

Supplemental Table 1. Characteristics of CKD patients included in this analysis

Variables	N	All (n=38,520)	Age<65 years (n=9019)	Age >65 years (n=29501)	Males (n=16818)	Females (n=21702)	White (N=33478)	Black (N=5042)
Age (years)		72.8±11.8	56.2±8.0	77.8±7.2	72.0±11.6	73.3±11.9	73.2±11.5	69.6±13.1
Male gender (n, %)		16818(43.7)	4191(46.5)	12627(42.8)	100%	0%	14824(44.3)	1994(39.5)
Blacks (n, %)		5042(13.1)	1639(18.2)	3403(11.5)	1994(11.9)	3048(14.0)	0%	100%
Diabetes (n, %)		8385(21.8)	2258(25.0)	6127(20.8)	3961(23.6)	4424(20.4)	6718(20.1)	1667(33.1)
Malignancy (n, %)		9100(23.6)	1861(20.6)	7239(24.5)	4697(27.9)	4403(20.3)	8143(24.3)	957(19.0)
Hypertension (n, %)		31742(82.4)	7274(80.7)	24468(82.9)	13891(82.6)	17851(82.3)	27422(81.9)	4320(85.7)
Hyperlipidemia (n, %)		29038(75.4)	6430(71.3)	22608(76.6)	12660(75.3)	16378(75.5)	25373(75.8)	3665(72.7)
Coronary artery disease (n, %)		7479(19.4)	1064(11.8)	6415(21.7)	4630(27.5)	2849(13.1)	6685(20.0)	794(15.7)
Congestive heart failure (n, %)		2812(7.3)	684(7.6)	2128(7.2)	1569(9.3)	1243(5.7)	2274(6.8)	538(10.7)
Body mass index (kg/m²)	36350	29.3±6.5	31.7±7.8	28.6±5.8	29.0±5.4	29.6±7.2	29.2±6.3	30.5±7.3
Stage of CKD								
3a (eGFR 45-59)		24639(64.0)	6039(67.0)	18600(63.0)	10796(64.2)	13843(63.8)	21707(64.8)	2932(58.2)
3b (eGFR 30-44)		10186(26.4)	2001(22.2)	8185(27.7)	4393(26.1)	5793(26.7)	8818(26.3)	1368(27.1)
4 (eGFR 15-29)		3149(8.2)	755(8.4)	2394(8.1)	1365(8.1)	1784(8.2)	2564(7.7)	585(11.6)
5 (eGFR<15)		546(1.4)	224(2.5)	322(1.1)	264(1.6)	282(1.3)	389(1.2)	157(3.1)
Outpatient visits per year, P50 [P25, P75]		5.2 [2.9, 9.0]	5.8 [3.0, 11.0]	5.1 [2.9, 8.5]	5.2 [2.9, 9.2]	5.3 [2.9, 8.8]	5.2 [2.9, 8.8]	5.7 [2.9, 9.7]
Serum albumin (g/dl)	31226	4.1±0.48	4.1±0.55	4.1±0.46	4.1±0.49	4.1±0.47	4.1±0.47	4.0±0.53
Hemoglobin (g/dl)	32262	12.8±1.8	12.8±2.0	12.8±1.7	13.2±1.9	12.6±1.6	12.9±1.8	12.1±1.8
ACEI/ARB use (n, %)		23620(61.3)	5350(59.3)	18270(61.9)	10907(64.9)	12713(58.6)	20096(60.0)	3524(69.9)
Statins use (n, %)		20984(54.5)	4424(49.1)	16560(56.1)	10072(59.9)	10912(50.3)	18229(54.5)	2755(54.6)
Beta-blocker use (n, %)		21198(55.0)	4505(50.0)	16693(56.6)	9908(58.9)	11290(52.0)	18223(54.4)	2975(59.0)
Insurance (n, %)								
Medicaid		258(0.67)	193(2.1)	65(0.22)	81(0.48)	177(0.82)	146(0.44)	112(2.2)
Medicare		31364(81.4)	4139(45.9)	27225(92.3)	13395(79.6)	17969(82.8)	27565(82.3)	3799(75.3)
Missing		1135(2.9)	553(6.1)	582(2.0)	520(3.1)	615(2.8)	842(2.5)	293(5.8)
Other		5763(15.0)	4134(45.8)	1629(5.5)	2822(16.8)	2941(13.6)	4925(14.7)	838(16.6)
Smoking Status (n, %)								
No		28705(74.5)	6280(69.6)	22425(76.0)	12377(73.6)	16328(75.2)	25113(75.0)	3592(71.2)
Yes		2586(6.7)	1039(11.5)	1547(5.2)	1287(7.7)	1299(6.0)	2054(6.1)	532(10.6)
Missing		7229(18.8)	1700(18.8)	5529(18.7)	3154(18.8)	4075(18.8)	6311(18.9)	918(18.2)

Values presented as mean ± SD or N (%) unless otherwise noted

Supplemental table 2. Unadjusted all-cause mortality rates among various subgroups

	All-cause mortality (per 1,000 years of follow up)
Age>65 years	83.3
Age<65 years	51.5
Males	90.6
Females	65.5
Whites	74.8
Blacks	84.6
Diabetics	69.2
Non-Diabetics	78.0
Stage 3a CKD	60.0
Stage 3b CKD	90.8
Stage 4 and 5 CKD	146.0

Supplemental table 3. Deaths related to specific types of malignancy

Types of malignancy	N (%) Total N = 2117
Malignant neoplasms of trachea, bronchus and lung	371 (17.5)
Malignant neoplasms of colon, rectum and anus	173 (8.2)
Leukemia	168 (7.9)
Malignant neoplasm of prostate	164 (7.8)*
Malignant neoplasm of breast	149 (7.0)*
Malignant neoplasms of kidney and renal pelvis	146 (6.9)
Malignant neoplasm of bladder	120 (5.7)
Multiple myeloma and immunoproliferative neoplasms	107 (5.1)
Non-Hodgkin's lymphoma	102 (4.8)
Malignant neoplasm of pancreas	81 (3.8)
Malignant neoplasm of ovary	72 (3.4)*
Malignant neoplasms of liver and intrahepatic bile ducts	56 (2.7)
Malignant neoplasm of esophagus	44 (2.1)
Malignant neoplasms of corpus uteri and uterus, part unspecified	35 (1.7)
Malignant neoplasms of meninges, brain and other parts of central nervous system	27 (1.3)
Malignant melanoma of skin	23 (1.1)
Malignant neoplasm of stomach	23 (1.1)
Malignant neoplasms of lip, oral cavity and pharynx	19 (0.9)
Malignant neoplasm of cervix uteri	12 (0.6)
Malignant neoplasm of larynx	7 (0.3)
Hodgkin's disease	5 (0.2)
Other and unspecified malignant neoplasms of lymphoid, hematopoietic and related tissue	1 (0.1)
All other and unspecified malignant neoplasms	212 (10.0)

*Prostate 14.5% among males, breast and ovary 15% and 7.3% respectively among females

Supplemental table 4. Associations between the covariates and various causes of mortality

	All-cause	Cardiovascular	Malignancy	Other
Blacks	1.04 (0.97, 1.12)	1.20 (1.06, 1.35)	0.89 (0.77, 1.02)	1.12 (0.99, 1.26)
Male gender	1.48 (1.41, 1.56)	1.56 (1.43, 1.71)	1.51 (1.38, 1.65)	1.39 (1.27, 1.53)
Diabetes	1.03 (0.96, 1.10)	1.01 (0.90, 1.13)	0.80 (0.70, 0.92)	1.36 (1.21, 1.53)
CKD stage				
eGFR 30-44	1.21 (1.14, 1.27)	1.35 (1.23, 1.48)	1.03 (0.93, 1.14)	1.29 (1.17, 1.42)
eGFR <30	1.58 (1.46, 1.70)	1.85 (1.64, 2.09)	1.00 (0.86, 1.16)	1.93 (1.71, 2.18)
Hypertension	0.87 (0.81, 0.94)	0.64 (0.57, 0.72)	0.93 (0.82, 1.05)	0.96 (0.85, 1.09)
Hyperlipidemia	0.73 (0.68, 0.79)	0.85 (0.75, 0.96)	0.69 (0.60, 0.78)	0.75 (0.66, 0.85)
BMI (kg/m ²)				
<18.5	1.72 (1.47, 2.01)	1.64 (1.18, 2.29)	1.58 (1.15, 2.17)	1.95 (1.54, 2.47)
25-29	0.74 (0.69, 0.79)	0.78 (0.70, 0.87)	0.69 (0.62, 0.77)	0.75 (0.66, 0.85)
>30	0.71 (0.66, 0.76)	0.76 (0.66, 0.88)	0.65 (0.57, 0.73)	0.79 (0.70, 0.88)
Malignancy	1.97 (1.87, 2.08)	0.82 (0.74, 0.92)	7.39 (6.70, 8.16)	0.92 (0.82, 1.03)
Coronary Artery Disease	1.01 (0.94, 1.08)	1.26 (1.13, 1.40)	0.75 (0.65, 0.86)	1.03 (0.91, 1.16)
Congestive Heart Failure	1.98 (1.84, 2.14)	2.98 (2.67, 3.32)	1.11 (0.92, 1.35)	1.57 (1.36, 1.81)
Insurance				
Medicare vs. other	0.75 (0.69, 0.82)	0.98 (0.83, 1.16)	0.60 (0.53, 0.69)	0.80 (0.68, 0.94)
Medicaid vs. other	2.14 (1.75, 2.60)	3.09 (2.16, 4.44)	1.59 (1.10, 2.30)	2.39 (1.73, 3.30)
ACEI/ARB use	0.94 (0.88, 0.99)	1.23 (1.11, 1.37)	0.77 (0.70, 0.85)	0.93 (0.83, 1.03)
Statins use	1.06 (0.99, 1.15)	1.02 (0.90, 1.15)	1.14 (1.00, 1.31)	0.99 (0.87, 1.13)
Beta-blocker use	1.22 (1.15, 1.29)	1.35 (1.22, 1.50)	1.14 (1.04, 1.25)	1.17 (1.06, 1.29)
Smoker	1.20 (1.09, 1.33)	1.30 (1.10, 1.54)	1.22 (1.02, 1.47)	1.15 (0.97, 1.37)
Age	*	*	*	*
Albumin	*	*	*	*
Hemoglobin	*	*	*	*

*Variable was modeled with splines and overall hazard ratio cannot be estimated.

Supplemental table 5. Associations between various causes of death based on eGFR for whom proteinuria data was available (N=18,347)

	HR (95%CI) adjusted*
<i>CKD Stage 3b vs. Stage 3a</i>	
All-cause mortality [#]	1.14 (1.06, 1.23)
Deaths due to malignancy	1.0 (0.87, 1.15)
Deaths due to cardiovascular disease	1.18 (1.04, 1.34)
Non-cardiovascular and non-malignancy deaths [^]	1.27 (1.11, 1.45)
<i>CKD Stage 4 and 5 vs. Stage 3a</i>	
All-cause mortality [#]	1.42 (1.28, 1.56)
Deaths due to malignancy	0.91 (0.74, 1.11)
Deaths due to cardiovascular disease	1.55 (1.32, 1.83)
Non-cardiovascular and non-malignancy deaths [^]	1.82 (1.54, 2.14)

*Model includes age, race gender, diabetes, HTN, hyperlipidemia, BMI group, albumin and hemoglobin, malignancy, CAD, CHF, insurance, ACE/ARB, statin, beta blocker, smoking, and proteinuria. HR shown were pooled using MIanalyze from 5 datasets created using multiple imputations. Each of the 5 datasets contained 18,347 patients with proteinuria data. # Includes all deaths related to non-disease causes.

[^] This does not include non-disease cause related deaths

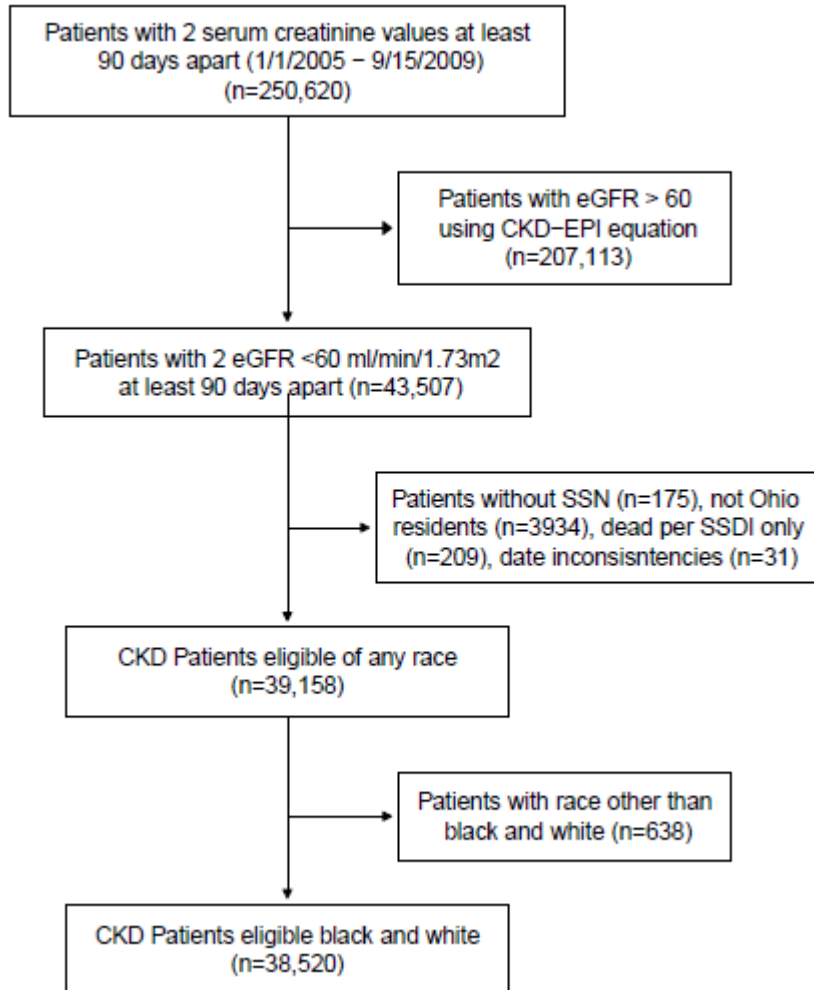
Supplemental Table 6. Associations of cardiovascular and malignancy-related death and kidney disease (excluding the presence of baselinedisease from model)

	HR (95%CI) adjusted
<i>CKD Stage 3b vs. Stage 3a</i>	
Deaths due to malignancy*	0.93 (0.84, 1.03)
Deaths due to cardiovascular disease**	1.39 (1.27, 1.53)
<i>CKD Stage 4 and 5 vs. Stage 3a</i>	
Deaths due to malignancy*	0.85 (0.74, 0.99)
Deaths due to cardiovascular disease**	1.95 (1.73, 2.19)

*Model includes age, race gender, diabetes, HTN, hyperlipidemia, BMI group, albumin and hemoglobin, CAD, CHF, insurance, ACE/ARB, statin, beta blocker, smoking, and proteinuria.

**Model includes age, race gender, diabetes, HTN, hyperlipidemia, BMI group, albumin and hemoglobin, malignancy, insurance, ACE/ARB, statin, beta blocker, smoking, and proteinuria.

HR shown were pooled using MIanalyze from 5 datasets created using multiple imputations.



Supplemental figure 1. Flow-chart showing how patients were selected for this analysis

Methods:

Sensitivity analyses

- a) We fit a model adjusting for proteinuria among the subset of patients with proteinuria data (n=18,347).
- b) To evaluate the association between CKD stage and cardiovascular disease irrespective of the presence of baseline coronary artery disease and heart failure, we also fit an adjusted model of cardiovascular mortality excluding from the model variables for coronary artery disease and heart failure. Similarly we evaluated the association between CKD stage and malignancy mortality in an adjusted model excluding baseline malignancy.
- c) To evaluate the impact of multiple imputation on the analysis results, we compared all-cause mortality models using multiple imputation, models using only complete case data, and models using mean value imputation with indicators of missing data.

Results

Sensitivity analyses

- a) In a subgroup of patients who had at least one urinary protein study (n=18,347, 48%), the risk for death and specific causes of death was similar to the primary analysis, with only slight attenuation of the associations (Supplemental Table 5).
- b) The model for cardiovascular mortality excluding from the model variables for coronary artery disease and heart failure showed a similar association between CKD stage and mortality as the primary model (Supplemental table 6). The model for malignancy mortality excluding baseline malignancy, showed no significant differences between stage 3a and 3b, but significantly lower mortality for stages 4 and 5 compared to stage 3a.

- c) Results from all-cause mortality models using multiple imputation, complete case data, and mean value imputation with missing data indicators were compared (data not shown).