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**Supplemental Table 1: *International Classification of Diseases, Ninth Edition, Clinical Modification* Codes for Invasive Infection**

<b>ICD-9-CM Code<sup>a</sup></b>	<b>Description</b>
001	Cholera
002	Typhoid/paratyphoid fever
003	Other salmonella infection
004	Shigellosis
005	Other food poisoning
008	Intestinal infection not otherwise classified
009	Ill-defined intestinal infection
010	Primary tuberculosis infection
011	Pulmonary tuberculosis
012	Other respiratory tuberculosis
013	Central nervous system tuberculosis
014	Intestinal tuberculosis
015	Tuberculosis of bone and joint
016	Genitourinary tuberculosis
017	Tuberculosis not otherwise classified
018	Miliary tuberculosis
020	Plague
021	Tularemia
022	Anthrax
023	Brucellosis
024	Glanders
025	Melioidosis
026	Rat-bite fever
027	Other bacterial zoonoses
030	Leprosy
031	Other mycobacterial disease
032	Diphtheria
033	Whooping cough
034	Streptococcal throat/scarlet fever
035	Erysipelas
036	Meningococcal infection
037	Tetanus

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038	Septicemia
039	Actinomycotic infections
040	Other bacterial diseases
041	Bacterial infection in other diseases not otherwise specified
090	Congenital syphilis
091	Early symptomatic syphilis
092	Early syphilis latent
093	Cardiovascular syphilis
094	neurosyphilis
095	Other late symptomatic syphilis
096	Late syphilis latent
097	Other and unspecified syphilis
098	Gonococcal infections
100	Leptosprosis
101	Vincent's angina
102	Yaws
103	Pinta
104	Other spirochetal infection
110	Dermatophytosis
111	Dermatomycosis not otherwise classified or specified
112	Candidiasis
114	Coccidioidomycosis
115	Histoplasmosis
116	Blastomycotic infection
117	Other mycoses
118	Opportunistic mycoses
320	Bacterial meningitis
322	Meningitis, unspecified
324	Central nervous system abscess
325	Phlebitis of intracranial sinus
420	Acute pericarditis
421	Acute or subacute endocarditis
451	Thrombophlebitis
461	Acute sinusitis
462	Acute pharyngitis

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463	Acute tonsillitis
464	Acute laryngitis/tracheitis
465	Acute upper respiratory infection of multiple sites/not otherwise specified
481	Pneumococcal pneumonia
482	Other bacterial pneumonia
485	Bronchopneumonia with organism not otherwise specified
486	Pneumonia, organism not otherwise specified
491.21	Acute exacerbation of obstructive chronic bronchitis
494	Bronchiectasis
510	Empyema
513	Lung/mediastinum abscess
540	Acute appendicitis
541	Appendicitis not otherwise specified
542	Other appendicitis
562.01	Diverticulitis of small intestine without hemorrhage
562.03	Diverticulitis of small intestine with hemorrhage
562.11	Diverticulitis of colon without hemorrhage
562.13	Diverticulitis of colon with hemorrhage
556	Anal and rectal abscess
567	Peritonitis
569.5	Intestinal abscess
569.83	Perforation of intestine
572	Abscess of liver
572.1	Portal pyemia
575.0	Acute cholecystitis
590	Kidney infection
597	Urethritis/urethral syndrome
599.0	Urinary tract infection not otherwise specified
601	Prostatic inflammation
614	Female pelvic inflammation disease
615	Uterine inflammatory disease
616	Other female genital inflammation
681	Cellulitis, finger/toe
682	Other cellulitis or abscess
683	Acute lymphadenitis

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686	Other local skin infection
711.0	Pyogenic arthritis
730	Osteomyelitis
790.7	Bacteremia
996.6	Infection or inflammation of device/graft
998.5	Postoperative infection
999.3	Infectious complication of medical care not otherwise classified

ICD-9-CM, International Classification of Disease, Ninth Revision, Clinical Modification

<sup>a</sup>Where 3 or 4 digit codes are listed, all associated subcodes were included

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**Supplemental Table 2: *International Classification of Diseases, Ninth Edition, Clinical Modification* Codes for Organ Dysfunction**

<b>ICD-9-CM Code<sup>a</sup></b>	<b>Description</b>
785.5	Shock without trauma
458	Hypotension
96.7	Mechanical ventilation
348.3	Encephalopathy
293	Transient organic psychosis
348.1	Anoxic brain damage
287.4	Secondary thrombocytopenia
287.5	Thrombocytopenia, unspecified
286.9	Other/unspecified coagulation defect
286.6	Defibrination syndrome
570	Acute and subacute necrosis of liver
573.4	Hepatic infarction
584	Acute kidney failure

ICD-9-CM, International Classification of Disease, Ninth Revision, Clinical Modification

<sup>a</sup>Where 3 or 4 digit codes are listed, all associated subcodes were included

**Supplemental Table 3: Nephrotoxic Injury Negated by Just-in-time Action (NINJA) Drugs**

<b>PHIS+ code and drug name</b>
127101 Acyclovir
125201 Amphotericin B
121101 Amikacin sulfate,
112205 Aspirin
135105 Captopril
171917 Carboplatin
112351 Celecoxib
127103 Cidofovir
171920 Cisplatin
124147 Colistimethate sodium
167115 Cyclosporine
119113 Deferasirox
174143 Diatrizoate meglumine
174145 Diatrizoate sodium
135111 Enalapril maleate (includes enalaprilat)
127107 Foscarnet sodium
127113 Ganciclovir
121105 Gentamicin
112260 Ibuprofen
171105 Ifosfamide
112264 Indomethacin
174123 Iodixanol
174107 Iohexol
174109 Iopamidol
174119 Iopromide
174115 Ioversol
174111 Ioxaglate meglumine and ioxaglate sodium
174121 Ioxilan
112270 Ketorolac tromethamine
135121 Lisinopril
113451 Lithium
135215 Losartan potassium
147450 Mesalamine

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171201 Methotrexate
171417 Mitomycin
121247 Nafcillin sodium
112288 Naproxen
151255 Pamidronate disodium
129121 Pentamidine isethionate
121261 Piperacillin sodium
121265 Piperacillin sodium and tazobactam sodium
124151 Polymyxin B sulfate
167137 Sirolimus
124431 Sulfasalazine
167135 Tacrolimus
127173 Tenofovir
121271 Ticarcillin disodium and clavulanate potassium
121135 Tobramycin sulfate
116061 Topiramate
127133 Valacyclovir HCl
127135 Valganciclovir HCl
135225 Valsartan
124133 Vancomycin (HCl)
151263 Zoledronic acid
116007 Zonisamide



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**Supplemental Table 4: Creatinine Values to Determine Baseline Kidney Function for Patients Without Measured Baseline Creatinine**

Age	Creatinine, Median (mg/dL)		Creatinine, Upper Limit Normal (mg/dL)	
	Male	Female	Male	Female
6 mos to <1 year		0.25		0.36
1 to < 2 years		0.27		0.39
2 to <3 years		0.30		0.42
3 to <4 years		0.33		0.46
4 to <5 years		0.36		0.50
5 to <6 years		0.38		0.53
6 to < 7 years		0.43		0.58
7 to < 8 years		0.45		0.60
8 to <9 years		0.47		0.62
9 to <10 years		0.50		0.69
10 to <11 years		0.52		0.71
11 to <12 years		0.54		0.71
12 to <13 years		0.57		0.74
13 to <14 years		0.61		0.83
	<b>Male</b>	<b>Female</b>	<b>Male</b>	<b>Female</b>
14 to <15 years	0.68	0.62	0.91	1.24
15 to < 16 years	0.78	0.68	1.01	1.36
16 to <17 years	0.82	0.70	1.07	1.40
17 to <18 years	0.85	0.71	1.10	1.42

**Supplemental Table 5: Imputed Versus Measured Baseline Creatinine Values in the Primary Analysis for Patients with Known Measured Baseline Creatinine after Excluding Those with Kidney and Urologic Complex Chronic Conditions**

Age	Sex	Measured Baseline Creatinine (mg/dL)			Imputed Baseline Creatinine (mg/dL)	Imputed Baseline Comparison to Actual Values
		Mean	LCL	UCL		
6 mos to <1 year	Both	0.17	0.15	0.19	0.25	Greater than UCL
1 to <2 years	Both	0.19	0.17	0.21	0.27	Greater than UCL
2 to <3 years	Both	0.19	0.18	0.21	0.3	Greater than UCL
3 to <4 years	Both	0.20	0.18	0.22	0.33	Greater than UCL
4 to <5 years	Both	0.21	0.19	0.24	0.36	Greater than UCL
5 to <6 years	Both	0.28	0.25	0.31	0.38	Greater than UCL
6 to <7 years	Both	0.24	0.21	0.27	0.43	Greater than UCL
7 to <8 years	Both	0.28	0.23	0.34	0.45	Greater than UCL
8 to <9 years	Both	0.27	0.23	0.32	0.47	Greater than UCL
9 to <10 years	Both	0.26	0.20	0.33	0.5	Greater than UCL
10 to <11 years	Both	0.32	0.28	0.36	0.52	Greater than UCL
11 to <12 years	Both	0.30	0.25	0.36	0.54	Greater than UCL
12 to <13 years	Both	0.36	0.31	0.41	0.57	Greater than UCL
13 to <14 years	Both	0.41	0.34	0.49	0.61	Greater than UCL
14 to <15 years	Male	0.38	0.28	0.51	0.68	Greater than UCL
14 to <15 years	Female	0.47	0.36	0.60	0.62	Greater than UCL
15 to <16 years	Male	0.47	0.37	0.60	0.78	Greater than UCL
15 to <16 years	Female	0.56	0.44	0.71	0.68	Between LCL and UCL
16 to <17 years	Male	0.47	0.41	0.53	0.82	Greater than UCL
16 to <17 years	Female	0.41	0.35	0.49	0.7	Greater than UCL
17 to <18 years	Male	0.45	0.38	0.52	0.85	Greater than UCL
17 to <18 years	Female	0.37	0.30	0.46	0.71	Greater than UCL

**Supplemental Table 6: Patient Encounter Characteristics by Components of MAKE30**

<b>Variable<sup>1</sup></b>	<b>No MAKE30</b>	<b>Death30<sup>2</sup></b>	<b>KRT30<sup>2</sup></b>	<b>PKD30<sup>2</sup></b>
N	1524	75	29	98
Age, years	8 (3-13)	8 (3-14)	12 (3-14)	10 (4-14)
<b>Age categories</b>				
6 months to <1 year	89 (6)	7 (9)	3 (10)	7 (7)
1 to <6 years	530 (35)	23 (31)	6 (21)	21 (21)
6 to <13 years	479 (31)	24 (32)	9 (31)	35 (36)
13 to <18 years	426 (28)	21 (28)	11 (38)	35 (36)
Sex, female	758 (50)	32 (44)	12 (41)	40 (41)
<b>Race</b>				
Non-Hispanic White	1,042 (68)	56 (75)	19 (66)	71 (72)
Non-Hispanic Black	209 (14)	5 (7)	4 (14)	10 (10)
Hispanic	121 (8)	5 (7)	1 (3)	6 (6)
Asian	47 (3)	2 (3)	1 (3)	2 (2)
Other	105 (7)	7 (9)	4 (14)	9 (9)
<b>Payer</b>				
Private	693 (45)	37 (50)	18 (62)	44 (45)
Government	696 (46)	28 (37)	10 (35)	39 (40)
Other payer	135 (9)	10 (13)	1 (3)	15 (15)
Admission through ED	1,284 (84)	55 (73)	24 (83)	73 (75)
Pediatric ICU admission	974 (64)	68 (91)	25 (86)	69 (70)
<b>Number of complex chronic conditions</b>				
None	272 (18)	1 (1)	0	10 (10)
One	259 (17)	19 (25)	0	14 (14)
Two	231 (15)	11 (15)	1 (3)	13 (13)
Three or more	762 (50)	44 (59)	28 (97)	61 (62)
<b>Type of complex chronic conditions</b>				
Cardiovascular	325 (21)	22 (29)	9 (31)	28 (29)
Respiratory	255 (17)	7 (9)	3 (10)	10 (10)
Neurologic/neuromuscular	483 (32)	36 (48)	5 (17)	25 (26)
Hematologic/immunodeficiency	201 (13)	14 (19)	10 (35)	20 (20)
Malignancy	307 (20)	20 (27)	11 (38)	24 (25)
Kidney/urologic	164 (11)	12 (16)	29 (100)	33 (34)
Gastrointestinal	660 (43)	17 (23)	10 (35)	35 (36)

Metabolic	231 (15)	23 (31)	9 (31)	26 (27)
Other congenital/genetic	194 (13)	8 (11)	2 (7)	14 (14.3)
Neonatal	50 (3)	4 (5)	0	3 (3)
Technology dependency	737 (48)	36 (48)	29 (100)	54 (55)
Transplantation	214 (14)	13 (17)	8 (28)	27 (28)
Creatinine (mg/dL), baseline <sup>3</sup>	0.3 (0.3-0.5)	0.3 (0.2-0.6)	0.5 (0.3 - 0.6)	0.4 (0.2 - 0.6)
Estimated GFR (mL/min/1.73 m <sup>2</sup> ), baseline <sup>4</sup>	107 (107-177)	107 (107- 193)	107 ( 107 - 144)	145 (107 - 204 )
Stage 2/3 AKI <sup>5</sup>	409 (27)	36 (48)	22 (76)	89 (91)
Therapies				
Non-invasive mechanical ventilation	209 (14)	11 (15)	9 (31)	17 (17)
Invasive mechanical ventilation, ETT	698 (46)	62 (83)	22 (76)	62 (63)
Invasive mechanical ventilation, tracheostomy	164 (11)	7 (9)	2 (7)	5 (5)
Lactated Ringer's fluid	30 (2)	1 (1)	0	2 (2)
Blood Transfusion	49 (3)	3 (4)	7 (24)	8 (8)
Vasoactive medication	574 (38)	61 (81)	23 (79)	57 (58)
Corticosteroids	559 (37)	44 (59)	20 (69)	56 (57)
Diuretics	537 (35)	40 (53)	25 (87)	60 (61)
Extracorporeal membrane oxygenation	19 (1)	9 (12)	3 (10)	4 (4)
NINJA drug exposure				
Aminoglycosides	491 (32)	32 (43)	10 (35)	37 (38)
≥2 non-aminoglycoside NINJA drugs	713 (47)	29 (38)	16 (55)	49 (50)
<2 NINJA drugs and no aminoglycoside	320 (21)	14 (19)	3 (10)	12 (12)

MAKE30, major adverse kidney events within 30 days; Death30, all-cause hospital mortality censored at discharge or 30 days; KRT30, new use of kidney replacement therapy censored at discharge or 30 days; PKD30, persistent kidney dysfunction censored at discharge or 30 days; ED, emergency department; ICU, intensive care unit; ETT, endotracheal tube; GFR, glomerular filtration rate; AKI, acute kidney injury; NINJA, Nephrotoxic Injury Negated by Just-in-time Action (reference 25)

<sup>1</sup>Data presented as n (%) or median (interquartile range)

<sup>2</sup>Groups are not mutually exclusive

<sup>3</sup>Baseline creatinine was measured for 988 (59%) and imputed for 697 (41%) of patients

<sup>4</sup>Baseline estimated GFR was calculated using the height-independent equation:  $eGFR \text{ mL/kg/1.73 m}^2 = 10.7.3 / (\text{measured or estimated baseline creatinine} / Q)$  with Q equal to the median serum creatinine concentration for children based on age and sex (see Supplemental Table 4 and Reference 30)

<sup>5</sup>Stage 2 and 3 AKI within the first seven days of admission was determined using the Kidney Disease Improving Global Outcomes (KDIGO) classification system (Reference 26)

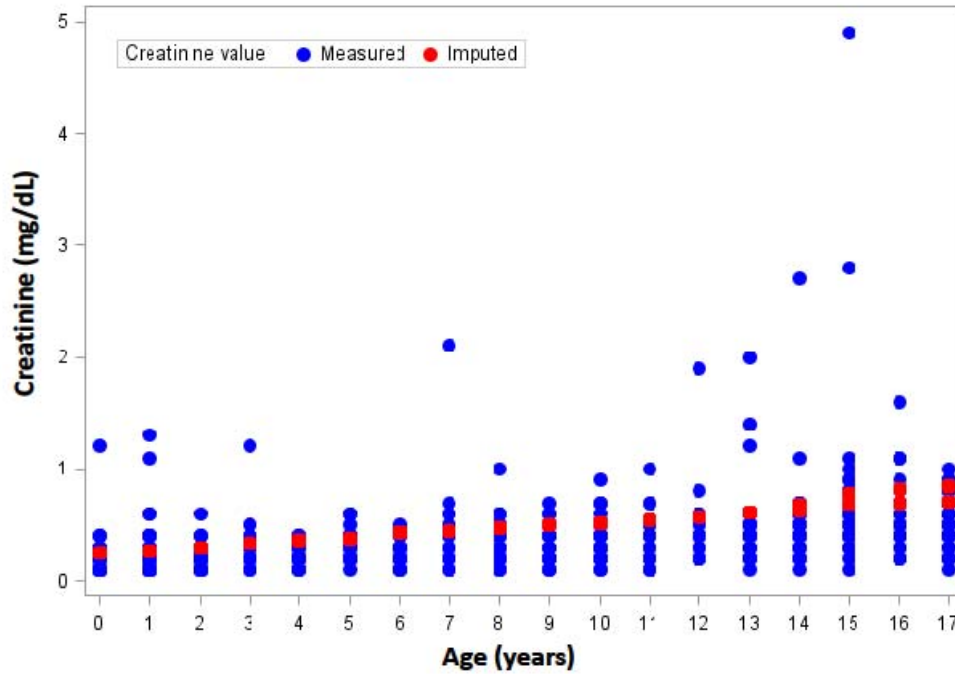
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**Supplemental Table 7: Distribution across Components of MAKE30**

<b>MAKE30 Component</b>	<b>Number</b>	<b>Percentage</b>
None	1524	90.4
Mortality, only	46	2.7
KRT, only	17	1.0
PKD, only	59	3.5
Mortality + KRT	0	0
Mortality + PKD	27	1.6
KRT + PKD	10	0.6
Mortality + KRT + PKD	2	0.1

MAKE30, major adverse kidney events within 30 days; KRT, kidney replacement therapy; PKD, persistent kidney dysfunction

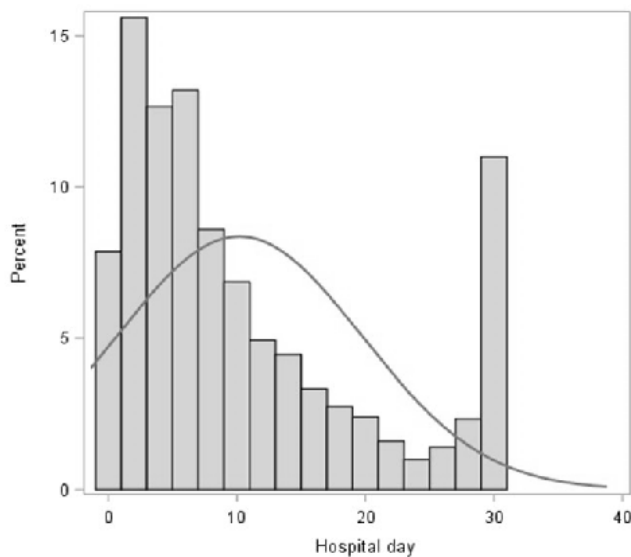
### Supplemental Figure 1: Imputed Versus Measured Baseline Creatinine Values



For the subset of patients with an available baseline creatinine value measured as the lowest recorded creatinine available between 12 months and 24 hours prior to the index hospital admission and who did not have kidney or urologic chronic comorbid conditions, the measured baseline creatinine value was compared to what the baseline would have been had an imputed value representing the median creatinine for age and sex been used. Imputed baseline creatinine (red values) overlap the approximate normal range indicated by the measured baseline creatinine (blue range), indicating that imputation closely approximated baseline creatinine. For patients age  $\geq 14$  years, the two imputed (red) values represent different imputed creatinine values for male and female patients.

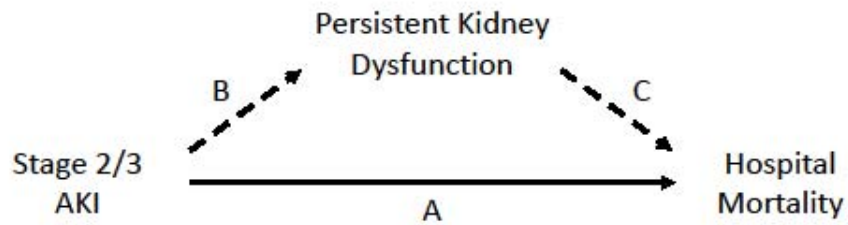
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## Supplemental Figure 2: Hospital Day on Which Serum Creatinine to Define Persistent Kidney Dysfunction was Measured



The serum creatinine value closest to discharge or 30 days after hospitalization, whichever came first, was used to determine persistent kidney dysfunction. The histogram depicts the hospital day on which kidney dysfunction was measured (median day 7 (IQR 3-15) of hospitalization).

**Supplemental Figure 3: Mediation Analysis of the Association of Stage 2/3 Acute Kidney Injury with Mortality at Hospital Discharge**



Model	Exposure	Outcome	OR	95% CI	P Value
A	Stage2/3 AKI	Hospital Mortality	2.9	1.9, 4.4	<0.001
B	Stage2/3 AKI	PKD	27.6	13.7, 55.8	<0.001
C	Stage2/3 AKI, adjusted for PKD	Hospital Mortality	1.5	0.9, 2.5	0.12
C	PKD, adjusted for stage 2/3 AKI	Hospital Mortality	8.0	4.4, 14.7	<0.001

Stage 2/3 acute kidney injury (AKI) within the first seven days of hospitalization was significantly associated with mortality at hospital discharge (model A) and with persistent kidney dysfunction (PKD) measured as the last available creatinine prior to hospital discharge or within 30 days of sepsis recognition, whichever came first (model B). However, stage 2/3 AKI was no longer significantly associated with mortality at hospital discharge after controlling for PKD (model C), supporting that the association of stage 2/3 AKI with hospital mortality is largely mediated through PKD.