Exploring Causal Methods to Assess Time-Sensitive Effects and Hospital Heterogeneity for Acute Kidney Injury Alerts

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BIGDATA SUMMER IMMERSION

The ELAIA-1 Trial

Background

- Acute kidney injury (AKI) affects ~ **15% of patients** but is asymptomatic and goes **vastly undocumented**.
- **ELAIA-1** implemented an alert to prompt AKI treatment:[1]
  - Randomized control trial at six Yale New Haven Health System hospitals ($n = 6{,}030$).
  - 22-month trial period with 14-day observation period.

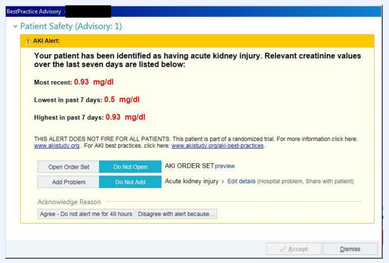


Fig. 1. *Screenshot of the AKI alert. Identifies the condition but only prompts testing and minimal risk treatment.*

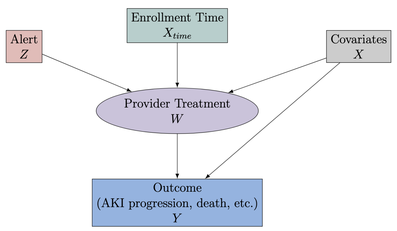


Fig. 2. *Direct acyclic graph illustrating causal mechanisms assumed in the ELAIA-1 trial.*

Objectives

- Wilson et al. prompted an exploration of hospital-level differences while exploratory analysis identified potential temporal effects.
- *Can **causal inference** methods be implemented to explore **temporal** and **population heterogeneity** while identifying **clinically relevant** patient subpopulations?*

Definitions & Causal Estimand

- Let X_i, Z_i denote patient i's covariates and alert status, respectively, for $i = 1, \dots, 6030$.
- We notate the counterfactual outcome as $Y_i(z)$ for each patient i and each $z \in \{0,1\}$.
- The **Average Treatment Effect (ATE)** of Alerts on a given outcome is $\mathbb{E}[Y_i(1) - Y_i(0)]$, where expectation is over all patients.[2]
- The **Conditional Average Treatment Effect (CATE)** for patient i is similarly $\tau(x) = \mathbb{E}[Y_i(1) - Y_i(0) | X = x_i]$.
- We focus on **CATE** of **alerts** on **death**, **AKI progression**, and **dialysis** within 14 days of the alert.

Methods & Models

- We use **Bayesian Additive Regression Trees (BART)** combined with a S-Learner meta-algorithm.[3]
- We define $\hat{\mu}(x) = \sum_{j=1}^{m} g(x; T_j, M_j) + \epsilon$, where T_j is the j^{th} binary tree with terminal parameters M_j and $\epsilon \sim N(0, \sigma^2)$ for m trees.
- We train $\hat{\mu}$ on the entire dataset using observed (X_i, Z_i) pairs.
- $\hat{\tau}(x) = \hat{\mu}(x_i, z_i = 1) - \hat{\mu}(x_i, z_i = 0)$ for each patient i.
- Lastly, we visualize important covariates using **Classification and Regression Trees (CART)**.[4]

Temporal Variance

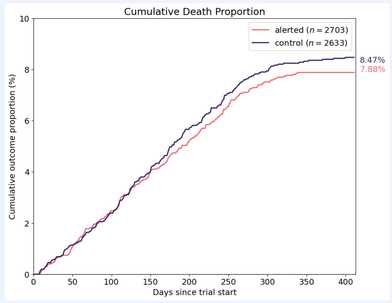


Fig. 3. *Patients in the alert group survive slightly more often than those in the control group.*

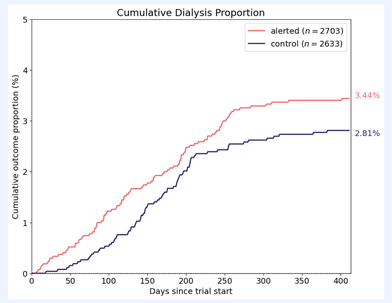


Fig. 4. *Patients in the alert group undergo dialysis quicker and more often than those in the control group.*

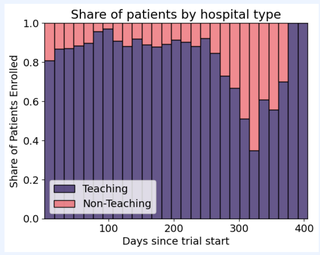
Alert Fatigue

Alert fatigue drives cognitive overload, desensitization over time; linked to adverse outcomes and ignorance of alerts.[5, 6]

Hospital Heterogeneity

Fig. 5 (right). *Non-teaching hospitals enroll patients towards the end of the trial.*

- Wilson et al. found significant differences between alert groups in teaching versus non-teaching hospitals.



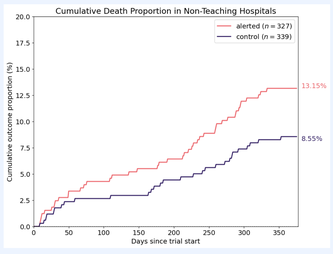
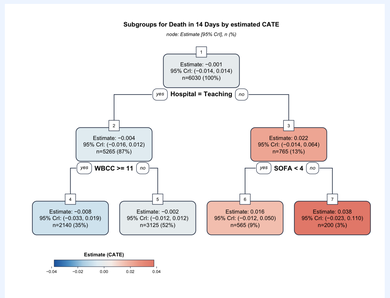


Fig. 6 (left). *Patients in the alert group survive less often than those in the control group in non-teaching hospitals.*

- Our findings suggest that time variance may contribute to the hospital heterogeneity in alert effects on patient outcomes.

Results



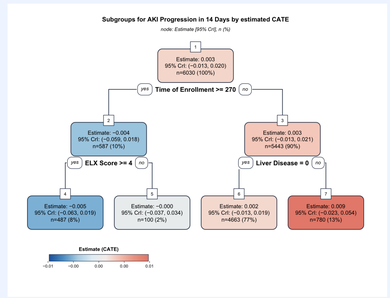
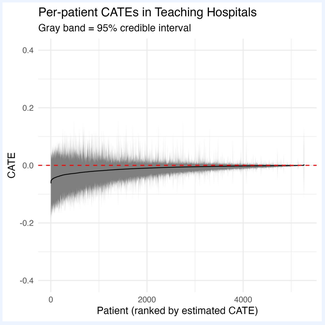


Fig. 7 (left). *Identified subgroups for death progression based on CATEs. Notably, type of hospital was the main split in the tree.* **Fig. 8 (right).** *Identified subgroups for AKI progression based on CATEs. Notably, time of enrollment in the trial was the main split in the tree.*



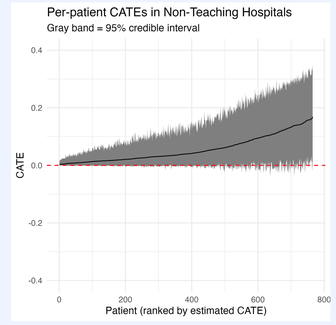


Fig. 9 (left). *Per-patient CATEs in teaching hospitals. Null results.* **Fig. 10 (right).** *Per-patient CATEs in non-teaching hospitals. Notably, nearly all CATEs are above 0, indicating our model predicts harm from alerts.*

Outcomes & Future Exploration

Findings

- No strong evidence of alert impact, but potential evidence of time-varying and hospital-based effect.
- Identified subgroups are minimal.
- Further analysis could explore alerts addressing specific causes for AKI and physician compliance.
- **Limitations:** collected data did not enable all potential analysis; lack of direct censoring variable; alert does not directly suggest physician action.

References

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