

Supplement to: **Candidate Surrogate Endpoints for ESRD After Acute Kidney Injury**

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Table S1: Baseline characteristics of veterans undergoing major surgery, 2004-2011, by the presence of post-discharge outpatient serum creatinine measurements within a given time period

	Overall	30 days ±15 days		60 days ±30 days		90 days ±30 days		180 day ±60 days		365 days ±90 days	
Post-discharge scr check		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
N	161,185	66,141	90,713	83,716	72,245	77,228	77,245	103,871	48,247	116,014	31,448
Demographics											
Age, years	64 (10)	64 (10)	63 (11)	64 (10)	63 (11)	64 (10)	63 (11)	64 (10)	63 (11)	64 (10)	62 (11)
Female, %	4	3	4	4	4	4	4	4	4	4	4
African American race, %	17	17	17	17	17	17	17	17	17	17	18
Comorbid conditions											
Systolic blood pressure, mmHg	133 (14)	133	133 (13)	133 (13)	133 (13)	133 (13)	133 (13)	133 (13)	133 (14)	133 (13)	133 (14)
Diastolic blood pressure,	76 (9)	75 (9)	76 (9)	75 (9)	76 (9)	75 (9)	76 (9)	75 (9)	76 (9)	76 (9)	76 (9)
Body mass index, kg/m ²	29 (6)	29 (6)	29 (6)	29 (6)	29 (6)	29 (6)	29 (6)	29 (6)	29 (6)	29 (6)	29 (6)
Baseline eGFR, ml/min/1.73m ²	80 (17)	79 (18)	81 (17)	79 (17)	81 (17)	79 (17)	81 (17)	79 (17)	81 (17)	80 (17)	82 (17)
% with eGFR<60	12	14	10	13	10	13	10	13	10	12	9
% with eGFR<45	2	3	2	3	1	3	2	2	1	2	1
Diabetes mellitus, %	35	41	31	40	30	40	30	39	27	38	24
Hypertension, %	75	79	73	78	72	78	72	78	70	77	67
Coronary artery disease, %	35	41	31	39	31	38	32	38	30	37	29
Congestive heart failure, %	10	13	8	12	8	12	8	11	7	10	7
Cerebral vascular disease, %	18	19	18	19	17	19	17	19	16	19	16
Peripheral arterial disease, %	20	21	19	21	18	21	18	21	17	20	17
Lung disease, %	33	35	30	35	30	35	30	34	28	33	27
Malignancy, %	30	33	27	33	26	34	25	31	25	29	25
Liver disease, %	1	2	1	1	1	1	1	1	1	1	1
Statin use, %	28	31	26	30	26	30	26	30	25	30	23
Diuretic use, %	26	30	24	26	23	29	23	28	22	27	21
ACE/ARB use, %	40	45	37	44	37	43	37	43	34	43	32
Laparoscopic, %	7	5	8	6	8	6	8	6	8	7	8

*All values reflect mean (SD) unless otherwise stated

Table S2: Number of participants, ESRD events, and mortality events by category of eGFR decline and AKI stage

Change in eGFR	Without AKI			AKI stage I			AKI stage II			AKI stage III or RRT		
	N	Died	ESRD	N	Died	ESRD	N	Died	ESRD	N	Died	ESRD
	30 days ± 15 days											
> 40 % decline	820	398	24	423	222	33	169	83	13	223	104	33
40 - 30 % decline	933	335	15	475	185	21	116	45	6	74	29	5
30 % decline- stable	18371	5042	88	3235	1007	70	572	193	12	247	86	10
stable - increase	36702	11649	119	3085	1101	34	482	188	4	214	83	3
Missing	82896	16525	164	6411	1634	84	934	284	19	472	166	29
	60 days ± 30 days											
> 40 % decline	790	408	33	378	201	41	149	79	16	156	78	39
40 - 30 % decline	1017	383	19	439	190	26	106	41	6	81	23	5
30 % decline- stable	23572	6296	118	3746	1173	74	617	201	14	311	114	15
stable - increase	47648	13851	124	3831	1242	42	599	208	4	276	97	2
Missing	65996	12335	116	5108	1216	59	776	238	14	365	115	18
	90 days ± 30 days											
> 40 % decline	779	415	42	332	153	46	113	61	15	132	63	44
40 - 30 % decline	994	370	16	381	153	23	101	34	6	59	18	0
30 % decline- stable	23381	6147	108	3407	1060	64	588	197	9	281	90	13
stable - increase	42562	12242	95	3328	1086	35	533	169	6	257	97	2
Missing	70121	12982	149	5858	1391	74	852	252	18	414	125	17
	180 day ± 60 days											
> 40 % decline	994	493	68	413	184	67	119	60	21	139	60	45
40 - 30 % decline	1417	536	34	506	182	33	116	35	5	71	18	6
30 % decline- stable	37008	8584	141	4812	1315	66	768	236	12	362	111	6
stable - increase	52560	12822	97	3766	1048	34	577	173	4	243	82	4
Missing	43898	7909	68	3530	856	41	542	152	12	277	79	11
	365 days ± 90 days											
> 40 % decline	1336	627	115	557	232	108	143	60	23	127	50	40
40 - 30 % decline	1962	654	41	652	199	23	114	28	5	73	18	6
30 % decline- stable	44304	8885	125	5389	1288	64	882	247	11	383	105	11
stable - increase	55672	11237	59	3640	870	16	548	138	3	232	58	2
Missing	28621	5340	63	2289	554	23	334	96	7	204	57	6

Table S3: Hazard ratios for all-cause mortality stable eGFR, 30% eGFR decline, and 40% eGFR decline after major surgery, by presence and stage of post-operative AKI at 30-days, 60-days, 90-days, 180-days, and 1-year post-hospital discharge

	Without AKI	AKI stage I	AKI stage II	AKI stage III or RRT	AKI Any Stage
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
30 days ± 15 days					
40 % decline	1.54 (1.43, 1.66)	1.83 (1.66, 2.02)	1.77 (1.50, 2.09)	1.62 (1.33, 1.97)	1.74 (1.60, 1.89)
30 % decline	1.34 (1.25, 1.43)	1.53 (1.39, 1.69)	1.55 (1.27, 1.88)	1.78 (1.36, 2.35)	1.55 (1.42, 1.69)
stable	Reference	1.24 (1.17, 1.32)	1.28 (1.11, 1.48)	1.23 (0.98, 1.53)	1.24 (1.17, 1.32)
60 days ± 30 days					
40 % decline	1.72 (1.60, 1.85)	2.11 (1.91, 2.33)	1.93 (1.62, 2.30)	1.68 (1.36, 2.07)	1.99 (1.83, 2.17)
30 % decline	1.48 (1.39, 1.57)	1.64 (1.49, 1.80)	1.40 (1.14, 1.73)	1.53 (1.16, 2.00)	1.59 (1.46, 1.73)
stable	Reference	1.25 (1.17, 1.33)	1.28 (1.11, 1.46)	1.52 (1.26, 1.85)	1.27 (1.20, 1.34)
90 days ± 30 days					
40 % decline	1.71 (1.59, 1.83)	1.97 (1.76, 2.19)	1.94 (1.60, 2.34)	1.65 (1.32, 2.07)	1.93 (1.77, 2.11)
30 % decline	1.49 (1.41, 1.58)	1.71 (1.55, 1.89)	1.79 (1.46, 2.18)	1.25 (0.90, 1.74)	1.68 (1.54, 1.83)
stable	Reference	1.24 (1.17, 1.32)	1.32 (1.15, 1.52)	1.64 (1.35, 1.99)	1.28 (1.21, 1.35)
180 day ± 60 days					
40 % decline	1.82 (1.71, 1.94)	1.76 (1.59, 1.94)	1.81 (1.50, 2.18)	1.52 (1.23, 1.90)	1.73 (1.60, 1.88)
30 % decline	1.46 (1.39, 1.54)	1.60 (1.46, 1.75)	1.64 (1.34, 2.00)	1.38 (1.05, 1.81)	1.58 (1.47, 1.71)
stable	Reference	1.20 (1.13, 1.27)	1.22 (1.07, 1.39)	1.77 (1.47, 2.15)	1.23 (1.21, 1.35)
365 days ± 90 days					
40 % decline	1.86 (1.76, 1.97)	1.94 (1.77, 2.12)	1.82 (1.50, 2.20)	1.82 (1.45, 2.29)	1.90 (1.77, 2.05)
30 % decline	1.43 (1.36, 1.50)	1.55 (1.42, 1.69)	1.93 (1.62, 2.30)	1.44 (1.08, 1.92)	1.60 (1.48, 1.72)
stable	Reference	1.25 (1.18, 1.33)	1.25 (1.08, 1.45)	1.77 (1.42, 2.20)	1.27 (1.21, 1.34)

*Adjusted for age, sex, race, BMI (linear spline, knot at 25 kg/m²), hypertension, baseline eGFR (linear spline with knots at 60 and 90 ml/min/1.73 m²), diabetes, congestive heart failure, peripheral arterial disease, cerebrovascular disease, lung disease, liver disease, BMI, ACE-I/ARB use, diuretic use, statin use, surgery type, laparoscopic procedure, hospital day of surgical procedure (hospital day 0-4, 5-14, 15-30), stage of AKI. The hazard ratio for AKI any stage is derived from separate regressions.

Table S4: International Classification of Diseases, 9th Clinical Modification, codes for major surgery

CCS Procedure Code	Surgery type	Major Class
10	Thyroidectomy; partial or complete	ENT
30	Tonsillectomy and/or adenoidectomy	ENT
33	Other OR therapeutic procedures on nose; mouth and pharynx	ENT
36	Lobectomy or pneumonectomy	Thoracic
42	Other OR Rx procedures on respiratory system and mediastinum	Thoracic
43	Heart valve procedures	Cardiac
44	Coronary artery bypass graft (CABG)	Cardiac
49	Other OR heart procedures	Cardiac
50	Extracorporeal circulation auxiliary to open heart procedures	Cardiac
51	Endarterectomy; vessel of head and neck	Vascular
52	Aortic resection; replacement or anastomosis	Vascular
53	Varicose vein stripping; lower limb	Vascular
54	Other vascular catheterization; not heart	Vascular
55	Peripheral vascular bypass	Vascular
56	Other vascular bypass and shunt; not heart	Vascular
59	Other OR procedures on vessels of head and neck	Vascular
60	Embolectomy and endarterectomy of lower limbs	Vascular
61	Other OR procedures on vessels other than head and neck	Vascular
66	Procedures on spleen	General
71	Gastrostomy; temporary and permanent	General
72	Colostomy; temporary and permanent	General
73	Ileostomy and other enterostomy	General
74	Gastrectomy; partial and total	General
75	Small bowel resection	General
80	Appendectomy	General
84	Cholecystectomy and common duct exploration	General
85	Inguinal and femoral hernia repair	General
86	Other hernia repair	General
89	Exploratory laparotomy	General
90	Excision; lysis peritoneal adhesions	General
94	Other OR upper GI therapeutic procedures	General
96	Other OR lower GI therapeutic procedures	General
99	Other OR gastrointestinal therapeutic procedures	General
113	Transurethral resection of prostate (TURP)	Urology
114	Open prostatectomy	Urology
118	Other OR therapeutic procedures; male genital	Urology
142	Partial excision bone	Ortho
153	Hip replacement; total and partial	Ortho
154	Arthroplasty other than hip or knee	Ortho
157	Amputation of lower extremity	Ortho
158	Spinal fusion	Ortho
161	Other OR therapeutic procedures on bone	Ortho
162	Other OR therapeutic procedures on joints	Ortho
164	Other OR therapeutic procedures on musculoskeletal system	Ortho
167	Mastectomy	Thoracic
175	Other OR therapeutic procedures on skin and breast	Thoracic

Table S5: International Classification of Diseases, 9th Clinical Modification, codes for comorbid conditions

Codes (inpatient or outpatient)

Comorbid Condition	ICD9
Hypertension	401-405
Diabetes mellitus	250-250.7
CAD	414.0, 414.8, 414.9, 410.x, 412, 36.1
CHF	428.x
Peripheral arterial disease	440.x, 443.x, 38.0, 38.1, 39.50, 39.22, 39.24, 39.25, 39.26, 39.28
Cerebrovascular disease	430-438
Chronic lung disease	490-496, 500-505, 506.4
Any malignancy	140-172, 174-195, 200-208
Moderate or severe liver disease	572.2 572.3 572.4 572.8, 456.0 456.1 456.2

Figure S1. Kaplan-Meier of post-discharge ESRD among survivors of major surgery, by the presence of >30% decline in eGFR at 30 days and post-operative AKI

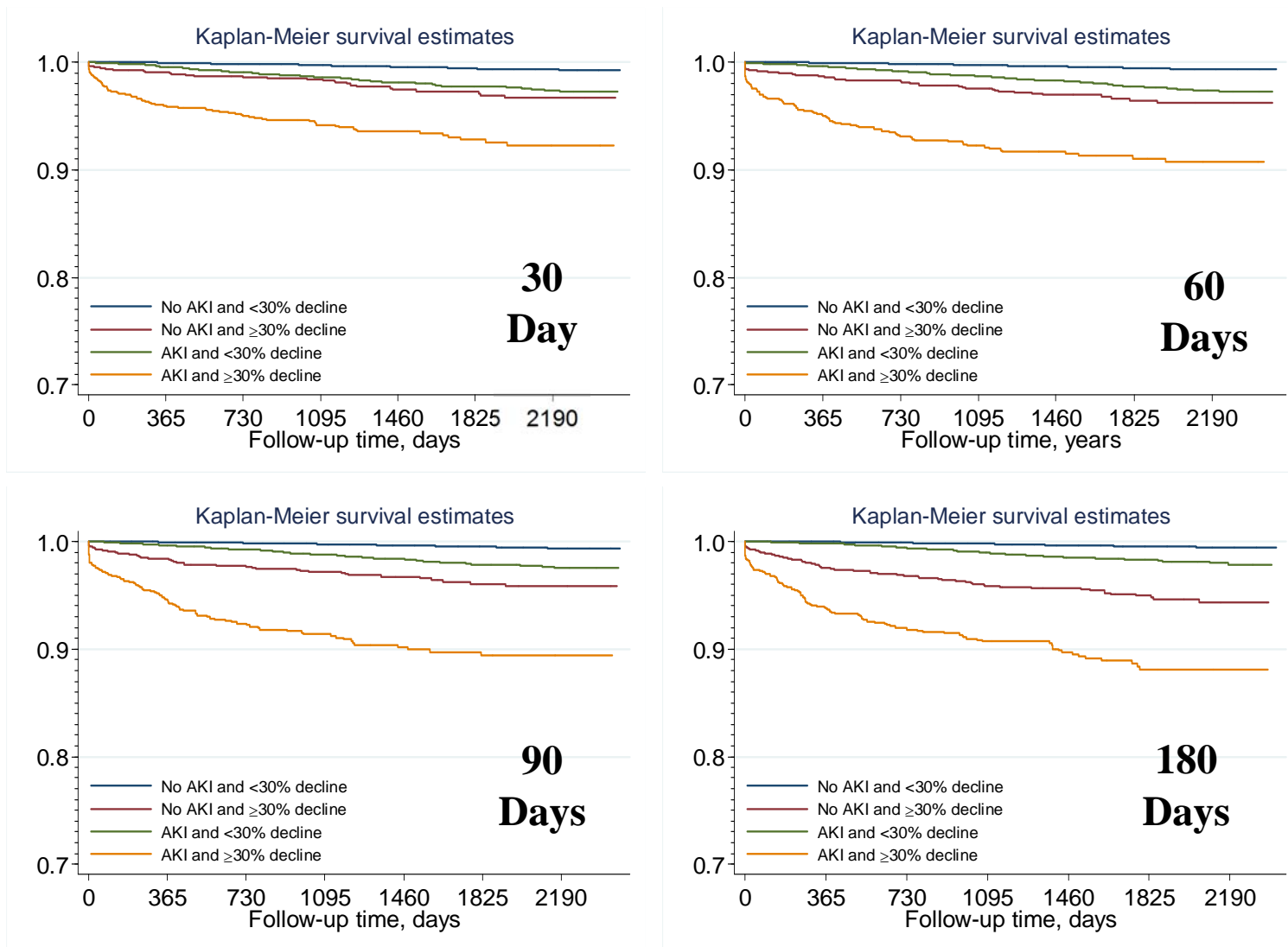
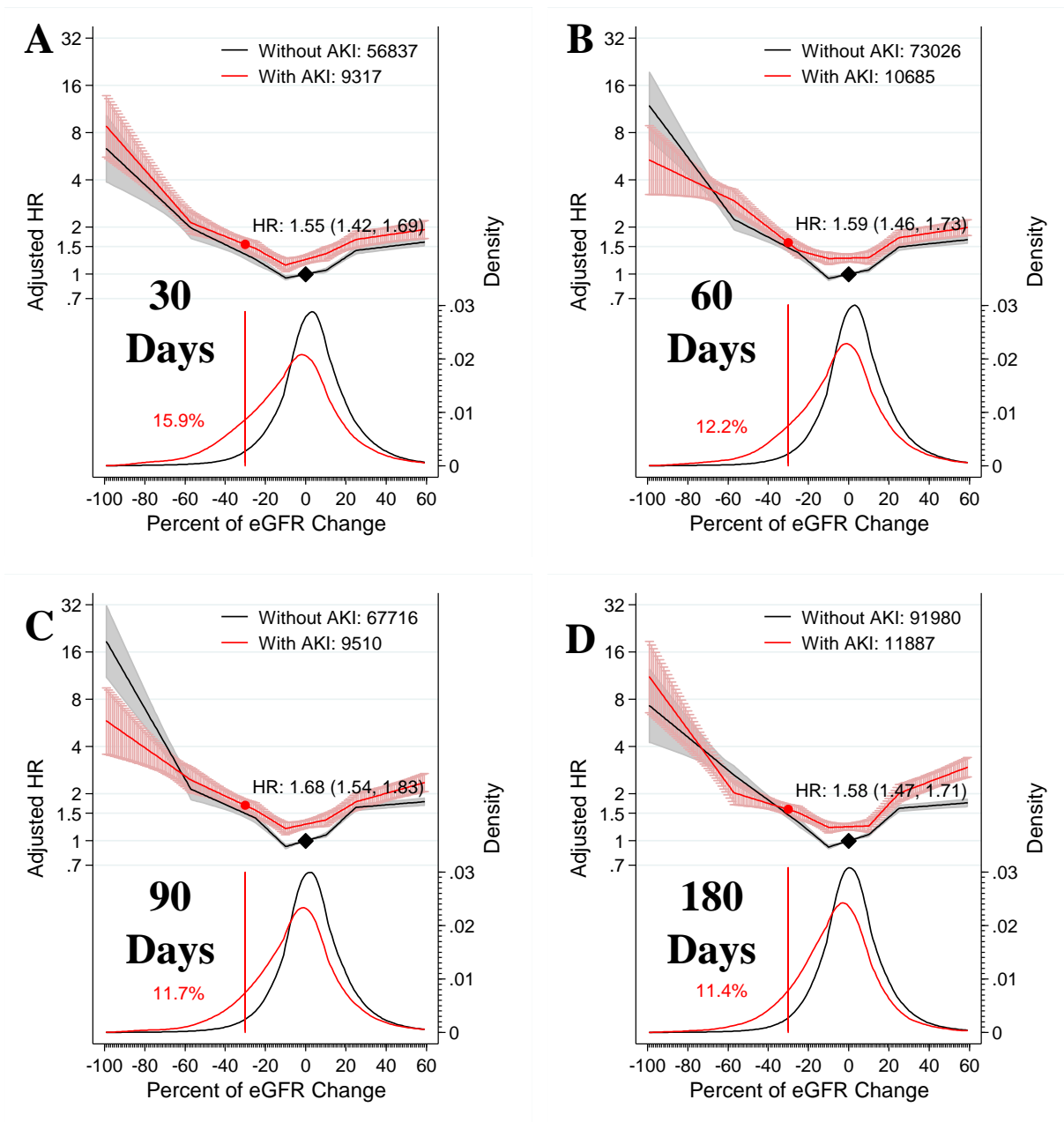
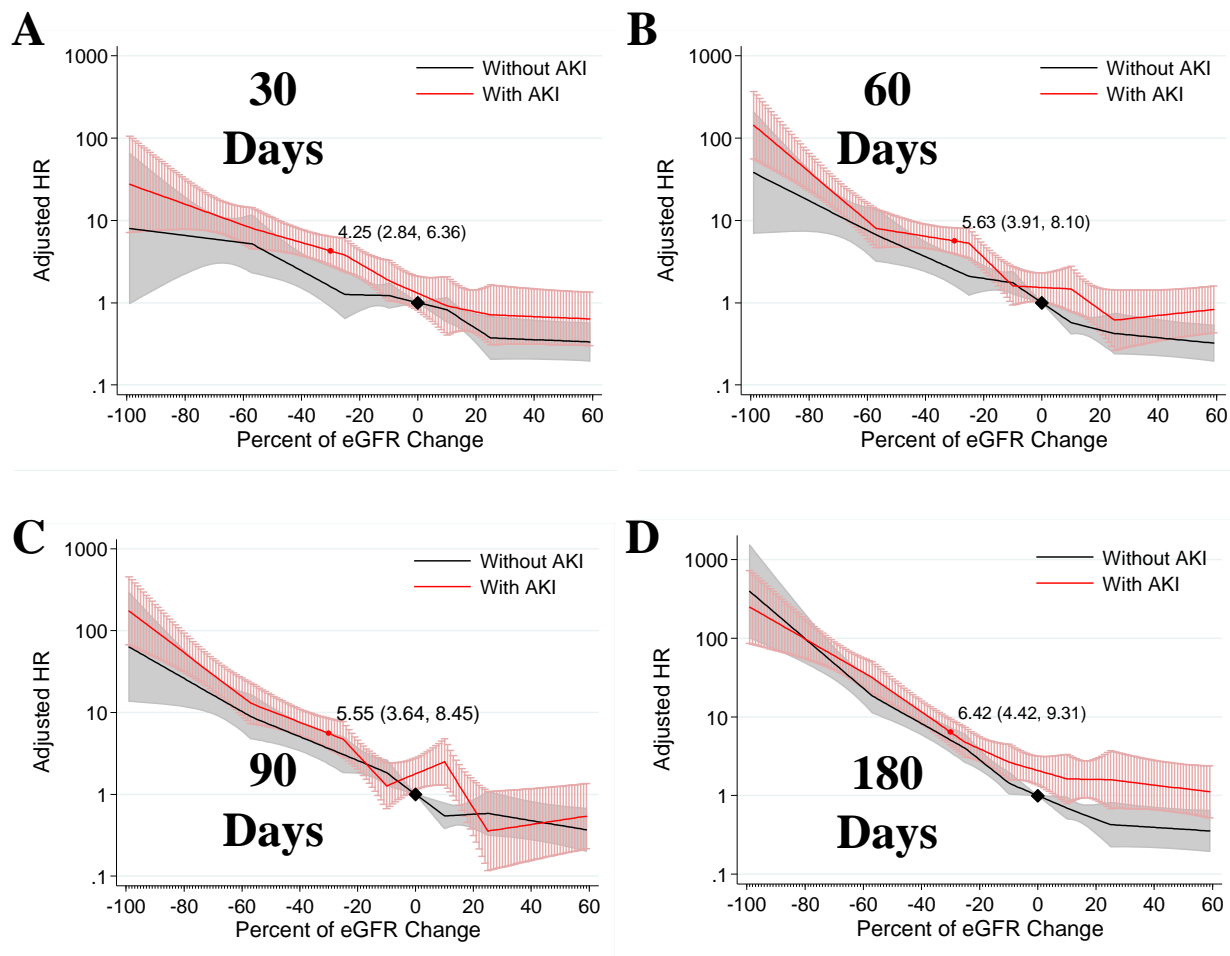


Figure S2: Risk of death associated with post-discharge change in eGFR after major surgery, by post-operative AKI status (upper half of graph); distribution of post-discharge change in eGFR after major surgery, by post-operative AKI status (lower half of graph); both estimates at 30-days (A), 60-days (B), 90-days (C), and 180-days (D) post-discharge.



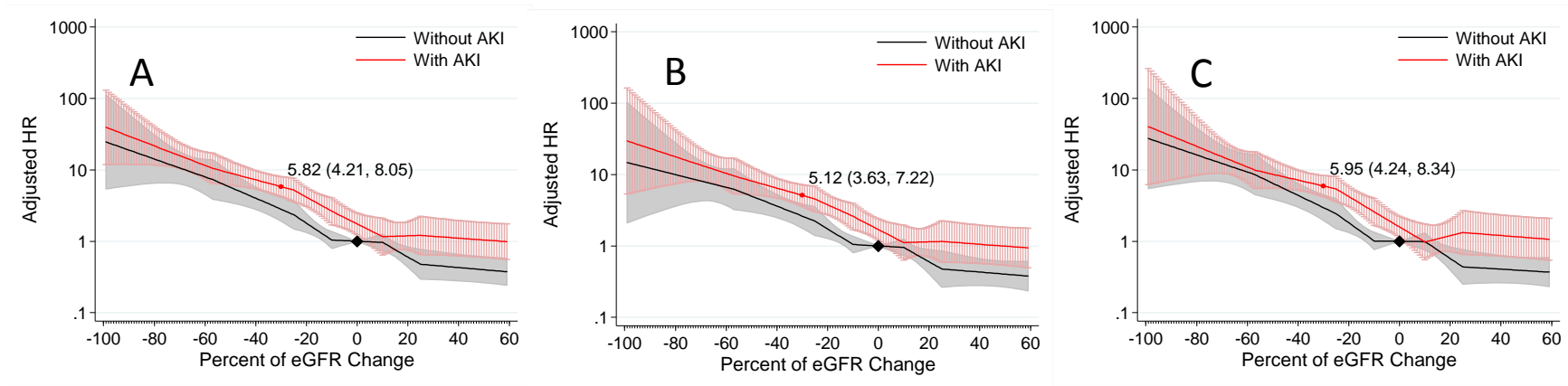
*Black diamond refers to stable eGFR among those without AKI, the reference. The red circle refers to an eGFR decline of 30% among those with AKI. The red line is at eGFR decline 30%, and the red percentage refers to the prevalence of eGFR decline $\geq 30\%$ among those survivors with post-operative AKI.

Figure S3. Risk of ESRD associated with post-discharge change in eGFR after major surgery, by post-operative AKI status, sensitivity analysis; estimates at 30-days (A), 60-days (B), 90-days (C), and 180-days (D) post-discharge. These analyses required that a patient have at least two creatinine measurements during the post-discharge window as a confirmation of eGFR decline.



*Black diamond refers to stable eGFR among those without AKI, the reference. The red circle refers to an eGFR decline of 30% among those with AKI.

Figure S4. Risk of ESRD associated with post-discharge change in eGFR after major surgery, by post-operative AKI status, additional sensitivity analyses for 30-day analysis; excluding ear-nose-throat surgeries (A), taking into account death as a competing risk (B), and weighting participants by the inverse of their probability of having a creatinine measurement during the time window (C).



*Black diamond refers to stable eGFR among those without AKI, the reference. The red circle refers to an eGFR decline of 30% among those with AKI.