Supplementary Appendix

Supplement to:

Biomarkers of Acute Kidney Injury Progression after Pediatric Cardiac Surgery

Table of Contents

Supplemental Table 1: Biomarker Level and Storage Time

Biomarker Name	Percent change over one month (95% CI)	P-value
Plasma IL1	0.35% (-0.44%, 1.16%)	0.38
Plasma IL2	0.72% (-1.67%, 3.17%)	0.55
Plasma IL4	0.64% (-1.37%, 2.69%)	0.53
Plasma IL6	1.96% (-0.82%, 4.8%)	0.17
Plasma IL8	0.04% (-2.08%, 2.21%)	0.97
Plasma IL10	1.79% (-1.5%, 5.19%)	0.29
Plasma IL12	-1.5% (-2.67%, -0.31%)	0.01
Plasma IL13	-0.08% (-1.5%, 1.36%)	0.91
Plasma IFN	-1.07% (-3.07%, 0.97%)	0.30
Plasma TNF	-0.8% (-1.79%, 0.2%)	0.11
Plasma NGAL	0.16% (-1.96%, 2.33%)	0.88
Plasma Cystatin	0.25% (-0.89%, 1.4%)	0.67
Urine L-FABP	-1.45% (-4.86%, 2.09%)	0.41
Urine NGAL	-0.04% (-7.73%, 8.28%)	0.99
Urine IL18	-1.63% (-9.64%, 7.09%)	0.70
Urine KIM-1	-0.25% (-2.31%, 1.86%)	0.82
Urine Albumin	0.23% (-1.92%, 2.43%)	0.83
Urine Cystatin	1.43% (0.06%, 2.81%)	0.04

Supplemental Table 2: Biomarkers and AKI Progression

Biomarker	AKI Without Progression (N=148)*	AKI With Progression (N=28)ǂ	P value
Traditional Biomarkers			
Serum Cr Rise (%)	67 (50, 100), N=148	80 (58, 133), N=28	0.05
Urine Albuminuria (mg/g)	33.2 (13.7, 96.8), N=103	76.3 (32.1, 142.6), N=15	0.05
Cystatin C			
Urine Cystatin C (mg/L)	0.12 (0.07, 0.2), N=136	0.2 (0.07, 0.32), N=24	0.13
Plasma Cystatin C (mg/L)	0.93 (0.71, 1.35), N=107	0.98 (0.86, 1.37), N=16	0.47
Kidney Injury Biomarkers			
Urine IL-18 (pg/ml)	40.67 (12.45, 131.05), N=106	79.2 (43.2, 492.9), N=17	0.01
Urine NGAL (ng/ml)	10.36 (4.95, 30.11), N=106	34.13 (12.49, 240.89), N=17	0.02
Urine KIM-1 (ng/ml)	0.63 (0.27, 2.28), N=138	0.95 (0.53, 2.3), N=26	0.27
Urine L-FABP (ng/ml)	32.05 (7.77, 151.53), N=138	257.29 (15.81, 591.98), N=26	0.001
Plasma NGAL (ng/ml)	129.59 (82.68, 217.31), N=98	177.56 (80.43, 192.26), N=15	0.94
Inflammatory Biomarkers			
Plasma IFN (pg/ml)	2.07 (1.02, 3.69), N=71	1.98 (1.28, 3.96), N=20	0.79
Plasma IL-1 (pg/ml)	0.18 (0.18, 0.18), N=71	0.18 (0.18, 0.22), N=20	0.01
Plasma IL-2 (pg/ml)	0.25 (0.13, 0.48), N=71	0.54 (0.26, 1.05), N=20	0.02
Plasma IL-4 (pg/ml)	0.05 (0.03, 0.12), N=71	0.07 (0.05, 0.17), N=20	0.23
Plasma IL-6 (pg/ml)	18.92 (9.28, 38.79), N=71	33.18 (22.75, 81.44), N=20	0.009
Plasma IL-8 (pg/ml)	22.68 (12.11, 43.23), N=71	63.81 (44.03, 159.9), N=20	<0.001
Plasma IL-10 (pg/ml)	33.66 (5.82, 88.09), N=71	94.3 (34.44, 163.39), N=20	0.03
Plasma IL-12 (pg/ml)	0.1 (0.07, 0.14), N=71	0.15 (0.07, 0.21), N=20	0.07
Plasma IL-13 (pg/ml)	0.44 (0.26, 1.04), N=71	0.55 (0.44, 1.77), N=20	0.02
Plasma TNF (pg/ml)	3.93 (2.85, 5.46), N=71	4.88 (3.89, 6.83), N=20	0.09

**p-values obtained by the Kruskal-Wallace test

Supplemental Table 3: Performance of AKI Progression Biomarkers

Biomarker	Unadjusted OR* (95%CI)	Biomarker AUC# (SE)
Traditional Biomarkers		
% Serum Cr Rise	3.7 (1.55, 8.81)	0.62 (0.06)
Urine Albuminuria	1.56 (0.99, 2.46)	0.66 (0.07)
Cystatin C		
Urine Cystatin C	1.74 (1.15, 2.64)	0.64 (0.07)
Blood Cystatin C	1.46 (0.43, 4.93)	0.56 (0.07)
Kidney Injury Biomarkers		
Urine IL-18	1.43 (1.09, 1.86)	0.69 (0.06)
Urine NGAL	1.39 (1.08, 1.8)	0.67 (0.08)
Urine KIM-1	1.17 (0.87, 1.57)	0.57 (0.06)
Urine L-FABP	1.43 (1.14, 1.8)	0.70 (0.06)
Plasma NGAL	1.25 (0.54, 2.9)	0.51 (0.08)
Inflammatory Biomarkers		
Plasma IFN	1.28 (0.82, 2)	0.52 (0.08)
Plasma IL-1	2.29 (0.83, 6.32)	0.58 (0.05)
Plasma IL-2	1.61 (1.07, 2.43)	0.67 (0.07)
Plasma IL-4	1.37 (0.85, 2.19)	0.59 (0.07)
Plasma IL-6	1.63 (1.02, 2.6)	0.69 (0.07)
Plasma IL-8	2.94 (1.66, 5.22)	0.80 (0.06)
Plasma IL-10	1.38 (0.98, 1.96)	0.66 (0.07)
Plasma IL-12	1.8 (0.89, 3.62)	0.62 (0.08)
Plasma IL-13	2.07 (1.08, 3.96)	0.67 (0.07)
Plasma TNF	1.95 (0.78, 4.9)	0.63 (0.07)

*, odds ratio for log-continuous biomarkers. #, without optimism correction. AKI, acute kidney injury. OR, odds ratio. AUC, area under the curve.

Supplemental Table 4: Biomarkers to Predict Progression from Stage I AKI to Higher AKI Stages

Biomarker	Unadjusted OR* (95%CL)	Biomarker unadjusted AUC# (SE)
Traditional Biomarkers		
Serum Cr % Rise	5.35 (0.85, 33.5)	0.61 (0.07)
Urine Microalbumin	1.82 (1.09, 3.05)	0.70 (0.07)
Cystatin C		
Urine Cystatin C	1.71 (1.1, 2.66)	0.61 (0.09)
Blood Cystatin C	1.51 (0.37, 6.13)	0.56 (0.08)
Kidney Injury Biomarkers		
Urine IL-18	1.54 (1.14, 2.07)	0.74 (0.07)
Urine NGAL	1.52 (1.15, 2.01)	0.73 (0.08)
Urine KIM-1	1.15 (0.8, 1.65)	0.57 (0.07)
Urine L-FABP	1.58 (1.18, 2.1)	0.73 (0.07)
Blood NGAL	1.5 (0.6, 3.75)	0.53 (0.09)
Inflammatory Biomarkers		
Blood IFN	1.19 (0.74, 1.94)	0.48 (0.09)
Blood IL-1	2.06 (0.72, 5.86)	0.57 (0.06)
Blood IL-2	1.91 (1.18, 3.09)	0.73 (0.06)
Blood IL-4	1.48 (0.86, 2.52)	0.60 (0.08)
Blood IL-6	2.18 (1.19, 4)	0.70 (0.07)
Blood IL-8	3.42 (1.74, 6.7)	0.83 (0.06)
Blood IL-10	1.44 (0.96, 2.16)	0.65 (0.07)
Blood IL-12	1.83 (0.84, 4)	0.59 (0.09)
Blood IL-13	1.84 (0.9, 3.77)	0.64 (0.08)
Blood TNF	1.62 (0.61, 4.34)	0.60 (0.08)

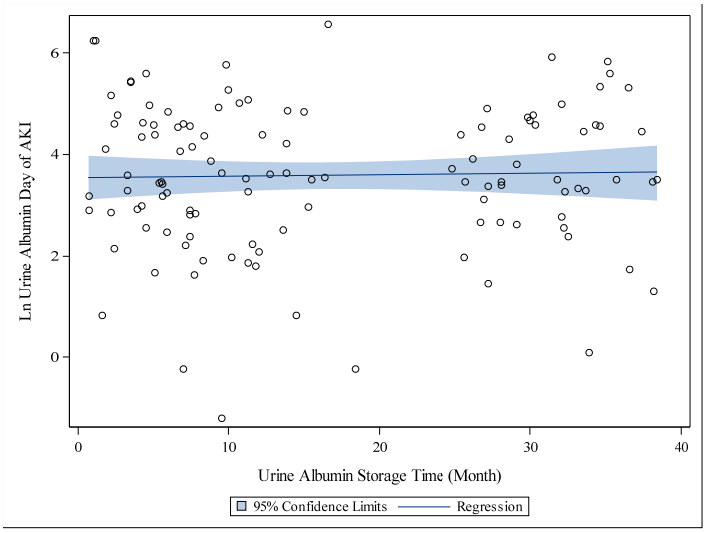
*, odds ratio for log-continuous biomarkers. #, without optimism correction. AKI, acute kidney injury. AUC, area under the curve. OR, odds ratio, SE, standard error.

Supplemental Table 5: Biomarkers to Predict Progression from Stage I and II AKI to Higher AKI Stages

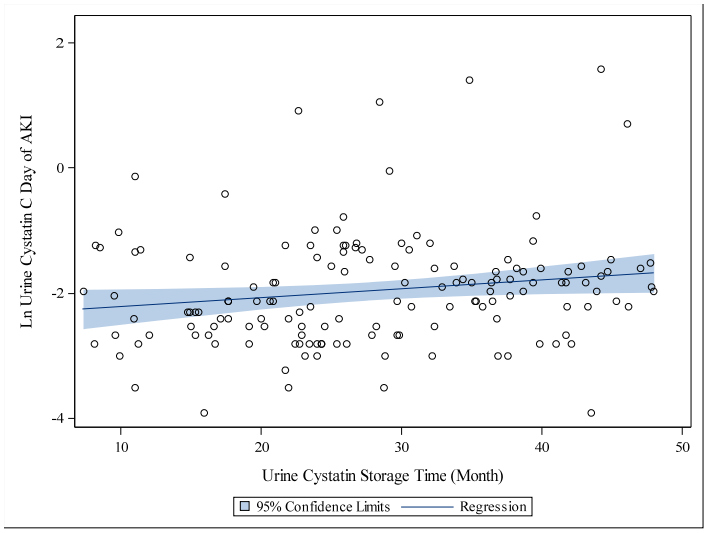
Biomarker	Unadjusted OR* (95%CL)	Biomarker unadjusted AUC# (SE)
Traditional Biomarkers		
Serum Cr % Rise	1.71 (0.54, 5.38)	0.56 (0.06)
Urine Microalbumin	1.62 (1.01, 2.6)	0.67 (0.07)
Cystatin C		
Urine Cystatin C	1.78 (1.15, 2.74)	0.63 (0.08)
Blood Cystatin C	1 (0.28, 3.55)	0.49 (0.08)
Kidney Injury Biomarkers		
Urine IL-18	1.52 (1.14, 2.03)	0.73 (0.06)
Urine NGAL	1.47 (1.13, 1.92)	0.71 (0.08)
Urine KIM-1	1.09 (0.78, 1.51)	0.54 (0.06)
Urine L-FABP	1.51 (1.16, 1.97)	0.71 (0.06)
Blood NGAL	1.22 (0.51, 2.88)	0.5 (0.09)
Inflammatory Biomarkers		
Blood IFN	1.26 (0.79, 2.02)	0.5 (0.08)
Blood IL-1	2.24 (0.79, 6.34)	0.57 (0.06)
Blood IL-2	1.74 (1.12, 2.71)	0.7 (0.07)
Blood IL-4	1.38 (0.84, 2.27)	0.59 (0.08)
Blood IL-6	1.54 (0.96, 2.47)	0.67 (0.08)
Blood IL-8	2.98 (1.62, 5.48)	0.79 (0.06)
Blood IL-10	1.24 (0.88, 1.75)	0.61 (0.08)
Blood IL-12	1.75 (0.85, 3.61)	0.6 (0.09)
Blood IL-13	1.84 (0.92, 3.66)	0.64 (0.07)
Blood TNF	1.85 (0.7, 4.9)	0.62 (0.07)

*, odds ratio for log-continuous biomarkers. #, without optimism correction. AKI, acute kidney injury. AUC, area under the curve. OR, odds ratio, SE, standard error.

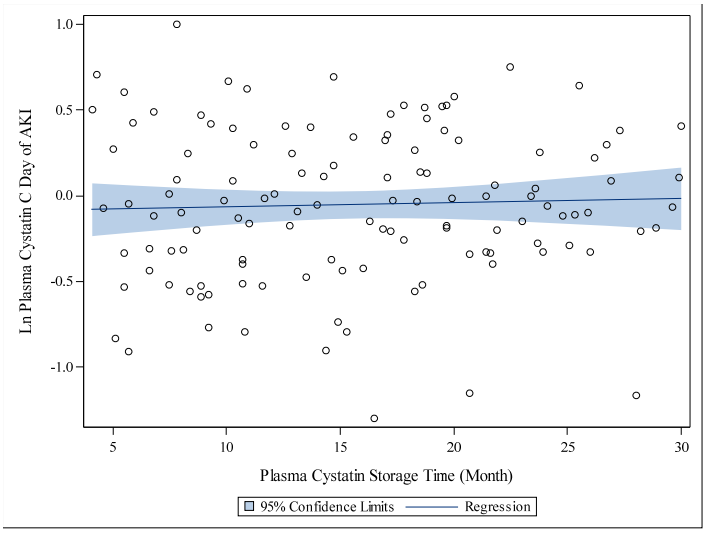
Supplemental Figure 1a: Biomarker Levels by Sample Storage Time



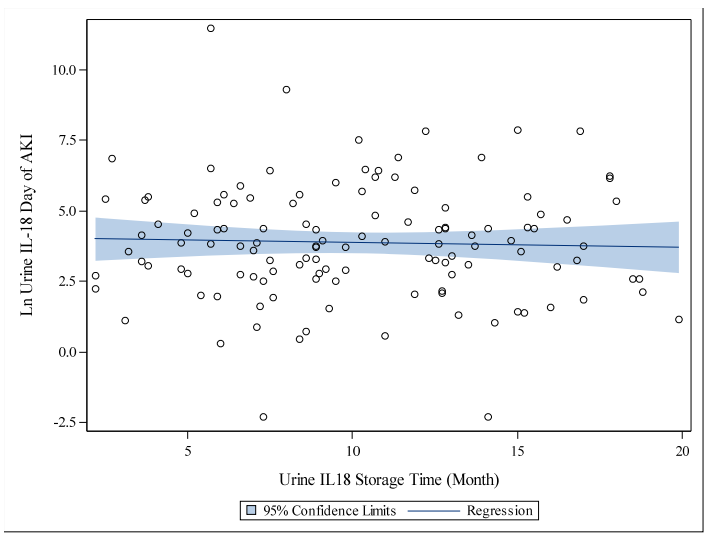
Supplemental Figure 1b Biomarker Levels by Sample Storage Time



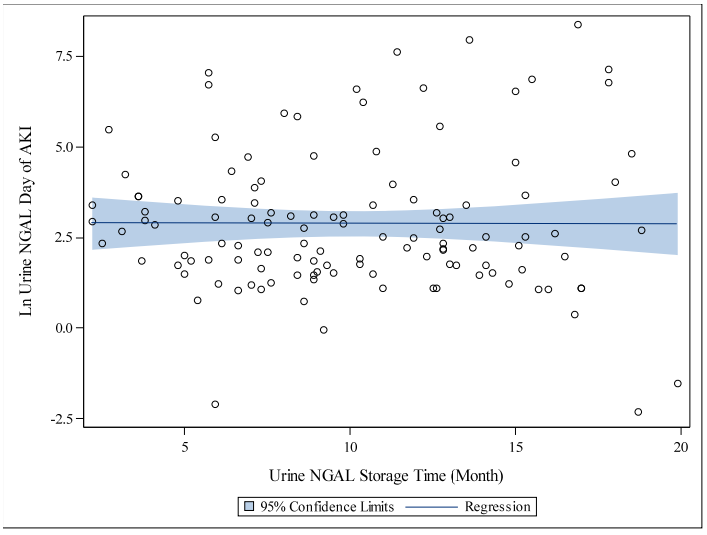
Supplemental Figure 1c: Biomarker Levels by Sample Storage Time



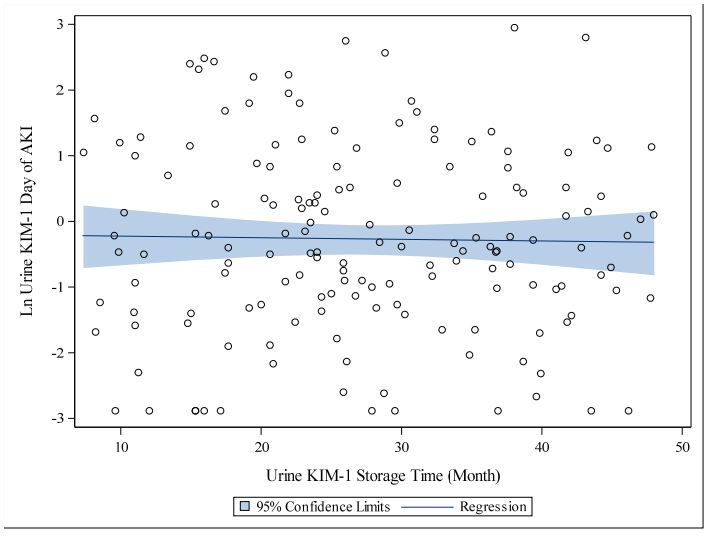
Supplemental Figure 1d Biomarker Levels by Sample Storage Time



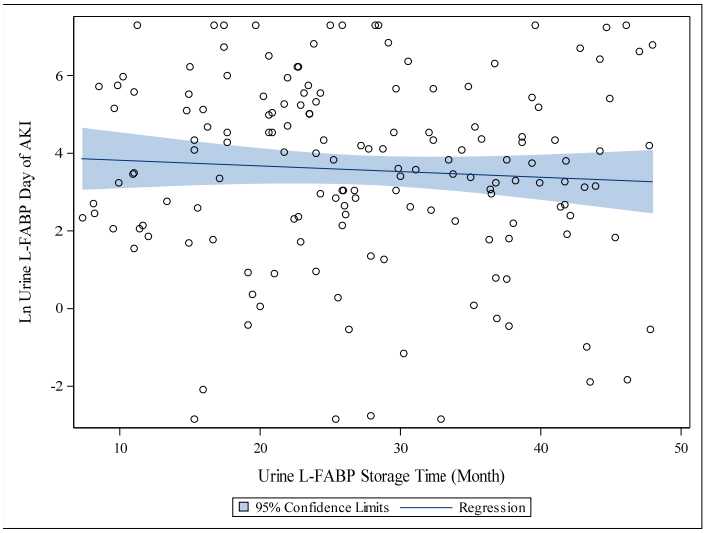
Supplemental Figure 1e: Biomarker Levels by Sample Storage Time



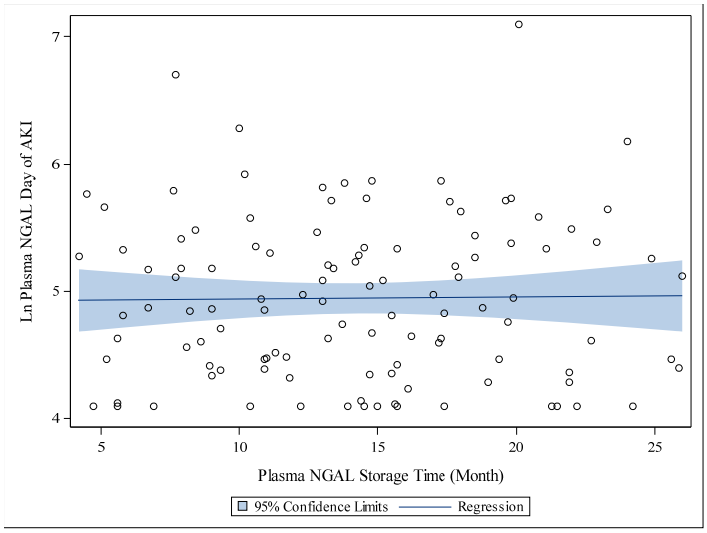
Supplemental Figure 1f Biomarker Levels by Sample Storage Time



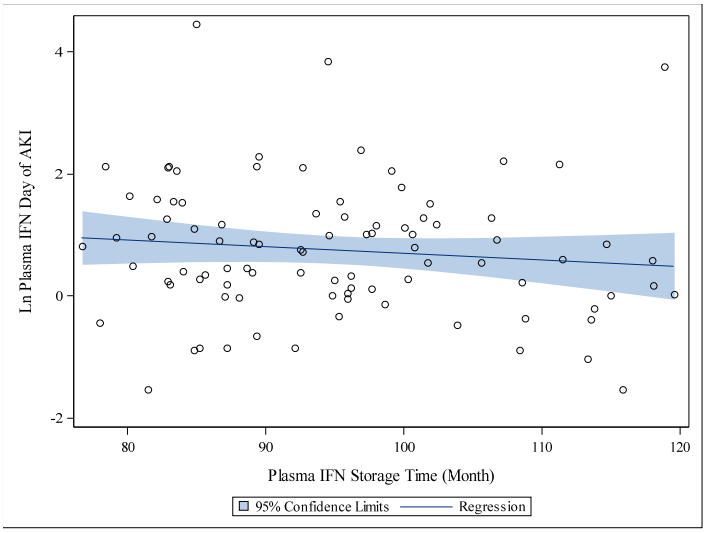
Supplemental Figure 1g: Biomarker Levels by Sample Storage Time



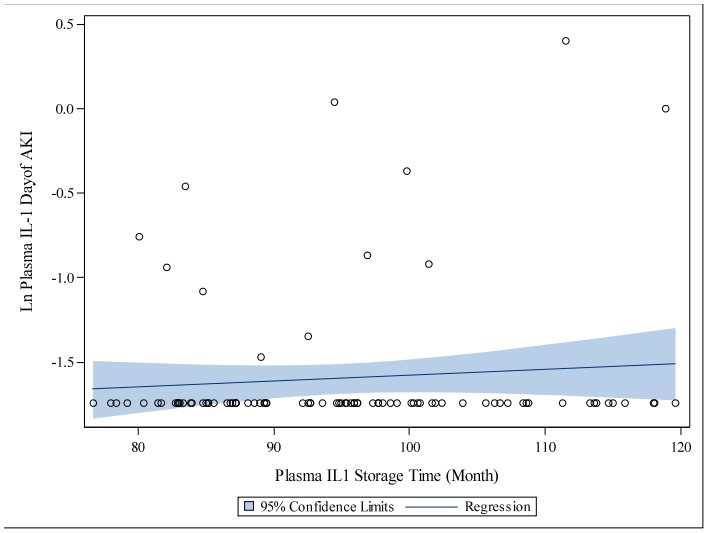
Supplemental Figure 1h Biomarker Levels by Sample Storage Time



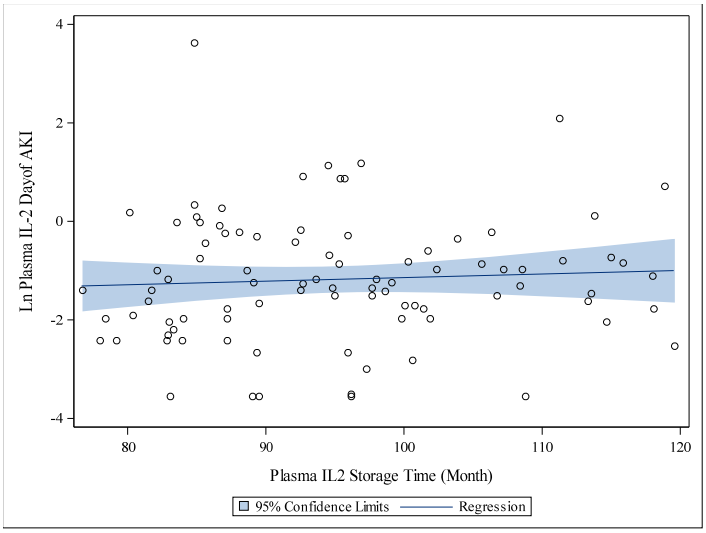
Supplemental Figure 1i: Biomarker Levels by Sample Storage Time



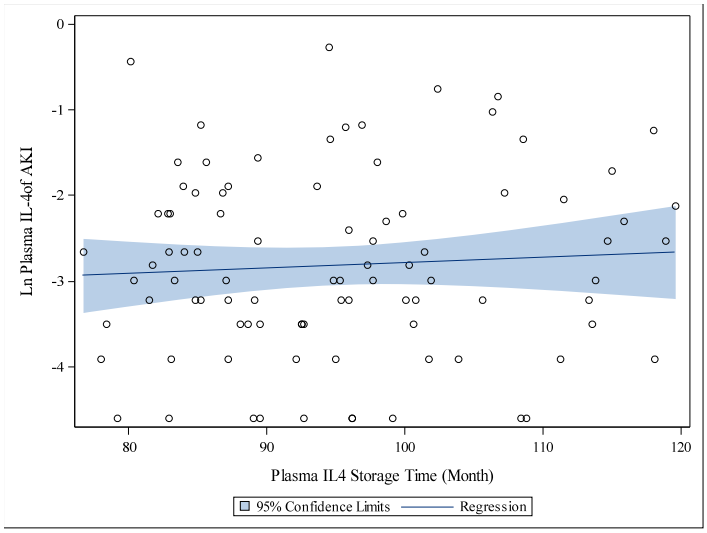
Supplemental Figure 1j Biomarker Levels by Sample Storage Time



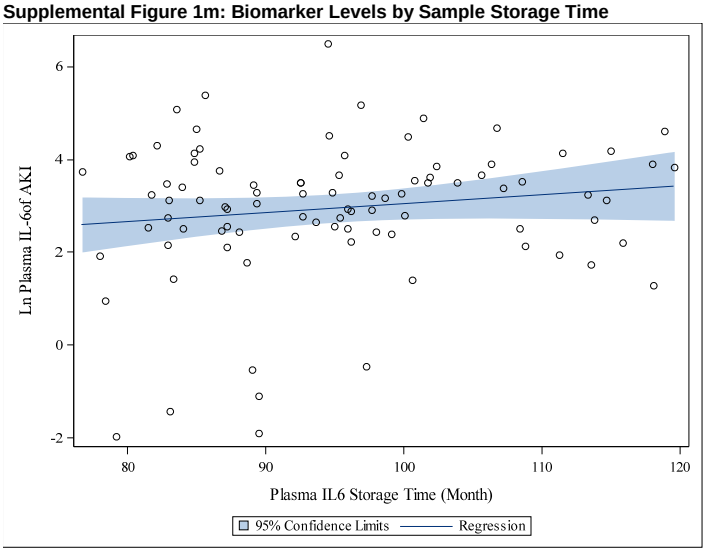
Supplemental Figure 1k: Biomarker Levels by Sample Storage Time



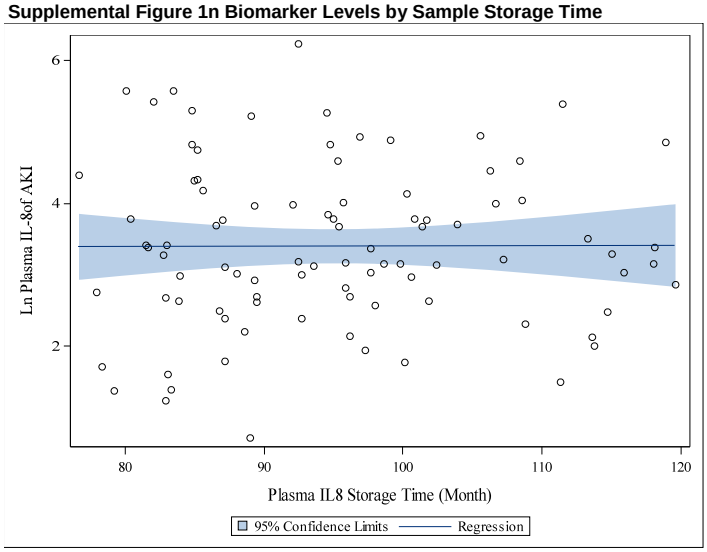
Supplemental Figure 1l Biomarker Levels by Sample Storage Time



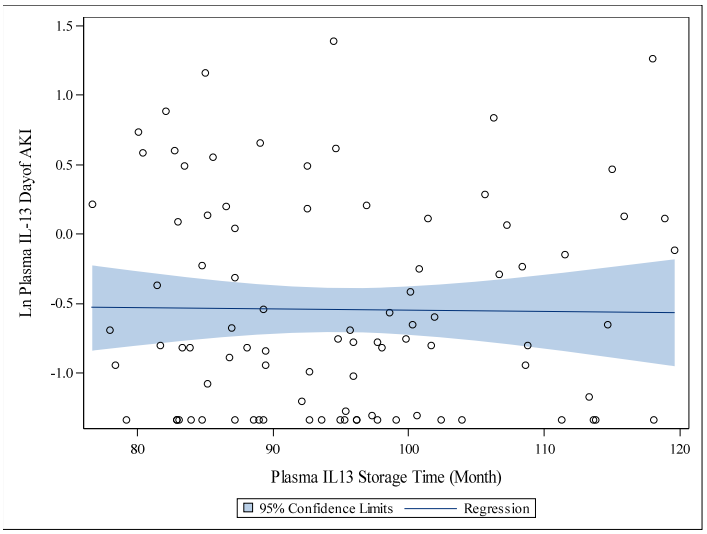
Supplemental Figure 1m: Biomarker Levels by Sample Storage Time



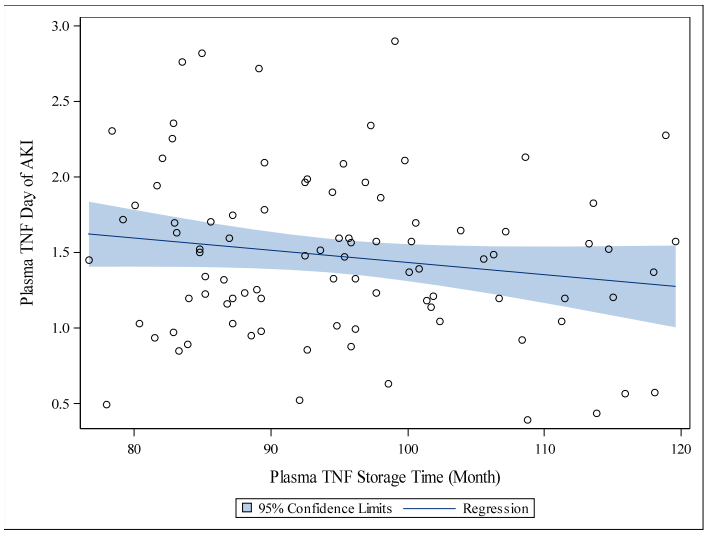
Supplemental Figure 1n Biomarker Levels by Sample Storage Time



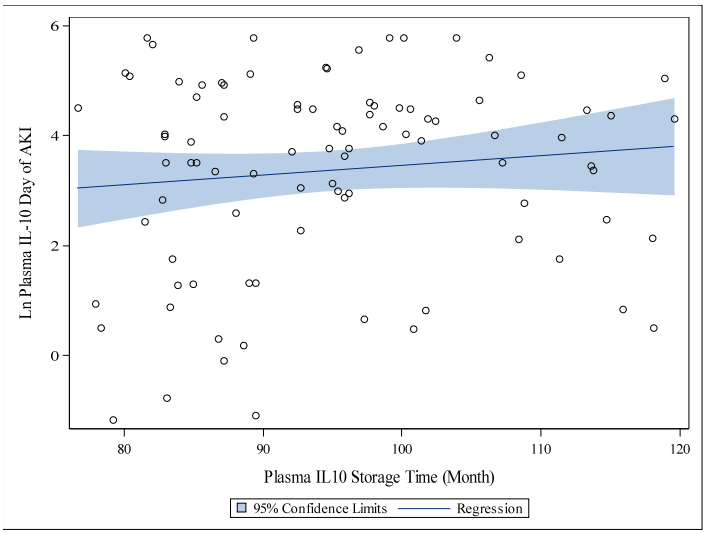
Supplemental Figure 1o: Biomarker Levels by Sample Storage Time



Supplemental Figure 1p Biomarker Levels by Sample Storage Time



Supplemental Figure 1q: Biomarker Levels by Sample Storage Time



Supplemental Figure 1r Biomarker Levels by Sample Storage Time