Supplemental Material

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Supplemental Table 1. Predictor variables used to create parsimonious prediction models.

Demographic variables (n=7)			
• Age • Ethnicity	• Height • Race	• Sex • Time since admission[a]	• Weight
Vital signs (n=6)			
• Arterial line diastolic blood pressure	• Diastolic blood pressure • Heart rate	• Oxygen saturation • Respiratory rate	• Systolic blood pressure
Locations variables (n=24)			
• Cardiology • Catheter lab • CTICU • Emergency room • Endoscopy suite • General pediatrics	• Hematology/oncology • Interventional radiology • Maternity • MICU • Neurological ICU • Neurology	• NICU • Nursery • Perioperative • PICU • Psychiatry	• SICU • Surgery • Surgical oncology • Transplant • Transport
Procedures variables (n=85)			
• Abdomen CT • Abdomen MR • Abdomen US • Abdomen XR • Arterial line placement • Autopsy • Biopsy • BiPAP • Blood culture • Bone XR • Car seat test • Cardiac catheter • Central line • Chest CT • Chest MR • Chest PT • Chest XR • Comfort code order • Consult DART • Contact precaution order • Contrast study • CPAP	• Critical care transport • Head CT • Head MR • Educational US • EEG • ETT adjustment • Extremities CT • Extremities MR • Extubation • Fall risk order • Feeding tube • Fluoroscopy study • Foley catheter • Foreign body XR • Full code status • Gadolinium study • Head US • HFOV • High flow oxygen • Hip US • Contrast IR procedure • Isolette placement	• Limited code order • Liver diet • Low salt diet • Mechanical ventilation • Neonatal abstinence score • NIPPV • Nitric oxide • NPO order • Nuclear scan • Oxygen • Paracentesis • Phototherapy • Physical therapy • PICC placement • PICU consult • Plasma transfusion • Plasmapheresis • Platelet transfusion • Posttransfusion reaction • RBC transfusion • Rectal tube	• Renal diet • Renal US • Restraints • SCD order • Sepsis trigger order • Soft tissue US • Speech swallow test • Spine MR • Spine US • TEE • Telemetry • TTE • Turn patient order • Umbilical line placement • Urine culture • Venous US • Ventilation order • Wound care • Wound VAC • 1:1 Order (Sitter)
Continuous laboratory variables (n=27)			
• Absolute lymphocyte count • Anion gap • Bicarbonate • BUN • BUN/creatinine ratio • Calcium • Carbon dioxide	• Chloride • Creatinine • eGFR • Eosinophils • Glucose • Hematocrit • Hemoglobin	• Lymphocytes • MCHC • MCV • Monocytes • MPV • Neutrophils • Platelet count	• Potassium • RBC count • RDW • Sodium • WBC count • Δ Creat 48

Medication groups variables (n=34)				
• ACEi/ARB • ACEi • Aminoglycosides • Antibiotics • Antidepressants • Antifungals • ARB	• Anti-thymocyte globulin • Breast milk • ß-blockers • ß-lactam antibiotics • Calcium channel blockers • Chemotherapy	• CMV immunoglobin • Diuretics • Fluoroquinolones • HAART • Immune globulin • Immunomodulators • Insulins • Iodine contrasts	• Potassium-sparing diuretics • Loop diuretics • Narcotics • NSAIDs • Pancreatic enzymes • Paralytic agents • PPIs	• Vasopressors • Sedatives • Statins • Steroids • Thiazide diuretics • Total parental nutrition

Continued Supplemental Table 1. Predictor variables used to create parsimonious prediction models.

Categorical laboratory variables (n=222)				
• 1,25 vitamin D • 25, vitamin-D2 • ABO group • Acetaminophen • Acetylcholine Ab • Activated Coagulation Time • Adrenocorticotropic hormone • ADAMTS13 • Adenovirus DFA • Adenovirus PCR • Adenovirus quantitative • AFP • Albumin • Aldolase • Alkaline phosphatase • Alpha 1 antitrypsin • ALT • Amikacin • Ammonia • amylase • ANA • ANA pattern • ANCA screen • Anticardiolipin • Anti-glial nuclear Ab • Arterial HCO3 • Arterial pCO • Arterial pCO2 • Arterial pO2 • ASO titer • AST/ALT ratio • Atypical lymphocytes • Atypical P-ANCA • Autopsy • Babesia Ab • Babesia PCR • Bands • Bartonella Ab • Base excess • Basophilic stippling • BK PCR • BK quantitative • Blasts • Blood culture • Blood ketones	• Blood smear • Carbamazepine • Brain natriuretic peptide • Bone marrow aspiration • Brucella Ab • C-peptide • C3 complement • C4 complement • Caffeine • Carboxyhemoglobin • Carnitine • Catheter culture • Complete blood count • CD-19 lymphocytes • CD-20 lymphocytes • CD-21 lymphocytes • CD-22 lymphocytes • Celiac disease screen • Chlamydia DNA • Cholesterol • Chromosomal analysis • C. difficile Ag • C. difficile PCR • C. difficile toxin • CK-MB • CMV Ab • CMV quantitative • CMV PCR • Copper • Cortisol • Coxackie-B Ab • C-reactive protein • Creatine kinase • CSF albumin • CSF culture • Cyclosporine • D-dimer • Direct bilirubin • Direct fluorescent Ab • DNAse • Double stranded DNA • E.Coli shiga toxin assay • Hep-B core Ab • EBV Ag	• EBV PCR • EKG heart rate • EKG QRS • EKG QRS axis • EKG R axis • Erythrocyte sedimentation rate • Ethanol • Ferritin • Fibrinogen • FiO2 • Flow cytometry • Gentamicin peak • Gentamicin trough • Gamma glutamyl transferase • GMB Ab • Haptoglobin • HbA1C • HDL • Heparin induced Ab • Hep-B E Ag • Hep-B quantitative • Hep-B surface Ab • Hep-B surface Ag • Hep-C Ab • Hep-C genotype • Hep-C quantitative • High sensitivity CRP • HIV Ab • HIV-1 Ab • HIV-1 RNA • HIV-2 Ab • Immature granulocytes • Influenza Ag • Influenza A Ab • Influenza A PCR • Influenza B Ab • Influenza PCR • INR • Intact PTH • Ionized calcium • Iron • Lactate • Lead • Leukemia panel	• LDH • Lipase • Lithium • Lyme Ab • Random urine creatinine • Magnesium • MCH • Methemoglobin • Mixed venous CO2 • Mixed venous pH • MRSA • Nucleated RBC • Osmolality • Oxygen saturation • pCO2 • P-ANCA • Pertussis Ab • pH • Phosphorous • Plasma amino acid • Plasma hemoglobin • Plasma metanephrines • pO2 • Prealbumin • Procalcitonin • PTH • Qualitative CMV • Random urine calcium • Rapamycin • RBC morphology • RDW • Relative eosinophils • Relative lymphocytes • Relative neutrophils • Renin • Reticulocytes • Rheumatoid factors • Salisylate • Serine protease 3 • Stool PCR • Tacrolimus • Tuberculosis test • Thrombin time • Thyroxine • Total bilirubin	• Total complement • Total creatine kinase • Total protein • Triglycerides • Troponin • TSH • Type/screen • UA appearance • UA bacteria • UA glucose • UA leukocyte esterase • Urine albumin/creatinine • Urea/nitrogen in urine • Urinalysis • Urine bacteria • Urine barbiturate • Urine ß-2 microglobulin • Urine BK • Urine calcium • Urine calcium oxalate • Urine calcium pyrophosphate • Urine chloride • Urine creatinine • Urine culture • Urine eosinophils • Urine fine casts • Urine glucose • Urine gram stain • Urine granular casts • Urine hyaline casts • Urine norepinephrine • Urine organic acids • Urine osmolality • Urine phosphate • Urine potassium • Urine RBC • Urine sodium • Urine uric acid • Urine waxy casts • Urine WBC cast • Valproate • Vancomycin trough • Venous O2 saturation • Venous pO2

Continued Supplemental Table 1. Predictor variables used to create parsimonious prediction models.

Individual medications variables (n=315)				
• Acetaminophen • Acetazolamide • Acetylcysteine • Acyclovir • Adalimumab • Adenosine • Albumin • Albuterol • Aldesleukin • Alemtuzumab • Allopurinol • Alprazolam • Alprostadil • Alteplase • Amantadine • Ambisome • Amikacin • Amiodarone • Amitriptyline • Amlodipine • Amoxicillin • Amoxicillin / clavulanate • Amphotericin • Ampicillin • Ampicillin / sulbactam • Anakinra • Anidulafungin • Aripiprazole • Asparaginase • Aspirin • Atenolol • Atorvastatin • Atovaquone • Atropine • Azathioprine • Azithromycin • Aztreonam • Baclofen • Barium • Basiliximab • Bleomycin • Budesonide • Bumetanide • Bupropion • Busulfan • Caffeine • Calcitriol • Calcium carbonate • Calcium chloride • Calcium citrate • Calcium glubionate	• Calcium gluconate • Captopril • Carbamazepine • Carboplatin • Carvedilol • Cefazolin • Cefdinir • Cefotaxime • Ceftazidime • Ceftriaxone • Cefuroxime • Celecoxib • Cephalexin • Certolizumab • Charcoal • Chlorpromazine • Ciprofloxacin • Cisatracurium • Cisplatin • Citalopram • Cladribin • Clarithromycin • Clindamycin • Clobazam • Clofarabin • Clonazepam • Clonidine • Clopidogrel • Codeine • Corticotropin • Cosyntropin • Creatine • Cyclophosphamide • Cyclosporine • Cyproheptadine • Cytarabine • Dactinomycin • Daptomycin • Daunorubicin • Decitabin • Deferasirox • Desmopressin • Dexamethasone • Dexmedetomidine • Dextrose drip • Diatrizoate • Diazepam • Diazoxide • Digoxin • Diltiazem • Dinutuximab	• Diphenhydramine • Dobutamine • Docusate • Dolutegravir • Dopamine • Dornase alpha • Doxazosin • Doxorubicin • Doxycycline • Dronabinol • Duloxetine • Eculizumab • Enalapril • Enoxaparin • Entecavir • Epinephrine • Epoetin alpha • Ertapenem • Erythromycin • Esmolol • Ethosuximide • Etoposide • Ezetimibe • Famotidine • Fentanyl • Ferrous sulfate • Ferrous sucrose • Filgrastim • Fluconazole • Fludarabin • Fludrocortisone • Fluorouracil • Fluoxetine • Foscarnet • Furosemide • Gabapentin • Ganciclovir • Gemcitabine • Gentamicin • Glucagon • Granisetron • Haloperidol • Heparin • Hydrochlorothiazide • Hydralazine • Hydrocodone • Hydrocortisone • Hydromorphone • Hydroxychloroquine • Hydroxyurea • Hypertonic saline	• Ibuprofen • Ifosfamide • Indomethacin • Iodixanol • Infliximab • Interferon alpha • Iohexol • Iopamidol • Ipratropium • Irinotecan • Isoniazid • Isradipine • Levetiracetam • Ketamine • Ketorolac • Labetalol • Lactulose • Lamotrigine • Lansoprazole • Leucovorin • Levocarnitine • Levofloxacin • Levothyroxine • Lidocaine • Lisinopril • Lithium • Loperamide • Lorazepam • Losartan • Magic mouthwash • Magnesium • Mannitol • Meclizine • Melatonin • Meperidine • Mercaptopurine • Meropenem • Mesalamine • Mesna • Metformin • Methadone • Methimazole • Methotrexate • Methylprednisolone • Metoclopramide • Metolazone • Metoprolol • Metronidazole • Midazolam • Midodrine	• Milrinone • Mirtazapine • Misoprostol • Mitoxantrone • Morphine • Moxifloxacin • Mycophenolate • Nadolol • Nafcillin • Naloxone • Naproxen • Neomycin • Nicardipine • Nifedipine • Nimodipine • Nitrofurantoin • Nitroprusside • Norepinephrine • Nortriptyline • Nystatin • Octreotide • Olanzapine • Omeprazole • Ondansetron • Oseltamivir • Oxacillin • Oxcarbazepine • Oxybutynin • Oxycodone • Paclitaxel • Palivizumab • Pantoprazole • Paroxetine • Pegaspargase • Penicillin • Pentamidine • Pentobarbital • Perphenazine • Phenazopyridine • Phenobarbital • Phenylephrine • Phenytoin • Piperacillin / tazobactam • Posaconazole • Potassium • Pravastatin • Prazosin • Prednisone • Pregabalin

Continued Supplemental Table 1. Predictor variables used to create parsimonious prediction models.

Individual medications variables (n=315)			
• Prochlorperazine • Propofol • Propranolol • Prostaglandin • Protamine • Pseudoephedrine • Pyridoxine • Quetiapine • Raltegravir • Ranitidine • Rasburicase • Rifampin • Rifaximin • Ringer lactate bolus • Ringer lactate drip • Risperidone	• Rituximab • Saline bolus • Saline drip • Sertraline • Sevelamer • Sildenafil • Simethicone • Sirolimus • Sodium acetate • Sodium bicarbonate • Sodium citrate • Sotalol • Spironolactone • Sulfamethoxazole / trimethoprim • Sulfasalazine • Tacrolimus	• Tamsulosin • Technetium • Temozolomide • Tenofovir • Terazosin • Terbutaline • Theophylline • Thymoglobulin • Tobramycin • Topiramate • Topotecan • Torsemide • Tramadol • Trazodone • Valganciclovir • Valproic	• Vancomycin • Vasopressin • Venlafaxine • Verapamil • Vinblastine • Vincristine • Vitamin C • Vitamin D • Vitamin K • Voriconazole • Warfarin • Ziprasidone • Zoledronic acid • Zolpidem • Zonisamide
Variables excluded from analysis due to high collinearity			
• 25, vitamin-D3 • A/G ratio • Absolute neutrophil count • Absolute nucleated RBC • Aldosterone • ANA titer • Arterial bicarbonate • Arterial pH • AST • Basophils • Basophils percent • C. difficile enzyme immunoassay • C-ANCA	• Catecholamines • CD-23 lymphocytes • EKG P wave • EKG PR interval • EKG PR interval • EKG qrs interval • Globulin • HIV-2 RNA • Influenza B PCR • Influenza DFA • Iron saturation • LDL • Mixed venous O2 • Oxygen saturation	• Prothrombin time • PTT • RH type • TIBC • UA blood • UA nitrite • UA pH • UA protein • UA specific gravity • Urine albumin • Urine benzodiazepine • Urine bilirubin • Urine clarity • Urine cocaine	• Urine color • Urine epinephrine • Urine ketones • Urine pH • Urine phencyclidine • Urine protein/creatinine ratio • Urine uric acid • Urine WBC • Vancomycin random • Venous bicarbonate • Venous pCO • Venous pCO2 • Venous pH

[a] log transformed as time since admission (log (time since addmission+1)). Ab, antibody; ACEi, angiotensin-converting enzyme inhibitor; Ag, antigen; A/G, albumin/globulin; ALT, alanine aminotransferase; ANA, antinuclear antibody; ANCA, antineutrophil cytoplasmic antibodies, ARB, angiotensin receptor blocker; ASO, antistreptolysin O; AST, aspartate aminotransferase; BiPAP, bilevel positive airway pressure; BUN, Blood urea nitrogen; CK-MB, creatine kinase-muscle/brain; CMV, cytomegalovirus; CPAP, continuous positive airway pressure; CSF, Cerebrospinal fluid; CT, computerized tomography; CTICU, Cardiothoracic Intensive Care Unit; DART, detection assessment research & treatment; HDL, high-density lipoproteins; DFA, direct fluorescent antibody; EBV, Epstein-Barr virus; EEG, electroencephalogram; eGFR, estimated glomerular filtration rate; EKG, electrocardiogram; ETT, endotracheal tube; FiO2, fraction of inspired oxygen; GBM, glomerular basement membrane; HAART, highly active antiretroviral therapy; HFOV, high frequency oscillatory ventilation; INR, international normalized ratio; IR, interventional radiology; LDH, lactate dehydrogenase; LDL, low-density lipoproteins; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin; MCV, mean corpuscular volume; MPV, mean platelet volume; MR, magnetic resonance imaging; MRSA, Methicillin-resistant Staphylococcus aureus; NICU, neonatal intensive care unit; NIPPV, noninvasive positive-pressure ventilation; NPO, nil per os; NSAID, nonsteroidal anti-inflammatory drugs; PACU, post-anesthesia care unit; pCO, partial pressure of carbon monoxide; pCO2, partial pressure of carbon dioxide; PCR, polymerase chain reaction; PICU, pediatric intensive care unit; pO2, partial pressure of oxygen; PPI, proton-pump inhibitors; PT, physical therapy; PTH, parathyroid hormone; PTT, partial thromboplastin time; SICU, surgical intensive care unit; RBC, red blood cells; RDW, red cell distribution width; SCD, sequential compression device; TEE, transesophageal echocardiography; TIBC, total iron binding capacity; TSH, thyroid stimulating hormone; TTE, transthoracic echocardiogram; UA, urinalysis; US, ultrasound; VAC, negative-pressure wound therapy; XR, x-ray; Δ Creat 48, Change in serum creatinine within the last 48 hours.

Supplemental Table 2. Comparing demographic and clinical characteristics according to development of AKI in the derivation cohort.

Variables	AKI (N=516)	Non-AKI (N=4556)	p-value
Demographic			
Age, yr (range)	2.9 (0,13.3)	5.4 (0.2,13.6)	<0.01
Ethnicity (Hispanic), n (%)	135 (26.2%)	1212 (26.6%)	0.85
Race (black), n (%)	126 (24.4%)	922 (20.2%)	0.05
Sex (Male), n (%)	289 (56%)	2467 (54.1%)	0.47
Medical History			
Congenital heart disease	149 (28.9%)	525 (11.5%)	<0.01
CKD	24 (4.7%)	53 (1.2%)	<0.01
Malignancy	105 (20.3%)	736 (16.2%)	0.05
Inpatient location, n (%)			
Pediatric ICU	90 (17.4%)	668 (14.7%)	0.09
Neonatal ICU	169 (32.8%)	649 (14.2%)	<0.01
General pediatrics	62 (12%)	1226 (26.9%)	<0.01
Pediatric Surgery	39 (7.6%)	479 (10.5%)	0.04
Hematology/Oncology	78 (15.1%)	615 (13.5%)	0.37
Nursery	21 (4.1%)	228 (5%)	0.35
Laboratory (first values)			
Serum creatinine, mg/dl	0.6 (0.4,0.8)	0.5 (0.3,0.7)	<0.01
eGFR, ml/min per 1.73 m2	73.6 (28.4,114.4)	101.8 (62.9,133.2)	<0.01
BUN, mg/dl	14 (10,21)	11 (8,16)	<0.01
Glucose, mg/dl	100 (76,129)	100 (83,128)	0.39
Bicarbonate, mmol/L	20.9 (18,23.1)	21 (18.8,23.6)	<0.01
Calcium, mg/dl	8.9 (7.9,9.5)	9.3 (8.7,9.8)	<0.01
Platelet count, x1000/µL	227 (156,313)	257 (186,344)	<0.01
Lymphocyte percent, %	21 (8,36)	21.8 (9,37.4)	0.89
INR measured (%)	311 (60.3%)	1345 (29.5%)	<0.01
Fibrinogen measured (%)	191 (37%)	306 (6.7%)	<0.01
Lactate measured (%)	302 (58.5%)	1645 (36.1%)	<0.01
Medication,[a] n (%)			
Loop diuretic	289 (56%)	633 (13.9%)	<0.01
Vasopressor	198 (38.4%)	331 (7.3%)	<0.01
Chemotherapy	72 (14%)	455 (10%)	0.01
Sodium bicarbonate	131 (25.4%)	222 (4.9%)	<0.01
Calcium gluconate	106 (20.5%)	110 (2.4%)	<0.01
Alprostadil	16 (3.1%)	27 (0.6%)	<0.01
Carboplatin	5 (1%)	8 (0.2%)	<0.01
Foscarnet	4 (0.8%)	1 (0%)	<0.01
Paclitaxel	1 (0.2%)	1 (0%)	<0.01
Nimodipine	1 (0.2%)	0 (0%)	<0.01
Procedures, n (%)			
Mechanical ventilation	150 (29.1%)	325 (7.1%)	<0.01
RBC Transfusion	305 (59.1%)	845 (18.5%)	<0.01
Secondary outcomes			
Inpatient mortality, n (%)	57 (11%)	41 (0.9%)	<0.01
Length of stay, days (range)	17.1 (6.4,52.3)	4.2 (2.1,9.3)	<0.01

Data are presented as median (IQR) or proportion. [a] If a medication was ever given during hospitalization for non-AKI encounters or prior to AKI for AKI encounters. INR, international normalized ratio; RBC, red blood cells.

Supplemental Table 3. Regression-based prediction models' coefficients and odds ratios.

	Coefficient	Standard Error	95% Confidence Interval		Odds Ratio	Standard Error	95% Confidence Interval		Z score	P>|z|
Clinical model										
Chemotherapy use	1.255421	0.172388	0.917546	1.593296	3.509316	0.604966	2.50314	4.91994	7.28	<0.001
BUN	0.033048	0.005163	0.022929	0.043168	1.0336	0.005337	1.023194	1.044113	6.40	<0.001
Calcium	-0.32967	0.059793	-0.44686	-0.21248	0.71916	0.043001	0.639632	0.808578	-5.51	<0.001
Lactate[a]	0.60651	0.115204	0.380715	0.832305	1.83402	0.211286	1.463331	2.298612	5.26	<0.001
ICU admission	0.595966	0.12527	0.350442	0.84149	1.814783	0.227337	1.419695	2.319821	4.76	<0.001
Creatinine	0.829801	0.197916	0.441892	1.217709	2.292861	0.453794	1.555648	3.379436	4.19	<0.001
Pressor use	0.516302	0.152033	0.218324	0.814281	1.67582	0.254779	1.24399	2.257551	3.40	0.001
Weight	0.008	0.002386	0.003323	0.012677	1.008032	0.002405	1.003329	1.012757	3.35	0.001
Bicarbonate	-0.00935	0.013795	-0.03638	0.01769	0.990697	0.013666	0.964271	1.017848	-0.68	0.498
Mechanical ventilation	0.073266	0.157288	-0.23501	0.381545	1.076017	0.169245	0.790561	1.464546	0.47	0.641
Intercept	-2.20092	0.693849	-3.56083	-0.841	0.110702	0.07681	0.028415	0.431281	-3.17	0.002
Lasso model										
Glucose	0.003391	0.000558	0.002298	0.004484	1.003397	0.00056	1.002301	1.004494	6.08	<0.001
Time since admission	-0.35862	0.059802	-0.47583	-0.24141	0.698642	0.04178	0.621371	0.785522	-6.00	<0.001
BUN	0.030068	0.005139	0.019996	0.04014	1.030525	0.005296	1.020198	1.040957	5.85	<0.001
INR[a]	0.59734	0.108152	0.385366	0.809313	1.817278	0.196542	1.470153	2.246364	5.52	<0.001
Δ creatinine 48 hours	3.133266	0.588987	1.978872	4.287659	22.9488	13.51655	7.234581	72.79585	5.32	<0.001
Sodium bicarbonate use	0.763901	0.181498	0.408171	1.11963	2.146633	0.38961	1.504064	3.063722	4.21	<0.001
Alprostadil use	1.374857	0.39072	0.60906	2.140653	3.954509	1.545104	1.838702	8.504989	3.52	<0.001
Calcium	-0.17351	0.059226	-0.2896	-0.05743	0.840705	0.049792	0.748566	0.944185	-2.93	0.003
Creatinine	0.462358	0.18594	0.097923	0.826793	1.587814	0.295238	1.102878	2.285977	2.49	0.013
Calcium gluconate use	0.43878	0.243384	-0.03824	0.915804	1.550814	0.377443	0.962478	2.498783	1.80	0.071
Intercept	-2.63584	0.555438	-3.72448	-1.5472	0.071659	0.039802	0.024126	0.212843	-4.75	<0.001
Top AUC model										
BUN	0.031084	0.004733	0.021808	0.04036	1.031572	0.004882	1.022047	1.041186	6.57	<0.001
Glucose	0.003321	0.000555	0.002234	0.004408	1.003327	0.000557	1.002236	1.004418	5.99	<0.001
Oxygen saturation	-0.0391	0.007343	-0.05349	-0.02471	0.961653	0.007061	0.947912	0.975592	-5.33	<0.001
Δ creatinine 48 hours	3.180922	0.599963	2.005016	4.356827	24.06893	14.44046	7.426213	78.00924	5.30	<0.001
Time since admission	-0.24528	0.06027	-0.3634	-0.12715	0.782489	0.047161	0.695307	0.880603	-4.07	<0.001
Respiratory rate	-0.00995	0.003029	-0.01588	-0.00401	0.990104	0.002999	0.984244	0.995999	-3.28	0.001
Calcium	-0.1994	0.062739	-0.32236	-0.07643	0.819224	0.051397	0.724434	0.926416	-3.18	0.001
Platelet count	-0.00125	0.000437	-0.00211	-0.0004	0.998747	0.000436	0.997893	0.999602	-2.87	0.004
Lymphocyte percent	-0.00592	0.003172	-0.01213	0.000301	0.994101	0.003154	0.987939	1.000301	-1.87	0.062
Creatinine	0.287709	0.189704	-0.0841	0.659522	1.333369	0.252946	0.919335	1.933868	1.52	0.129
Intercept	2.497134	0.965801	0.6042	4.390068	12.14763	11.73219	1.829787	80.64593	2.59	0.010
Forward model										
Nimodipine use	3.837853	0.121538	3.599644	4.076063	46.42571	5.642484	36.58519	58.91309	31.58	<0.001
Time since admission	-0.7377	0.05763	-0.85065	-0.62475	0.478213	0.02756	0.427136	0.535397	-12.80	<0.001
Foscarnet use	3.239226	0.355951	2.541576	3.936876	25.51396	9.081707	12.69966	51.25822	9.10	<0.001
BUN	0.036629	0.004052	0.028687	0.04457	1.037308	0.004203	1.029102	1.045579	9.04	<0.001
Carboplatin use	2.734362	0.369992	2.009191	3.459533	15.39992	5.697848	7.457285	31.80213	7.39	<0.001
RBC Transfusion	0.640064	0.121263	0.402393	0.877735	1.896602	0.229987	1.495399	2.405444	5.28	<0.001
Loop diuretic use	0.674762	0.137812	0.404656	0.944869	1.963566	0.270603	1.498786	2.572477	4.90	<0.001
Sodium bicarbonate use	0.857524	0.180742	0.503277	1.211772	2.357317	0.426066	1.654132	3.359432	4.74	<0.001
Fibrinogen[a]	0.614002	0.14651	0.326848	0.901157	1.847812	0.270723	1.386591	2.46245	4.19	<0.001
Paclitaxel use	6.129291	1.647324	2.900596	9.357986	459.1106	756.3037	18.18498	11591.02	3.72	<0.001
Intercept	-3.35249	0.119794	-3.58728	-3.1177	0.034997	0.004192	0.027674	0.044259	-27.99	<0.001
Genetic model										
Time since admission	-0.64517	0.060229	-0.76322	-0.52713	0.524572	0.031594	0.466163	0.590299	-10.71	<0.001
General Pediatrics admission	-1.29355	0.198857	-1.68331	-0.9038	0.274294	0.054545	0.185759	0.405027	-6.50	<0.001
Loop diuretic use	0.810097	0.140097	0.535511	1.084683	2.248126	0.314957	1.708321	2.958501	5.78	<0.001
BUN	0.029493	0.005114	0.01947	0.039516	1.029932	0.005267	1.019661	1.040307	5.77	<0.001
RBC Transfusion	0.680983	0.118269	0.449181	0.912785	1.975819	0.233677	1.567028	2.491251	5.76	<0.001
Glucose	0.003262	0.000579	0.002128	0.004396	1.003267	0.000581	1.00213	1.004406	5.64	<0.001
Sodium bicarbonate use	0.857802	0.172809	0.519103	1.196502	2.357973	0.407479	1.68052	3.308522	4.96	<0.001
Chemotherapy use	0.821921	0.175061	0.478808	1.165035	2.274867	0.39824	1.614149	3.206034	4.70	<0.001
Creatinine	0.752208	0.19168	0.376522	1.127894	2.121679	0.406683	1.457207	3.089142	3.92	<0.001
Alprostadil use	1.113824	0.414417	0.301581	1.926067	3.045983	1.262308	1.351994	6.862465	2.69	0.007
Intercept	-4.05392	0.182843	-4.41229	-3.69556	0.017354	0.003173	0.012127	0.024834	-22.17	<0.001

[a] Transformed into categorical variables (measured vs not measured) due to missingness > 25%. BUN, blood urea nitrogen; ICU, intensive care unit; INR, international normalized ratio; RBC, red blood cells; Spo2, oxygen saturation; Δ creatinine 48 hours, change in serum creatinine within the last 48 hours.

Supplemental Table 4: Genetic algorithm model operating points applied to the internal validation cohort. The choice of threshold points should be decided based on the risk of the potential intervention and individual health systems may have to make their own choices. A suggested low-risk cut-off threshold point of 0.08 shows a high negative predictive value of 97.9%, includes a large number of patients but a small proportion were falsely negative and therefore it can aid in low-risk, screening interventions. A suggested high-risk cut-off threshold point of 0.24 is a highly specific operating point (specificity of 99.6%) at which the ratio of true positive to false positive alerts is 1:2.8, therefore it can be used to identify patients at imminent AKI to implement more intensive interventions. Given the low baseline rate of AKI episodes (2.8%), it would be hard to make a test with a high PPV, but a PPV of 26.6% represents a 12-fold increase over baseline (LR+ of 12.5).

Cut point	True positive[a]	False positive[a]	TP:FP[a]	True negative[a]	False negative[a]	Sensitivity	Specificity	PPV	NPV	LR+	LR-	OR	Median (IQR) time from alert to AKI, hours
0[b]	14,099	486,003	1:34.5	0	0	100.0%	0.0%	2.8%	-	1.0	-	-	159.1 (52.3-384.1)
0.04	7,593	99,111	1:13.1	386,892	6,506	53.9%	79.6%	7.1%	98.3%	2.6	0.6	4.6	136.6 (42.7-299.7)
0.08	4,055	28,526	1:7.0	457,477	10,044	28.8%	94.1%	12.4%	97.9%	4.9	0.8	6.5	142.7 (32.7-300.3)
0.12	2,396	11,993	1:5.0	474,010	11,703	17.0%	97.5%	16.7%	97.6%	6.9	0.9	8.1	124.9 (24.7-284.5)
0.16	1,420	5,620	1:4.0	480,383	12,679	10.1%	98.8%	20.2%	97.4%	8.7	0.9	9.6	113.7 (13.3-252.9)
0.20	953	3,274	1:3.4	482,729	13,146	6.8%	99.3%	22.5%	97.3%	10.0	0.9	10.7	116.2 (8.8-259.7)
0.24	749	2,071	1:2.8	483,932	13,350	5.3%	99.6%	26.6%	97.3%	12.5	1.0	13.1	23.7 (5.3-343.7)
0.28	642	1,394	1:2.2	484,609	13,457	4.6%	99.7%	31.5%	97.3%	15.9	1.0	16.6	10 (4.2-328.9)
0.32	440	781	1:1.8	485,222	13,659	3.1%	99.8%	36.0%	97.3%	19.4	1.0	20.0	7.6 (3.3-24.5)
0.36	355	558	1:1.6	485,445	13,744	2.5%	99.9%	38.9%	97.2%	21.9	1.0	22.5	7.1 (2.5-19.5)

[a] The sensitivity analysis was performed at the timepoint level. For example, there were 749 timepoints in all the 2299 encounters in the internal validation cohort that crossed the 0.24 threshold point (alert) and lead to an AKI in the next 48 hours compared to 2,071 timepoints that did not lead to an AKI in the next 48 hours. [B] The cut point of 0 represents a baseline rate of all timepoints of the 2299 encounters in the validation cohort. At baseline, 14,099/486,003 (2.8%) timepoints were associated with AKI events afterwards. LR+, positive likelihood ratio; LR-, negative likelihood ratio; NPV, negative predictive value; OR, odds ratio; PPV, positive predictive value; TP:FP, true positive to false positive ratio.

Supplemental Table 5: Genetic algorithm model operating points applied to the external validation cohort. The suggested low-risk threshold point of 0.08 showed a comparable performance to the internal validation cohort, but the high-risk threshold point had no true positives due to the small number of patients that crossed this threshold in this low-acuity cohort.

Cut point	True positive[a]	False positive[a]	TP:FP[a]	True negative[a]	False negative[a]	Sensitivity	Specificity	PPV	NPV	LR+	LR-	OR	Median (IQR) time from alert to AKI, hours
0[b]	1,981	278,045	1:140.4	0	0	100.0%	0.0%	0.7%	-	1.0	-	-	153.3(57.8-336.2)
0.04	1,109	36,049	1:32.5	241,996	872	56.0%	87.0%	3.0%	99.6%	4.3	0.5	8.5	148.6(59.6-338.9)
0.08	526	7,416	1:14.1	270,629	1,455	26.6%	97.3%	6.6%	99.5%	10.0	0.8	13.2	139.3(65.9-393.6)
0.12	337	2,240	1:6.6	275,805	1,644	17.0%	99.2%	13.1%	99.4%	21.1	0.8	25.2	87.6(26.5-171.1)
0.16	104	764	1:7.3	277,281	1,877	5.2%	99.7%	12.0%	99.3%	19.1	1.0	20.1	23.6(5.1-58.2)
0.20	4	500	1:125.0	277,545	1,977	0.2%	99.8%	0.8%	99.3%	1.1	1.0	1.1	421.1(14.6-422.8)
0.24	0	341	-	277,704	1,981	0.0%	99.9%	0.0%	99.3%	0.0	1.0	0.0	422.2(420.7-423)

[a] The sensitivity analysis was performed at the timepoint level. For example, there were 526 timepoints in all the 1102 encounters in external validation cohort that crossed the 0.08 threshold point (alert) and lead to an AKI in the next 48 hours compared to 7,416 timepoints that did not lead to an AKI in the next 48 hours. [B] The cut point of 0 represents a baseline rate of all timepoints of the 1102 encounters in the external validation cohort. At baseline, 1,981/278,045 (0.7%) timepoints were associated with AKI events afterwards. LR+, positive likelihood ratio; LR-, negative likelihood ratio; NPV, negative predictive value; OR, odds ratio; PPV, positive predictive value; TP:FP, true positive to false positive ratio.

Supplemental Table 6: Low-risk cut-off threshold (0.08) analysis using the genetic algorithm model in age subgroups (on the internal validation cohort).

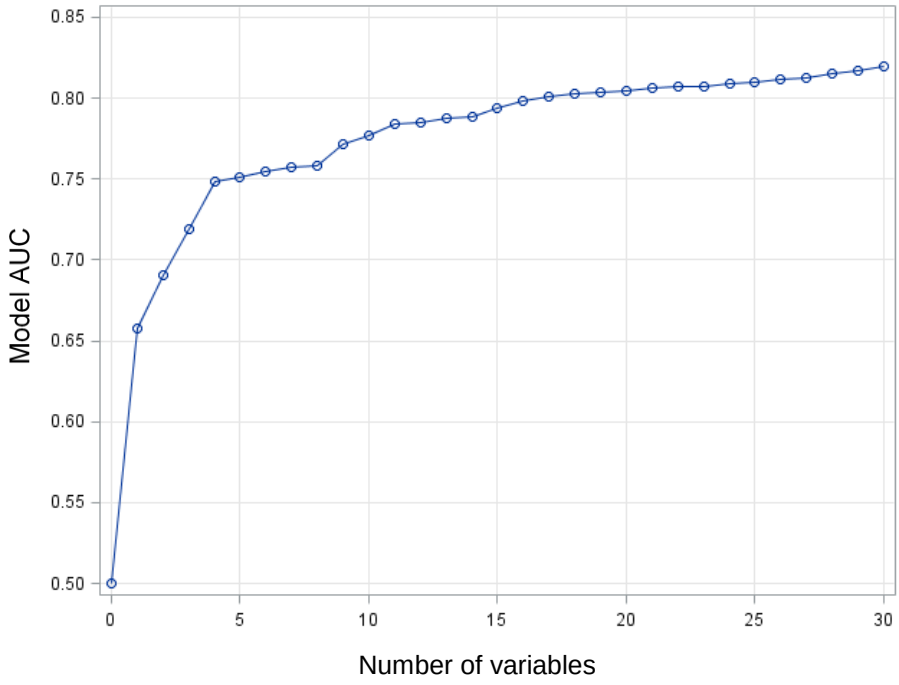
Cohort	Sensitivity	Specificity	PPV	NPV
Entire validation cohort n=2299 (AKI=207, 9%)	28.8%	94.1%	12.4%	97.9%
Newborns (birth–27 days) n=492 (AKI=70, 14.2%)	32.8%	76.4%	24.2%	83.2%
Infants (28 days–12 months) n=256 (AKI=16, 6.2%)	27.0%	90.5%	49.5%	78.3%
Children (1-12 years) n=913 (AKI=68, 7.4%)	30.7%	89.8%	58.7%	73.2%
Adolescents (12-18 years) n=632 (AKI=53, 8.3%)	21.5%	67.1%	25.3%	62.2%

NPV, negative predictive value; PPV, positive predictive value

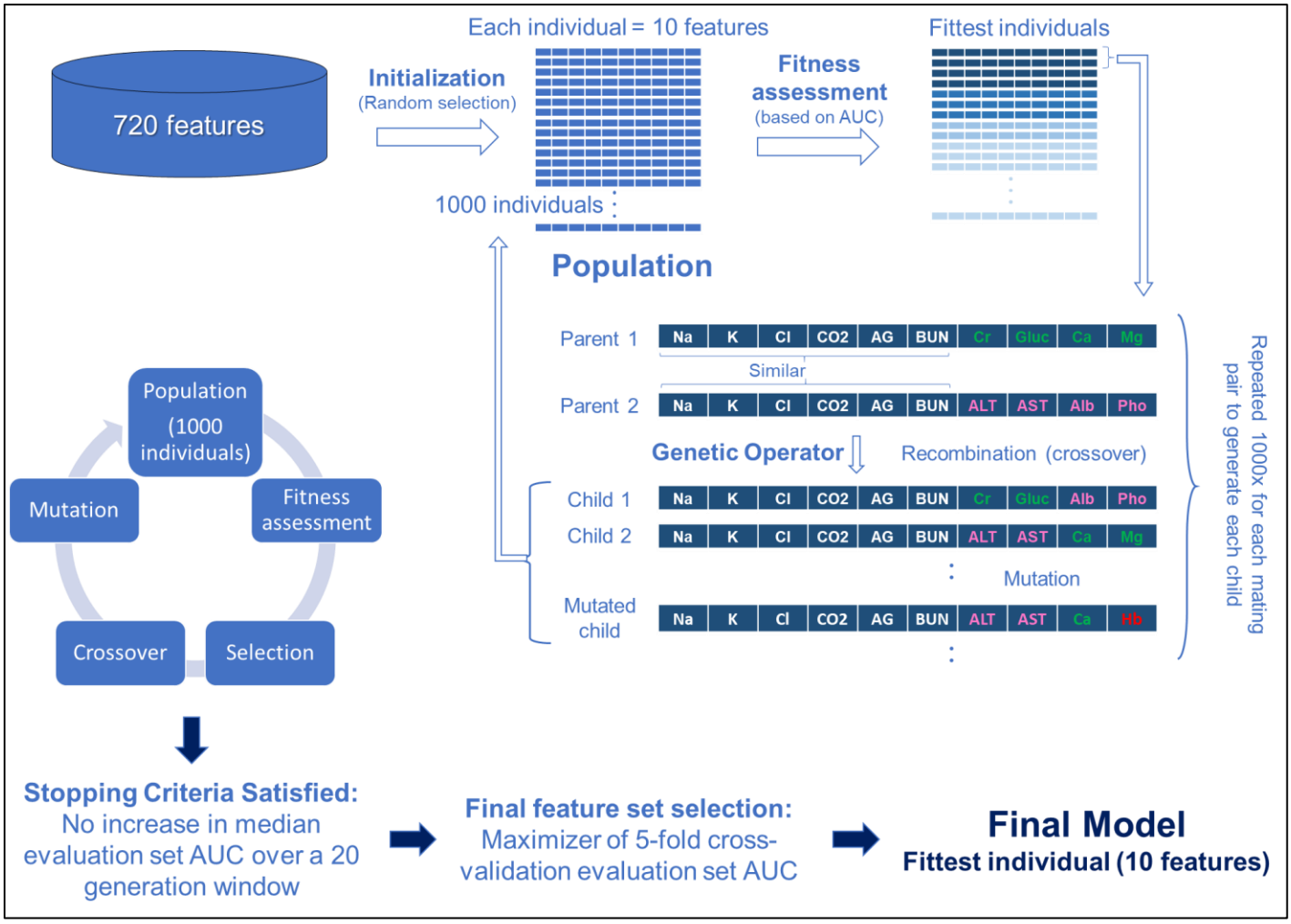
Supplemental Table 7: High-risk cut-off threshold (0.24) analysis using the genetic algorithm model in age subgroups (on the internal validation cohort).

Cohort	Sensitivity	Specificity	PPV	NPV
Entire validation cohort n=2299 (AKI=207, 9%)	5.3%	99.6%	26.6%	97.3%
Newborns (birth–27 days) n=492 (AKI=70, 14.2%)	3.8%	99.1%	48.3%	81.7%
Infants (28 days–12 months) n=256 (AKI=16, 6.2%)	0.2%	99.2%	6.7%	74.3%
Children (1-12 years) n=913 (AKI=68, 7.4%)	9.8%	100.0%	100.0%	70.0%
Adolescents (12-18 years) n=632 (AKI=53, 8.3%)	5.9%	95.4%	40.1%	66.1%

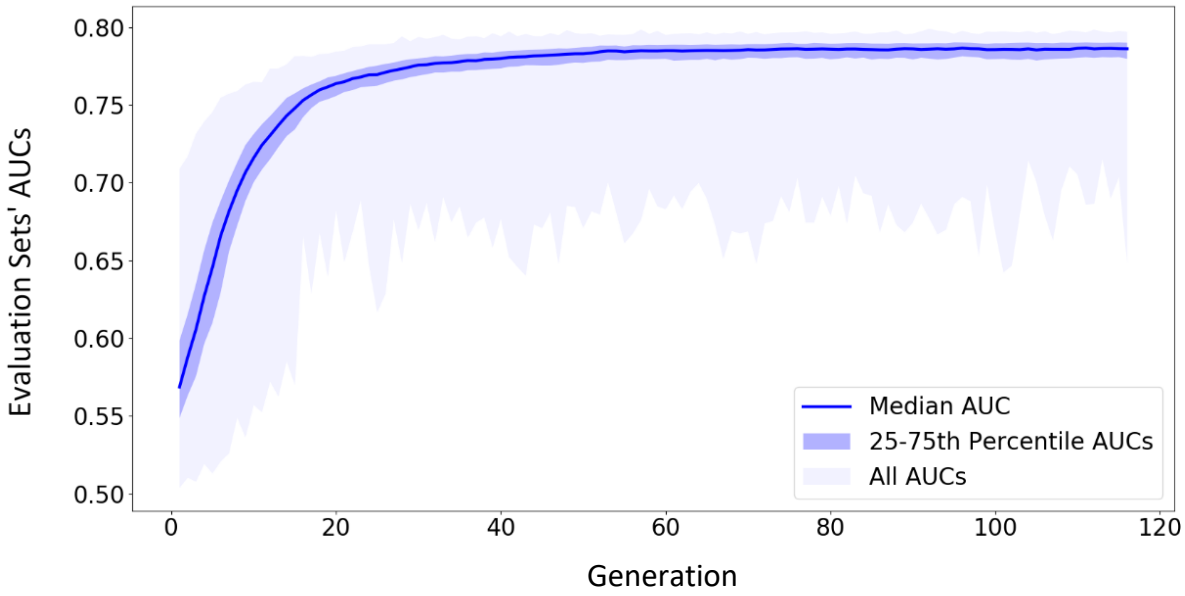
NPV, negative predictive value; PPV, positive predictive value



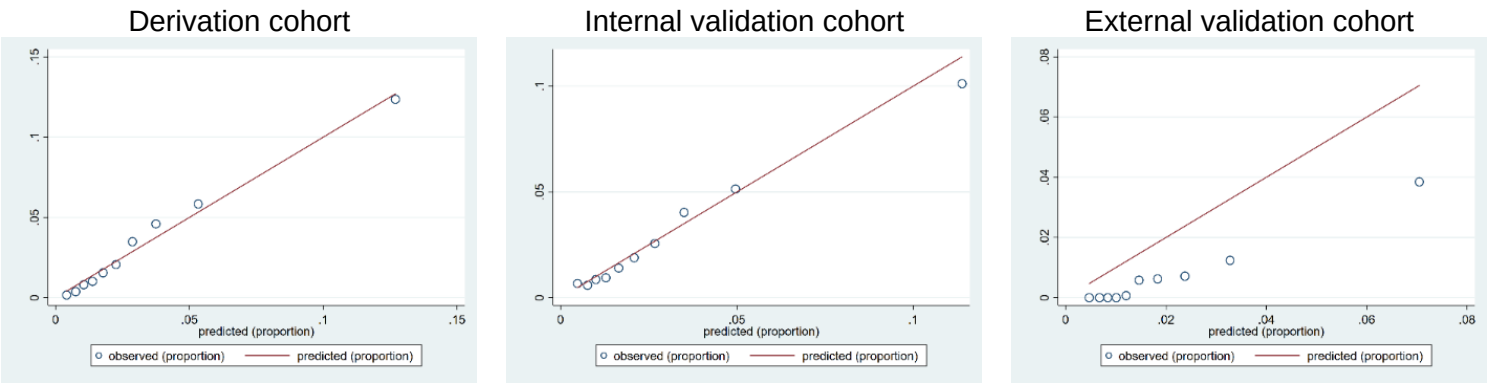
Supplemental Figure 1: Logistic regression analyses of incremental numbers of variables of the stepwise forward selection model. Model performance increases as additional variables are added, but there are diminishing returns after the first 10 variables.



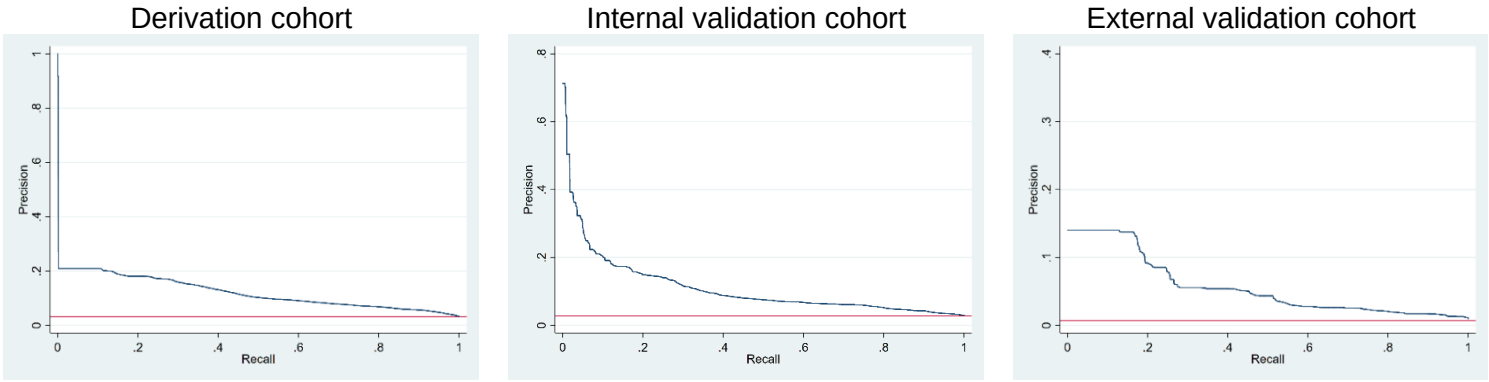
Supplemental Figure 2. Genetic algorithm feature selection process.



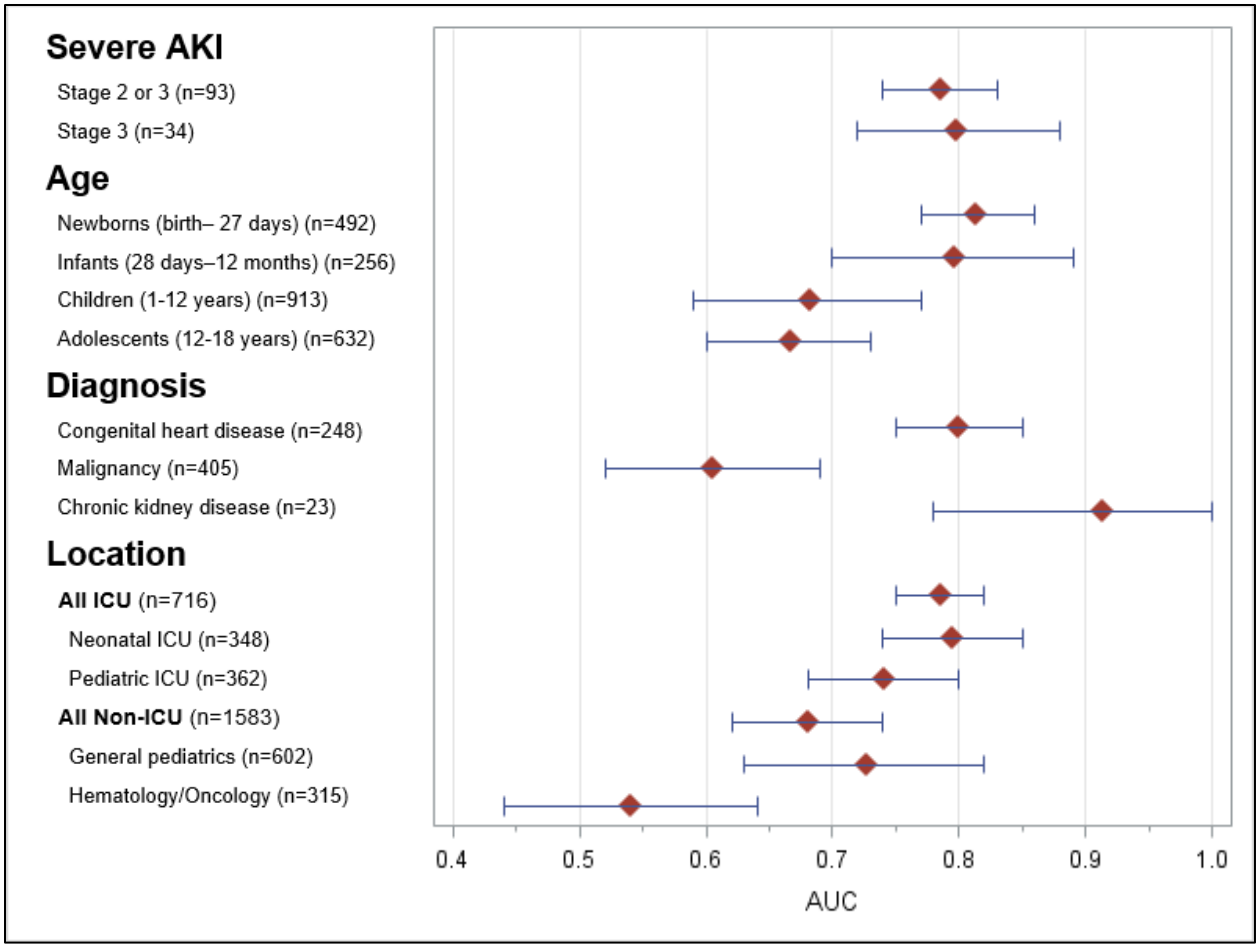
Supplemental Figure 3: Convergence in evaluation set (of derivation cohort) area under the receiver operating characteristic curve (AUC) of the genetic algorithm's population.



Supplemental Figure 4: Genetic algorithm model calibration curves. The prediction model is well calibrated in both derivation and internal validation cohorts. For prospective and external implementation, it would be appropriate to recalibrate the model on the local cohort.



Supplemental Figure 5: Genetic algorithm model performance illustrated by a precision-recall curve. PR-AUC, the area under the precision–recall curve.



Supplemental Figure 6. Genetic model for the prediction of severe AKI and subgroup analyses in the internal validation cohort. The AUC is 0.79 (95% CI 0.74-0.83) for predicting severe AKI (stage 2 or 3) and 0.80 (95% 0.72-0.88) for stage 3 AKI. In newborns, the AUC is 0.81 (95% CI 0.77-0.86).

Supplemental Methods. Genetic Algorithm Methodology:

Genetic algorithms model a population of genotypes and its temporal evolution, discretized as a sequence of generations. Several key components must be defined: a genotype representation, a fitness function and mating rules, and genetic recombination and mutation rules. These key components are used to produce the next generation in the sequence from the current one. A general implementation of genetic algorithms for feature selection is described below.

- Genotype Representation: A genotype is defined as a subset of k features chosen from the full feature set.
- Fitness Function: The derivation set is randomly split into training and evaluation sets with proportions α and $1-\alpha$, respectively. A model M is fit to the training set restricted to only the features in the genotype representation. The fitness function is defined as a performance metric P of the model when applied to the evaluation set. This procedure occurs for every genotype.
- Mating Rules: The fitness values over the population are used to generate a distribution F over the population describing their probability of being selected for mating. Mating pairs are then generated by randomly sampling from this distribution until the number of pairs equals the current population size n.
- Genetic Recombination: For each mating pair, overlapping features of the parent genotypes are first placed into the child genotype. The remaining non-overlapping features are uniformly sampled without replacement and given to the child until the child has k features.
- Genetic Mutation: After recombination, each child has their k features iterated through and randomly replaced by a new feature from the full feature set according to a probability set by the mutation rate r.

For our particular implementation, the hyperparameters chosen were $\alpha = 2/3$, $n = 1000$, $k = 10$, $r = 0.05$, M is logistic regression, P is the area under the receiving operator characteristic curve (AUC), and F is a linearly decreasing probability mass function (PMF) defined over the indices of the population reordered by fitness such that the worst performing genotype has probability 0. Furthermore, we incorporated elitism, a technique commonly used with genetic algorithms, which improves the rate of convergence. Elitism chooses the t best genotypes for a generation and produces a clone of them in the next generation; we set $t = 3$. We initialize the algorithm with uniformly randomly selected genotypes. The algorithm runs until a stopping criteria is met: a lack of improvement in the median evaluation AUC in the population over a 20 generation window. Once the stopping criteria is met, 5-fold cross validation is used to estimate a mean AUC for every genotype in the population. The algorithm returns the genotype that maximizes this statistic.