

Supplemental Table 1. Multivariable-Adjusted Associations of Urine Biomarkers with Rapid Decline by eGFR_{creat} in HIV-Infected WIHS Participants

Cut-Off Points	ACR		IL-18		KIM-1	
	Tertile 2	Tertile 3	Tertile 2	Tertile 3	Tertile 2	Tertile 3
	7.1-15.7 mg/g	>15.7 mg/g	81-196 pg/mL	>196 pg/mL	318-721 pg/mL	>721 pg/mL
3% (N=546)^a						
Model 1 ^b	0.97 (0.74, 1.27) p=0.80	1.16 (0.86, 1.58) p=0.33	1.01 (0.74, 1.37) p=0.97	1.11 (0.83, 1.49) p=0.49	0.98 (0.77, 1.26) p=0.89	1.30 (1.02, 1.66) p=0.032
Model 2 ^c	0.95 (0.73, 1.25) p=0.73	1.12 (0.83, 1.51) p=0.45	1.00 (0.77, 1.28) p=0.97	1.12 (0.87, 1.44) p=0.37	0.95 (0.75, 1.20) p=0.68	1.22 (0.98, 1.53) p=0.078
Model 3 ^d	0.95 (0.74, 1.21) p=0.68	1.08 (0.83, 1.40) p=0.58	0.97 (0.75, 1.26) p=0.82	1.03 (0.78, 1.35) p=0.83	0.96 (0.77, 1.20) p=0.72	1.22 (0.97, 1.54) p=0.097
5% (N=323)^a						
Model 1 ^b	0.93 (0.61, 1.41) p=0.74	1.23 (0.77, 1.96) p=0.39	1.03 (0.63, 1.68) p=0.91	1.16 (0.70, 1.90) p=0.57	1.19 (0.83, 1.71) p=0.36	1.88 (1.31, 2.71) p=0.0007
Model 2 ^c	1.03 (0.69, 1.55) p=0.87	1.27 (0.82, 1.96) p=0.28	0.95 (0.66, 1.35) p=0.76	1.18 (0.85, 1.65) p=0.33	1.05 (0.74, 1.50) p=0.77	1.64 (1.21, 2.22) p=0.0013
Model 3 ^d	1.03 (0.72, 1.46) p=0.88	1.17 (0.81, 1.70) p=0.40	0.87 (0.61, 1.22) p=0.42	0.94 (0.67, 1.31) p=0.71	1.10 (0.80, 1.52) p=0.56	1.71 (1.25, 2.33) p=0.0007
10% (N=113)^a						
Model 1 ^b	1.00 (0.50, 2.00) p=0.99	1.64 (0.94, 2.86) p=0.084	2.15 (1.16, 3.98) p=0.015	2.12 (1.08, 4.16) p=0.029	1.21 (0.62, 2.35) p=0.58	2.22 (1.27, 3.85) p=0.0048
Model 2 ^c	1.07 (0.52, 2.19) p=0.85	1.57 (0.89, 2.80) p=0.12	1.92 (1.05, 3.49) p=0.034	2.06 (1.09, 3.91) p=0.026	1.06 (0.57, 1.98) p=0.84	1.94 (1.15, 3.26) p=0.012
Model 3 ^d	1.10 (0.61, 1.99) p=0.76	1.63 (0.91, 2.94) p=0.10	1.96 (1.05, 3.65) p=0.034	1.97 (1.00, 3.87) p=0.050	1.01 (0.55, 1.85) p=0.98	1.78 (1.07, 2.96) p=0.027

+ $p < 0.05$, * $p < .01$, ** $p < .001$, *** $p < .0001$ denotes statistical significance of estimates above.

Results reported as risk of eGFR decline of $\geq 3\%$, $\geq 5\%$, or $\geq 10\%$ per year (95% confidence interval).

^aN=number of participants with at least one outcome.

^bModel 1: Demographic-adjusted model controls for age, ethnicity, and single biomarker.

^cModel 2: Multivariable-adjusted full model controls for Model 1 plus traditional kidney risk factors, HIV-related risk factors, and ACR.

^dModel 3: Multivariable-adjusted full model controls for Model 2 plus all four biomarkers (ACR, IL-18, KIM-1, NGAL).

Estimates are calculated from GEE relative risk models to account for multiple episodes of rapid decline, with inverse probability weighting to account for dropout, and multiple imputation for missing covariates.

Tertile 1 is reference category, and represents those with lowest amount of biomarker; cutoff points for Tertile 1 of each biomarker are as follows:

ACR < 7.1 mg/g; IL-18 < 81 pg/mL; KIM-1 < 318 pg/mL.

Supplemental Table 2. Multivariable-Adjusted Associations of Urine Biomarkers with Rapid Decline by eGFRcreat in HIV-Uninfected

WIHS Participants

Cut-Off Points	ACR		IL-18		KIM-1	
	Tertile 2	Tertile 3	Tertile 2	Tertile 3	Tertile 2	Tertile 3
	6.1-10.0 mg/g	>10.0 mg/g	53-132 pg/mL	>132 pg/mL	272-645 pg/mL	>645 pg/mL
3% (N=155)^a						
Model 1 ^b	0.67 (0.46, 0.97) p=0.033	0.83 (0.58, 1.20) p=0.33	1.38 (0.93, 2.06) p=0.11	1.30 (0.94, 1.80) p=0.12	1.57 (1.08, 2.29) p=0.018	1.38 (0.98, 1.95) p=0.067
Model 2 ^c	0.66 (0.47, 0.93) p=0.017	0.80 (0.57, 1.13) p=0.21	1.23 (0.85, 1.80) p=0.27	1.16 (0.82, 1.63) p=0.40	1.50 (1.07, 2.12) p=0.019	1.31 (0.93, 1.85) p=0.12
Model 3 ^d	0.69 (0.51, 0.94) p=0.018	0.90 (0.67, 1.22) p=0.50	1.16 (0.80, 1.69) p=0.43	1.16 (0.78, 1.71) p=0.47	1.44 (1.04, 2.00) p=0.028	1.27 (0.87, 1.85) p=0.22
5% (N=77)^a						
Model 1 ^b	0.37 (0.20, 0.67) p=0.0011	0.65 (0.35, 1.19) p=0.16	2.23 (1.12, 4.47) p=0.023	1.86 (1.09, 3.16) p=0.023	2.77 (1.39, 5.50) p=0.0037	1.96 (1.10, 3.47) p=0.021
Model 2 ^c	0.37 (0.22, 0.61) p=0.0001	0.64 (0.39, 1.07) p=0.087	1.67 (0.95, 2.91) p=0.073	1.56 (0.92, 2.66) p=0.10	2.24 (1.30, 3.88) p=0.0039	1.81 (1.08, 3.02) p=0.023
Model 3 ^d	0.41 (0.25, 0.65) p=0.0002	0.81 (0.51, 1.26) p=0.35	1.41 (0.78, 2.55) p=0.26	1.42 (0.76, 2.64) p=0.27	2.02 (1.17, 3.50) p=0.012	1.66 (0.93, 2.96) p=0.088
10% (N=23)^a						
Model 1 ^b	0.69 (0.25, 1.93) p=0.48	1.23 (0.45, 3.36) p=0.69	1.46 (0.42, 5.14) p=0.56	3.87 (1.17, 12.79) p=0.026	1.39 (0.39, 4.91) p=0.61	2.78 (0.93, 8.31) p=0.067
Model 2 ^c	0.65 (0.24, 1.77) p=0.39	1.01 (0.38, 2.67) p=0.98	1.82 (0.52, 6.36) p=0.35	3.69 (1.16, 11.67) p=0.026	1.50 (0.43, 5.25) p=0.52	2.64 (0.95, 7.33) p=0.062
Model 3 ^d	0.63 (0.23, 1.69) p=0.35	1.14 (0.42, 3.09) p=0.80	1.50 (0.41, 5.45) p=0.54	2.97 (0.87, 10.08) p=0.081	1.21 (0.36, 4.03) p=0.76	1.87 (0.67, 5.22) p=0.23

+ p<0.05, * p<.01, ** p<.001, *** p<.0001 denotes statistical significance of estimates above.

Results reported as risk of eGFR decline of $\geq 3\%$, $\geq 5\%$, or $\geq 10\%$ per year (95% confidence interval).

^aN=number of participants with at least one outcome.

^bModel 1: Demographic-adjusted model controls for age, ethnicity, and single biomarker.

^cModel 2: Multivariable-adjusted full model controls for Model 1 plus traditional kidney risk factors, and ACR.

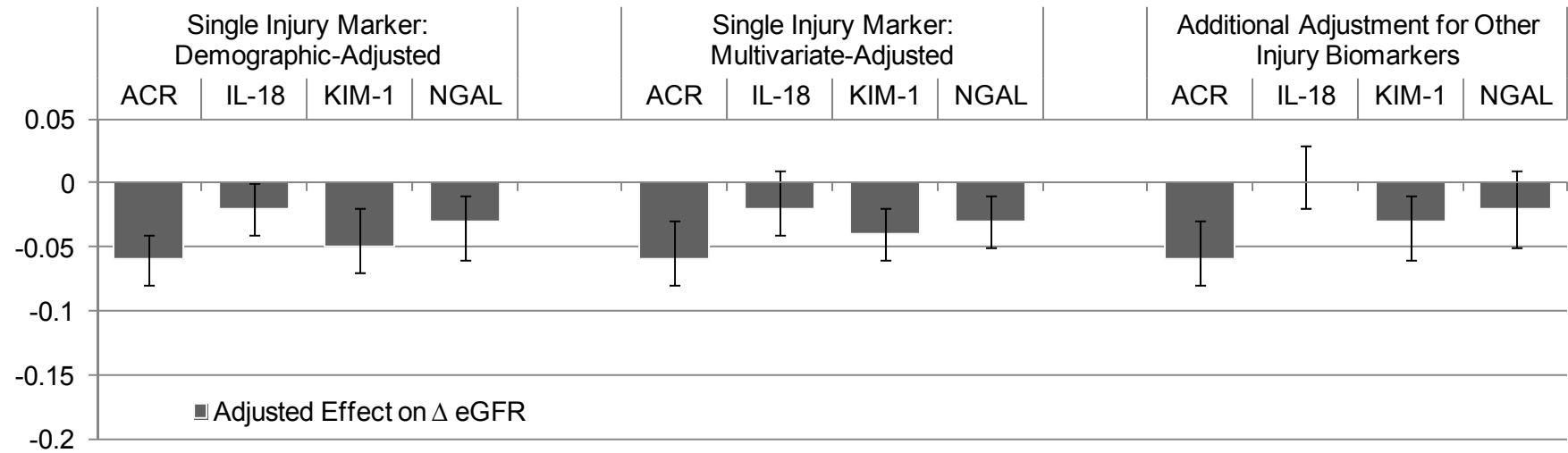
^dModel 3: Multivariable-adjusted full model controls for Model 2 plus all four biomarkers (ACR, IL-18, KIM-1, NGAL).

Estimates are calculated from GEE relative risk models to account for multiple episodes of rapid decline, with inverse probability weighting to account for dropout, and multiple imputation for missing covariates.

Tertile 1 is reference category, and represents those with lowest amount of biomarker; cutoff points for Tertile 1 of each biomarker are as follows: ACR <6.1 mg/g; IL-18 <53 pg/mL; KIM-1 <272 pg/mL.

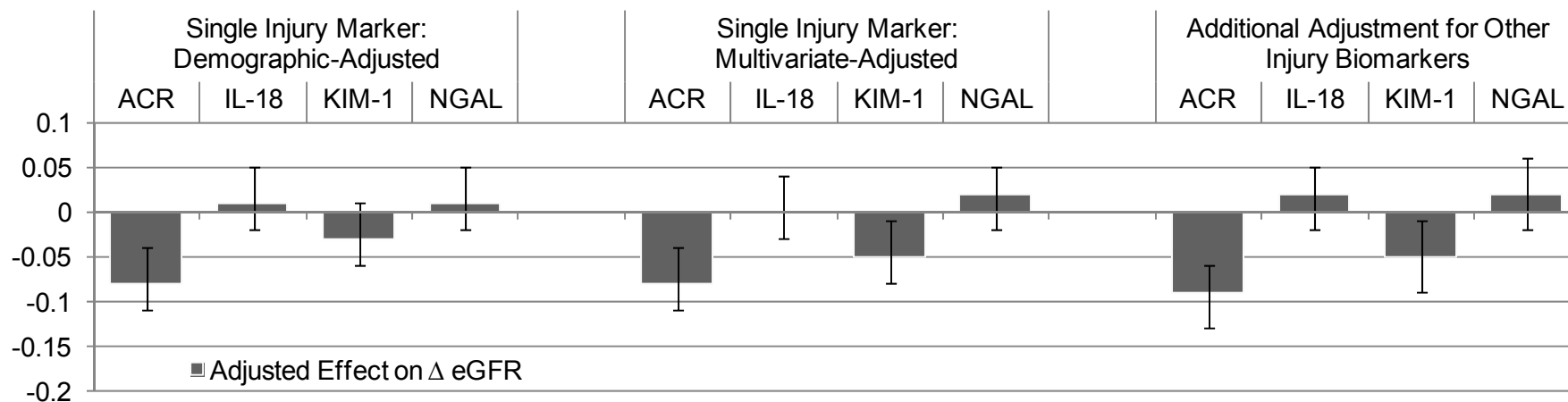
Supplemental Figures 1 and 2. Multivariable-Adjusted Associations of Urine Biomarkers with Annual Change in eGFR_{creat} in 908 WIHS HIV-Infected and 289 WIHS Control Participants

Supplemental Figure 1. HIV-Infected Participants



Supplemental Figure 1 Legend. Note: Estimates are highest versus lowest biomarker tertile. Tertile 1 is reference category, and represents those with lowest amount of biomarker; Tertile 3 results shown. Cutoff points for biomarker tertiles are as follows: ACR T1: <7.1 mg/g, T2: 7.1-15.8 mg/g, T3: >15.8 mg/g; IL-18 T1: <81 pg/mL, T2: 81-196 pg/mL, T3: >196 pg/mL; KIM-1 T1: <319 pg/mL, T2: 319-723 pg/mL, T3: >723 pg/mL; NGAL T1: <22 ng/mL, T2: 22-57 ng/mL, T3: >57 ng/mL. Results reported as estimated annual change in eGFR from baseline in mL/min/1.73m² (95% confidence interval). Demographic-adjusted model includes single biomarker, age, and ethnicity. Single injury marker multivariable model includes age, ethnicity, traditional kidney risk factors, HIV-related risk factors, and ACR. Additional adjustment for other injury biomarker model includes single injury biomarker multivariable model and all 4 markers.

Supplemental Figure 2. Control Participants



Supplemental Figure 2. Tertile 1 is reference category, and represents those with lowest amount of biomarker; Tertile 3 results shown. Cutoff points for biomarker tertiles are as follows: ACR T1: <6.1 mg/g, T2: 6.1-10.0 mg/g, T3: >10.0 mg/g; IL-18 T1: <53 pg/mL, T2: 53-132 pg/mL, T3: >132 pg/mL; KIM-1 T1: <272 pg/mL, T2: 272-645 pg/mL, T3: >645 pg/mL; NGAL T1: <21 ng/mL, T2: 21-53 ng/mL, T3: >53 ng/mL. Results reported as estimated annual change in eGFR from baseline in mL/min/1.73m² (95% confidence interval). Demographic-adjusted model includes single biomarker, age, and ethnicity. Single injury marker multivariable model includes age, ethnicity, traditional kidney risk factors, and ACR. Additional adjustment for other injury biomarker model includes single injury biomarker multivariable model and all 4 markers.