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A G-Transformer–Based Longitudinal Causal Framework for Personalized Vasopressor and Fluid Recommendations to Reduce Major Adverse Kidney Events in Sepsis

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Objectives : Early sepsis management requires repeated decisions regarding vasopressors and fluid therapy, yet the individualized treatment pattern associated with lower risk of major adverse kidney events within 30 days (MAKE30) remains uncertain.

Methods : We developed a G-transformer–based longitudinal causal modeling framework using hourly sepsis trajectories from MIMIC-IV for model development and internal evaluation and eICU for external evaluation. The action space included discretized norepinephrine, vasopressin, normal saline, lactated Ringer's solution, and albumin. Time-varying physiologic and laboratory variables were combined with static clinical features and cumulative treatment-history summaries. A G-transformer was trained as an action-conditional MAKE30 risk model, and nuisance models for treatment assignment and censoring were incorporated within an augmented inverse probability weighting (AIPW) framework. For each subject, candidate treatment combinations were evaluated and the action associated with the lowest estimated MAKE30 risk was selected as the recommended action.

Results : In the internal MIMIC-IV cohort, the AIPW-estimated MAKE30 risk was 0.237 under the observed policy and 0.104 under the recommended policy, corresponding to an estimated risk difference of 0.133 (95% confidence interval [CI], 0.121–0.145). In the external eICU cohort, the corresponding risks were 0.257 and 0.104, yielding an estimated risk difference of 0.153 (95% CI, 0.148–0.158). Subgroup analyses suggested larger estimated risk reductions in subjects with chronic kidney disease, baseline vasopressor exposure, and elevated lactate levels. Representative patient-level comparisons also showed lower estimated risk under recommended than observed actions.

Conclusions : In this proof-of-concept analysis, a G-transformer–based longitudinal causal modeling framework identified treatment patterns associated with lower estimated MAKE30 risk than observed care in internal and external cohorts. These findings should be interpreted cautiously and viewed as exploratory rather than practice-changing.

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Table. AIPW-estimated MAKE30 risk under observed and recommended policies

Dataset	Observed policy risk (AIPW)	Recommended policy risk (AIPW)	Risk difference (95% CI)
MIMIC-IV (internal validation)	0.237	0.104	0.133 (0.121–0.145)
eICU (external validation)	0.257	0.104	0.153 (0.148–0.158)

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Figure: Subgroup Risk Heterogeneity (MIMIC-Test)

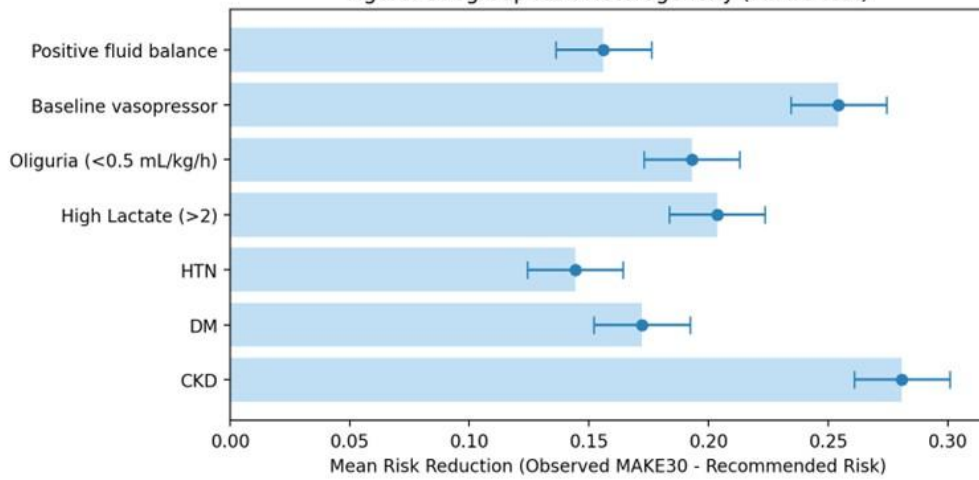


Figure 5: Representative Patient-level Comparison - Observed vs Recommended Risk

