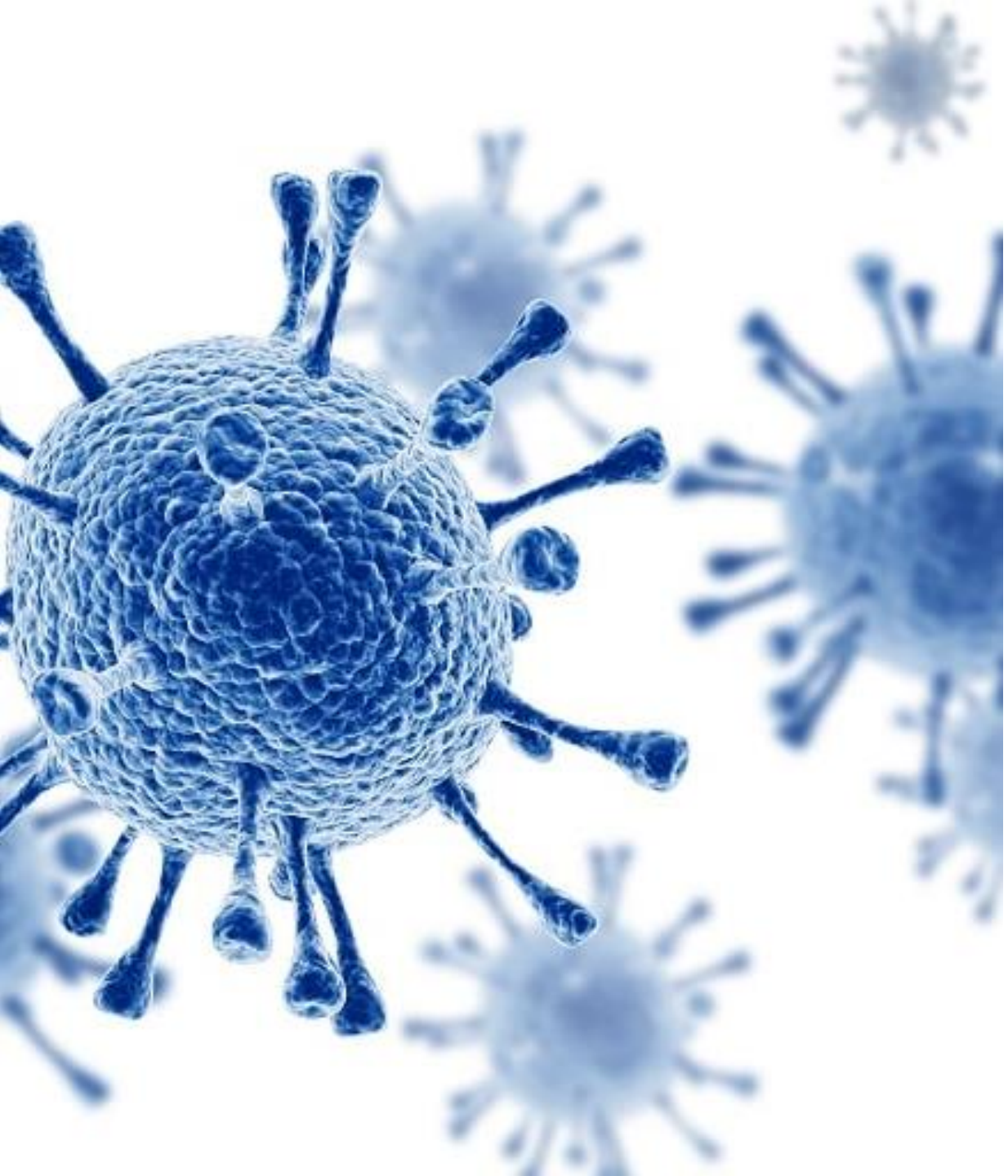


Evaluating ART Regimen Efficacy:

Using HIV Viral Suppression Outcomes to Improve Care

Team Personality Hires (D8)
Matthew Rui, Haiyan Wang, Lauren Khine

Executive Summary

Objectives

- **Classify** and identify potential ART regimens
- **Evaluate** regimen efficacy by key health metrics:
  - Viral load (<50 copies/mL, <250 copies/mL)
  - CD4 cell count and percentage
- **Inform providers** of best regimens for patients without any *a priori* metric for effectiveness

Proposal

1. Which regimens efficiently achieve **HEDIS goals?**
2. How can we best **tailor** treatment to improve individual patient outcomes?
3. How can we best **empower** healthcare providers to **leverage** our analyses?

ART Efficacy

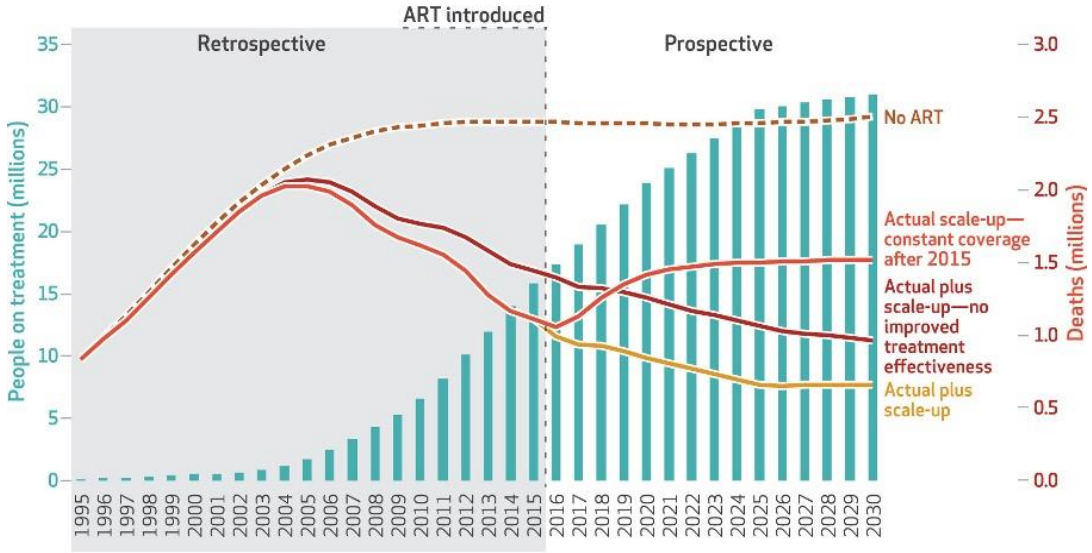
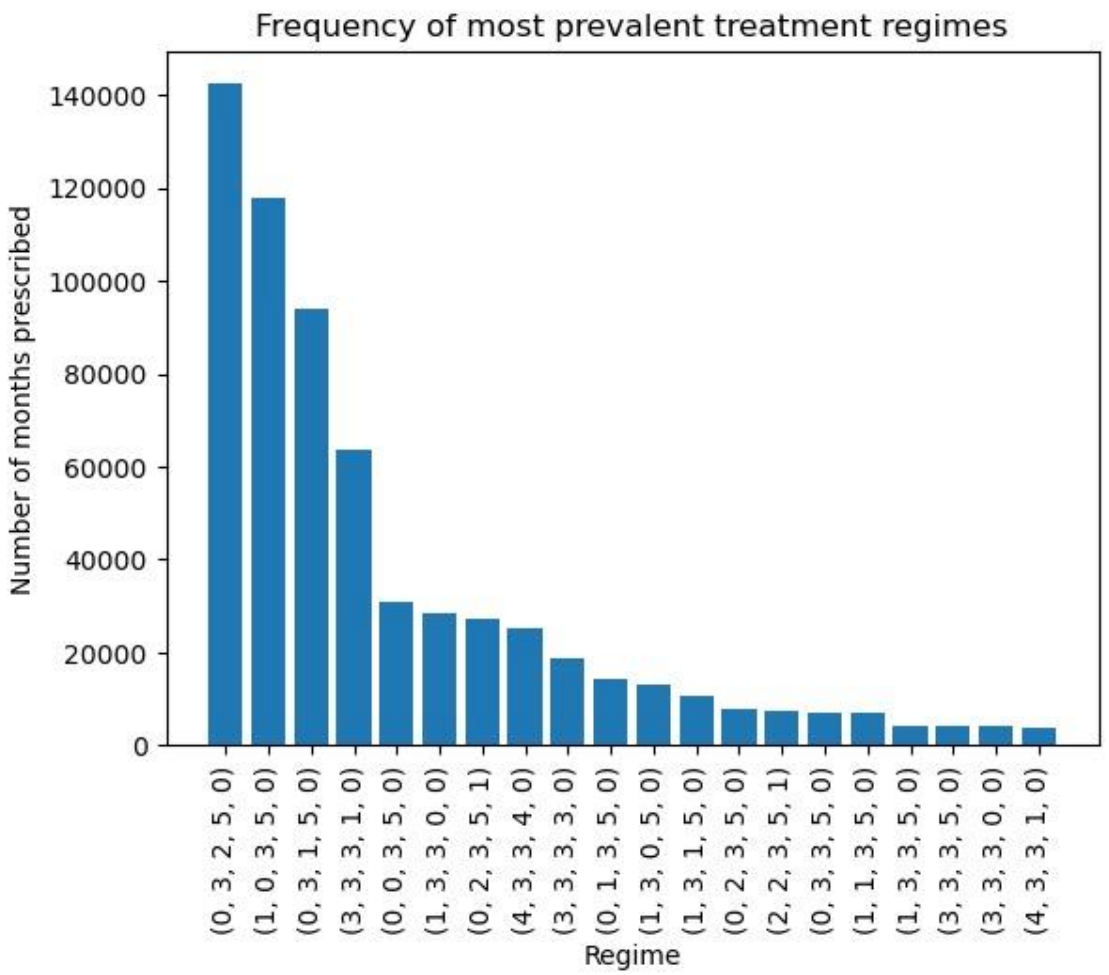


Figure 1. https://www.healthaffairs.org/doi/10.1377/hlthaff.2018.05391

- Global HIV burden is **~39.9 million** people; the disease exposes **healthcare disparities**[1]
- **Interpretive models** enable **accessible** adoption by providers and greater **generalizability**[2]

[1] https://www.hiv.gov/hiv-basics/overview/data-and-trends/global-statistics
[2] https://bmcmedinformdecismak.biomedcentral.com/articles/10.1186/s12911-023-02193-5

Data Preparation & Exploration



Treatment Regimens

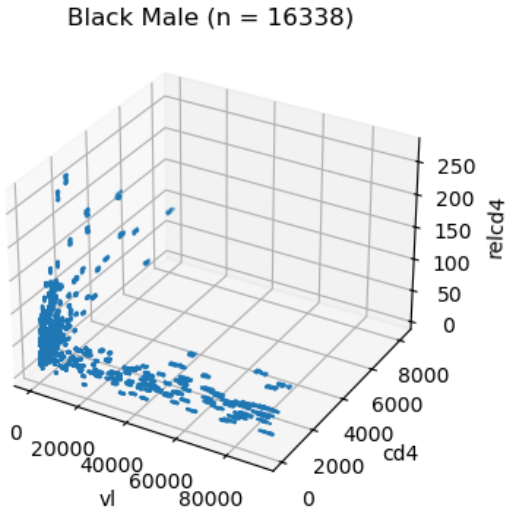
- Dataset consists of **135 realized treatment regimens** defined by five classes of drugs in ART:
  1. Base drug
  2. Integrase inhibitor
  3. Reverse transcriptase inhibitor
  4. Protease inhibitor
  5. Pharmacokinetic enhancer

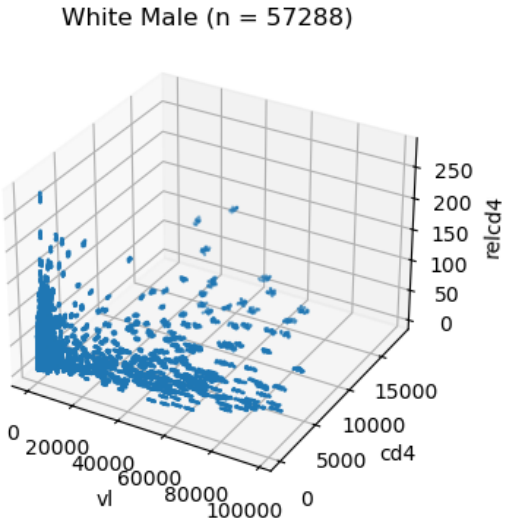
Dataset Challenges

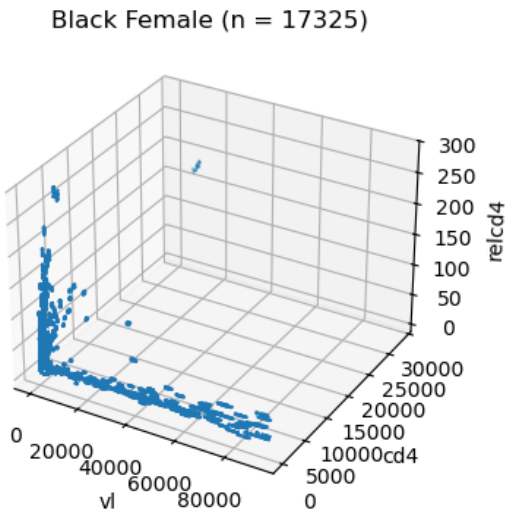
- Few observed confounders and control variables
  - **Comprehensive** history integral to HIV care[3]
- Lack of baseline
  - Observational study vs. randomized trial
- Class imbalance
  - 90% of dataset achieves HEDIS goals; attention to efficiency in reaching **undetectable**

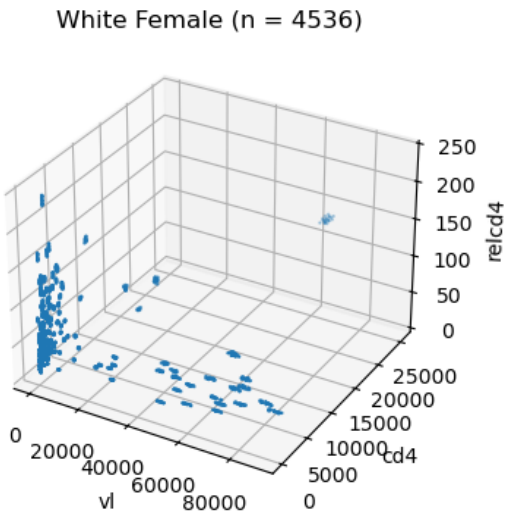
[3] https://pmc.ncbi.nlm.nih.gov/articles/PMC9025375/

Patient Clustering



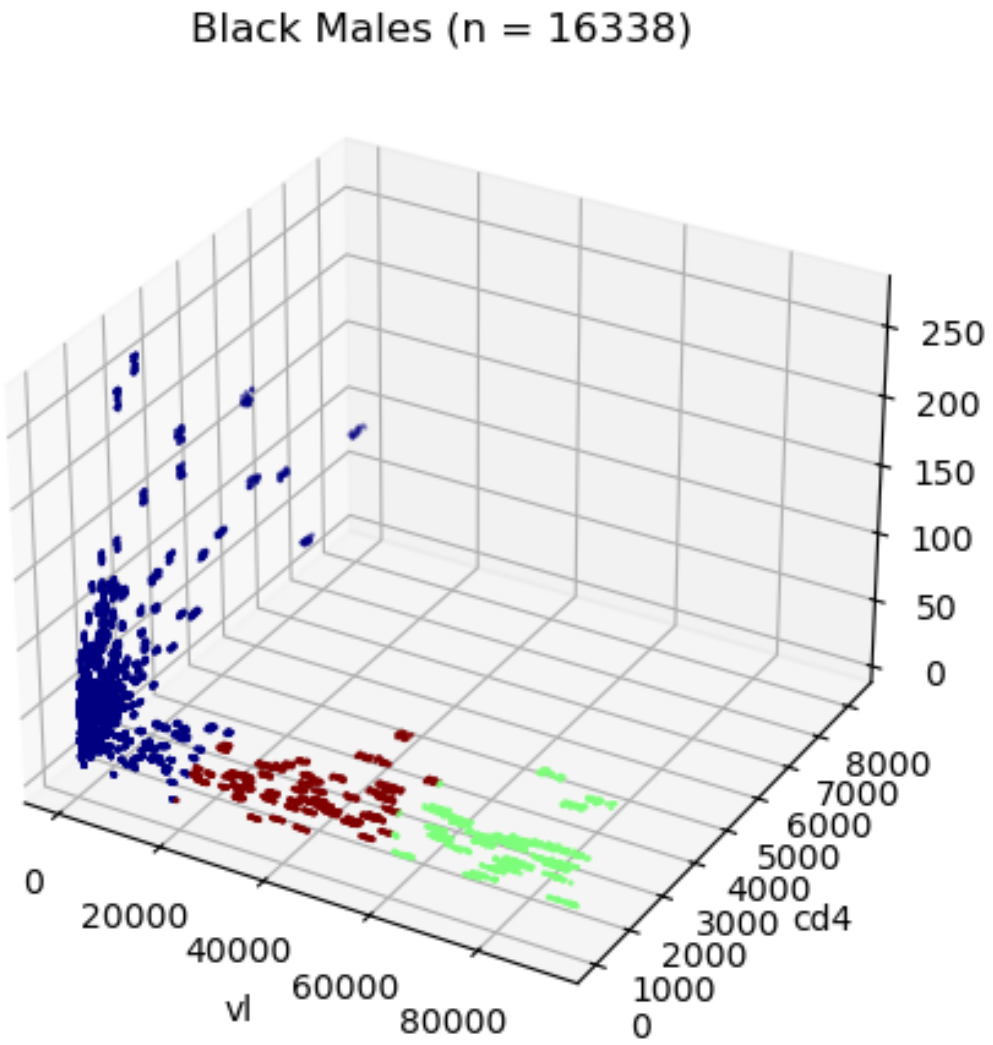






- Assume a new patient with known race, gender, and infection characteristics but unknown medical history (i.e. identical to our dataset parameters) is seeking treatment. **How do we use existing data to suggest an ART regimen?**
- Match to similar patients in dataset with known outcomes; prescribe optimal trial based on these outcomes
- Group patients exactly on demographic data and visualize infection characteristics
- Patients clustered in large number of small, dense groups – impractical for later analysis

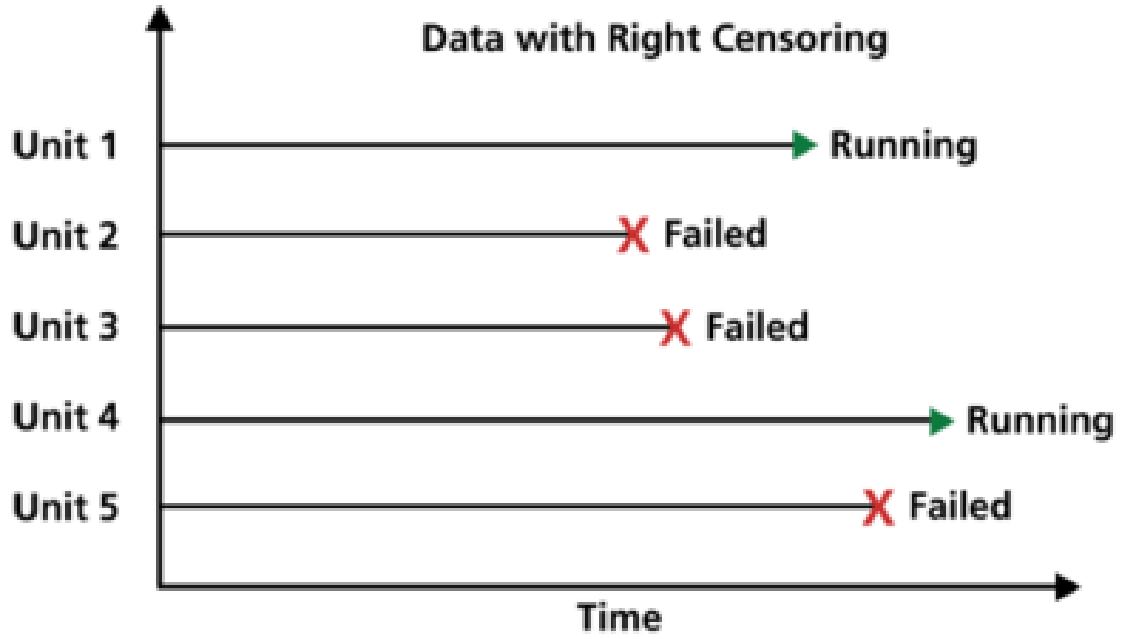
Patient Clustering



- Distributions are expected: high concentration along coordinate axes
  - Viral load and CD4 cell populations are opposing forces – HIV attacks CD4 cells
- K-means clustering – not an optimal clustering but sufficient for our purposes
- Group patients into three categories:
  - High viral load/low CD4 (active infection)
  - Low viral load/low CD4 (recovering)
  - Low viral load/high CD4 (controlled infection)

“Right-Censored” Data

- Construct "censored" dataset: Focus on intervals of patient data with **constant treatment**.
  - Baseline VL, CD4, CD4%
  - Indicator Variable (Every Treatment Regime)
  - Censor Indicators (for VL, CD4, CD4%)



Proportional Hazards

- We employ Cox's **Proportional Hazard Model** to estimate the hazard function:
  - Hazard: Likelihood of achieving HEDIS target outcomes over time
  - Coefficients interpreted as how many times more likely we are to achieve our target outcome
  - Estimate p-values to assess statistical significance

- Using **Mixture of Experts** (MoE) framework, we train proportional hazard models on every data cluster
  - Better capture localized patterns and dependencies
  - Reduce computational complexity and memory constraints
  - Ensure correct covariate interactions modeling (e.g., between treatment and patient demographics)

VL50 (Select Coefficients)

Covariate	Exp (Coef)	P-Value
DRV + FTC + TDF, -, -, RTVB	1.684809	<0.005
FTC + TDF, -, EFV, -	1.783005	<0.005
FTC + TDF, -, RPV, -	0.486272	<0.005
FTC + TDF, RAL, -, -	1.040211	0.11

Recommendation Algorithm

Procedure

Given a new patient:

1. Use demographic and medical data to label patient with its cluster group
2. Retrieve (compute) hazard ratio estimates for patient's cluster group for all three HEDIS targets
3. Compute and assign a score to each treatment regimen to formulate individualized recommendations

Individualized Scoring

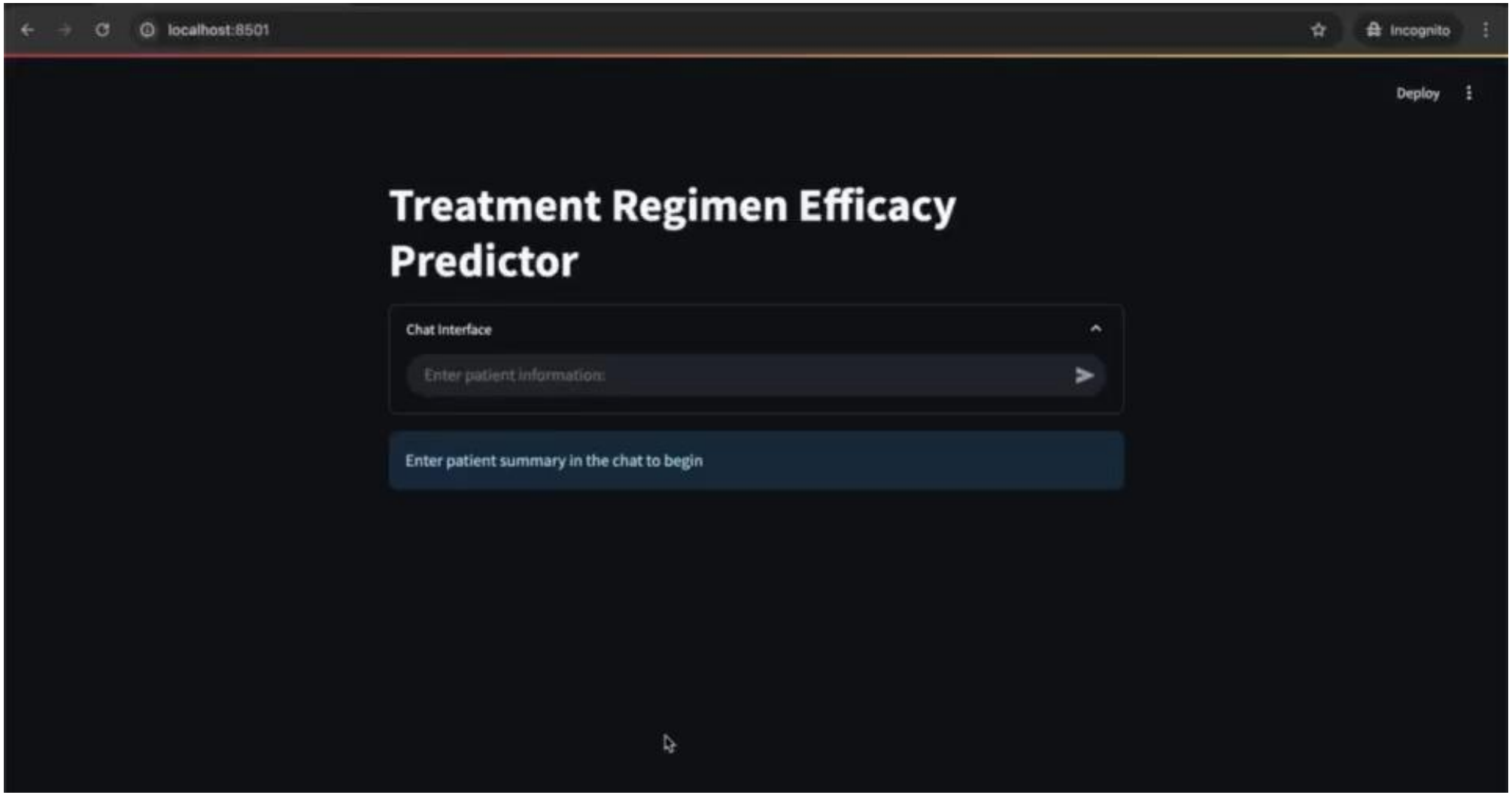
- Weighted geometric mean of the three hazard ratios
  - Weights are **dynamically adjusted** based on the patient's **current viral load and CD4 count** relative to the HEDIS thresholds

Generative AI

- Created **Generative AI**-based Platform to promote accessibility to recommendations
  - Leverage Gemini to extract key demographic and medical metrics from **natural language** to use as input for recommendation algorithm.

Web Application

Input: “I have a patient who is a black male with a viral load of 400, cd4 of 50, and cd4 percentage of 25%”



Interpretability

- Barriers to Adoption
  - Unknown **biases** in AI prevent application population-wide[4]
  - Predictive models may be **unreliable** over time in **clinical settings**[5]
  - Limited transparency **prevents trust** from both patients and providers

- Building Interpretable Models
  - **Intuitive interpretation of clustering** enables providers to verify recommendation output alignment with clinical expertise
  - Easy interpretability of hazard ratios **bridge accessibility** of traditional tools and accuracy of black box models
  - **Tailor tools** for healthcare provider usage

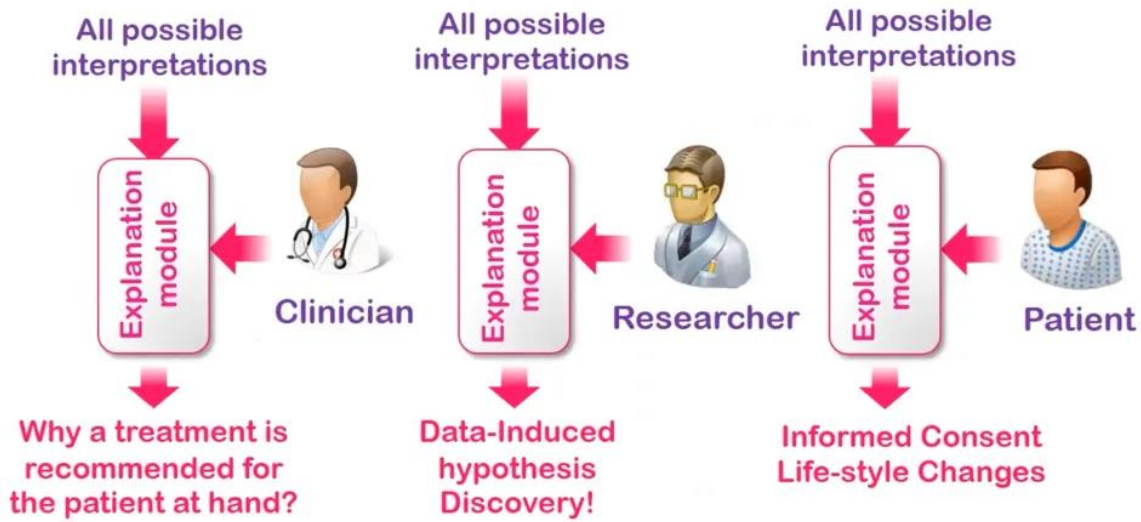


Figure 2. https://www.vanderschaar-lab.com/making-machine-learning-interpretable-a-dialog-with-clinicians/

[4] https://bmcmedinformdecismak.biomedcentral.com/articles/10.1186/s12911-023-02193-5
[5] https://medicalxpress.com/news/2023-10-ai-shown-unreliable-clinical.html

Accessibility

Distribution of new HIV infections by population, global, 2018

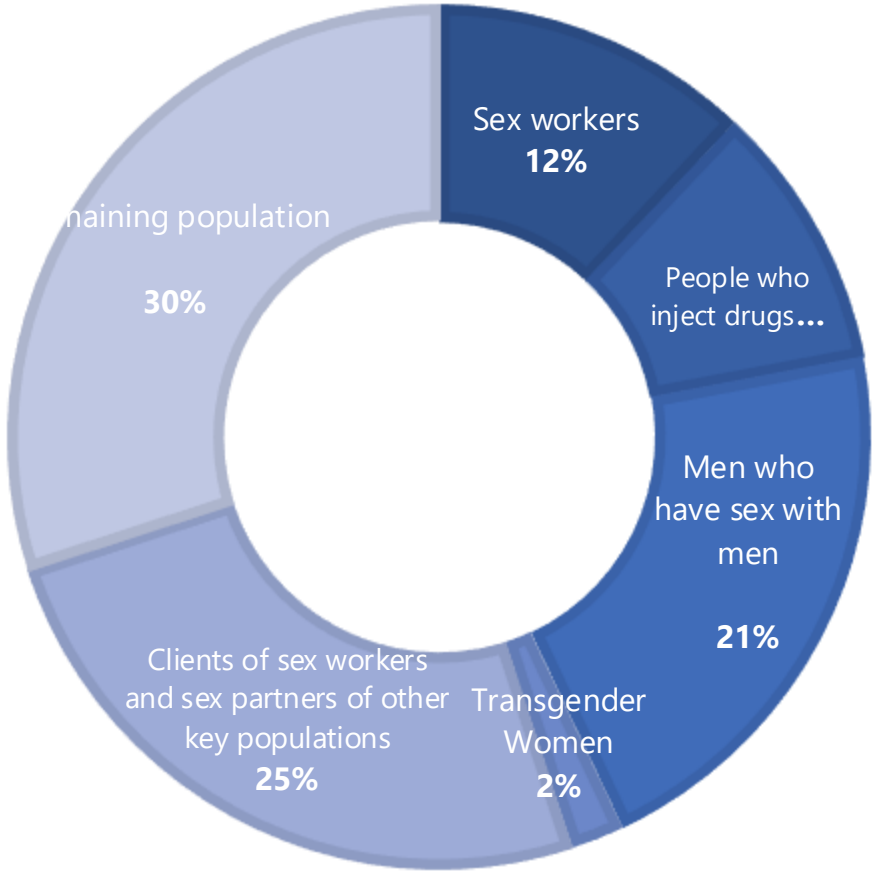
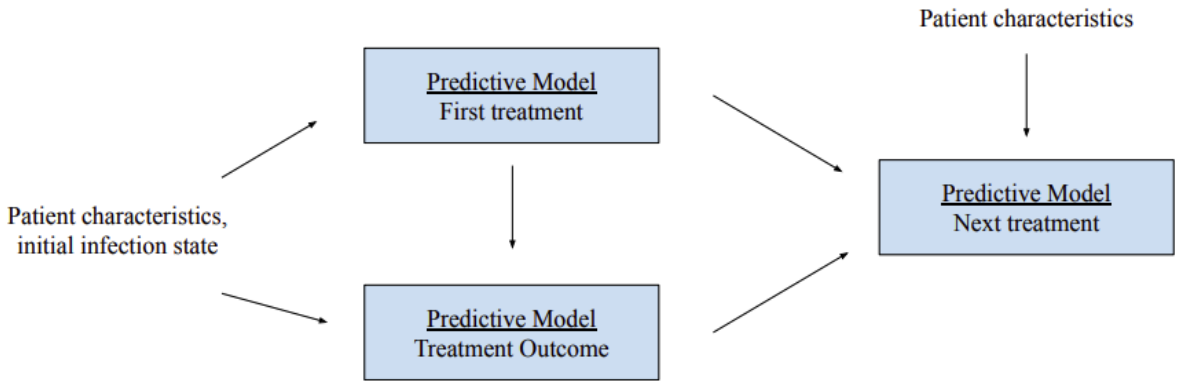


Figure 3. https://news.un.org/en/story/2022/07/1123332

- Inequity in HIV Burden
  - Marginalized populations are **disproportionally** affected by HIV
  - **Geographic**, **cultural**, and **economic** accessibility is necessary globally
- Our Approach to Access
  - The **Mixture of Experts'** decentralization allows implementation in low-resource healthcare systems
  - Addressing **limited access** to high-performance computing infrastructure
  - Natural **language-based** chat interface allows ease of provider input

Stronger Assumptions

- What if decisions made in the dataset are informed by some underlying objective?
  - i.e. a doctor prescribes drugs with the intent treating a given patient as effectively as possible
- Assume there is some underlying motivation behind treatment regime decisions. For example, what if this dataset records a physician's actual prescriptions to patients over time? How does this assumption allow us to learn optimal treatment regimens?
- Framework: Learn to predict **what a doctor would do next** given a dataset about a physician's decisions for a group of patients
- Three criteria of effectiveness:
  - Accuracy – promising benchmark results from experiments
  - Interpretability – choice of predictive models is highly flexible
  - Accessibility – widespread data, low computational cost, highly adaptable and portable



Future Applications and Directions

Improving Medical Decision-Making

- Accessible machine learning models combine ease of use and accuracy in predictions
- Providers are institutionally **empowered** to **evaluate** and **improve** predictive frameworks

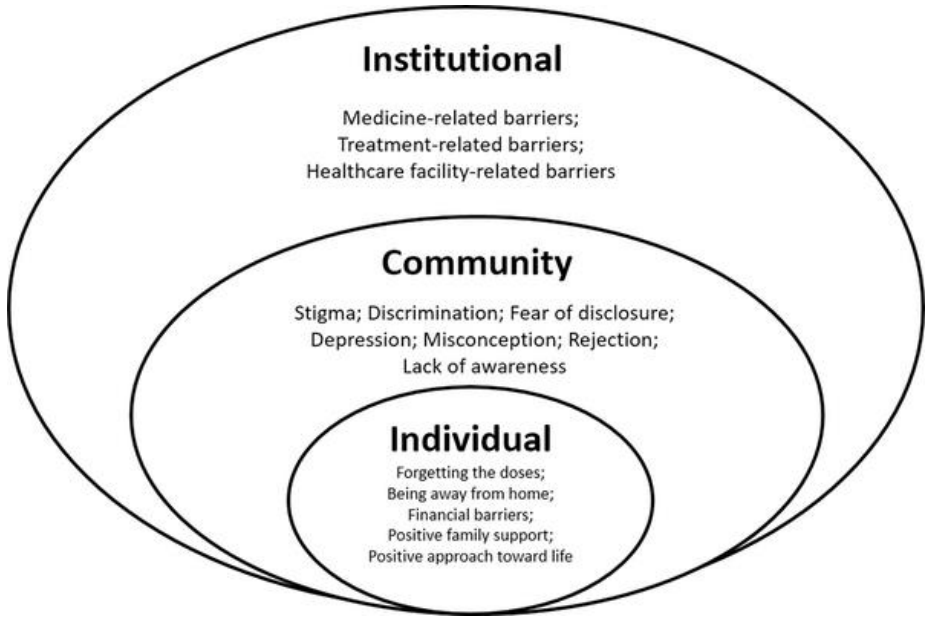
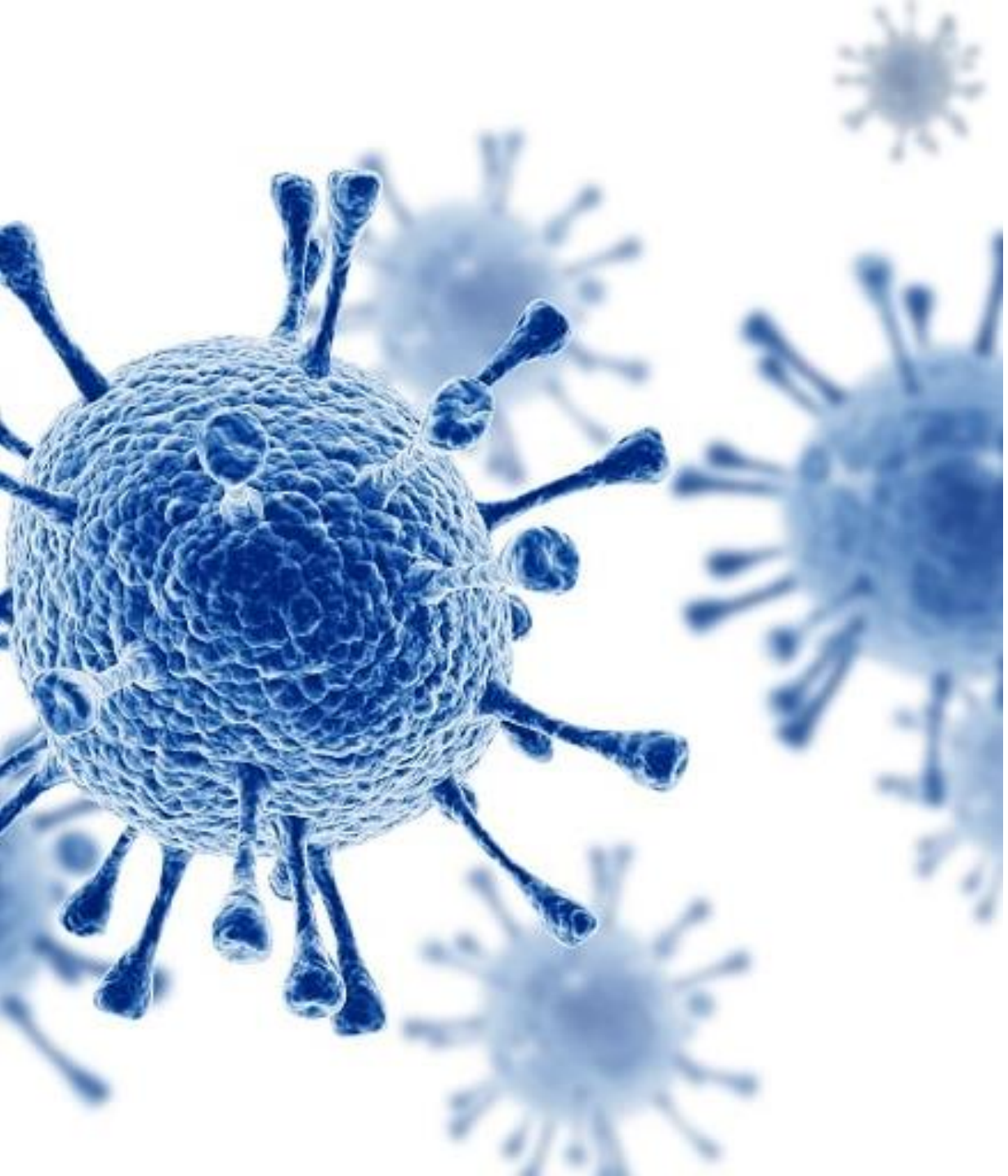


Figure 3. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0276575

Addressing Healthcare Disparities

- **Individualized** treatment requires **multi-disciplinary** teams and tools and effective **resource allocation**
- **Interpretable models** like ours can **mitigate** unequal HIV burden and **transform** global aid and care
- **Comorbidities** and **social barriers** to ART adherence in marginalized groups can be addressed by greater treatment efficacy and **transparent** recommendations
- Facilitating global **epidemiological transition** through acute infectious and chronic **disease control**



Questions?