Pediatric Dehydration: Drug Effect on Serum Sodium

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1) Introduction

- Dehydration is a critical consideration when treating children, where even a small degree of dehydration → increased morbidity, mortality for infants and young children
- A method to quantifiably measure one's dehydration is through their **serum sodium** levels, a vital electrolyte that's crucial in fluid balance
- Low serum sodium often indicates *hyponatremia*, which leads to nausea and vomiting, loss of energy and confusion, and in serious cases, seizures, coma, and death
- Given the variety of patients that come into the emergency department, doctors can find themselves guessing the effectiveness of different drugs on improving their serum sodium levels

In our study, we quantify the effect of different drugs on groups of patient's serum sodium levels (dehydration).
This allows us to measure how different drugs affect different patient's serum sodium levels.
Analysis can ***help medical professionals reduce the potential of over/under-correcting serum sodium levels.***

2) Data

We used 9 Emergency Department datasets from CHOC from Jan 6th, 2023 - Jan 6th, 2024.

- Information was deidentified (no names & age)
- Contains vitals and labs taken during visits, drug administration information, oncology reports, and ICD-10 codes assigned to each visit
- Serum sodium measurements taken sparsely and irregularly

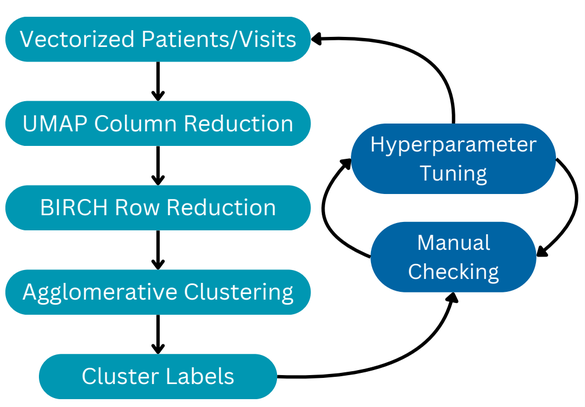
3) Methods

The project was designed for personalized dehydration treatment for pediatric patients. This involves **2 models**:

- **A Prediction model** that can determine the effectiveness of drugs/drug combinations on increasing/decreasing a patient's serum sodium levels
  a. Normalize drug measurements
  b. Quantify the effects of different drugs/drug combinations on patients' serum sodium levels
  c. Determine drug effectiveness in relation to time (when drugs are administered, time between serum sodium measurements, etc.)

- **A Clustering model** that groups patients and visits into different clusters based on demographics & ICD-10 codes (Codes for diagnoses).
  a. Allows us to find underline patterns within and between patients and visits
  b. Determine the accuracy of our model for subgroups in the CHOC ED population

4) Clustering Methods



5) Regression Methods

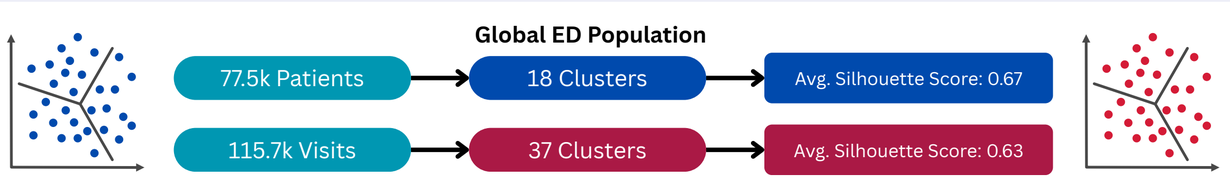
Models were tested & deployed for different purposes:

- **Robust & Lasso Linear Regression**: Regression but less sensitive to outliers. Lasso also used for feature selection
- **Bayesian Mixed Effect Models** : Quantify the distribution of probable effectiveness of different drugs on different groups of patients
- **Random Forest**: Used to estimate feature importance and validate top predictive variables (e.g., specific drugs, baseline sodium)

Given two sodium measurements (*sodium_before, sodium_after*), our outcome variable captured either absolute **sodium change** or **% change**.

We personalized our analysis by combining our clustering model and a Bayesian regression model to predict sodium change per group. This approach helped identify which drugs were more effective for specific patient clusters based on traits like family history and demographics.

Metrics such as r^2 , RSME and visualizations such as residual plots help validate and guide our model making.



Patient Cluster #0
No Identifiable Health History
Primarily Female

Patient Cluster #3
Type I & Type II Diabetes
Slight Male Majority

Visit Cluster #0
E86.0: Dehydration
R11.10: Nausea & Vomiting
R50.9: Fever

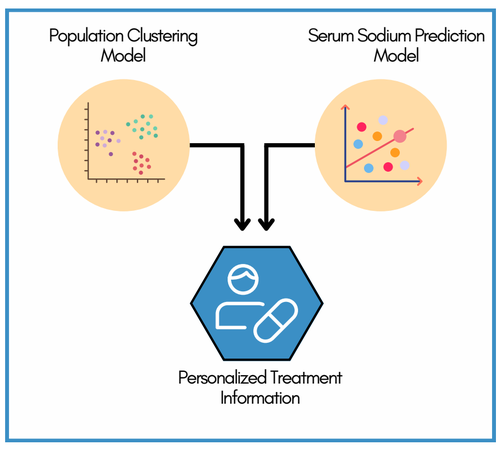
Visit Cluster #18
L60.0: Disorders of Skin Appendages
L03.90: Cellulitis
L02.91: Infection of Skin Tissue

998 Patients, 1106 Visits → **>= 2 Serum Sodium Measurements**

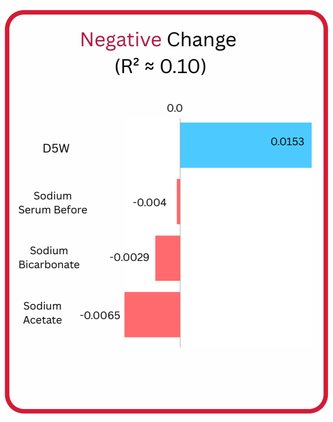
35/37 Visit Clusters
- ~39% of visits with measurements are from Cluster 0 (see above)
- Second biggest is 7% of visits, primarily around nervous system diseases

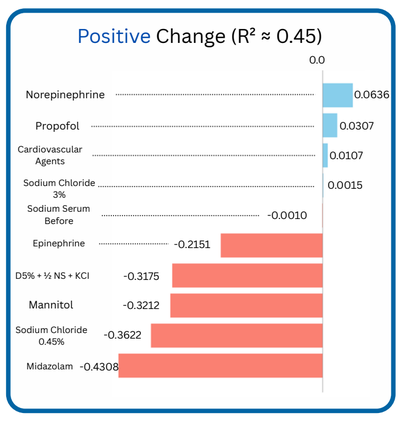
16/18 Patient Clusters
- ~70% of selected patients are in 2 clusters ("no identifiable health history")
- Rest are scattered among 15 clusters, each being <4% of total selection

Personalized Treatment Model



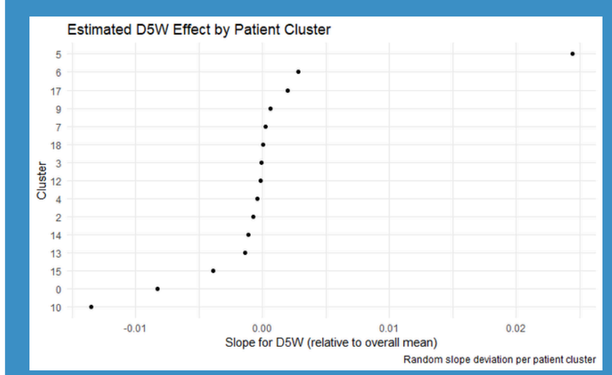
Factors Influencing Sodium Sereum % Change

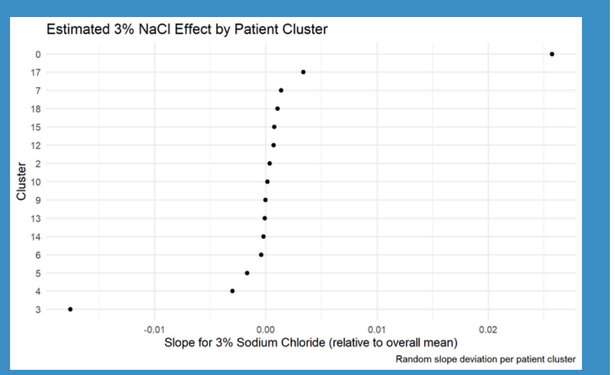




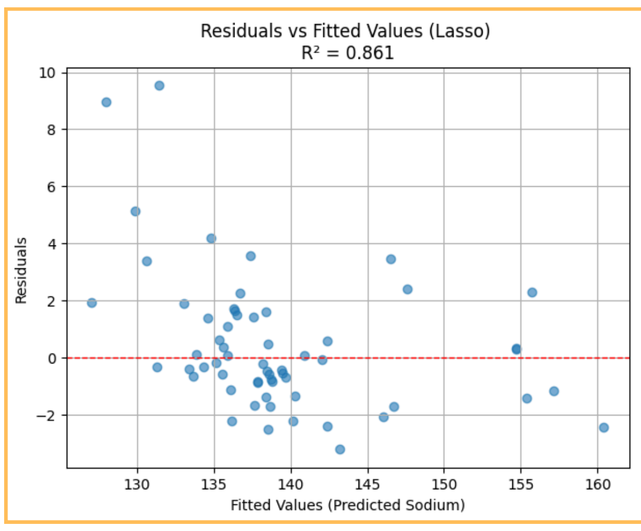
Notable Regression Parameters	# Rows	Model Info	(Avg) RSME	(Avg) R^2
sodium_after ~ sodium_before + drug_zscores + binary_drug_class_indicator + time_btwn_measurement_hrs	1,243	Lasso	3.24	0.640
sodium_after ~ sodium_before + drug_zscores + binary_drug_class_indicator + bun/creatine_zscore + time_btwn_measurement_hrs	299	Lasso	2.46	0.859
sodium_after ~ [Same as Model 2 but only non-zero features determined by Lasso where alpha = 0.01]	299	Robust	2.51	0.853
sodium_after ~ sodium_before + drug_zscores + binary_drug_class_indicator + time_btwn_measurement_hrs *(only on pairs which have bun/creatine scores)*	299	Best Lasso	2.44	0.861

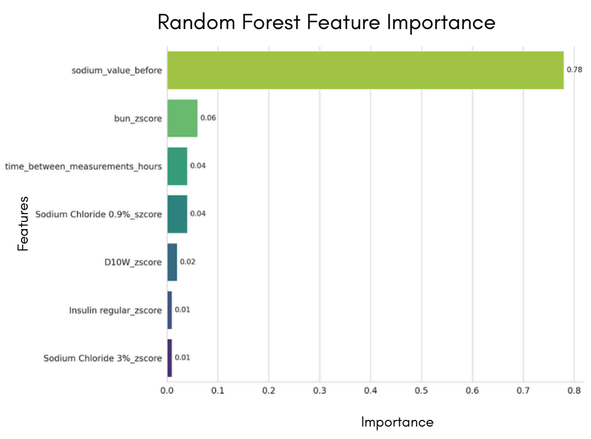
Variation in Drug Effects by Patient Cluster





Interpretation:
Patient clusters differed in their response to D5W and 3% NaCl. Some clusters showed stronger associations with sodium increases, while others showed minimal or even negative effects. This suggests fluid impact is not uniform across subgroups





6) Analysis

Clusters (Population vs. 998 patients)

- Effective in capturing global ED population variability, not as effective in capturing group variation among selected patients & visits with >= 2 S.S measurements

Serum Sodium Model

- Heavy dependent on first serum sodium measurement
- Unclear how effective the bun/creatine values are. Suffers from small sample size

Personalized Treatment

- Cluster-specific random slope modeling allowed us to estimate drug effects across patient subgroups, providing insight into response heterogeneity
- The model for negative sodium changes had limited explanatory power ($R^2 \approx 0.10$), but significantly associated D5W with a less negative change, while higher initial sodium, sodium acetate, and sodium bicarbonate were linked to more negative changes. Conversely, the model for positive sodium changes explained a moderate amount of variance ($R^2 \approx 0.45$). It found that higher initial sodium, several IV fluids (like 0.45% NaCl, D5% + 1/2 NS + KCl), and numerous medications (including epinephrine, fentanyl, heparin, mannitol, and midazolam) were associated with a smaller positive increase. Conversely, 3% NaCl, norepinephrine, propofol, and the administration of cardiovascular agents were linked to a larger positive increase in sodium.

7) Conclusion

This project aimed to understand how different drugs affect serum sodium levels in dehydrated pediatric patients. We combined clustering and regression methods—including Lasso, Robust, and Bayesian models—to explore both general and personalized patterns of drug effectiveness.

Among the models tested, Lasso regression performed best overall, helping us select key features and achieve more stable predictions. However, model performance was limited by several factors: a high number of missing values, especially in kidney markers like BUN and creatinine, and strong dependence on the baseline serum sodium level. In many cases, this baseline dominated the model's predictive power, making it difficult to isolate drug effects.

Even with those limitations, we found that drug response varied by cluster. For D5W and 3% NaCl, some clusters had stronger associations with sodium increase, while others had lower-than-average responses. Cluster-level modeling uncovered heterogeneity in fluid response, offering a potential path toward individualized sodium correction strategies

8) Future Work

Given the sparsity of serum sodium, gathering more measurements, as well as bun/creatine measurements could vastly improve our work. For clustering, doing more research on ICD-10 codes can provide deeper insight into our population clusters. We can could also explore explore different textual embedding methods (e.g. semantic embeddings) as its likely that vectorization may provide better accuracies. For the regression models, running grid search on regression parameters could provide parameters for better results. Finally we may transition into writing a paper over the summer!

References:

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Acknowledgements:

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