Electronic Supplemental Material

1. *AKIN Criteria*

Table E1 - Classification of acute kidney injury proposed by AKIN [7]

Stage	Serum creatinine criteria (over 48-hour period)	Urine output criteria
1	↑ Serum creatinine ≥ 0.3 mg/dl (≥ 26.4 µmol/l) or ↑ 150-200 % (1.5- to 2-fold) from baseline	< 0.5 ml/kg/h for more than 6 h
2	↑ Serum creatinine 200-300 % (> 2- to 3-fold) from baseline	< 0.5 ml/kg/h for more than 12 h
3	↑ Serum creatinine > 300 % (> 3-fold) from baseline or serum creatinine ≥ 4 mg/dl (≥ 354 µmol/l) with an acute increase of at least 0.5 mg/dl (44 µmol/l) or need for renal replacement therapy	< 0.3 ml/kg/h for more than 24 h or anuria for 12 h

2. *Final Analytic Cohort*

The final analytic cohort used for the creatinine analyses (absolute and percentage) consisted of 17,227 patients. Of these, 14,526 had sufficient data for the urine output analysis. 9,080 patients fulfilled the AKIN criteria at least once during their ICU stay. The cohort consisted of 7,453 women (43.3%). The median age on admission was 65.3 years (interquartile range (IQR): 51.3, 77.7). The median SOFA score on admission was 5 (IQR: 2, 8). Other demographic data are presented in Table E2.

Table E2- Patient characteristics, stratified by in-hospital mortality

	Survivors	Expired	Total
Number of patients: N (%)	15,353(89.1)	1,874 (10.9)	17,227 (100)
Female: N (%)	6,536 (42.6)	917 (48.9)	7,453 (43.3)
Age, years: median (IQR)	64.2 (50.4, 76.8)	74.6 (60.4, 83)	65.3 (51.3, 77.7)
SOFA: median (IQR)	5 (2,8)	8(5,11)	5 (2, 8)

Vasoactive therapy: N (%)	5,177 (33.7)	1,103 (58.9)	6,280 (36.5)
Mechanical ventilation: N (%)	7,856 (51.2)	1,419 (75.7)	9,275 (53.8)
Renal replacement therapy: N (%)	157 (1.0)	136 (7.3)	293 (1.7)
Medical service: N (%)	7,667 (49.9)	1,177 (62.8)	8,844 (51.3)
Selected Elixhauser comorbidities: N (%)			
Congestive heart failure	2,476 (16.1)	532 (28.4)	3,008 (17.5)
Cardiac arrhythmias	2,398 (15.6)	490 (26.1)	2,888 (16.8)
Hypertension	4,824 (31.4)	550 (29.3)	5,374 (31.2)
Chronic pulmonary disease	2,411 (15.7)	318 (17.0)	2,729 (15.8)
Diabetes	3,399 (22.1)	355 (18.9)	3,754 (21.8)
Renal failure	460 (3.0)	101 (5.4)	561 (3.3)
Liver disease	603 (3.9)	124 (6.6)	727 (4.2)
Lymphoma	212 (1.4)	59 (3.1)	271 (1.6)
Coagulopathy	796 (5.2)	161 (8.6)	957 (5.6)

A total of 417 patients were excluded from this study due to missing data. The median age and SOFA score of these excluded patients were 62.2 years (IQR: 47.3, 76.2) and 5 (IQR: 2, 9), respectively. Also, 41.2% were women and 68.1% were medical patients. In-hospital mortality and RRT rates were 9.4% and 2.2%, respectively. Besides the higher percentage of medical patients, the excluded patients were similar to the included patients with respect to descriptive statistics.

3. Cross-sections of Figures 1 and 2 at the AKIN Criteria

Figures E1 and E2 draw parallels to the AKIN criteria by showing the cross-sections of Figs. 1 and 2, respectively, at the observation periods utilized by AKIN. Figures E1(A) and E2(A) show a near-linear relationship between mortality/RRT rate and absolute creatinine increase. Figures E1(B) and E2(B) also show an approximately linear relationship between mortality/RRT and percentage creatinine increase up to a creatinine increase of 300%. In Fig. E1(B), creatinine increases above 350% actually resulted in decreased mortality rates, which may again be due to a

small number of deemed AKI patients (<100). As seen in Figs. E1(C) and E2(C), mortality and RRT rates increased rapidly as urine output decreased below 0.4 ml/kg/h. Also, longer observation periods were associated with higher mortality and RRT rates.

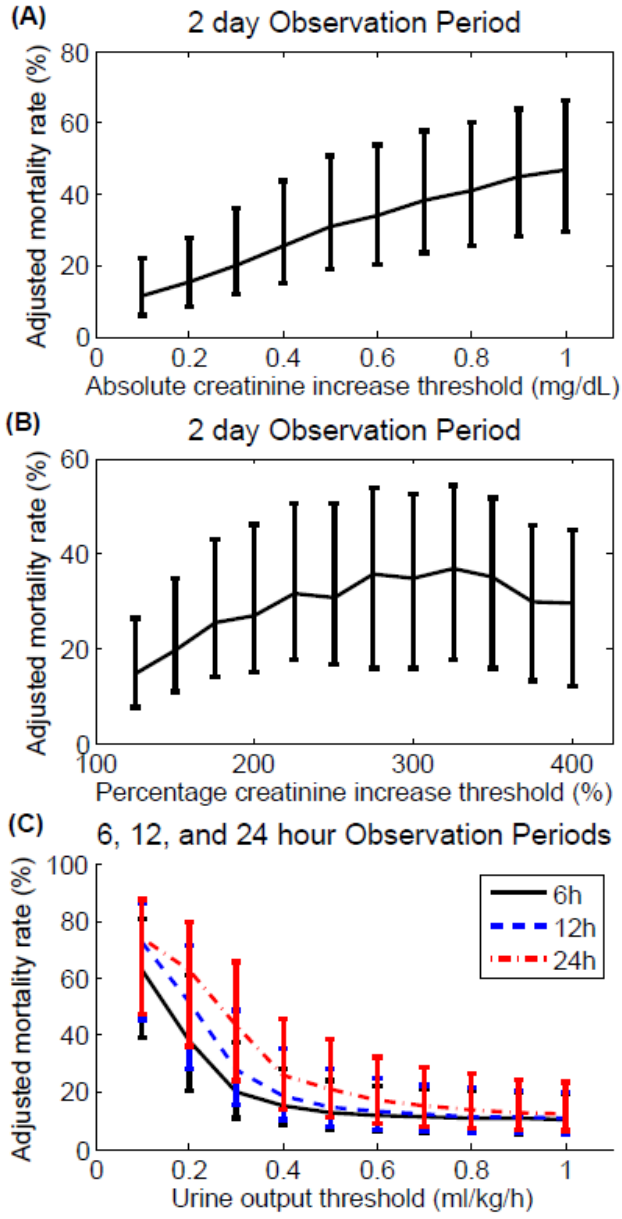

Figure E1 – Cross-sections of Fig. 1 at the AKIN observation periods illustrating the relationship between adjusted in-hospital mortality rate and (A) absolute increase in serum creatinine at 2 days (N=17,227), (B) percentage increase in serum creatinine at 2 days (N=17,227), and (C) urine output at 6, 12, 24 hours (N=14,526).

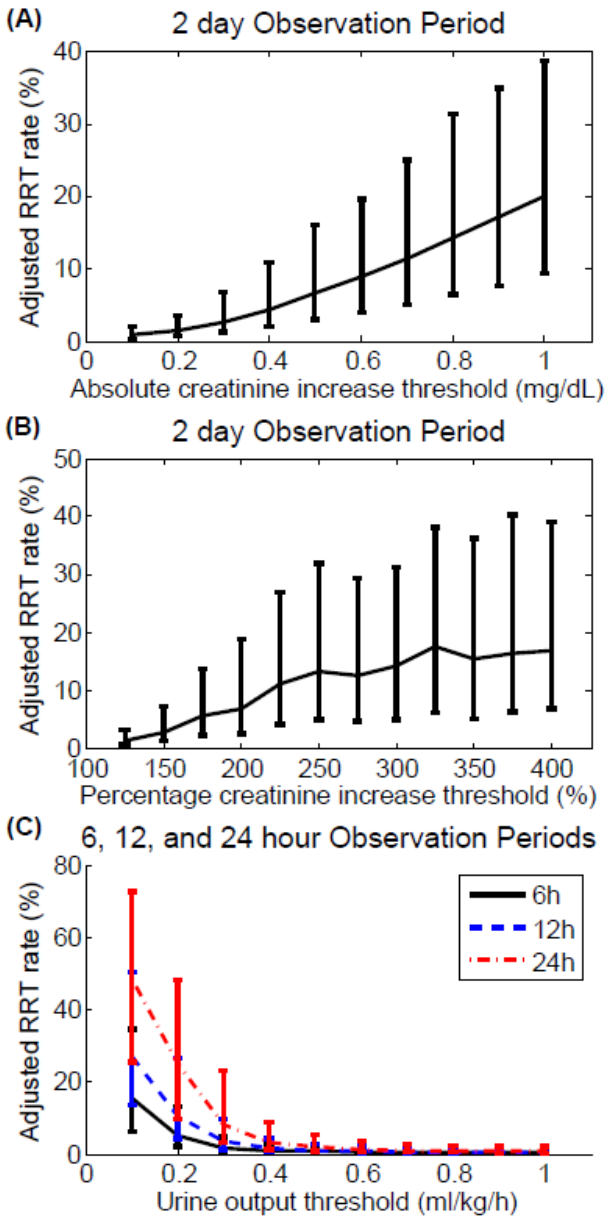

Figure E2 – Cross-sections of Fig. 2 at the AKIN observation periods illustrating the relationship between adjusted renal replacement therapy rate and (A) absolute increase in serum creatinine at 2 days (N=17,227), (B) percentage increase in serum creatinine at 2 days (N=17,227), and (C) urine output at 6, 12, 24 hours (N=14,526).

4. AUC Contour Plots for In-hospital Mortality and RRT Predictions

Figures E3 and E4 show AUC contour plots for in-hospital mortality and RRT predictions, respectively. In both figures, some specific combinations of threshold and observation period are associated with the highest AUCs (e.g., 170 % and 6 days in Fig. E3(B)). However, the variability in AUC is small in each plot (the following shown in median (IQR)): Fig. E3(A) – 0.790 (0.788, 0.791); Fig. E3(B) – 0.784 (0.782, 0.786); Fig. E3(C) – 0.806 (0.801, 0.809); Fig. E4(A) – 0.932 (0.922, 0.935); Fig. E4(B) – 0.908 (0.901, 0.915); Fig. E4(C) – 0.904 (0.896, 0.914).

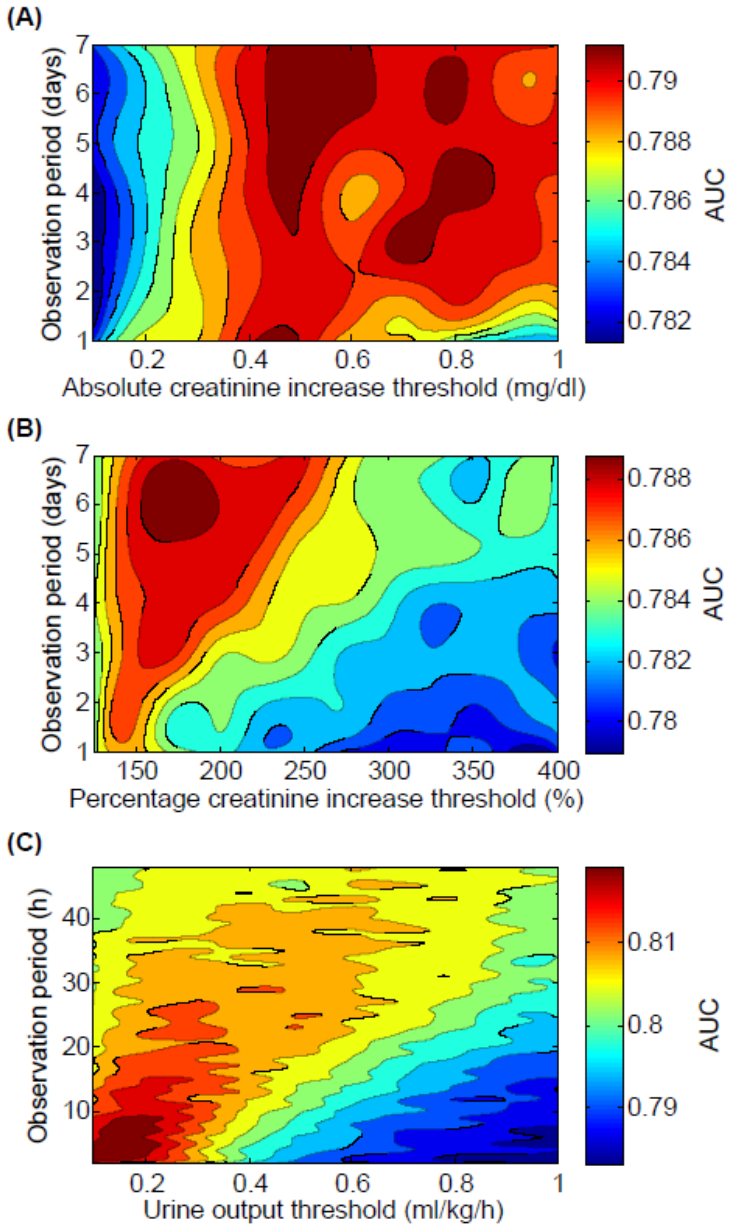

Figure E3 – In-hospital mortality prediction AUC contour plots for (A) absolute increase in serum creatinine (N=17,227), (B) percentage increase in serum creatinine (N=17,227), and (C) urine output (N=14,526). The predictive performance of the corresponding regression models in Fig. 1 is shown. AUCs were evaluated at a fine grid of observation periods and thresholds (steps of 1 day, 1 h, 0.1 mg/dl, 25 %-points, and 0.1 ml/kg/h), and the contour plots were produced using cubic spline interpolation.

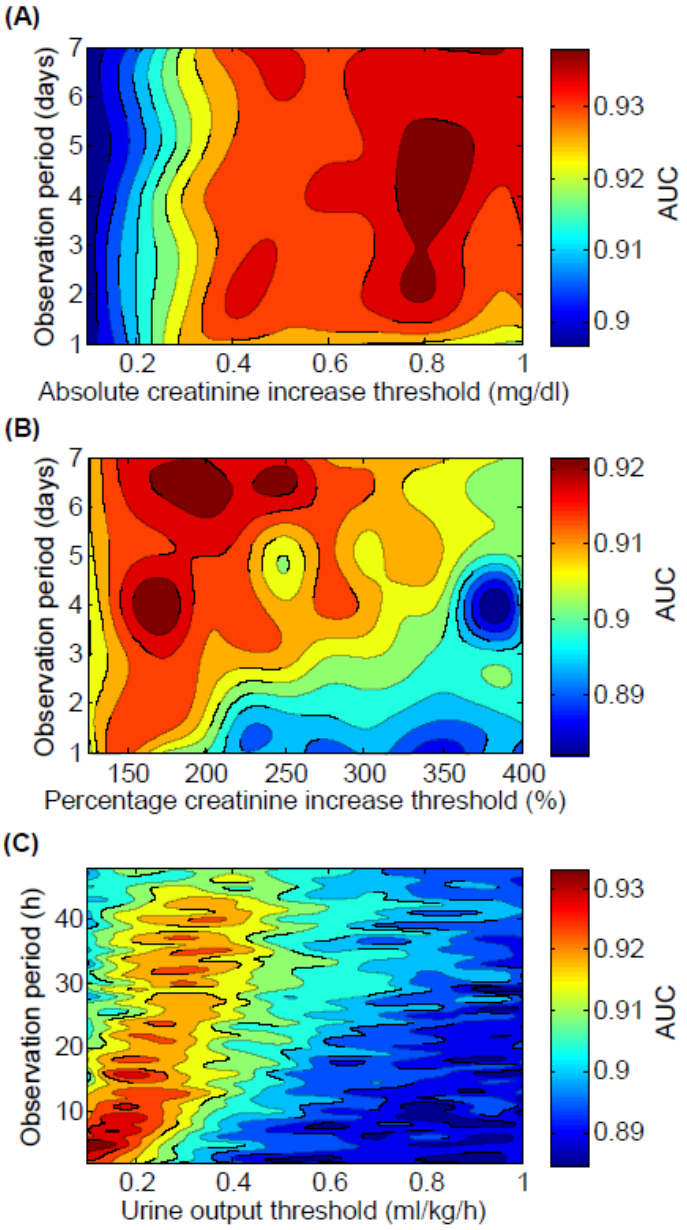

Figure E4 - Renal replacement therapy prediction AUC contour plots for (A) absolute increase in serum creatinine (N=17,227), (B) percentage increase in serum creatinine (N=17,227), and (C) urine output (N=14,526). The predictive performance of the corresponding regression models in Fig. 2 is shown. AUCs were evaluated at a fine grid of observation periods and thresholds (steps of 1 day, 1 h, 0.1 mg/dl, 25 %-points, and 0.1 ml/kg/h), and the contour plots were produced using cubic spline interpolation.