.14 - 2.18)	0.006	1.31 (0.94 - 1.84)	0.11	1.22 (0.86 - 1.74)	0.26	1.23 (0.85 - 1.78)	0.26	1.22 (0.83 - 1.77)	0.30
Cardiovascular events	PAP (each SD increase)	1.62 (1.29 - 2.04)	<0.001	1.53 (1.20 - 1.95)	<0.001	1.24 (0.95 - 1.63)	0.11	1.24 (0.95 - 1.63)	0.11	1.17 (0.89 - 1.53)	0.25
Cardiovascular events	TRV (each SD increase)	1.63 (1.34 - 1.98)	<0.001	1.54 (1.24 - 1.90)	<0.001	1.32 (1.05 - 1.67)	0.01	1.29 (1.02 - 1.63)	0.03	1.22 (0.97 - 1.53)	0.08
CHF	PH (Yes vs. No)	2.08 (1.42 - 3.06)	<0.001	1.71 (1.14 - 2.56)	0.009	1.48 (0.97 - 2.26)	0.06	1.59 (1.02 - 2.46)	0.03	1.63 (1.03 - 2.57)	0.03
CHF	PAP (each SD increase)	1.98 (1.52 - 2.59)	<0.001	1.85 (1.40 - 2.45)	<0.001	1.41 (1.01 - 1.96)	0.04	1.42 (1.03 - 1.97)	0.03	1.34 (0.96 - 1.85)	0.08
CHF	TRV (each SD increase)	1.88 (1.50 - 2.37)	<0.001	1.76 (1.38 - 2.26)	<0.001	1.46 (1.11 - 1.93)	0.007	1.42 (1.08 - 1.87)	0.01	1.34 (1.03 - 1.75)	0.02
MI	PH (Yes vs. No)	1.02 (0.56 - 1.85)	0.95	0.77 (0.41 - 1.43)	0.40	0.71 (0.37 - 1.36)	0.30	0.70 (0.36 - 1.36)	0.29	0.63 (0.32 - 1.25)	0.18
MI	PAP (each SD increase)	1.10 (0.75 - 1.62)	0.62	1.01 (0.67 - 1.52)	0.95	0.87 (0.55 - 1.36)	0.53	0.94 (0.60 - 1.46)	0.76	0.91 (0.59 - 1.40)	0.68
MI	TRV (each SD increase)	1.13 (0.82 - 1.58)	0.45	1.03 (0.72 - 1.48)	0.85	0.92 (0.62 - 1.36)	0.68	0.95 (0.64 - 1.40)	0.78	0.91 (0.62 - 1.33)	0.63
CVA	PH (Yes vs. No)	1.26 (0.58 - 2.74)	0.56	1.15 (0.51 - 2.57)	0.74	1.16 (0.49 - 2.72)	0.74	0.88 (0.34 - 2.31)	0.79	0.89 (0.34 - 2.35)	0.81
CVA	PAP (each SD increase)	1.72 (1.02 - 2.90)	0.04	1.54 (0.90 - 2.63)	0.11	1.46 (0.75 - 2.84)	0.26	1.26 (0.61 - 2.59)	0.53	1.22 (0.58 - 2.58)	0.59
CVA	TRV (each SD increase)	1.79 (1.13 - 2.82)	0.01	1.62 (1.01 - 2.59)	0.04	1.53 (0.89 - 2.62)	0.12	1.53 (0.80 - 2.92)	0.19	1.57 (0.81 - 3.04)	0.18

Model A- Adjusted for age, gender, race and clinical center

Model B – Adjusted for model A plus smoking, diabetes, hypertension, previous cardiovascular disease, COPD, BMI, albumin, hemoglobin, LDL cholesterol, use of RAS blockers, diuretics, statins and beta-blockers,

Model C- Adjusted for model B plus LVEF and diastolic dysfunction

Model D- Adjusted for model C plus eGFR and UACR

Table S6: Associations between PH, TRV, PASP and ESRD/ESRD and death composite events

	<i>HR(95% CI)*</i>	<i>p-value</i>
PH vs no PH		
ESRD	1.16(0.92- 1.45)	0.20
ESRD/Death composite	1.24(1.04 -1.46)	0.01
TRV (per one SD increase)		
ESRD	1.13(0.99 – 1.29)	0.07
ESRD/Death composite	1.10(1.00 – 1.21)	0.05
PASP (per one SD increase)		
ESRD	1.12(0.96 – 1.30)	0.14
ESRD/Death composite	1.07(0.96 – 1.18)	0.22

*Adjusted for age, gender, race and clinical center, smoking, diabetes, hypertension, previous cardiovascular disease, COPD, BMI, albumin, hemoglobin, LDL cholesterol, use of RAS blockers, diuretics, statins and beta-blockers, BNP, LVEF, LVH, eGFR and UACR

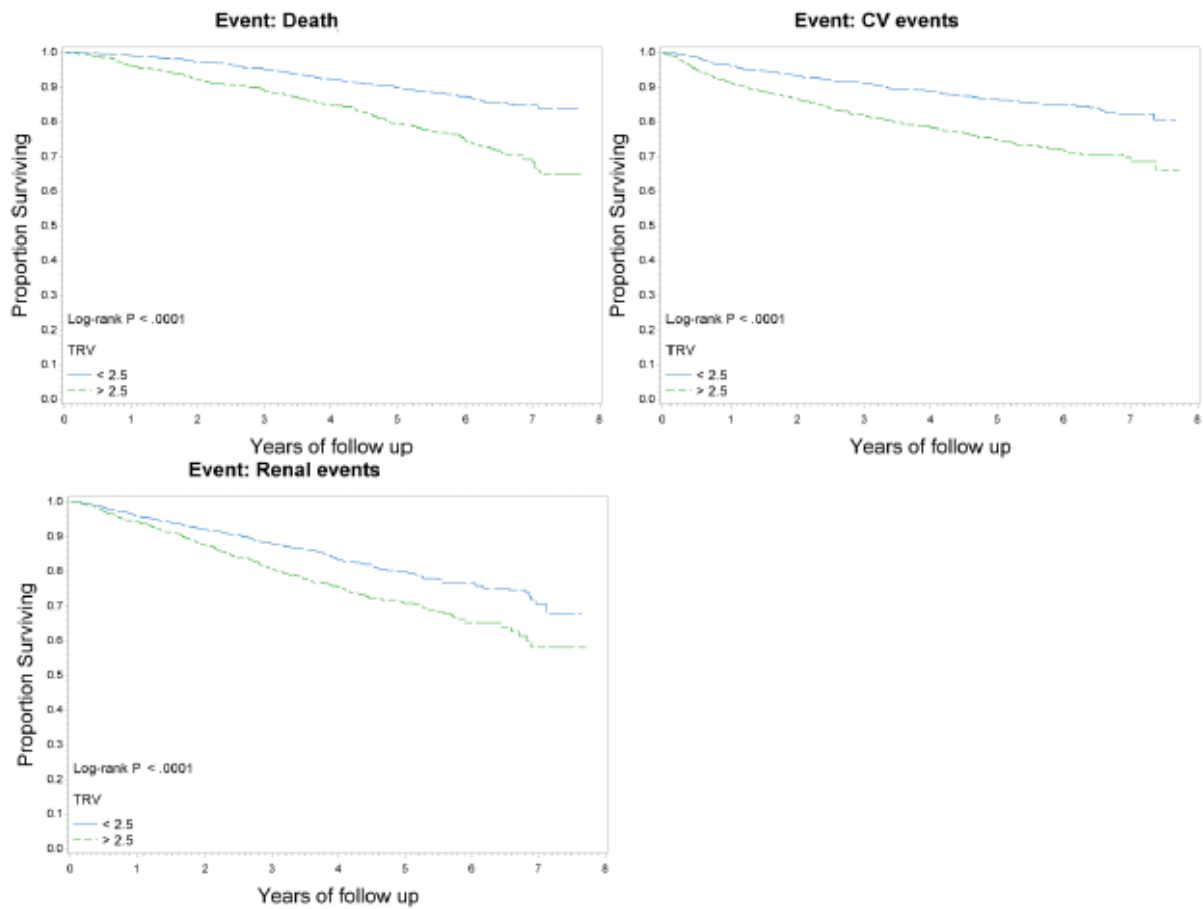


Figure S1- Kaplan Meier curve for mortality, CV events and renal events for those with TRV ≥ 2.5 vs. < 2.5 m/sec

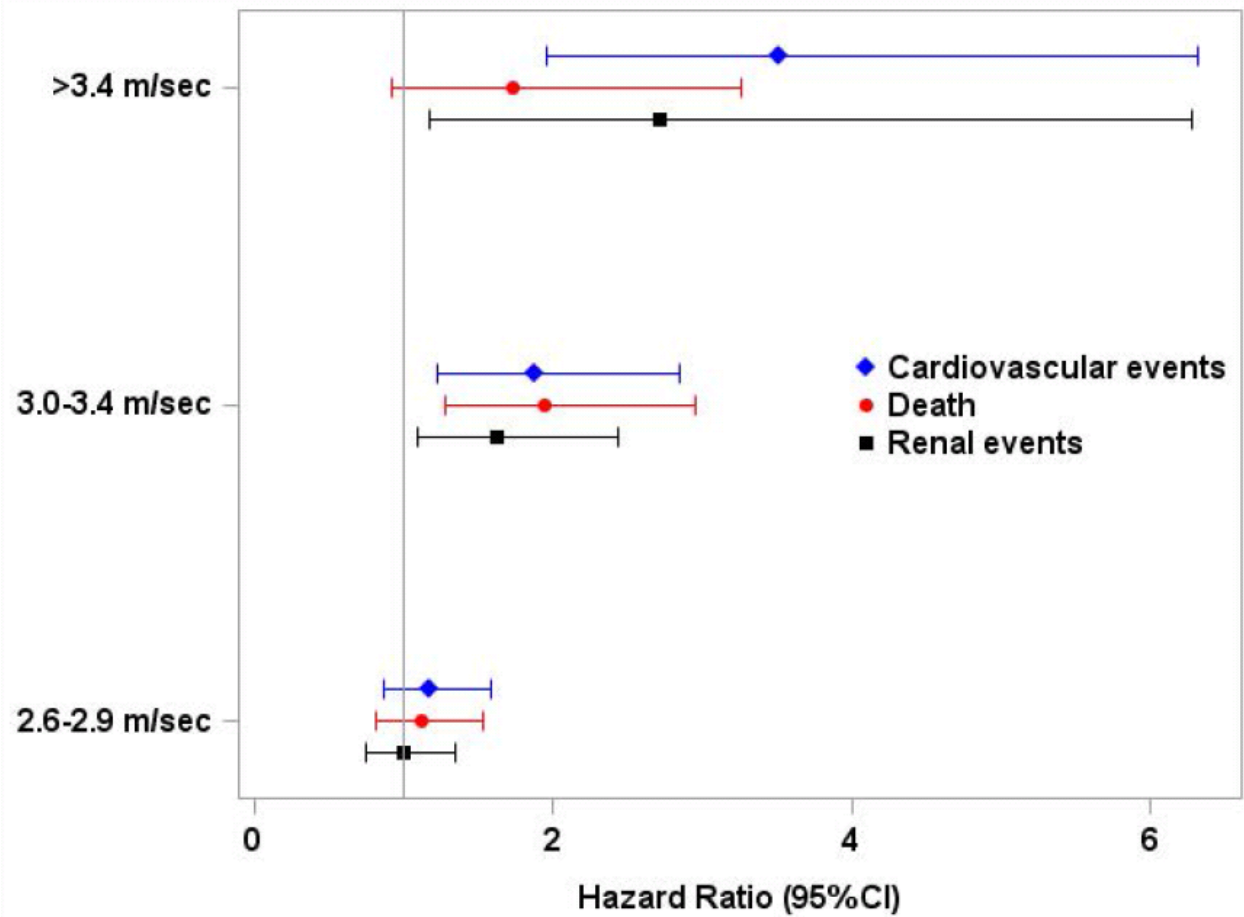


Figure S2. Associations between TRV categories and outcomes in CRIC cohort (compared to TRV <2.5 m/sec)

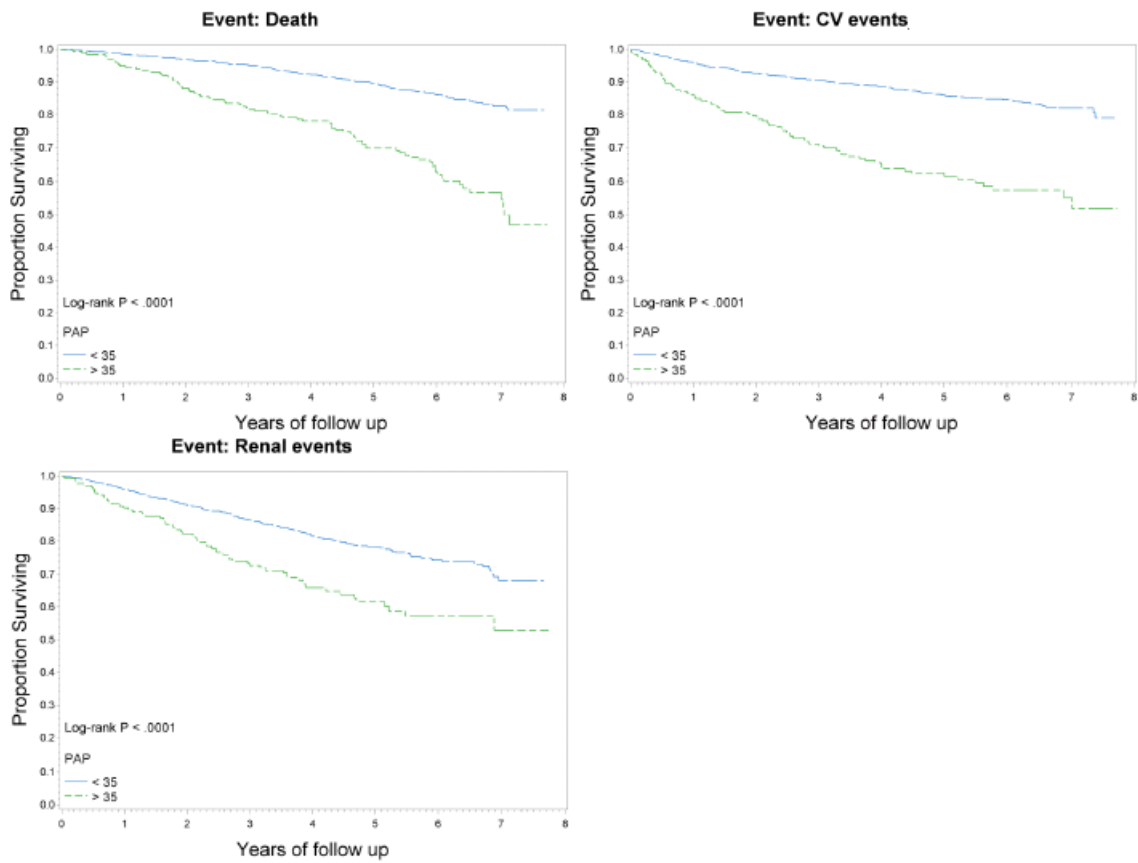


Figure S3. Kaplan Meier curve for mortality, CV events and renal events for those with PASP ≥ 35 mm Hg vs. < 35 mm Hg

Figure S4. Kaplan Meier curve for mortality, CV events and renal events for those with PH (Males).

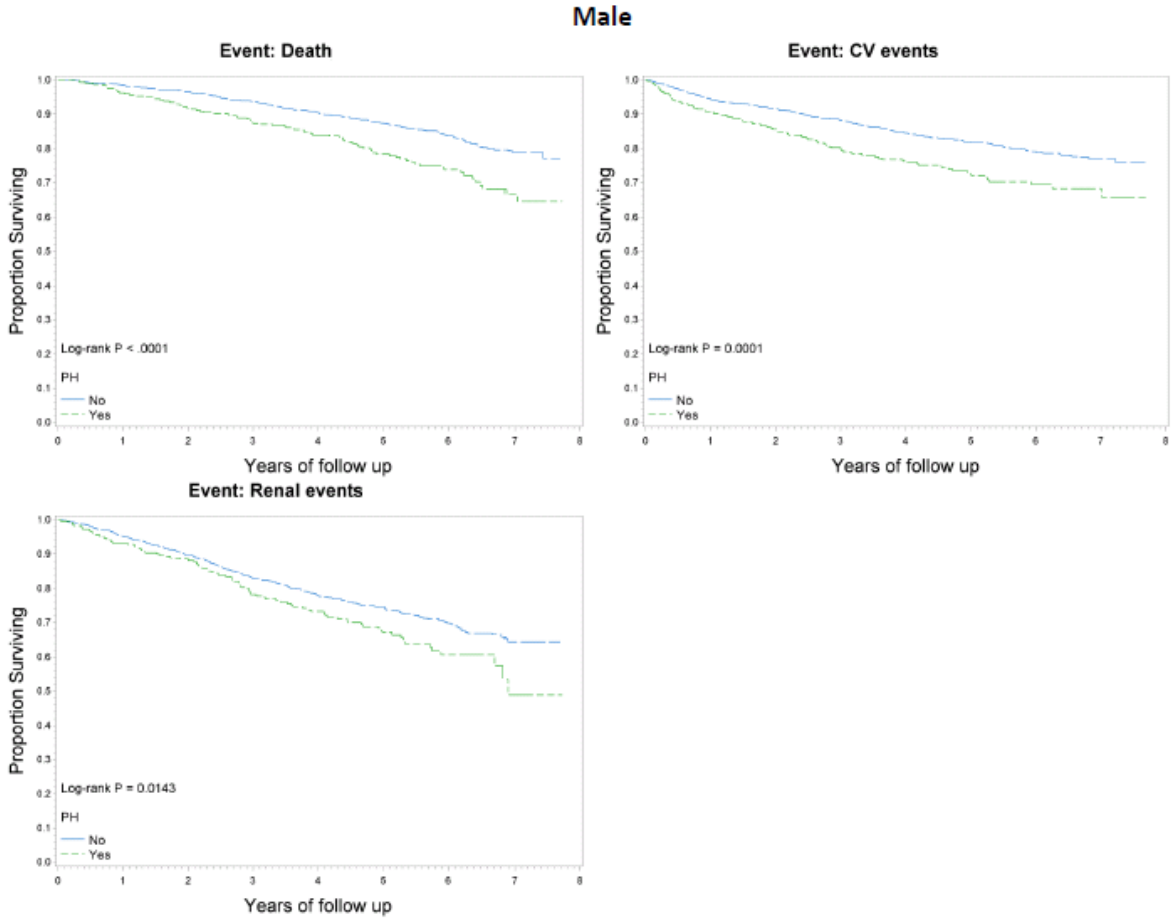
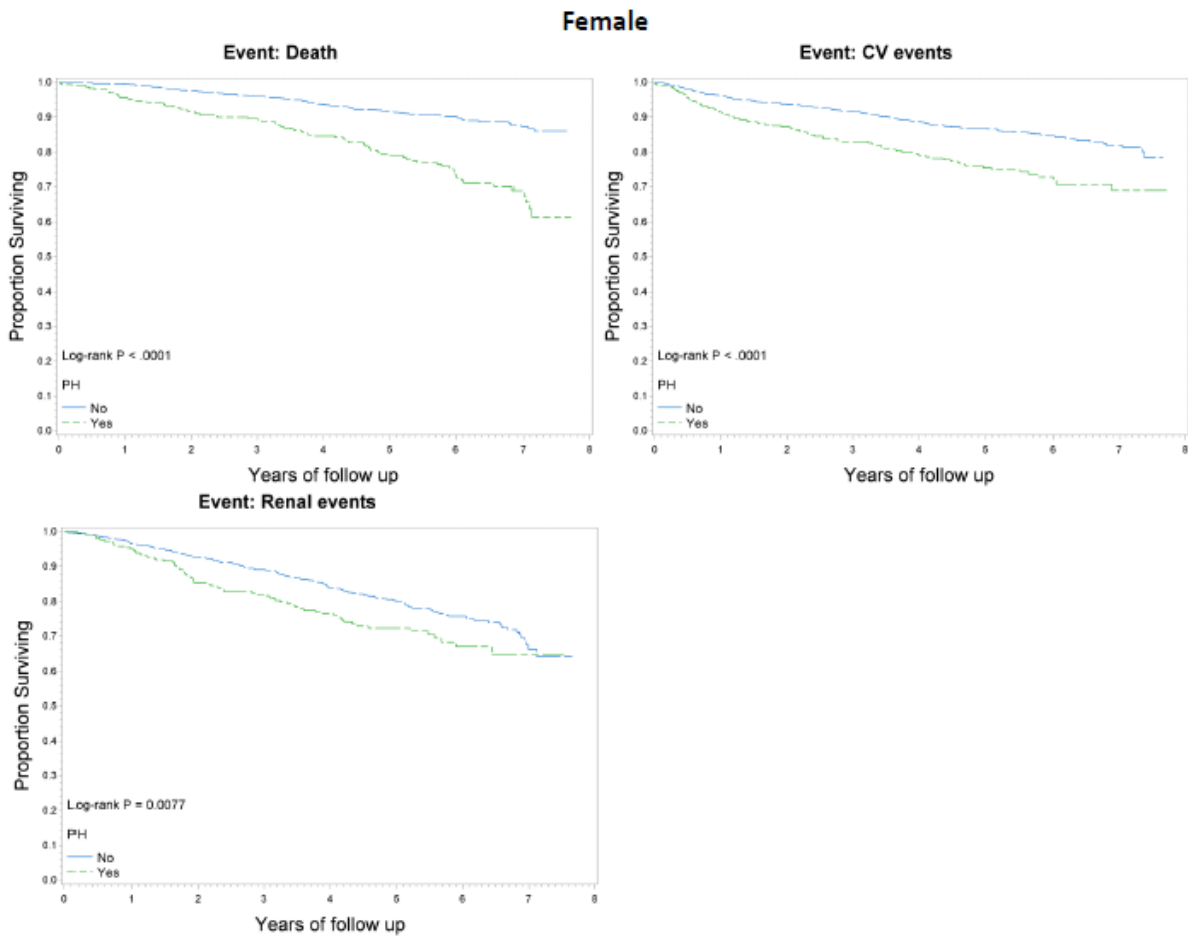


Figure S5. Kaplan Meier curve for mortality, CV events and renal events for those with PH (Females).



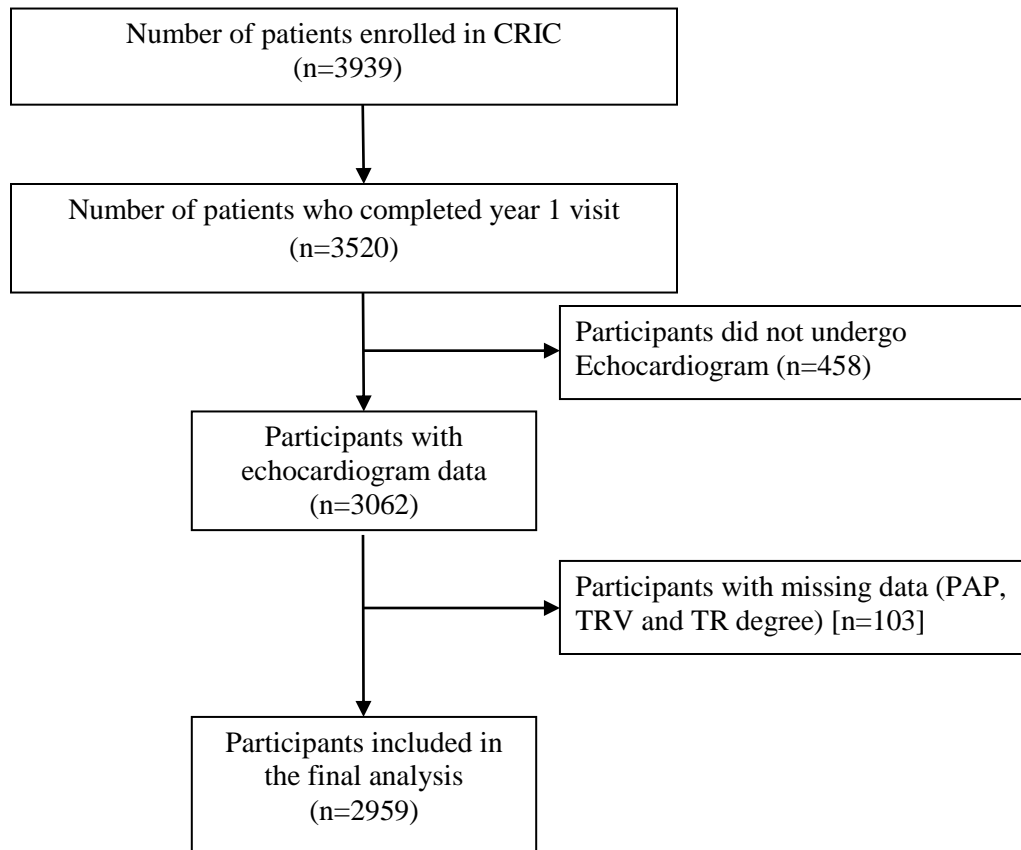


Figure S6. Flow chart describing how participants were selected for this analysis