K-MIMIC

Prediction Model for Neonatal Acute Kidney Injury Adjusted for Regional Characteristics: A Retrospective Cohort Study of the K-MIMIC Database

Team SMILE:D

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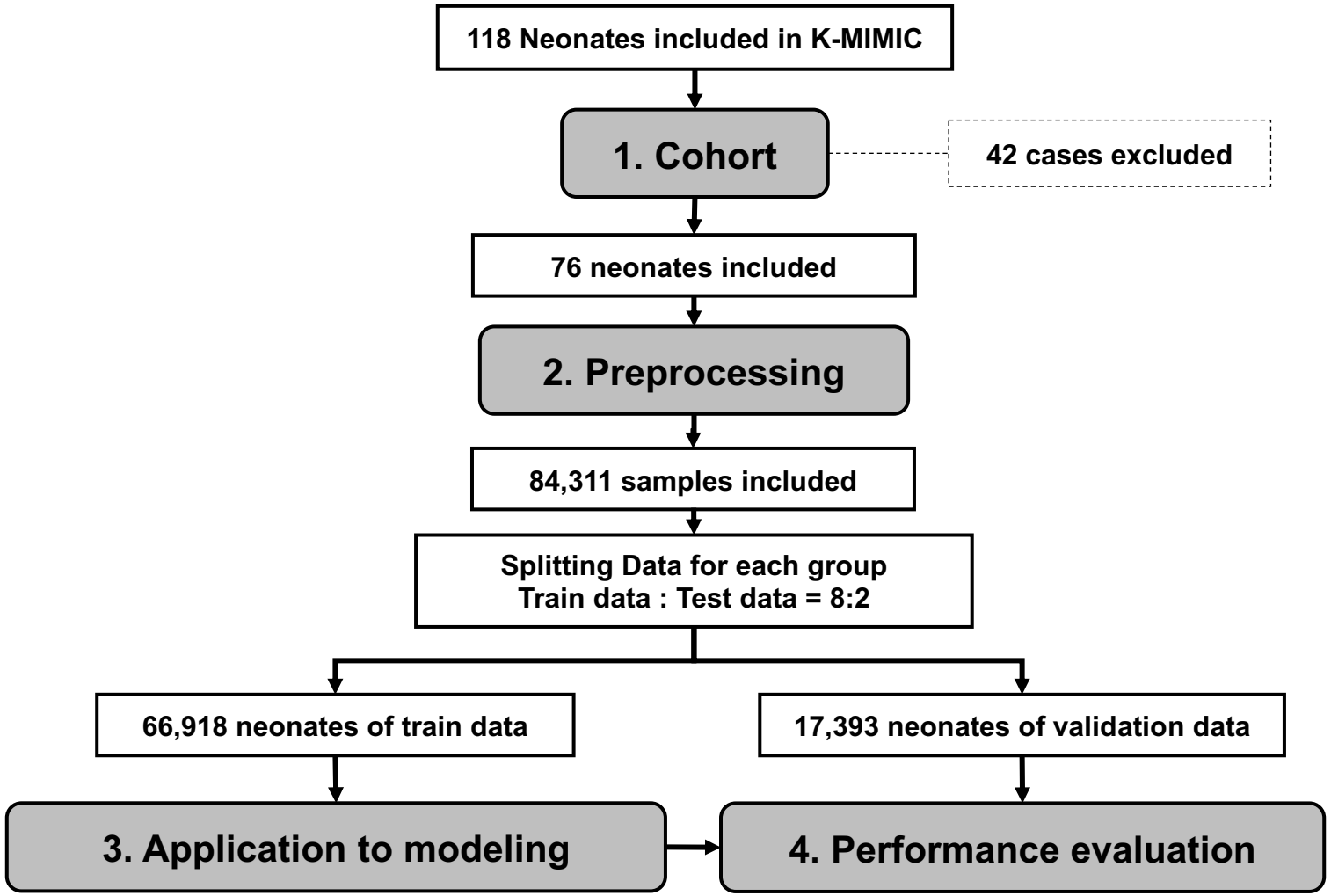
Aim

- To develop an AKI prediction model that extracts data characteristics from K-MIMIC neonatal ICU data collected from multiple institutions in South Korea, considering and adjusting for regional characteristics.

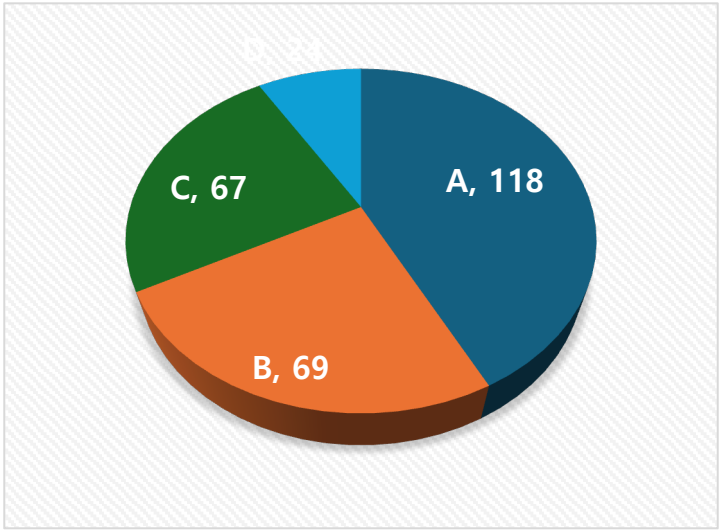
Methods

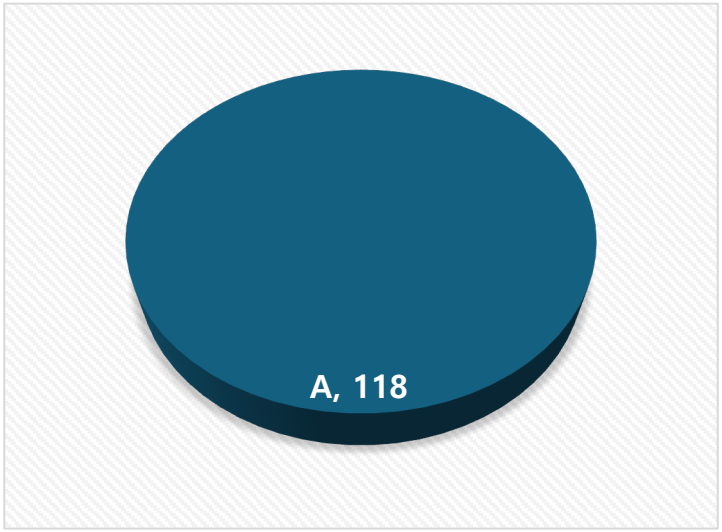
A study flow diagram



Cohorts

- **Inclusion criteria: Neonates**
  - B (69) hospital: ‘NICU’ is not a Neonatal Intensive Care Unit
- **Exclusion criteria**
  - No vital sign data: C (67) and D (24) Hospital
  - Major congenital anomaly in ICD 10
    - The Circulatory System (Heart and Lung): Q20 - Q28
    - The Urinary system: Q60 - Q64
- **One hospital’s 118 neonates enrolled in this study.**





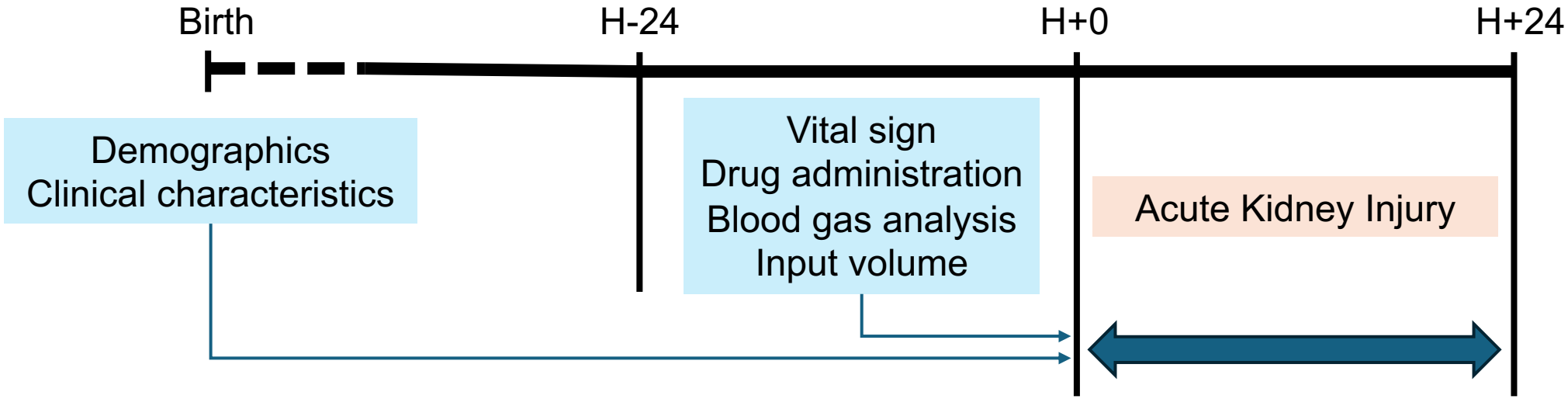
Aim

- To develop an AKI prediction model that extracts data characteristics from K-MIMIC neonatal ICU data collected from multiple institutions in South Korea, considering and adjusting for regional characteristics.

- → To develop an AKI prediction model that extracts data characteristics from K-MIMIC neonatal ICU data, considering uncontrolled bias.

Preprocessing

- **Sampling**
  - Hospital days: from 7 to 27 days (2nd - 4th week)
  - Sampling frequency: once an hour



- **Vital sign and outlier**
  - Systolic Blood Pressure: <0, >200, >±2SD
  - Heart Rate: <0, >±2SD
  - SpO2: > ±2SD

Preprocessing: Input features

- **Demographics and clinical characteristics**

Neonate	Mother
Sex, Weight Gestational age, C-section Small for gestational age Multiple births	Nationality Maternal age DM (Overt DM, GDM) Hypertension (Gestational HTN, Chronic HTN) PROM, Chorioamnionitis, IVF Antenatal steroid Maternal antibiotics

Preprocessing: Input features

- **Drug administration**

Category	Drug
Antibiotics	Acyclovir, Amikacin Amphotericin B Vancomycin Meropenem Piperacillin/Tazobactam
Methylxanthines	Aminophylline
Steroid	Dexamethasone
NSAID	Ibuprofen
Inotropic	Dopamine, Dobutamine Epinephrine
Diuretics	Furosemide

Nephrotoxicity drug

Medication	Mechanism of action	Site of kidney damage	Nephrotoxicity	Notes
Acyclovir	Inhibits DNA synthesis and viral replication *via* inhibition of viral DNA polymerase	Tubule	Crystallization and obstruction occur causing tubular damage, particularly when in low urinary flow state	Can be used for prophylaxis (CMV, HSV, varicella, herpes zoster), suppression (HSV), and treatment (varicella zoster, herpes zoster, HSV, varicella). Dosage adjustment for renal impairment available (93).
Amikacin	Inhibits protein synthesis *via* binding to 30S ribosomal subunits	Proximal tubule, S1 and S2 segments, late changes in S3	Proximal tubular damage after accumulation of aminoglycoside	Dosage adjustment for renal impairment as well as augmented renal clearance available (93).
Amphotericin B	Disrupts fungal cell wall synthesis and cell membrane permeability *via* binding to ergosterol which causes leakage of cellular components and subsequent cell death	Distal tubule	Vasoconstriction and direct distal tubular toxicity	Hydration and sodium repletion prior to administration of amphotericin B may reduce risk of renal toxicity. Dosage adjustment for renal impairment available (93).
Gentamicin	Disrupts bacterial protein synthesis and cell membrane integrity *via* biding to 30S ribosomal subunit	Proximal tubule, S1 and S2 segments, late changes in S3	Proximal tubular damage after accumulation of aminoglycoside	Dosage adjustment for renal impairment available (93).
Indomethacin	Non-selective cyclooxygenase inhibitor decreasing prostaglandin synthesis	Afferent arteriole	Hemodynamically mediated: causes afferent arteriole vasoconstriction and reduced GFR	Dosage adjustment for renal impairment available (93).
Piperacillin/Tazobactam	Inhibits bacterial cell wall synthesis leading to bacteria lysis	Tubule, particularly proximal tubule	Inhibits tubular secretion and clearance, direct toxicity	Dosage adjustment for renal impairment available (93).
Vancomycin	Inhibits cell wall synthesis of gram-positive bacteria *via* blocking glycol-peptide polymerization	Proximal tubule	Direct toxicity, otherwise unclear	Dosage adjustment for renal impairment available (93).

Coleman C, et al. Neonatal Acute Kidney Injury. Front Pediatr. 2022;10:842544.

Preprocessing : Outcome

- **Outcome: Acute Kidney Injury in neonates**

Table 2 Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury (AKI) Classification including neonatal modifications

	Pediatric		Neonatal	
Stage	Serum creatinine	Urine output	Serum creatinine	Urine output[a]
1	1.5–1.9 times baseline OR ≥ 0.3 mg/dl increase*	< 0.5 ml/kg/h for 6–12 h	≥ 0.3 rise within 48 h or ≥ 1.5–1.9 × rise from baseline (previous lowest value) within 7 days	≤ 1 ml/kg/h for 24 h
2	2.0–2.9 times baseline	< 0.5 ml/kg/h for ≥ 12 h	2.0–2.9 times baseline	≤ 0.5 ml/kg/h for 24 h
3	3.0 times baseline OR Increase in serum creatinine to ≥ 4.0 mg/dl OR Initiation of renal replacement therapy OR In patients < 18 years, decrease in eGFR to < 35 ml/min per 1.73 m^2	< 0.3 ml/kg/h for ≥ 24 h OR Anuria for ≥ 12 h	≥ 3 × rise from baseline or serum creatinine ≥ 2.5 mg/dl or renal replacement therapy initiation	≤ 0.3 ml/kg/h for 24 h

[a] Urine output criteria utilized in the AWAKEN study. May also consider utilizing the pediatric urine output data for neonates if the granularity of data allows

* Increase in SCr by X0.3 mg/dl within 48 hours; or K Increase in SCr toX1.5 times baseline, which is known or presumed to have occurred within the prior 7 days

mg/dl milligrams per deciliter, *eGFR* estimated golumerular filtration rate, *ml/min* milliliters per min, *ml/k/h* milliliters per kilogram

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Results

Cohort characteristics

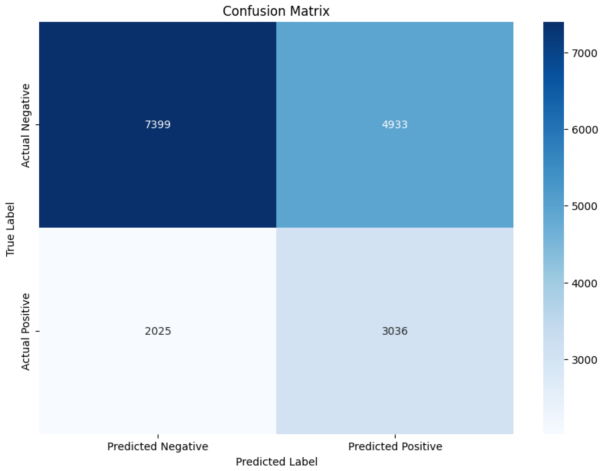
Value	AKI (N = 6)	No AKI (N=70)	P value
Male	2 (33.33)	37 (52.86)	0.359
Birth weight	2.83 ±0.91	2.87 ±1.21	0.938
Gestational age	29.67 ±2.94	32.90 ±4.54	0.092
Admission duration	53.83 ±40.18	49.08 ±49.47	0.835
urine output (per once, ml)	26.61 ±3.93	33.61 ±11.31	<0.001
Blood Creatinine (per once, mg/dl)	0.43 ±0.07	0.42 ±0.09	0.737

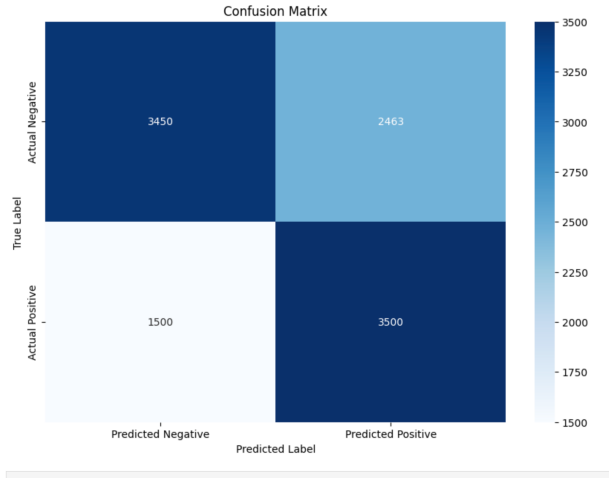
Train vs test set feature

Target variable	Train set (N = 66,918)	Test set (N = 17,393)
AKI	19,406 (29.0%)	5,044 (29.7%)

Performance of test set

- **GRU model**
  - Accuracy: 60.0
  - Sensitivity (Recall): 0.60 / Specificity: 0.60
  - Precision: 0.38 / F1 Score: 0.47
  - AUROC: 0.56 / AUPRC: 0.55
- **MLP model**
  - Accuracy: 0.59
  - Recall (Sensitivity): 0.64 Specificity: 0.71
  - Precision: 0.71 / F1 Score: 0.67
  - AUPRC: 0.64 / AUPRC:0.71





Evaluating potential biases within the model

- **Fairness**
  - Nationality, Gender, Insurance: Correlation with Prediction Results
- **Accountability**
  - Accuracy of the predictive model and Safeguards against misdiagnosis
- **Transparency**
  - Data Selection: Imbalance issue due to a high amount of normal data
  - ICD Code Discrepancy
    - Variables substituted based on operational definitions
    - Suspected NEC, Sepsis: Suspected infectious Disease (NEC, Sepsis) By Antibiotics
    - Hypotension By Inotropics and/or Steroid
    - Acute kidney injury by Serum Creatinine and/or Urine output

Evaluating potential biases within the model

- **Transparency**
  - Feature Selection: Frequency and type of creatinine tests adjusted as variables

	AKI	No AKI
Blood Cr (times)	7.5	11.8
Blood Cr ↑ (times)	2.3	4.4
Hospital duration (day)	42.2	44.7

Discussion

Conclusion

- **Based on the modified neonatal KDIGO criteria, the prevalence of AKI in the NICU is 8.0%.**
- **A GRU and MPL model was attempted to be developed to predict Neonatal AKI one hour earlier using clinical characteristics and time-series vital sign data.**
- **Solved Bias**
  - Spares and Imbalance data: Unbalance cohort → Time shift sampling
  - ICD Code Discrepancy → Definition by EMR and laboratory
  - The number of test - influenced feature selection s → not significant
- **Unsolved Bias**
  - Accountability → performance tunning
  - Fairness: Nationality, Gender, Insurance → Covariance
  - Important feature → Feature importance, Shapley plot

THANK YOU!!