Supplemental Materials

Supplemental Figure 1. Cumulative incidence of all-cause mortality according to annually-updated tobacco smoking, alcohol drinking, marijuana use, and hard illicit drug use

Supplemental Table 1. Characteristics of 3939 patients with CKD according to CKD progression and all-cause mortality (the CRIC Study)
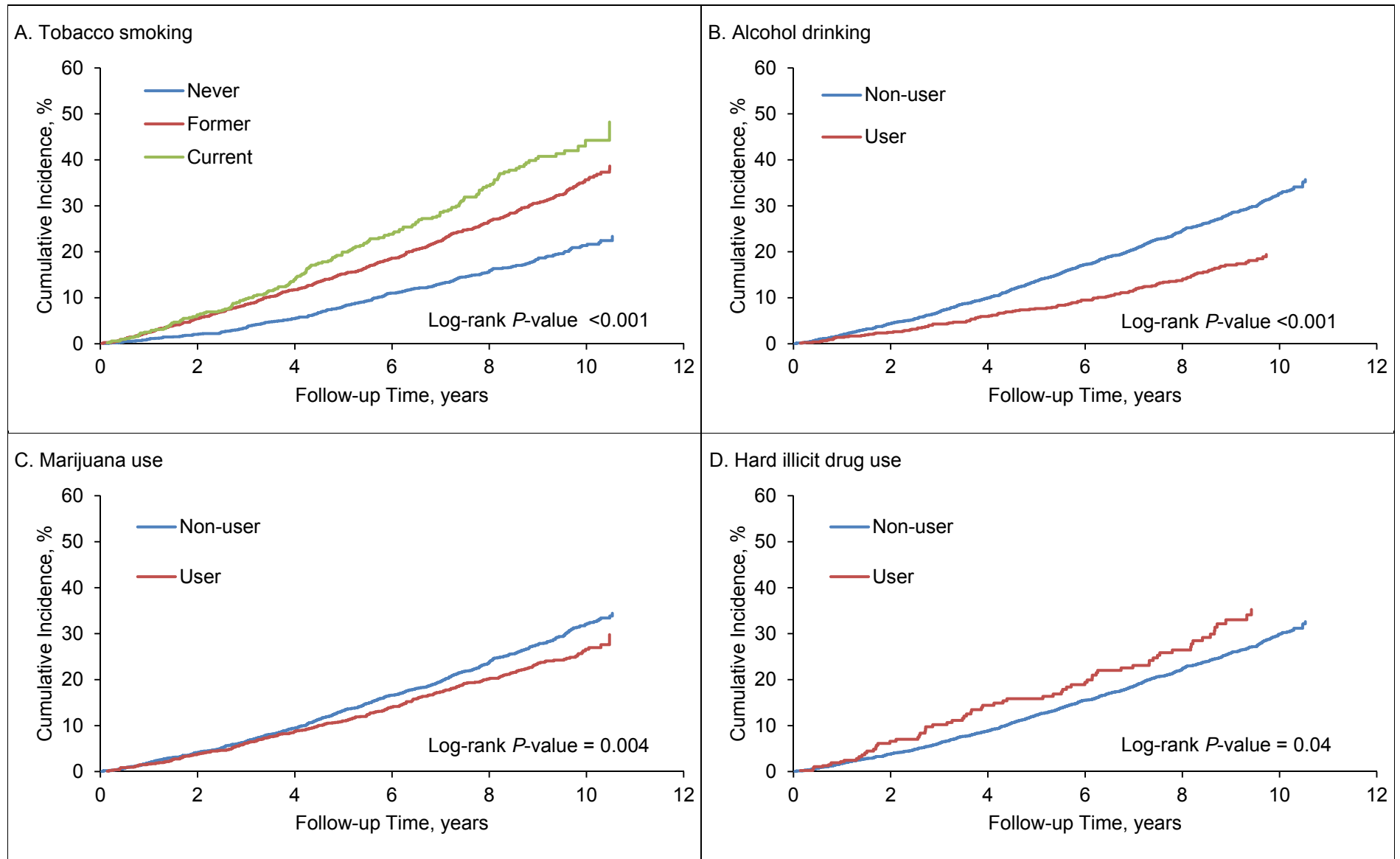
Supplemental Table 2. Number of events, incidence, and hazard ratios and 95% confidence intervals of CKD progression and all-cause mortality associated with baseline tobacco smoking, alcohol drinking, marijuana use, and hard illicit drug use among 3939 patients with CKD

Supplemental Table 3. Hazard ratios and 95% confidence intervals of CKD progression and all-cause mortality associated with annually-updated tobacco smoking, alcohol drinking, marijuana use, and hard illicit drug use among 3939 patients with CKD

Supplemental Table 4. Hazard ratios and 95% confidence intervals of all-cause mortality associated with cumulative average tobacco smoking, alcohol drinking, marijuana use, and hard illicit drug use by subgroups

Supplemental Table 5. Hazard ratios and 95% confidence intervals of CKD progression or all-cause mortality associated with cumulative average tobacco smoking, alcohol drinking, marijuana use, and hard illicit drug use by subgroups

Supplemental Figure 1. Cumulative incidence of all-cause mortality according to annually-updated tobacco smoking, alcohol drinking, marijuana use, and hard illicit drug use

Panel A Cumulative incidence of all-cause mortality among never, former, and current tobacco smokers. Panel B Cumulative incidence of all-cause mortality for alcohol drinkers and non-drinkers. Panel C Cumulative incidence of all-cause mortality among marijuana users and non-users. Panel D Cumulative incidence of all-cause mortality among hard illicit drug users and non-users. CKD, chronic kidney disease

Supplemental Table 1. Characteristics of 3939 patients with CKD according to CKD progression and all-cause mortality (the CRIC Study)

Variable	CKD progression		All-cause Mortality	
	No Progression (n=2652)	**Progression (n=1287)**	**No Death (n=2938)**	**Death (n=1001)**
Age, mean ± SD, years	59 ± 11	56 ± 12	56 ± 11	62 ± 9
Female, no. (%)	1243 (47)	535 (42)	1398 (48)	380 (38)
Race/ethnicity, no. (%)				
Non-Hispanic white	1279 (48)	359 (28)	1270 (43)	368 (37)
Non-Hispanic black	1019 (38)	631 (49)	1167 (40)	483 (48)
Hispanic	253 (10)	244 (19)	376 (13)	121 (12)
Other	101 (4)	53 (4)	125 (4)	29 (3)
High school graduate, no. (%)	2175 (82)	935 (73)	2396 (82)	714 (71)
Physical activity, mean ± SD, METs/wk	200 (140)	194 (156)	209 (149)	167 (131)
Former tobacco smoking, no. (%)	1117 (48)	524 (48)	1155 (44)	486 (60)
Current tobacco smoking, no. (%)	316 (21)	201 (26)	320 (18)	197 (38)
Alcohol drinking, no. (%) [a]	600 (23)	193 (15)	635 (22)	158 (16)
Marijuana use, no. (%) [b]	882 (33)	411 (32)	1001 (34)	292 (29)
Hard illicit drug use, no. (%) [b,c]	324 (12)	150 (12)	356 (12)	118 (12)
Body mass index, mean ± SD, kg/m^2	32 ± 8	32 ± 8	32 ± 8	32 ± 8
History of CVD, no. (%)	821 (31)	495 (39)	756 (26)	560 (56)
Hypertension, no. (%)	2195 (83)	1196 (93)	2459 (84)	932 (93)
Diabetes, no. (%)	1076 (41)	832 (65)	1270 (43)	638 (64)
Antihypertensive medication, no. (%)	2363 (90)	1229 (96)	2621 (90)	971 (98)

NSAIDs, no. (%)	1416 (54)	598 (47)	1466 (50)	548 (55)
Systolic BP, mean ± SD, mm Hg	124 ± 21	137 ± 23	127 ± 21	134 ± 24
Diastolic BP, mean ± SD, mm Hg	70 ± 12	74 ± 13	72 ± 13	71 ± 14
LDL cholesterol, mean ± SD, mg/dL	102 ± 34	103 ± 39	104 ± 35	100 ± 37
HDL cholesterol, mean ± SD, mg/dL	48 ± 16	46 ± 15	48 ± 15	46 ± 16
Hemoglobin, mean ± SD, g/dL	12.9 (1.7)	12.0 (1.8)	12.7 (1.8)	12.2 (1.8)
eGFR, mean ± SD, ml/min/1.73 m^2	49 ± 17	36 ± 13	48 ± 17	37 ± 13
Urinary protein, median (IQR), g/24 h	0.1 (0.1, 0.3)	1.2 (0.4, 3.1)	0.2 (0.1, 0.7)	0.4 (0.1, 1.8)

BP, blood pressure; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein; NSAIDs, non-steroidal anti-inflammatory drugs; SD, standard deviation

[a] Participants were classified as users of alcohol if they reported having one or more alcoholic drinks per week

[b] Participants were classified as users of marijuana and hard illicit drugs if they reported any lifetime history of use

[c] Hard illicit drug use is defined as self-reported use of cocaine, heroin, or methamphetamine

Supplemental Table 2. Number of events, incidence, and hazard ratios of CKD progression and all-cause mortality according to baseline tobacco smoking, alcohol drinking, marijuana use, and illicit drug use among 3939 patients with CKD

Variable	Number of events, user vs. non-user	Incidence per 1000 PYs, user vs. non-user	Univariable		Age, sex, race/ethnicity, and clinical site adjusted		Multivariable adjusted	
			HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
CKD progression								
Former tobacco smoking	524 vs. 562	60.2 vs. 55.9	1.08 (0.96-1.22)	0.21	1.17 (1.03-1.32)	0.01	1.00 (0.88-1.14)	0.95
Current tobacco smoking	201 vs. 562	86.9 vs. 55.9	1.57 (1.33-1.84)	<0.001	1.36 (1.15-1.61)	<0.001	1.15 (0.97-1.37)	0.12
Alcohol drinking	193 vs. 1094	41.0 vs. 66.8	0.61 (0.52-0.71)	<0.001	0.75 (0.64-0.88)	<0.001	0.99 (0.84-1.17)	0.91
Marijuana use	411 vs. 876	58.1 vs. 62.5	0.93 (0.83-1.05)	0.23	0.92 (0.81-1.04)	0.17	0.90 (0.79-1.03)	0.12
Hard illicit drug use	150 vs. 1137	59.9 vs. 61.2	0.98 (0.83-1.16)	0.82	0.91 (0.77-1.09)	0.30	0.94 (0.79-1.13)	0.54
Cocaine use	129 vs. 1158	56.3 vs. 61.6	0.91 (0.76-1.10)	0.33	0.82 (0.68-0.99)	0.04	0.85 (0.70-1.03)	0.09
Heroin use	28 vs. 1259	136.6 vs. 60.3	2.32 (1.60-3.38)	<0.001	1.69 (1.16-2.46)	0.007	1.47 (0.99-2.19)	0.06
Methamphetamine use	47 vs. 1240	63.2 vs. 61.0	1.04 (0.78-1.39)	0.81	1.27 (0.94-1.70)	0.12	1.22 (0.90-1.65)	0.20
All-cause mortality								
Former tobacco smoking	486 vs. 318	39.3 vs. 22.2	1.80 (1.56-2.07)	<0.001	1.46 (1.27-1.69)	<0.001	1.38 (1.18-1.60)	<0.001
Current tobacco smoking	197 vs. 318	53.7 vs. 22.2	2.49 (2.08-2.97)	<0.001	2.32 (1.93-2.79)	<0.001	2.09 (1.72-2.55)	<0.001
Alcohol drinking	158 vs. 843	24.9 vs. 35.1	0.70 (0.59-0.83)	<0.001	0.78 (0.65-0.93)	0.005	0.91 (0.76-1.10)	0.34
Marijuana use	292 vs. 709	28.8 vs. 35.1	0.81 (0.71-0.93)	0.003	1.10 (0.95-1.27)	0.21	1.06 (0.91-1.24)	0.45
Hard illicit drug use	118 vs. 883	32.7 vs. 33.0	0.99 (0.82-1.20)	0.94	1.35 (1.11-1.66)	0.003	1.24 (1.00-1.53)	0.049
Cocaine use	99 vs. 902	30.2 vs. 33.3	0.91 (0.74-1.12)	0.36	1.26 (1.02-1.57)	0.04	1.24 (0.98-1.56)	0.07
Heroin use	25 vs. 976	68.6 vs. 32.5	2.18 (1.47-3.24)	<0.001	2.08 (1.39-3.12)	<0.001	1.40 (0.91-2.16)	0.12

Methamphetamine use	36 vs. 965	32.5 vs. 33.0	0.99 (0.71-1.38)	0.94	1.36 (0.97-1.90)	0.08	1.20 (0.85-1.69)	0.31
CKD progression or all-cause mortality								
Former tobacco smoking	804 vs. 748	88.1 vs. 72.3	1.22 (1.11-1.35)	<0.001	1.22 (1.10-1.35)	<0.001	1.09 (0.98-1.22)	0.10
Current tobacco smoking	304 vs. 804	124.6 vs. 72.3	1.76 (1.54-2.01)	<0.001	1.56 (1.36-1.79)	<0.001	1.33 (1.15-1.54)	<0.001
Alcohol drinking	296 vs. 1560	61.1 vs. 91.4	0.66 (0.59-0.75)	<0.001	0.79 (0.70-0.90)	<0.001	1.02 (0.89-1.17)	0.79
Marijuana use	573 vs. 1283	78.4 vs. 87.8	0.89 (0.81-0.98)	0.02	0.94 (0.85-1.05)	0.28	0.92 (0.82-1.03)	0.14
Hard illicit drug use	213 vs. 1643	82.2 vs. 85.0	0.97 (0.84-1.12)	0.67	0.99 (0.85-1.14)	0.85	0.96 (0.82-1.12)	0.58
Cocaine use	183 vs. 1673	77.2 vs. 85.6	0.90 (0.77-1.05)	0.18	0.89 (0.76-1.05)	0.17	0.87 (0.74-1.03)	0.11
Heroin use	36 vs. 1820	166.3 vs. 83.9	2.05 (1.48-2.86)	<0.001	1.63 (1.17-2.27)	0.004	1.23 (0.86-1.76)	0.25
Methamphetamine use	66 vs. 1790	86.1 vs. 84.6	1.02 (0.80-1.30)	0.88	1.26 (0.99-1.62)	0.06	1.22 (0.95-1.57)	0.13

Hazard ratios compare former and current tobacco smoking with never smoking, alcohol drinking with non-drinking, marijuana use with no marijuana use, and hard illicit drug use (use of cocaine, heroin, or methamphetamine) with no hard illicit drug use. Multivariable-adjusted: adjusted for age, sex, race/ethnicity, clinical site, education, estimated glomerular filtration rate, proteinuria, history of diabetes, body mass index, systolic blood pressure, hemoglobin, use of non-steroidal anti-inflammatory drugs; current tobacco smoking was additionally adjusted in models of weekly alcohol drinking, marijuana use, and hard illicit drug use. CI, confidence interval; CKD, chronic kidney disease; HR, hazard ratio.

Supplemental Table 3. Hazard ratios and 95% confidence intervals of CKD progression and all-cause mortality associated with annually-updated tobacco smoking, alcohol drinking, marijuana use, and hard illicit drug use among 3939 patients with CKD

Variable	Univariable		Age, sex, race/ethnicity, and clinical site adjusted		Multivariable adjusted	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
CKD progression						
Former tobacco smoking	1.11 (0.99-1.25)	0.08	1.20 (1.06-1.36)	0.003	1.05 (0.93-1.20)	0.41
Current tobacco smoking	1.49 (1.26-1.76)	<0.001	1.29 (1.08-1.53)	0.004	1.02 (0.86-1.23)	0.79
Alcohol drinking	0.51 (0.44-0.61)	<0.001	0.63 (0.53-0.75)	<0.001	1.03 (0.86-1.22)	0.76
Marijuana use	0.93 (0.83-1.05)	0.24	0.92 (0.81-1.04)	0.18	0.94 (0.83-1.07)	0.36
Hard illicit drug use	1.32 (1.07-1.63)	0.01	1.34 (1.08-1.65)	0.008	1.30 (1.04-1.62)	0.02
Cocaine use	1.29 (0.91-1.83)	0.15	1.15 (0.81-1.63)	0.44	1.43 (0.99-2.07)	0.06
Heroin use	2.45 (1.71-3.49)	<0.001	1.79 (1.25-2.56)	0.002	1.59 (1.10-2.31)	0.01
Methamphetamine use	1.06 (0.80-1.41)	0.68	1.28 (0.96-1.70)	0.10	1.12 (0.83-1.50)	0.47
All-cause mortality						
Former tobacco smoking	1.82 (1.59-2.10)	<0.001	1.50 (1.30-1.73)	<0.001	1.41 (1.21-1.63)	<0.001
Current tobacco smoking	2.48 (2.05-2.98)	<0.001	2.31 (1.91-2.80)	<0.001	2.15 (1.76-2.64)	<0.001
Alcohol drinking	0.56 (0.46-0.67)	<0.001	0.64 (0.53-0.78)	<0.001	0.79 (0.64-0.96)	0.02

Marijuana use	0.81 (0.71-0.93)	0.003	1.11 (0.96-1.28)	0.16	1.12 (0.96-1.30)	0.15
Hard illicit drug use	1.30 (1.03-1.65)	0.03	1.64 (1.29-2.09)	<0.001	1.35 (1.05-1.73)	0.02
Cocaine use	1.43 (0.97-2.09)	0.07	1.90 (1.29-2.81)	0.001	1.76 (1.17-2.66)	0.007
Heroin use	2.23 (1.52-3.27)	<0.001	2.11 (1.43-3.12)	<0.001	1.45 (0.97-2.15)	0.07
Methamphetamine use	1.05 (0.76-1.45)	0.76	1.43 (1.03-1.97)	0.03	1.26 (0.91-1.75)	0.17
CKD progression or all-cause mortality						
Former tobacco smoking	1.25 (1.13-1.38)	<0.001	1.24 (1.12-1.38)	<0.001	1.11 (1.00-1.24)	0.048
Current tobacco smoking	1.69 (1.47-1.94)	<0.001	1.49 (1.29-1.72)	<0.001	1.19 (1.03-1.39)	0.02
Alcohol drinking	0.56 (0.49-0.64)	<0.001	0.67 (0.59-0.77)	<0.001	0.98 (0.85-1.13)	0.78
Marijuana use	0.89 (0.81-0.98)	0.02	0.94 (0.85-1.05)	0.29	0.97 (0.87-1.08)	0.58
Hard illicit drug use	1.30 (1.09-1.55)	0.003	1.38 (1.15-1.65)	<0.001	1.28 (1.07-1.54)	0.008
Cocaine use	1.40 (1.07-1.84)	0.02	1.35 (1.02-1.77)	0.03	1.47 (1.10-1.97)	0.009
Heroin use	2.17 (1.59-2.97)	<0.001	1.72 (1.26-2.37)	0.001	1.40 (1.02-1.94)	0.04
Methamphetamine use	1.05 (0.82-1.33)	0.71	1.28 (1.00-1.63)	0.05	1.16 (0.90-1.48)	0.25

Hazard ratios compare former and current tobacco smoking with never smoking, alcohol drinking with non-drinking, marijuana use with no marijuana use, and hard illicit drug use (use of cocaine, heroin, or methamphetamine) with no hard illicit drug use. Multivariable-adjusted: adjusted for age, sex, race/ethnicity, clinical site, education, estimated glomerular filtration rate, proteinuria, history of diabetes, body mass index, systolic blood pressure, hemoglobin, use of non-steroidal anti-inflammatory drugs; current tobacco smoking was additionally adjusted in models of weekly alcohol drinking, marijuana use, and hard illicit drug use. CI, confidence interval; CKD, chronic kidney disease; HR, hazard ratio.

Supplemental Table 4. Hazard ratios and 95% confidence intervals of all-cause mortality associated with cumulative average tobacco smoking, alcohol drinking, marijuana use, and hard illicit drug use by subgroups

Subgroups	HR (95% CI)	*P* Value	*P* Value for Interaction	HR (95% CI)	*P* Value	*P* Value for Interaction
	Tobacco Smoking			**Alcohol Drinking**		
Sex						
Men	1.96 (1.56-2.46)	<0.001	0.45	0.74 (0.58-0.95)	0.02	0.71
Women	1.70 (1.25-2.30)	0.001		0.67 (0.42-1.08)	0.10	
Race						
White	2.32 (1.70-3.18)	<0.001	0.15	0.69 (0.51-0.92)	0.01	0.53
Non-white	1.76 (1.41-2.19)	<0.001		0.79 (0.56-1.11)	0.18	
Age						
Age <65 years	1.97 (1.58-2.45)	<0.001	0.40	0.69 (0.51-0.93)	0.02	0.58
Age ≥65 years	1.66 (1.18-2.33)	0.004		0.78 (0.56-1.08)	0.13	
Baseline eGFR						
eGFR <45	1.68 (1.36-2.08)	<0.001	0.08	0.66 (0.50-0.87)	0.004	0.22
eGFR ≥45	2.45 (1.69-3.54)	<0.001		0.87 (0.61-1.25)	0.46	
	Marijuana Use			**Hard Illicit Drug Use**		
Sex						
Men	1.06 (0.89-1.27)	0.49	0.35	1.29 (0.97-1.72)	0.09	0.17
Women	1.23 (0.95-1.58)	0.11		1.88 (1.18-2.98)	0.007	
Race						
White	1.03 (0.81-1.31)	0.83	0.32	1.17 (0.77-1.78)	0.45	0.23
Non-white	1.19 (0.99-1.43)	0.06		1.60 (1.19-2.17)	0.002	

Age						
Age <65 years	1.20 (1.00-1.43)	0.05	0.19	1.47 (1.12-1.92)	0.006	0.66
Age ≥65 years	0.96 (0.73-1.27)	0.79		1.26 (0.67-2.36)	0.48	
Baseline eGFR						
eGFR <45	1.09 (0.92-1.30)	0.32	0.67	1.42 (1.07-1.88)	0.01	0.93
eGFR ≥45	1.17 (0.88-1.55)	0.28		1.39 (0.84-2.29)	0.20	

Hazard ratios compare persistent tobacco smoking throughout follow-up with non-smoking, persistent alcohol drinking throughout follow-up with non-drinking, persistent marijuana use throughout follow-up with no marijuana use, and persistent hard illicit drug use (use of cocaine, heroin, or methamphetamine) throughout follow-up with no hard illicit drug use. Adjusted for age, sex, race/ethnicity, clinical site, education, estimated glomerular filtration rate, proteinuria, history of diabetes, body mass index, systolic blood pressure, hemoglobin, use of non-steroidal anti-inflammatory drugs; current tobacco smoking was additionally adjusted in models of weekly alcohol drinking, marijuana use, and hard illicit drug use. CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated-glomerular filtration rate; HR, hazard ratio.

Supplemental Table 5. Hazard ratios and 95% confidence intervals of CKD progression or all-cause mortality associated with cumulative average tobacco smoking, alcohol drinking, marijuana use, and hard illicit drug use by subgroups

Subgroups	HR (95% CI)	*P* Value	*P* Value for Interaction	HR (95% CI)	*P* Value	*P* Value for Interaction
	Tobacco Smoking			**Alcohol Drinking**		
Sex						
Men	1.25 (1.05-1.50)	0.01	0.20	1.01 (0.85-1.21)	0.88	0.67
Women	1.05 (0.84-1.31)	0.69		0.94 (0.68-1.29)	0.69	
Race						
White	1.24 (0.96-1.61)	0.10	0.65	1.00 (0.80-1.24)	0.99	0.93
Non-white	1.16 (0.99-1.36)	0.08		0.99 (0.79-1.23)	0.90	
Age						
Age <65 years	1.19 (1.02-1.40)	0.03	0.68	1.00 (0.83-1.21)	0.99	0.91
Age ≥65 years	1.11 (0.82-1.51)	0.50		0.98 (0.75-1.29)	0.90	
Baseline eGFR						
eGFR <45	1.10 (0.94-1.30)	0.23	0.11	1.01 (0.84-1.22)	0.88	0.92
eGFR ≥45	1.43 (1.08-1.89)	0.01		1.00 (0.76-1.31)	0.99	
	Marijuana Use			**Hard Illicit Drug Use**		
Sex						
Men	0.95 (0.84-1.09)	0.49	0.73	1.34 (1.08-1.66)	0.007	0.26
Women	0.99 (0.83-1.19)	0.93		1.06 (0.74-1.51)	0.77	
Race						
White	0.83 (0.69-0.99)	0.04	0.03	1.15 (0.84-1.57)	0.39	0.45
Non-white	1.05 (0.93-1.20)	0.43		1.33 (1.06-1.66)	0.01	

Age						
Age <65 years	0.98 (0.86-1.11)	0.73	0.81	1.27 (1.04-1.54)	0.02	0.93
Age ≥65 years	0.95 (0.75-1.20)	0.66		1.30 (0.74-2.29)	0.36	
Baseline eGFR						
eGFR <45	0.97 (0.85-1.10)	0.62	0.99	1.23 (1.00-1.52)	0.05	0.65
eGFR ≥45	0.97 (0.79-1.19)	0.77		1.36 (0.94-1.97)	0.11	

Hazard ratios compare persistent tobacco smoking throughout follow-up with non-smoking, persistent alcohol drinking throughout follow-up with non-drinking, persistent marijuana use throughout follow-up with no marijuana use, and persistent hard illicit drug use (use of cocaine, heroin, or methamphetamine) throughout follow-up with no hard illicit drug use. Adjusted for age, sex, race/ethnicity, clinical site, education, estimated glomerular filtration rate, proteinuria, history of diabetes, body mass index, systolic blood pressure, hemoglobin, use of non-steroidal anti-inflammatory drugs; current tobacco smoking was additionally adjusted in models of weekly alcohol drinking, marijuana use, and hard illicit drug use. CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated-glomerular filtration rate; HR, hazard ratio.