Validating an open source electronic health record pipeline to phenotype pneumonia

ehrapy: an open source Python framework for EHR data

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EHR data contains a wealth of information

However working with it is extremely challenging

- EHRs = rich but messy (hierarchical, sparse, missing)
- Need better tooling for data processing, joining, organization, cohort tracking, analysis + phenotyping
- ehrapy: Python framework designed for EHR analysis [1]

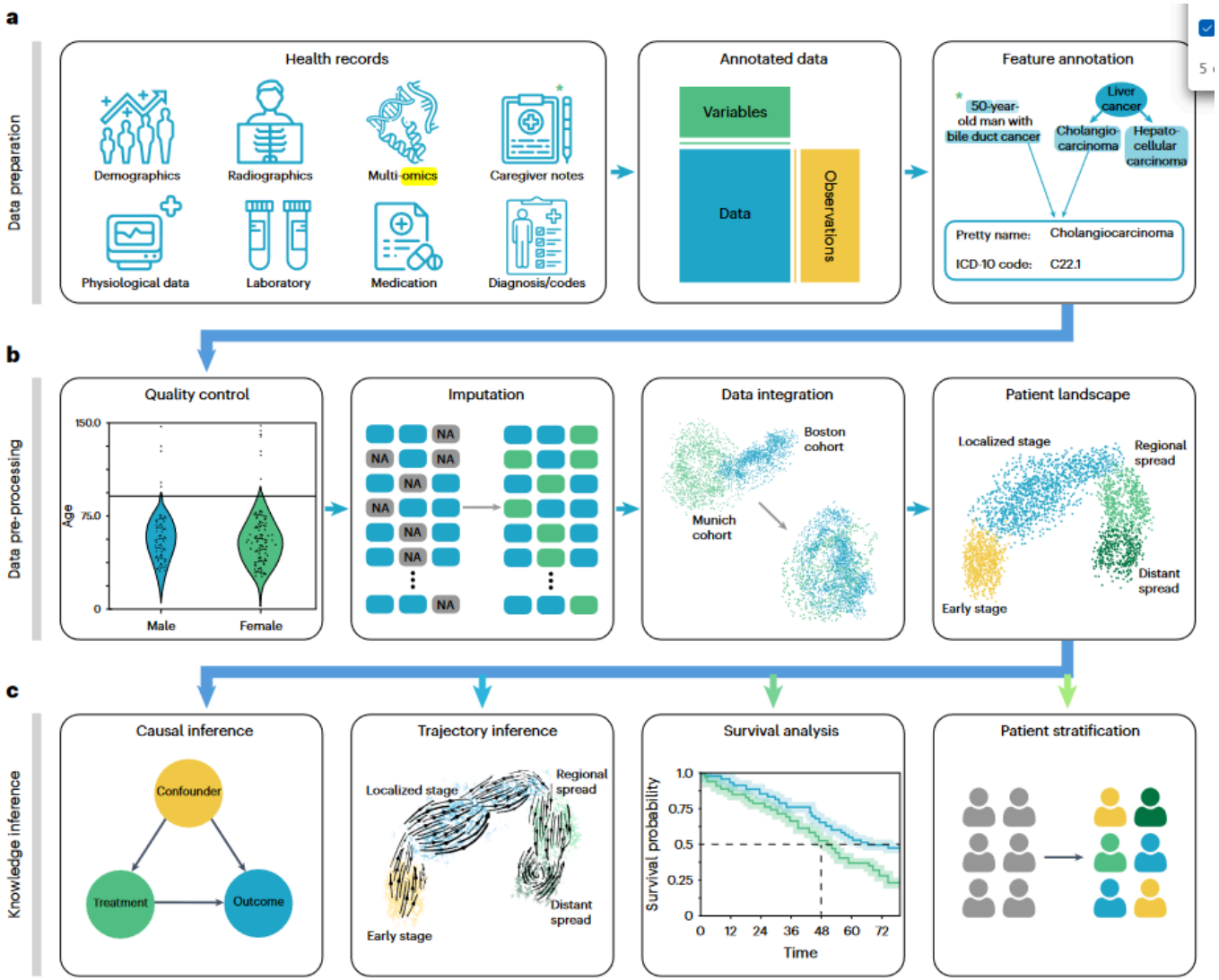
Phenotyping pneumonia unspecified

Learn to process a large EHR dataset for clustering and modelling

1. ✅ Validate ehrapy with MIMIC-IV
2. 🧬 Replicate Gupta and colleagues original paper that phenotype pediatric pneumonia [2]
    i. 🔀 Stratify pneumonia patients into subtypes (unsupervised)
    ii. 🔧 Extend with supervised ML to predict hospital mortality

> **Tip**
>
> The process of identifying and grouping patients based on shared clinical characteristics, patterns, or outcomes — often using unsupervised learning to uncover hidden subtypes within a population [3].

ehrapy Workflow



ehrapy EHR data pipeline. Retrieved from: [2]

Dataset

MIMIC-IV

Adult pneumonia unspecified cohort

- ~70,000 ICU and non-ICU adult patient admissions (2008–2019)
- Structured: vitals, labs, meds, diagnoses, procedures
- Credentialed access to MIMIC-IV can be obtained via PhysioNet [4]

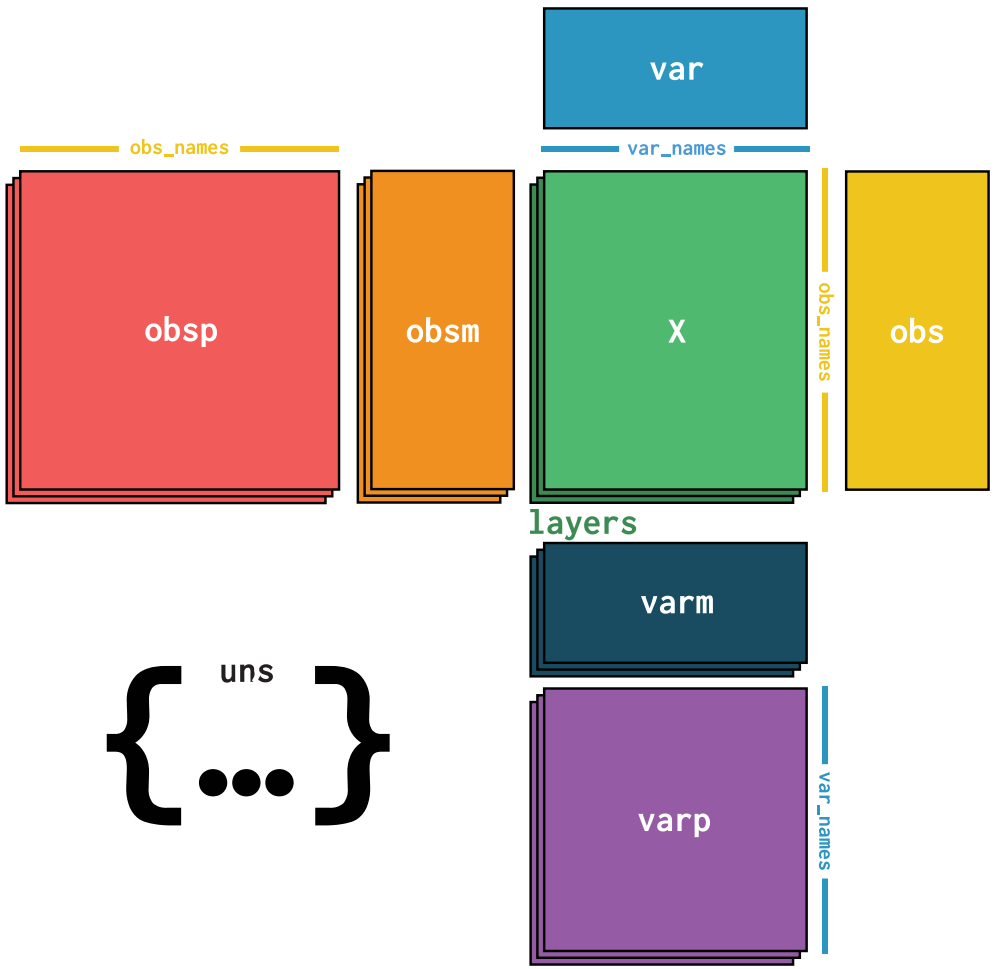
Characteristic	Value
Average Age	63.04
Average Hospital Mortality	7.14%
Average ICU Stay (days)	3.63
Average ICU Visits per Admission	1.11
Patients with >1 ICU Visit (%)	9.03%
Male (%)	55.98%
Female (%)	44.02%

The plan

Phase 1 - Framework Validation

ehrapy data processing pipeline

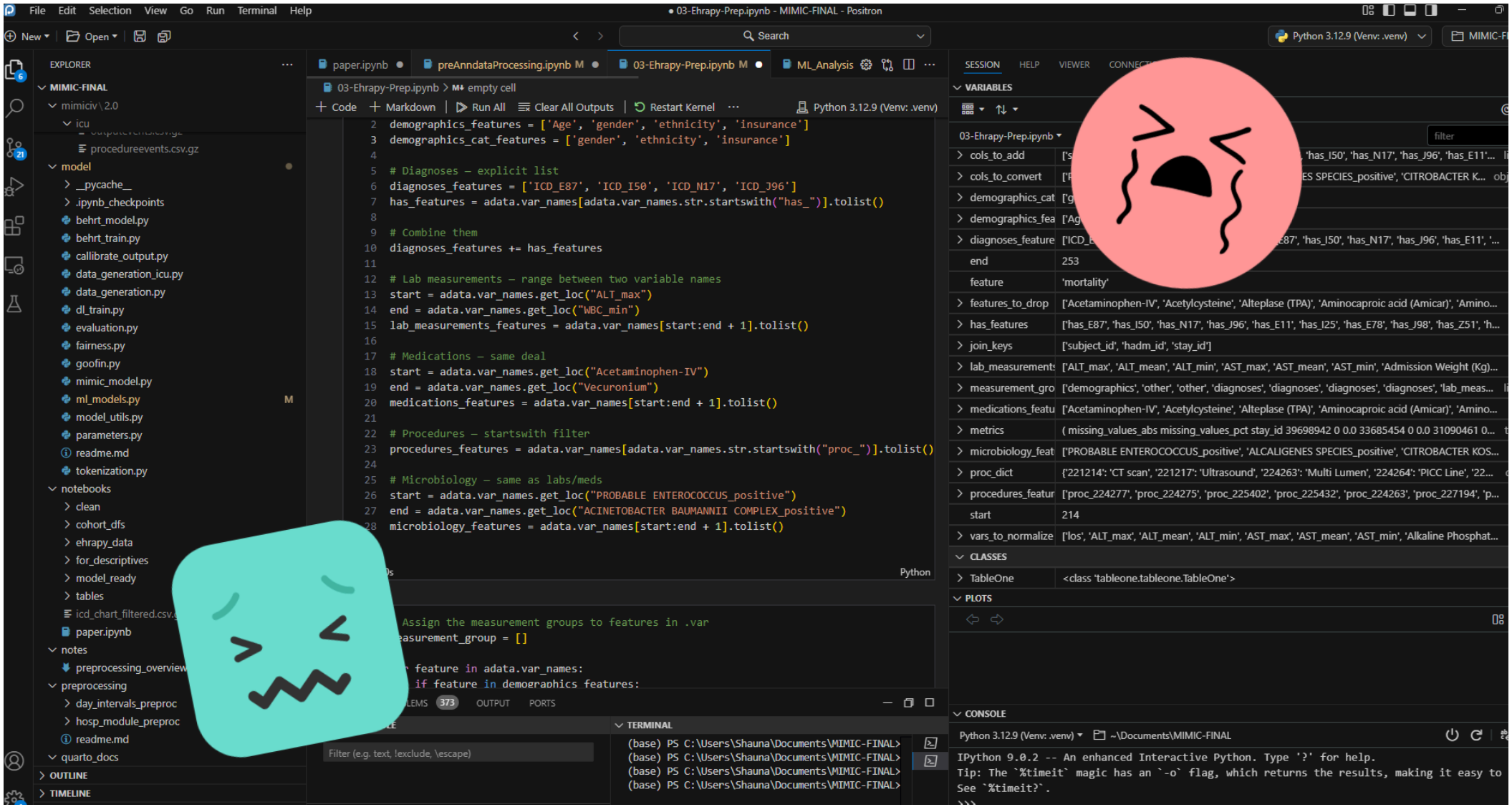
- Wrangle data into vectors for converting to anndata object [5]
- Use ehrapy's built-in clustering pipeline to prepare and preprocess data
- Identify pneumonia subgroups (phenotypes)
- Compare with original paper (PIC) subgroups [2]
- Use new subgroups to predict 30 day in hospital mortality



Anndata Structure. Retrieved from [5]

Reality…

Trials and tribulations



Phase 1 - Technical Challenges

Did I bite off more than I can chew?

> **Caution**
>
> Wrangling 9.8 GB worth of datasets and > 30 individual datasets into a cohesive, single cohort fit for analysis is HARD on your 🧠 AND on your RAM

- What to include or not include in terms of chart data, medication data, icu versus hospital data, etc.
- Iterative pipeline testing to get it right
- Lots of late nights & hair pulling

Phase 1 - Data Wrangling

ICU data - All features with > 60% coverage

```
   import ehrapy as ep

① adata = ep.io.read_csv(pic_data_path)          # Read in the dataset into an AnnData object
② ep.pp.winsorize(adata)                         # Winsorize extreme values
③ ep.pp.summarize_measurements(adata)            # Summarize measurements to obtain min, average and max values
④ ep.pp.knn_impute(adata)                        # Impute missing values with k-nearest-neighbors imputation
⑤ ep.pp.log_norm(adata)                          # Log normalize numerical values
⑥ ep.pp.encode(adata, encodings="one-hot")       # One-hot encode categorical values
   ep.pp.pca(adata)                              # Reduce the dimensionality of the data using PCA
   ep.pp.neighbors(adata)                        # Compute the neighborhood graph
⑦ ep.tl.umap(adata)                              # Embed the graph in two dimensions using UMAP
   ep.pl.umap(adata, color="LOS")                # Plot the UMAP colored by the length of stay
```

ehrapy basic data pipeline functions. Retrieved from [2]

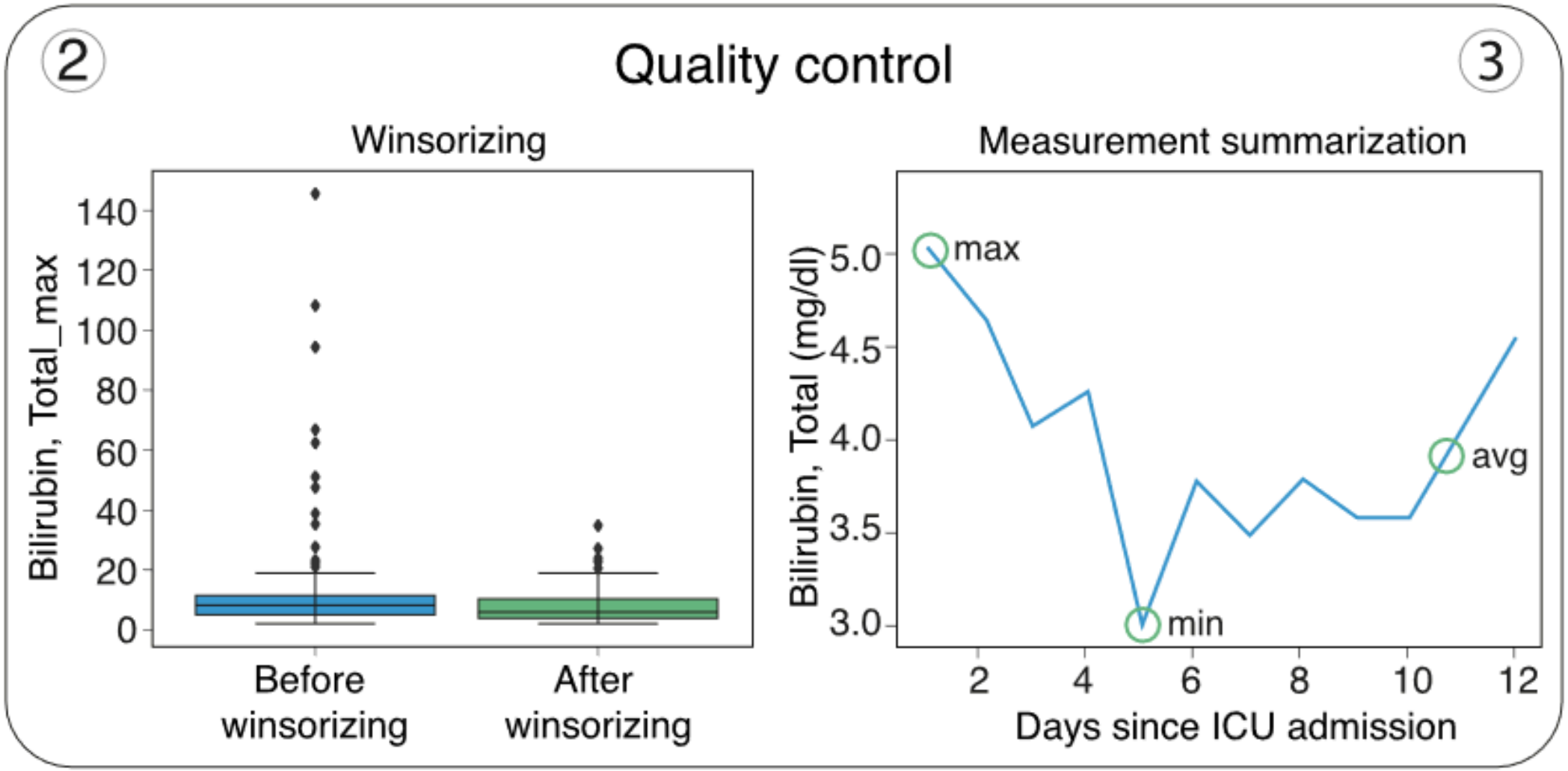
The unspecified pneumonia cohort

ICD-J18

Characteristic	Value
Unique Patients	7518
Average Age	65.56
Average Hospital Mortality	13.69%
Average ICU Stay (days)	4.98
Average ICU Visits per Admission	1.20
Patients with >1 ICU Visit (%)	16.23%
Male (%)	55.00%
Female (%)	45.00%
TOTAL OBSERVATIONS	9864
TOTAL FEATURES	180

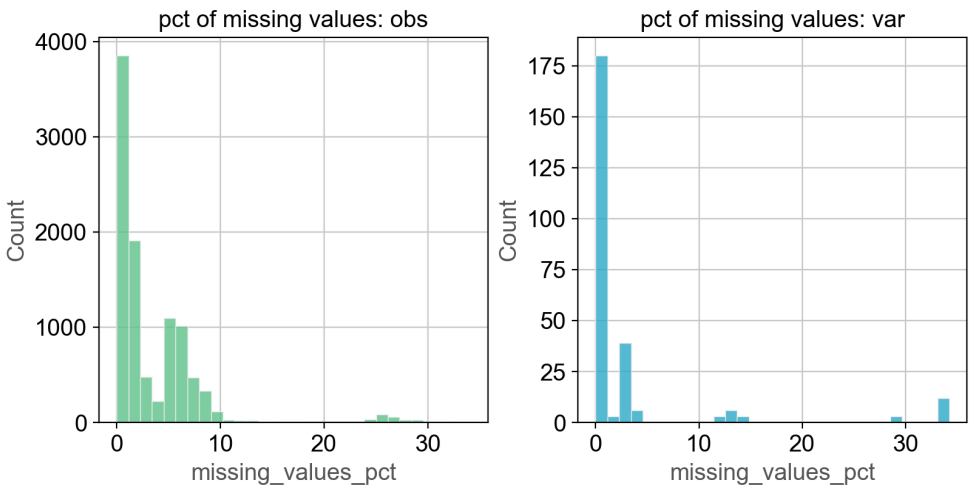
Winsorizing & summarization

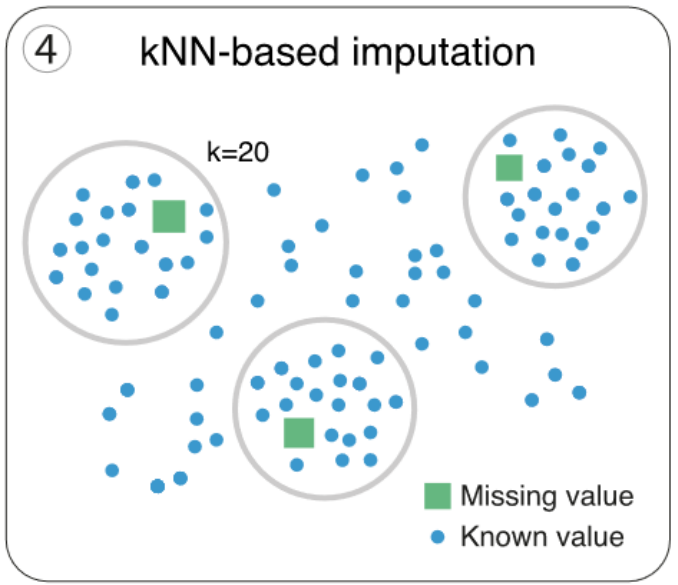
✅ *Helps reduce outlier influence while keeping data shape*



Missing Data

KNN - 20 neighbors



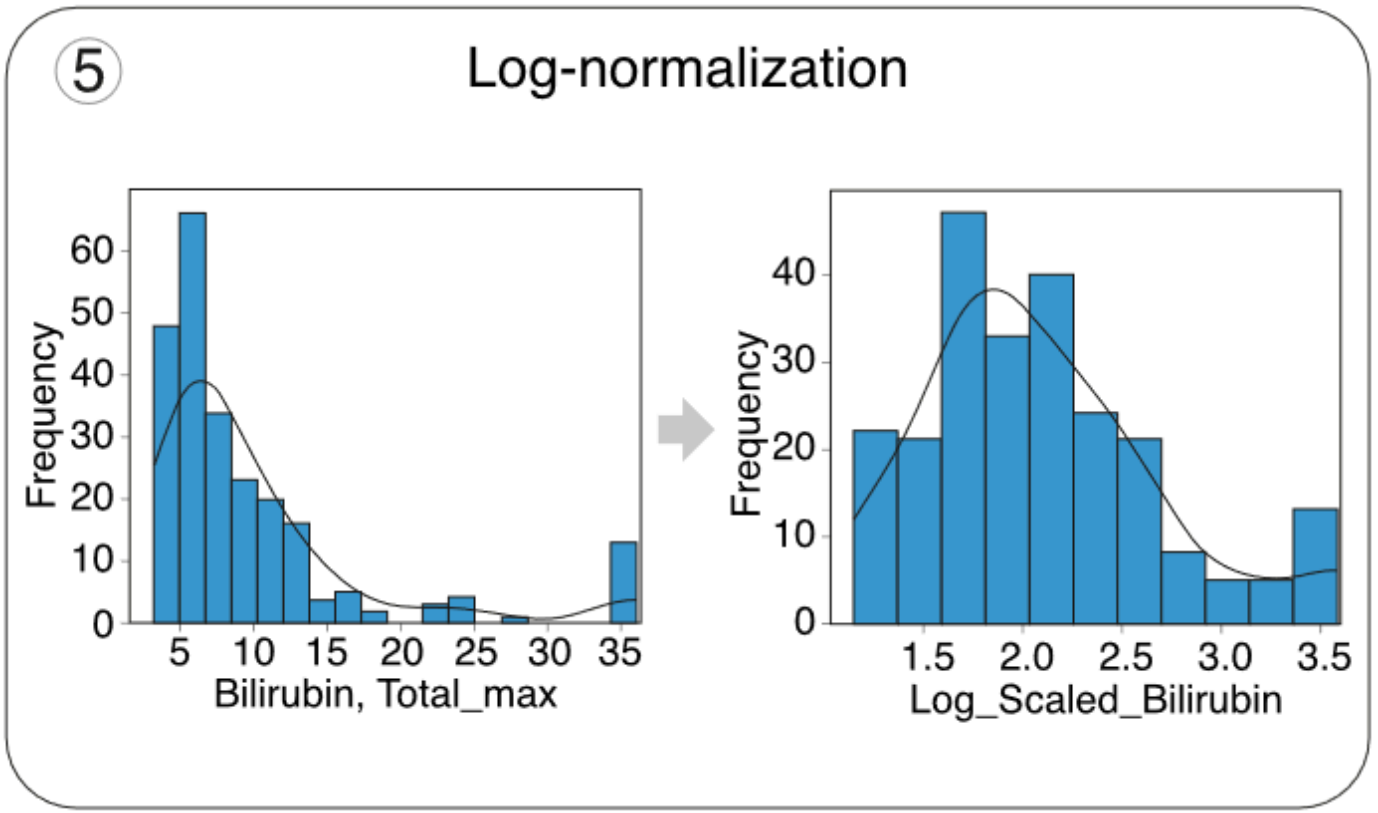


Tip

the percentage of missing values in all features did not exceed 40%, however, some features were not complete. We used K-nearest neighbors imputation (with K = 20) to fill in missing values. Each missing value was estimated by averaging the same feature across its 20 nearest neighbors.

Normalization

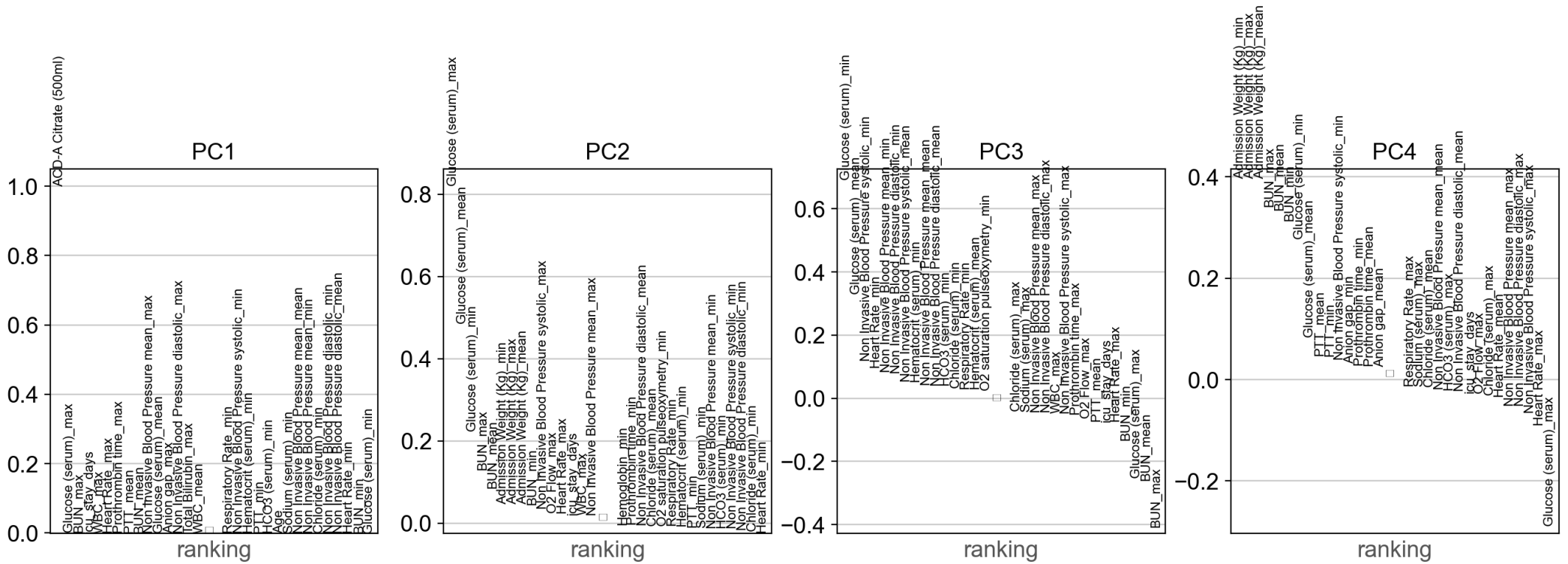
Log normalization




```
adata.var["coefficient.variation"] = (
    adata.var["standard_deviation"] / adata.var["mean"]
) * 100
adata.var.loc[(adata.var["coefficient.variation"] > 50) & (adata.var["mean"] > 50),]
ep.pp.log_norm(adata, vars=vars_to_normalize, offset=1)
```

Principal Component Analysis (PCA)

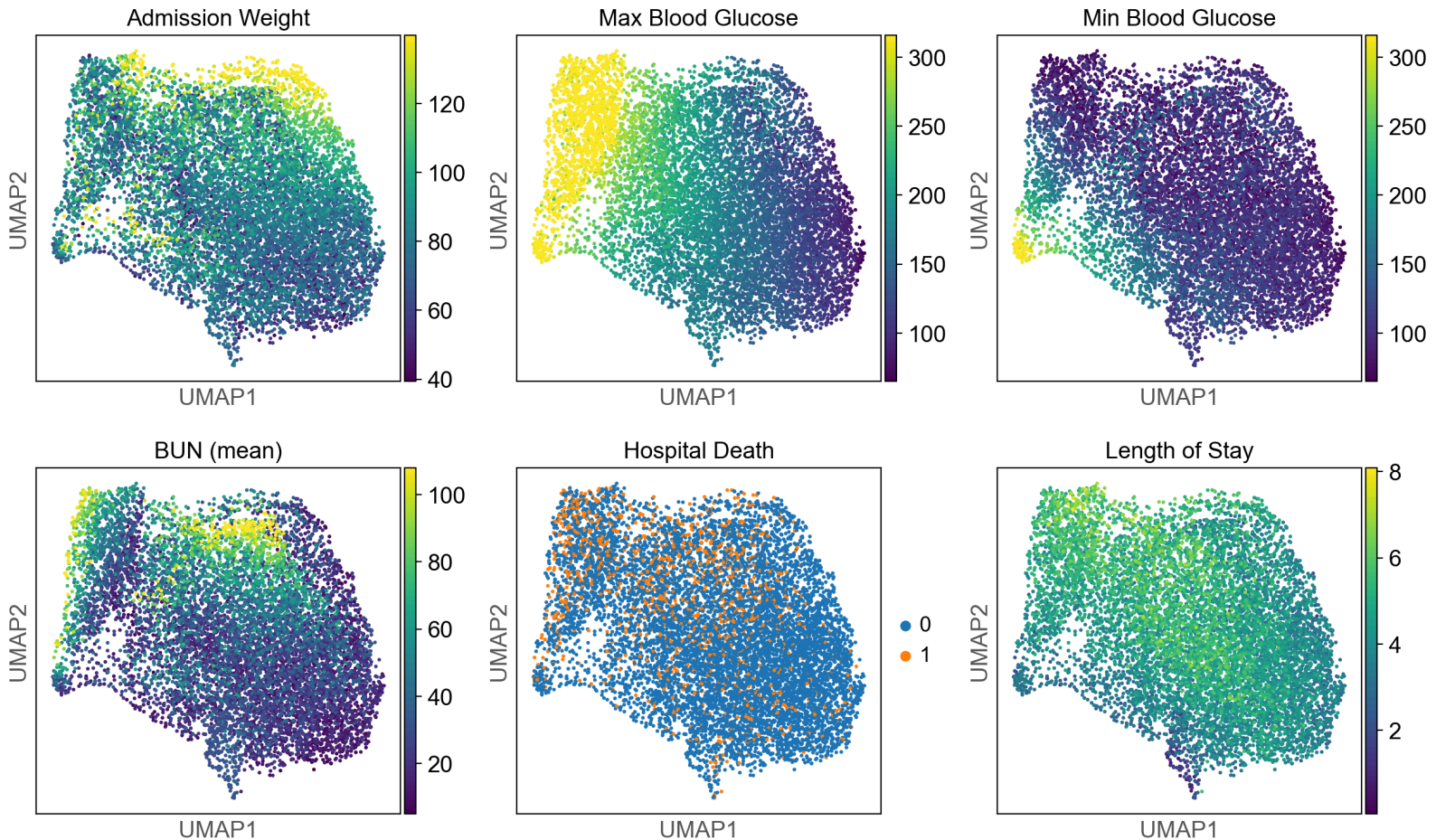
Dimensionality reduction



PCA was used to transform our high-dimension data into a smaller set of uncorrelated components. The reduced representation was then used as input for the neighbors graph calculation.

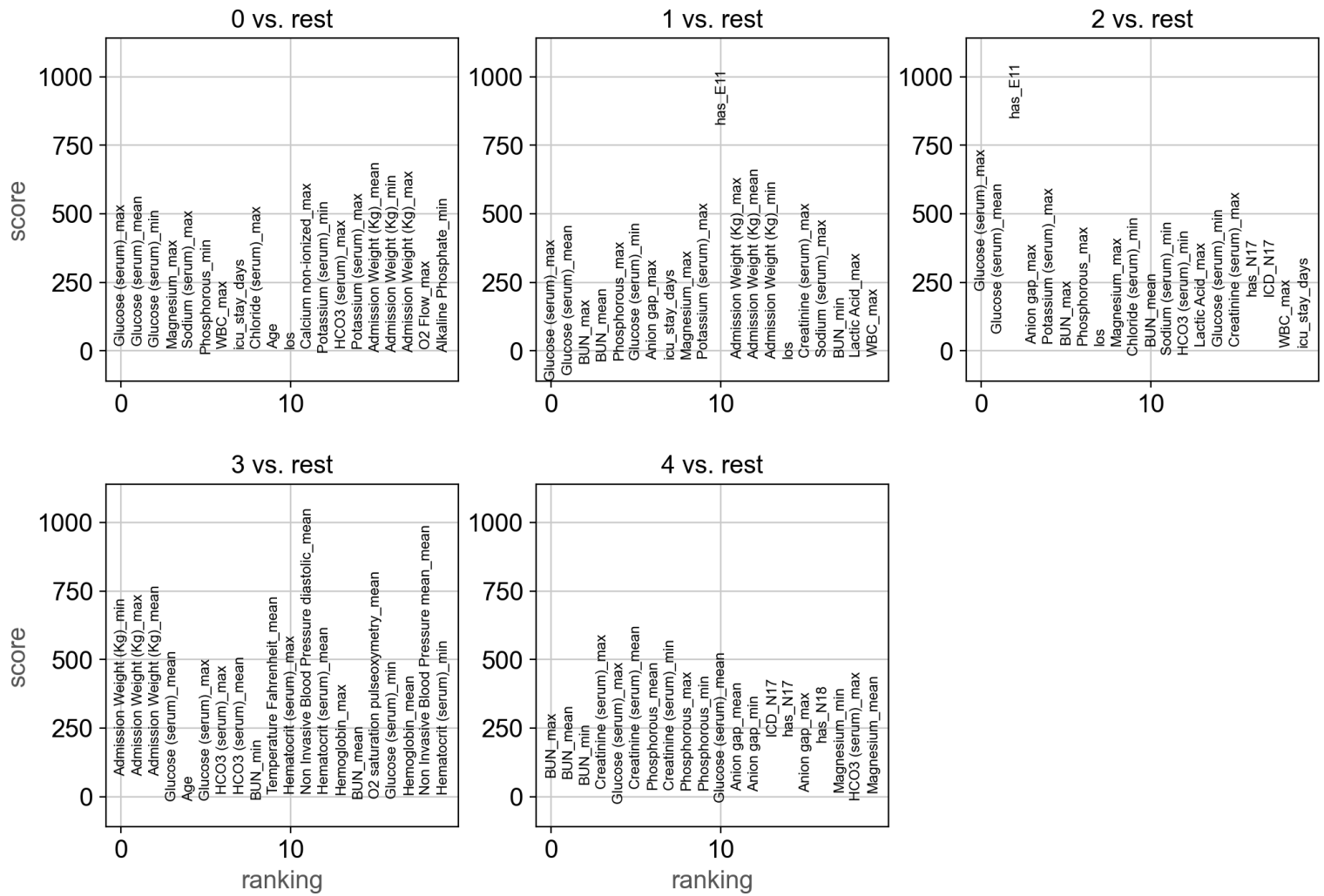
UMAP

Uniform Manifold Approximation and Projection (UMAP)



This figure shows a UMAP embedding of our dataset after dimensionality reduction with PCA. Each dot is an ICU stay, positioned based on similarity across high-dimensional vitals, labs, and demographics.

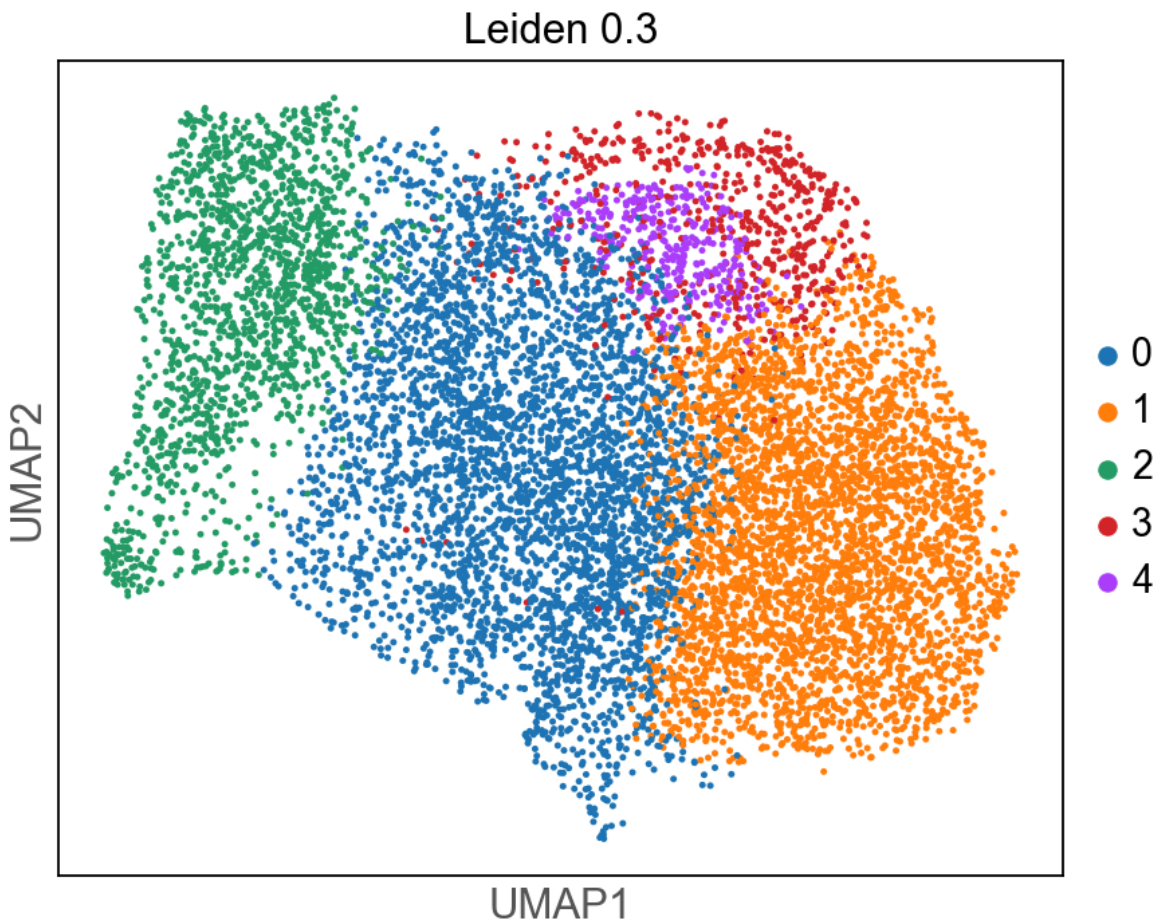
Leiden Clusters



After projecting patient data into UMAP space, we applied Leiden clustering to identify subgroups. The y-axis represents importance scores, while the x-axis ranks features from most to least informative for each cluster. How strongly this variable distinguishes this cluster from the rest, based on the Wilcoxon test statistic.

Cluster identification

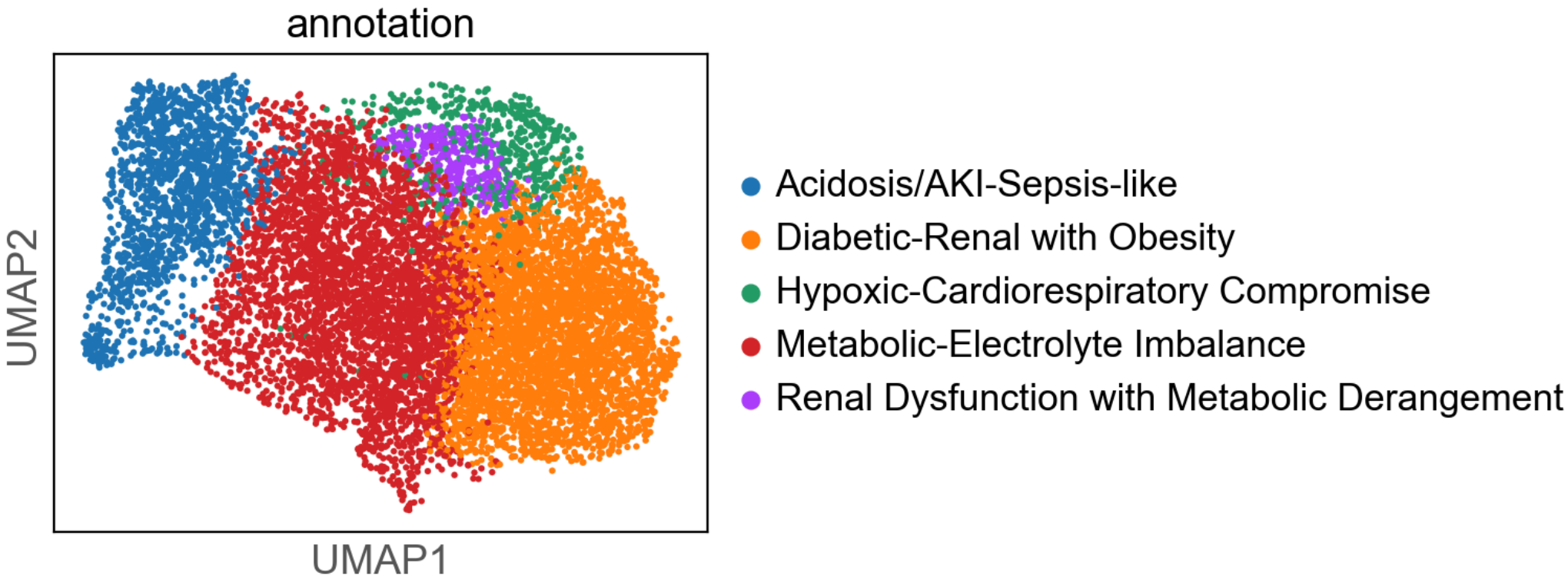
Leiden 0.4



Leiden is a fast, community detection algorithm that improves on Louvain by guaranteeing well-connected, high-quality clusters. Often used in network and single cell data. Optimizes the modularity of Louvain where clusters can become disconnected.

Phase 1 - Results

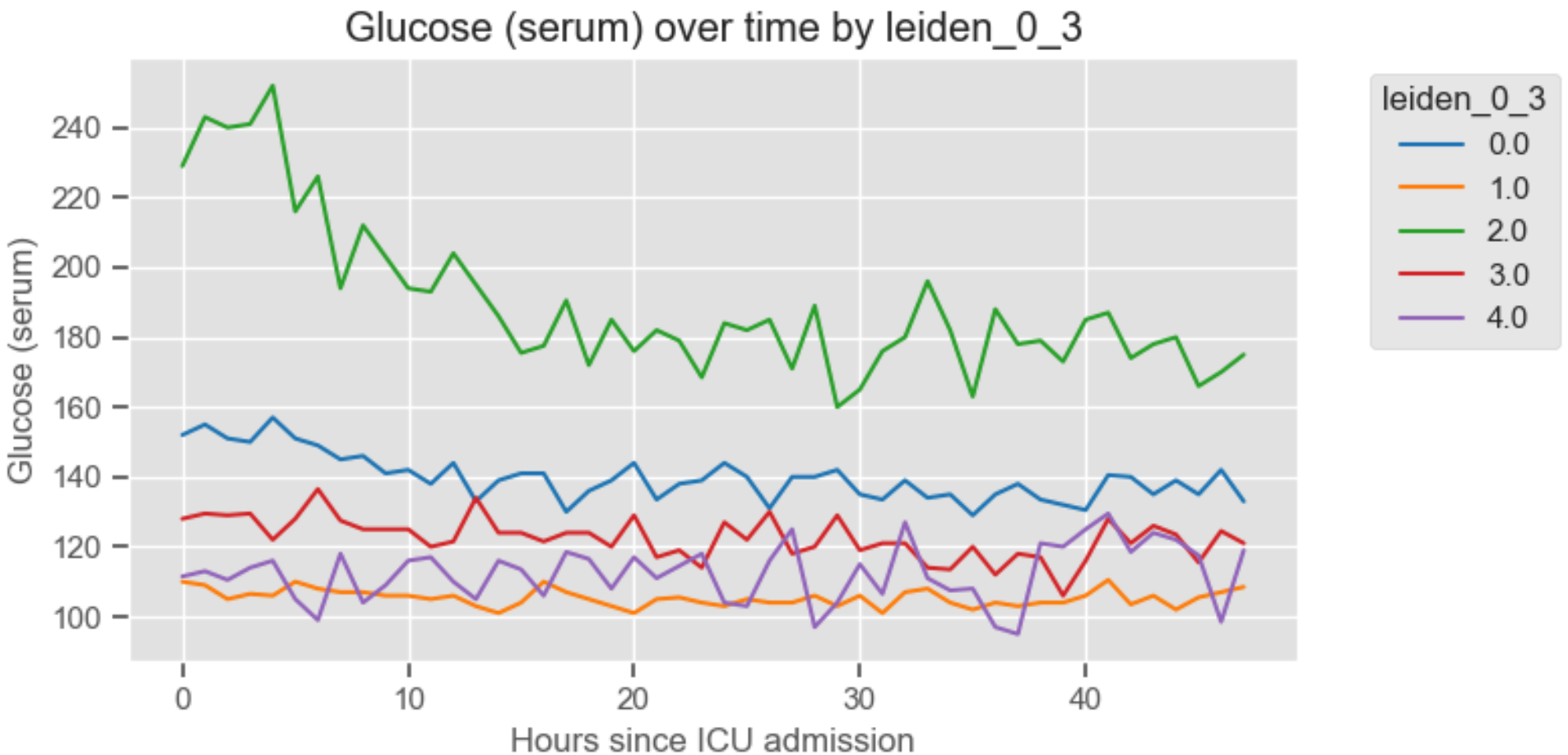
GPT-Assisted annotation of clusters for disease phenotypes



Gupta and colleagues had a group of physicians evaluate and annotate their subgroups; we used reached out to ChatGPT for assistance [6].

Glucose levels measured over time

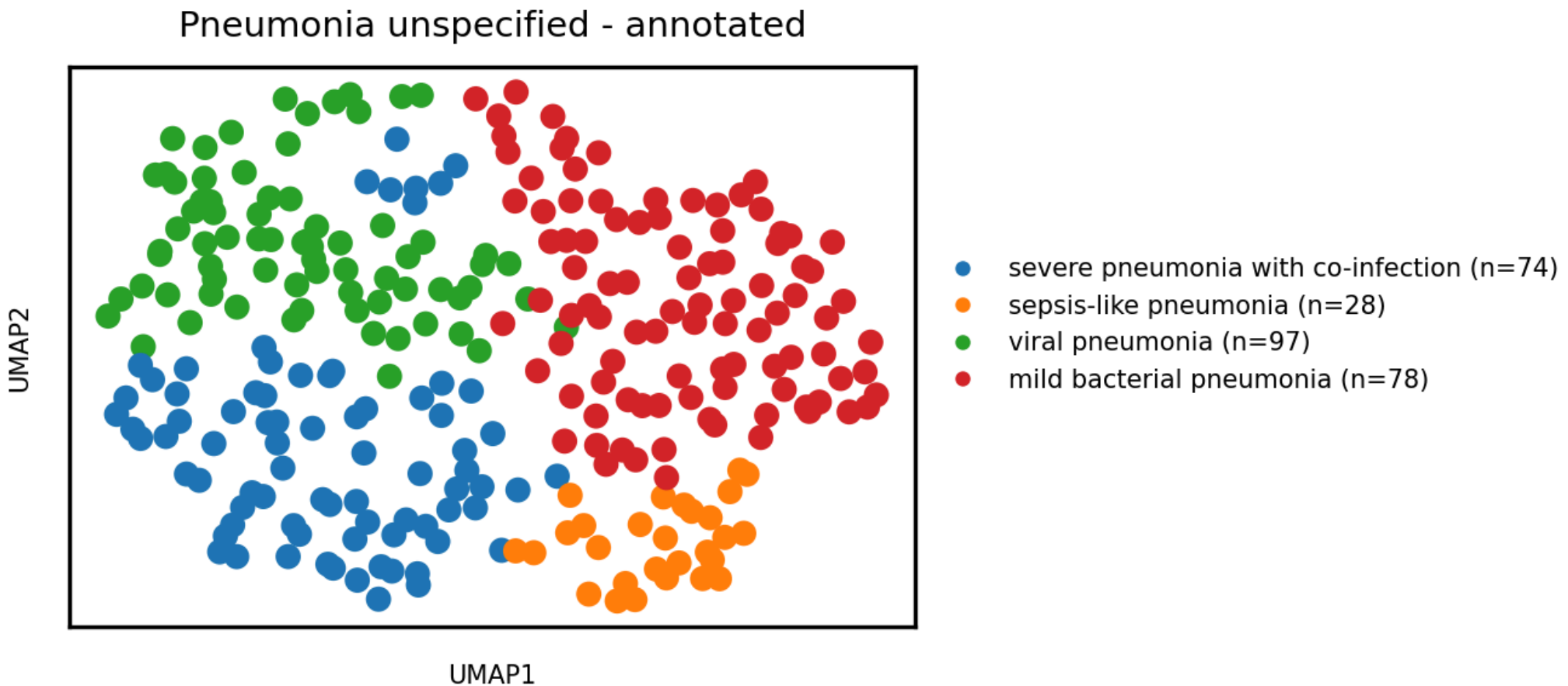
By cluster



This is an example of how the groups differ in one specific measure (glucose serum) over time. Note the most severe cluster w/diabetic sepsis enters the ICU with very high sugars.

Comparison with ehrapy paper

Pediatric cohort [2]



Pediatric clusters. Retrieved from [2]

Comparing Adult & Pediatric Phenotypes

Validation with original pediatric cohort

Pediatric Phenotype	Adult Cluster	Shared Signals
Sepsis-like	Cluster 0 / 2	↑ Creatinine, Hypotension, Acidosis, possibly ↑ mortality
Severe w/ Co-infection	Cluster 2 / 4	↑ LOS, AKI, Electrolyte imbalance
Mild bacterial	Cluster 1	Low inflammation, metabolic comorbidity (e.g., diabetes/obesity)
Viral pneumonia	Cluster 3	Stable BP, ↑ O2 sat, less renal involvement

Adult & pediatric clusters overlap but also reflect comorbidity burden (e.g., diabetes) not observed in pediatric patients.

Phase 2: predicting in-hospital mortality

Phase 2 - ML Extension

Goal: Build temporal ML model using pneumonia cluster labels

- Predict in-hospital mortality from early ICU data

  → Binary target: `hospital_death` (0 = survived, 1 = died)

- Vitals, labs, and structured demographic features (first 48h)

  → Cluster info (Leiden groups) included as one-hot encoded features

- Stratified dataset for train-test split of (80/20)

  → Class imbalance handled by undersampling survivors (only 24% mortality in df)

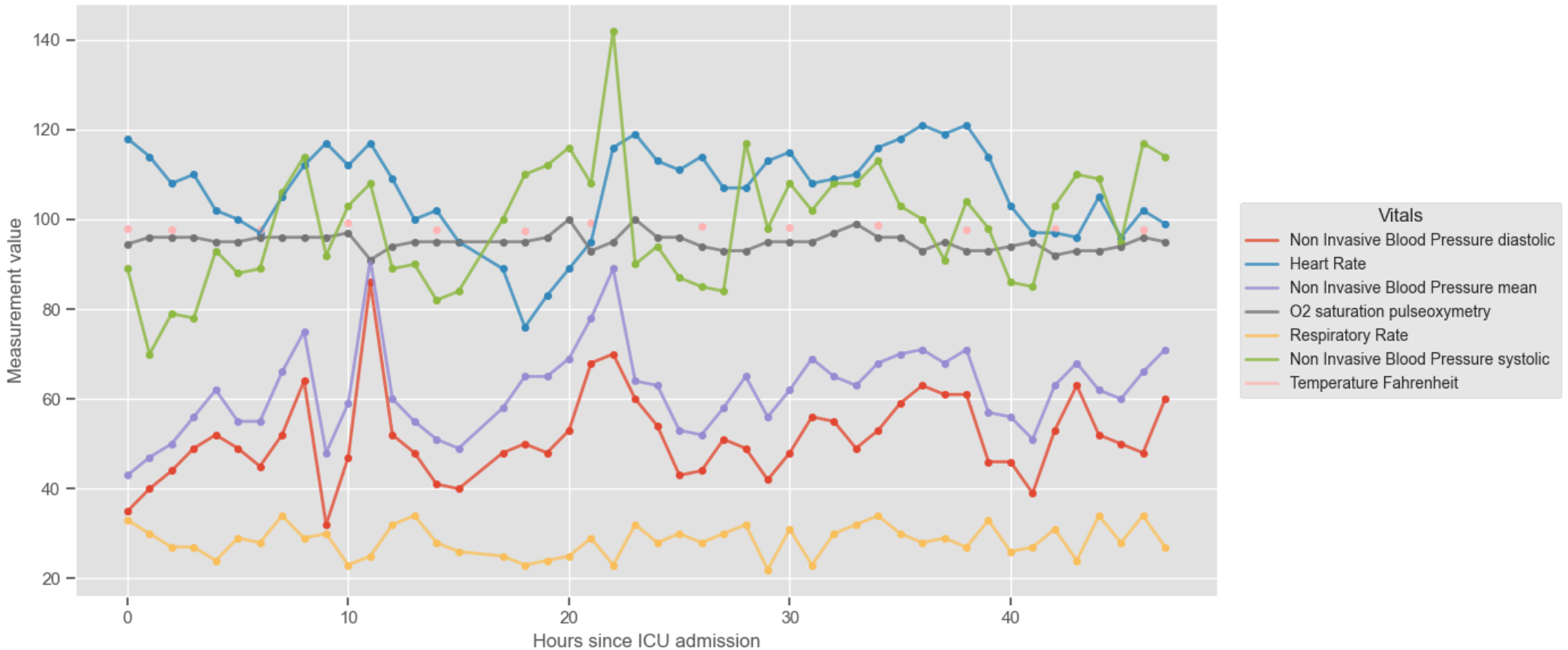
Phase 2 - Model Architecture

Predicting in-hospital mortality from first 48 hours

- Random Forest (GridSearchCV, hyperparameter tuning)
- XGBoost (tree boosting baseline)
- Neural Net (MLP-Classifier, small feedforward network)

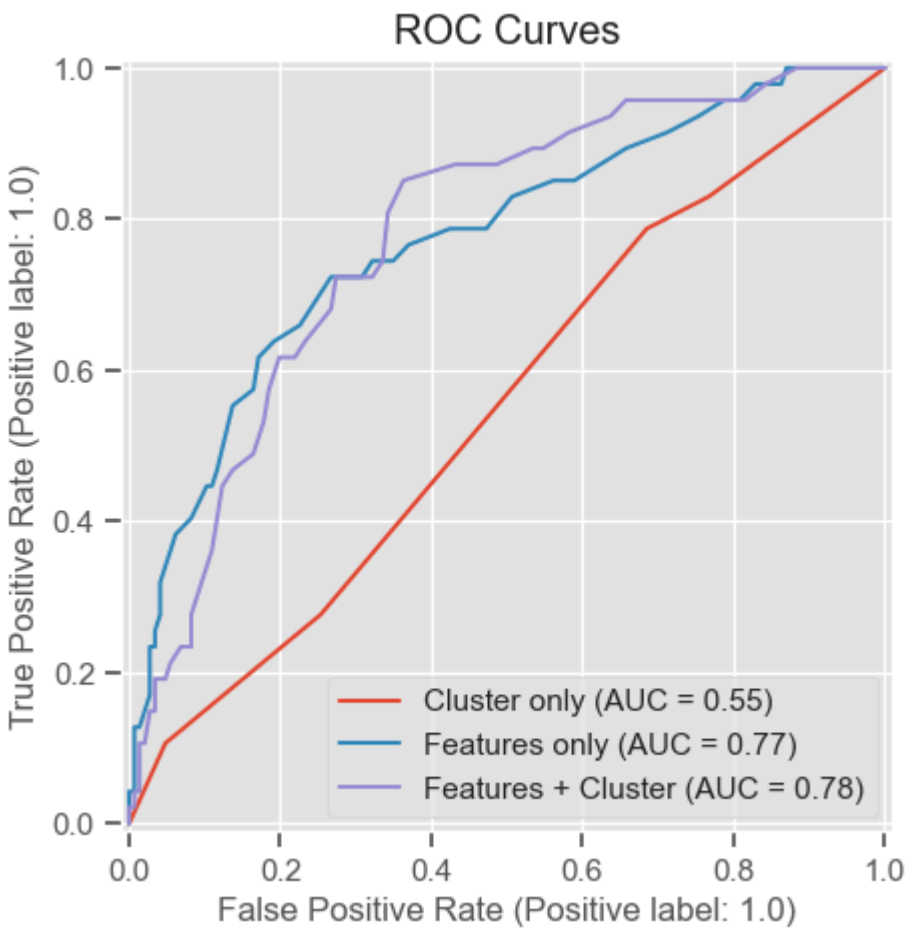
Time Series Extraction

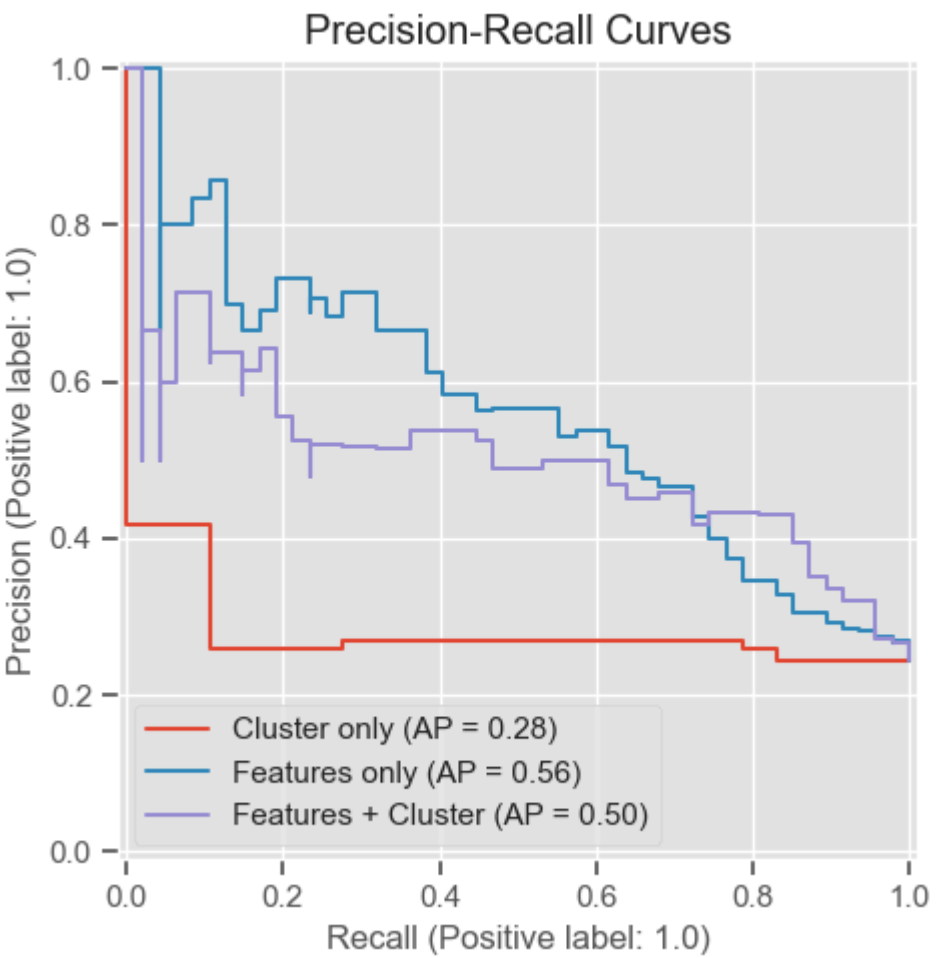
Vitals were aggregated (min, mean, max) every hour for first 48 hrs



Results: RF Feature Comparison

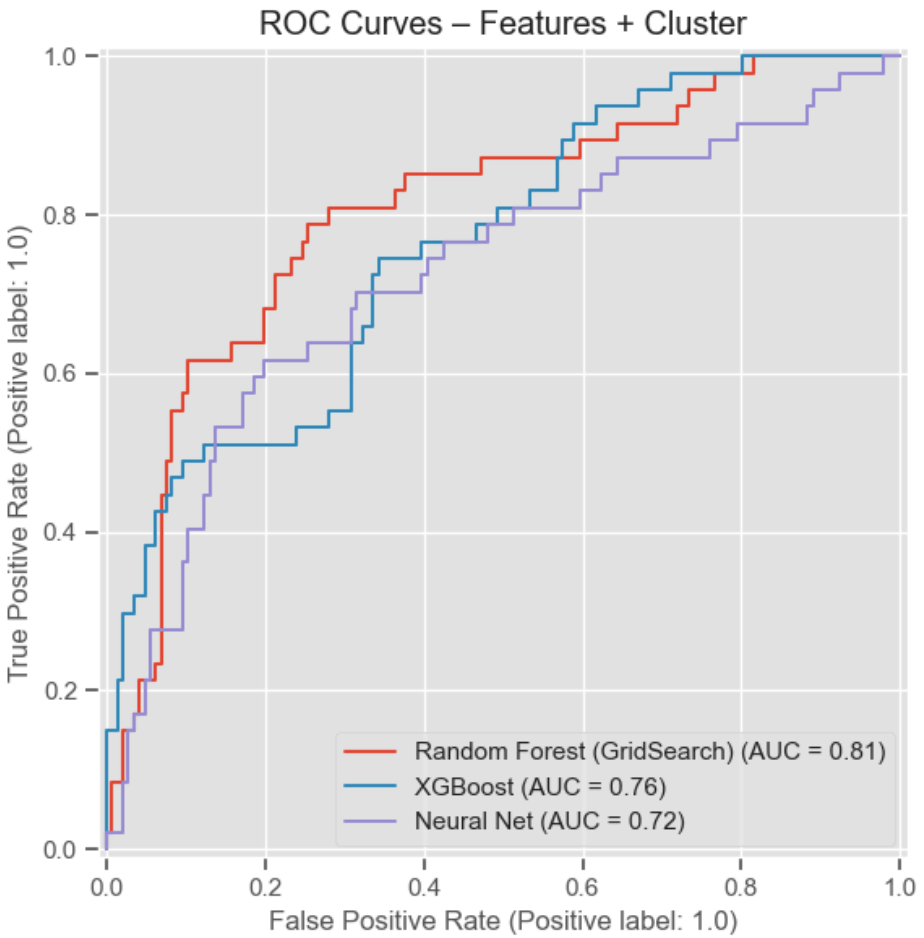
With and without leiden clusters





Results: RF, XGB & NN Race

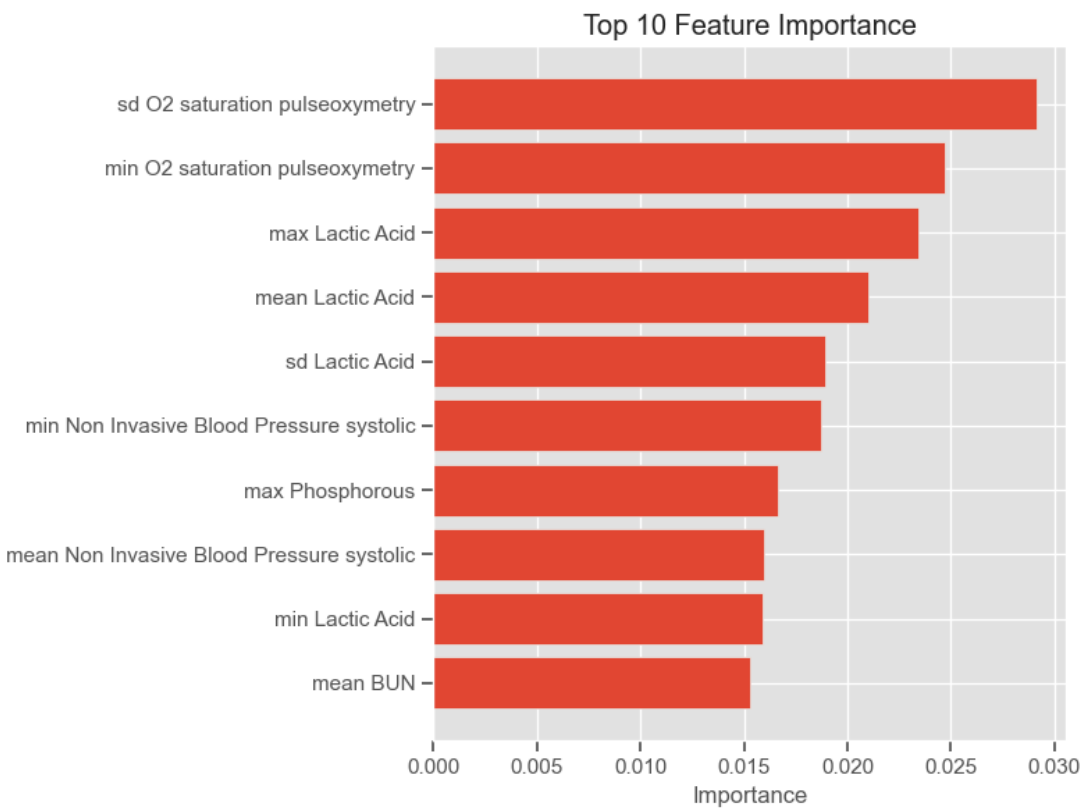
Random Forest + clusters for the win



The model does well at identifying survivors but struggles with catching true deaths (low recall).High AUC suggests the model still ranks high-risk patients reasonably well, which could be improved with better threshold tuning or resampling

Features that contribute most to predicting in-hospital death in pneumonia patients

SHAP



O^2 sat., lactic acid levels, and BP stability are 💪 contributors to mortality prediction. These align well with clinical expectations around respiratory failure, sepsis, and hemodynamic instability in high-risk pneumonia patients.

Next Steps

- **Robust Modeling & Tuning**
  Explore advanced ML pipelines with deeper hyperparameter tuning, model ensembles, and uncertainty quantification.
  Limited by time and compute.
- **Temporal Modeling**
  Incorporate trends across time using time-series models or RNNs to better capture clinical trajectories.
- **Validation on External Cohorts**
  Evaluate model generalizability and phenotype stability on new datasets or hospital systems.
- **Interpretability & Explainability**
  Use SHAP or similar tools to explore feature importance and clinical relevance of phenotypes.

Clinical Collaboration

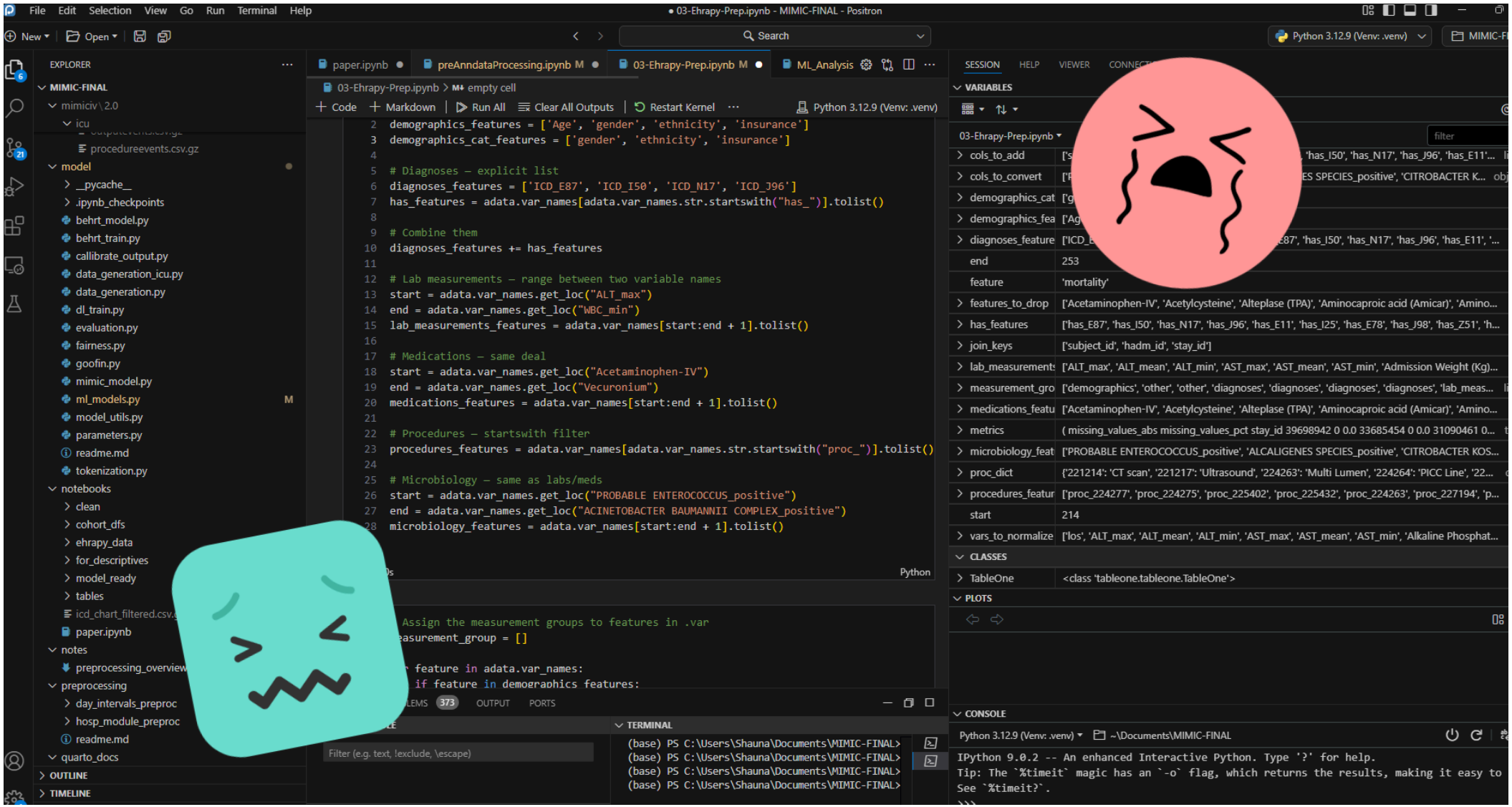
It would be important to work with actual clinicians to validate clusters and explore practical applications in care delivery.

Key Takeaways

Conclusion

- ehrapy has a steep learning curve; but may be worth it
- EHR phenotyping benefits from hybrid unsupervised + supervised approaches
- Open-source workflows like ehrapy + PyTorch are promising for real-world EHR work

Trials and tribulations



Math

Winsorization

For a value $\boldsymbol{x_i}$ in feature $\boldsymbol{X}$:

$$x_i^{\text{win}} = \begin{cases} P_1(X), & \text{if } x_i < P_1(X) \\ x_i, & \text{if } P_1(X) \leq x_i \leq P_{99}(X) \\ P_{99}(X), & \text{if } x_i > P_{99}(X) \end{cases}$$

Where:

- $P_1(X)$ = 1st % of X
- $P_{99}(X)$ = 99th % of X
- x_i^{win}

KNN

For a missing value $\boldsymbol{x}_{i,j}$ in row $\boldsymbol{i}$, column $\boldsymbol{j}$:

$$\hat{\boldsymbol{x}}_{i,j} = \frac{1}{K} \sum_{k \in \mathcal{N}_K(i)} \boldsymbol{x}_{k,j}$$

References

[1] M. Gupta, B. Gallamoza, N. Cutrona, P. Dhakal, R. Poulain, and R. Beheshti, “An Extensive Data Processing Pipeline for MIMIC-IV,” in *Proceedings of the 2nd machine learning for health symposium*, in Proceedings of machine learning research, vol. 193. PMLR, 2022, pp. 311–325. Available: https://proceedings.mlr.press/v193/gupta22a.html

[2] M. Gupta, B. Gallamoza, N. Cutrona, P. Dhakal, R. Poulain, and R. Beheshti, “An extensive data processing pipeline for MIMIC-IV,” *Proceedings of machine learning research*, vol. 193, pp. 311–325, Nov. 2022, Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9854277/

[3] S. Yang, P. Varghese, E. Stephenson, K. Tu, and J. Gronsbell, “Machine learning approaches for electronic health records phenotyping: A methodical review,” *Journal of the American Medical Informatics Association*, vol. 30, no. 2, pp. 367–381, Feb. 2023, doi: 10.1093/jamia/ocac216. Available: https://doi.org/10.1093/jamia/ocac216

[4] A. E. W. Johnson *et al.*, “MIMIC-IV, a freely accessible electronic health record dataset,” *Scientific Data*, vol. 10, no. 1, p. 1, Jan. 2023, doi: 10.1038/s41597-022-01899-x. Available: https://www.nature.com/articles/s41597-022-01899-x

[5] I. Virshup, S. Rybakov, F. J. Theis, P. Angerer, and F. A. Wolf, “anndata: Annotated data,” 2021, doi: 10.1101/2021.12.16.473007

[6] OpenAI, “ChatGPT (april 2024 version).” https://chat.openai.com, 2024.