Harnessing the Power of Machine Learning Methods for Enhancing HIV Care and Treatment Within Resource-Limited Settings

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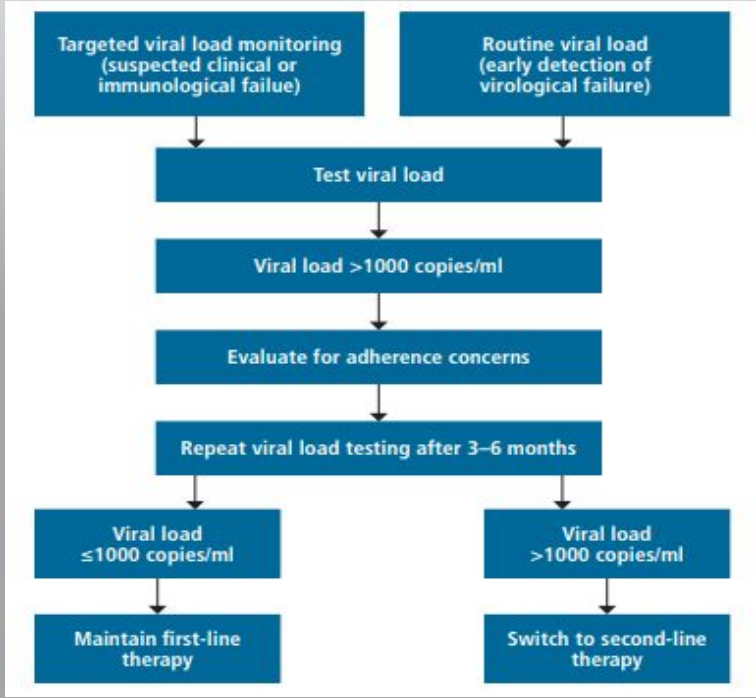

- As a measure to achieve the last **90%** of the ambitious **UNAIDS 90-90-90** targets, WHO guidelines recommend that, where possible, HIV viral load suppression to be assessed **six months** immediately after starting ART and **annually or semi-annually** thereafter.
- However, a major deficiency of the current model is in its inability to detect **virologic failures** early enough.

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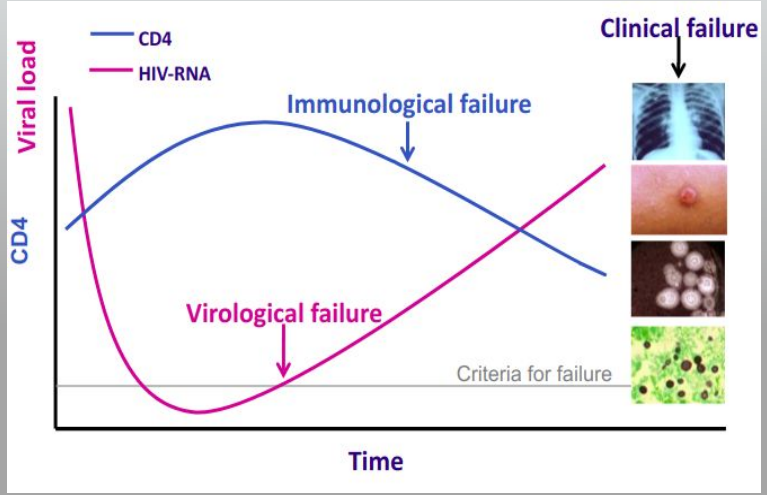

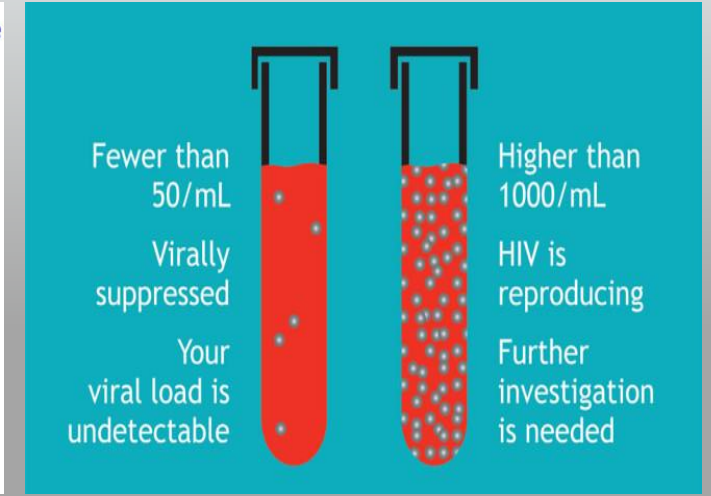

- Delays in efforts to detect and address potential virologic failures ultimately lead to **adverse clinical trajectories** such as patient-level treatment failures, immunological failures as well as clinical failures.
- Not only does virologic failure increases morbidity for the patient, but also creates a significant **public health risk** for **HIV transmission**.

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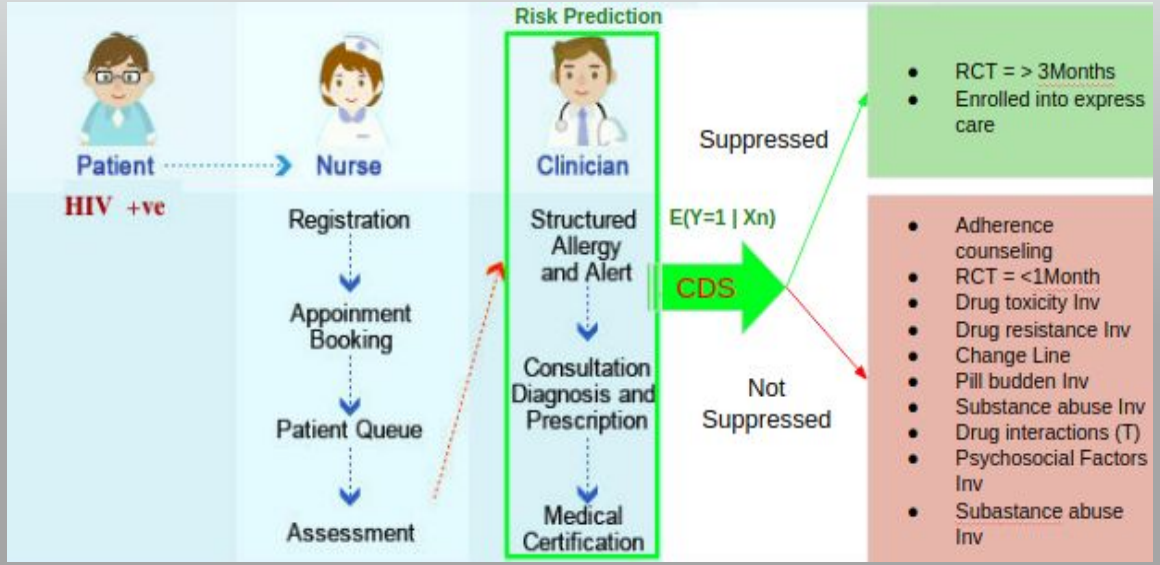

- To achieve most of the benefits of the current WHO HIV model, timely detection of potential virologic failure is critical in administering essential **patient-centered interventions**. As such, this study aims to disseminate some techniques that can potentially be utilized in HIV clinical settings with rich, structured EHR to **proactively** anticipate and mitigate potential **risk of virologic failure** before they manifest.

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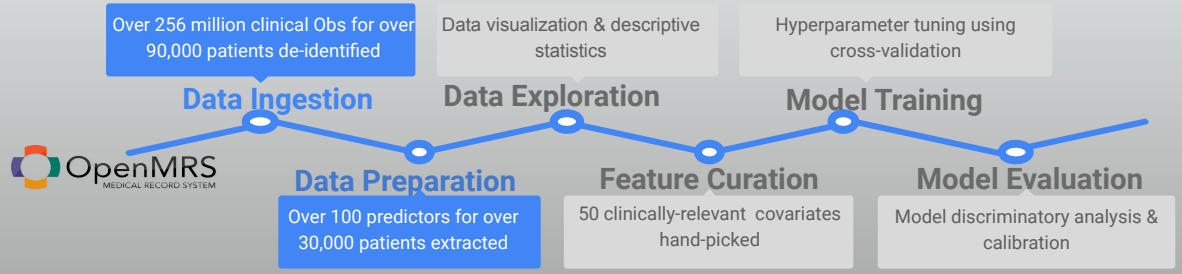

Study Design: A retrospective observational study was conducted by analyzing and creating *virologic failure risk prediction model* using vast amounts of clinical & non-clinical profile collected between ***January 2014*** and ***March 2018***.

Population Setting: The de-identified training & validation dataset was extracted from AMPATH's EHR serving over ***90,000 HIV patients in Kenya***. All patients ***younger than 18 years old*** or patients with ***less than 2 viral load tests*** were excluded from the dataset, thereby decreasing the sample size to ***30,039 patients***.

Risk Predictive Modeling: A comparative analysis was conducted by training a series of ML models using 50 clinically-relevant covariates that were handpicked and curated by domain experts. The risk model can be expressed as:

$$\mathbf{E(Y_t|V_{t-1})} \text{ or } \mathbf{Pr(Y_t = 1|V_{t-1}) = \pi} \qquad Y \sim Bern(\pi)$$

where $\mathbf{V_{t-1}}$ denotes baseline covariates before time point **t**, $\mathbf{Y_t}$ is a binary outcome for virologic failure while t is the time point relative to viral load count measurements. The primary focus of this study: $\mathbf{E(Y_1|V_0)}$ **and** $\mathbf{E(Y_2|Y_1,V_0)}$

Evaluation Criteria: ***Internal validation*** (sensitivity, AUC and specificity), as well as ***calibration & discriminatory,*** were used to assess the discriminatory ability of each model in distinguishing between low-risk and high-risk patients.

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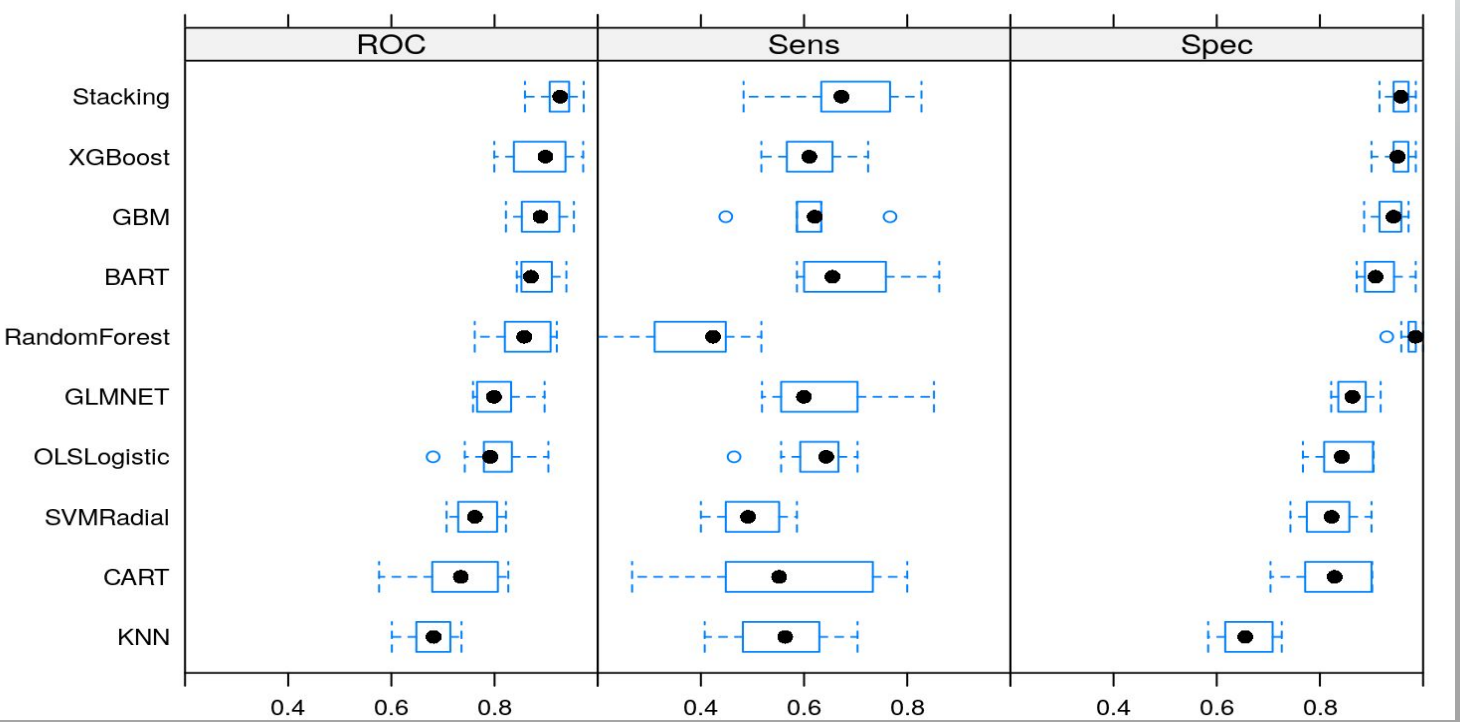

Holding the cutoff at .5, the **10-fold cross-validated** performance summary for predicting the first risk of virologic failure at baseline using only baseline covariates is illustrated above (**newly enrolled patients**).

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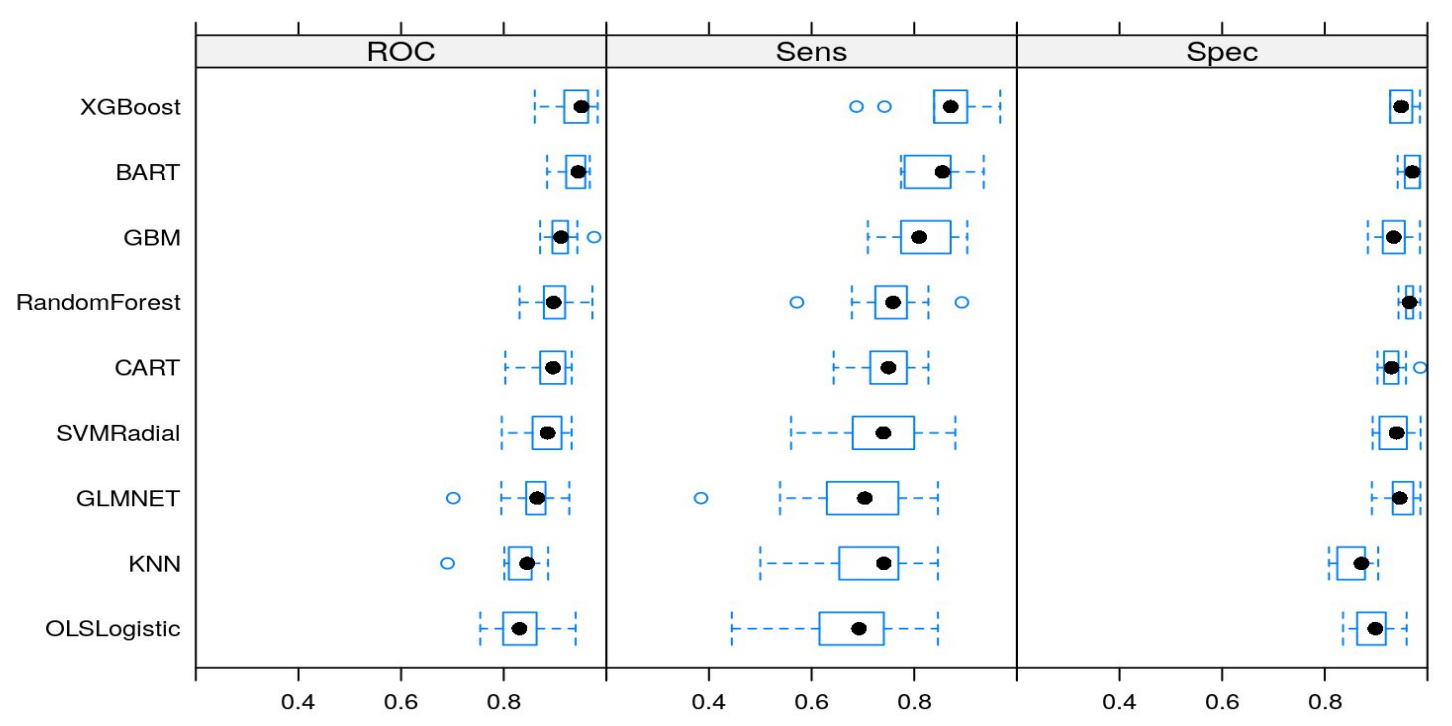

Holding the cutoff at .5, the **10-fold cross-validated** performance summary for predicting the second risk of virologic failure using baseline covariates & Y1 is illustrated above (**currently enrolled patients**).

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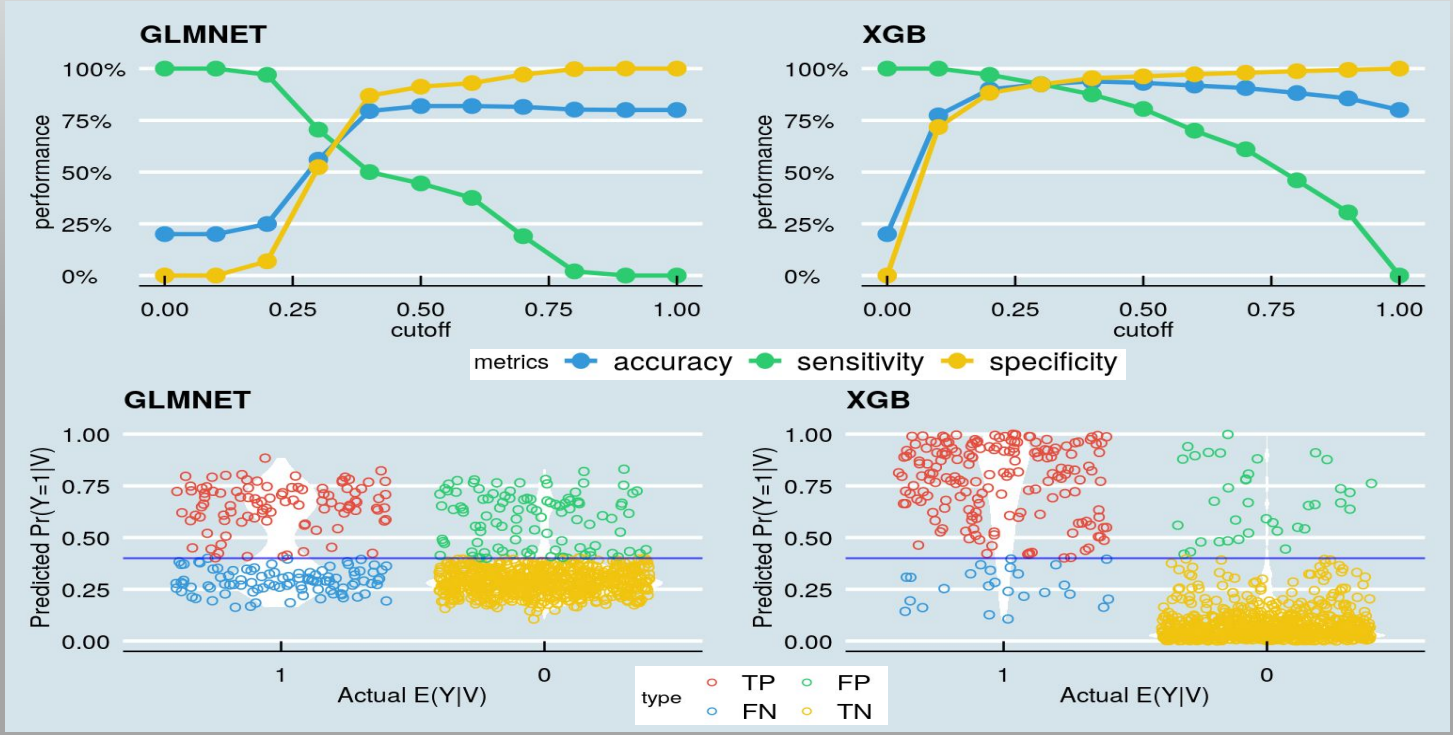

The panel above illustrates the tradeoff faced upon selecting a reasonable probability threshold other than .5. Using a cutoff value of .3, gave better performance in most classifiers. Adjusting the cutoff to .25 boosted the sensitivity of some methods like XGBoost, GBM, and BART to .92, .87, and .90 respectively.

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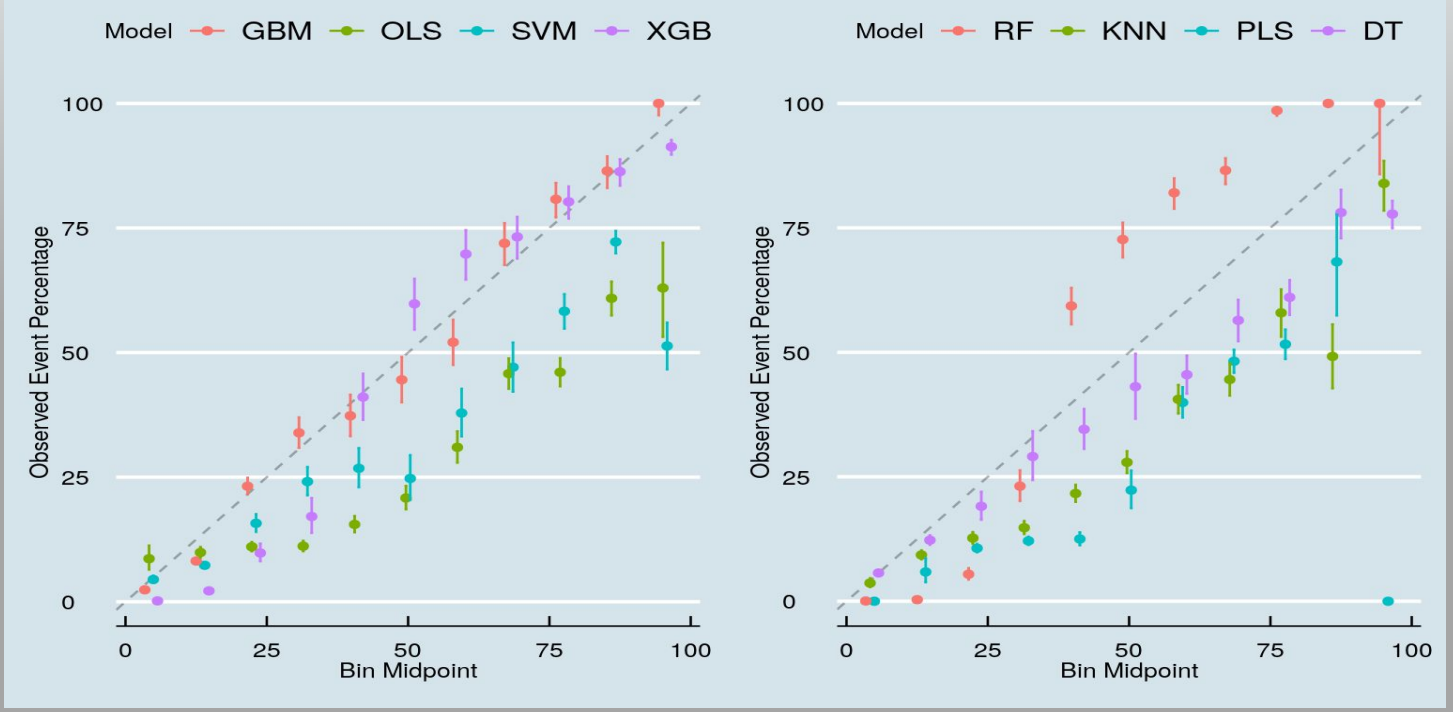

Ensemble methods such as XGBoost and GBM were naturally well calibrated while some were not. RF, for instance, exhibited "optimism," i.e., its predictions for Pr(Y_2=1)>0.5 were extremely high relative to the observed event rate; while others like KNN, OLS, SVM, PLS were unrealistically underconfident.

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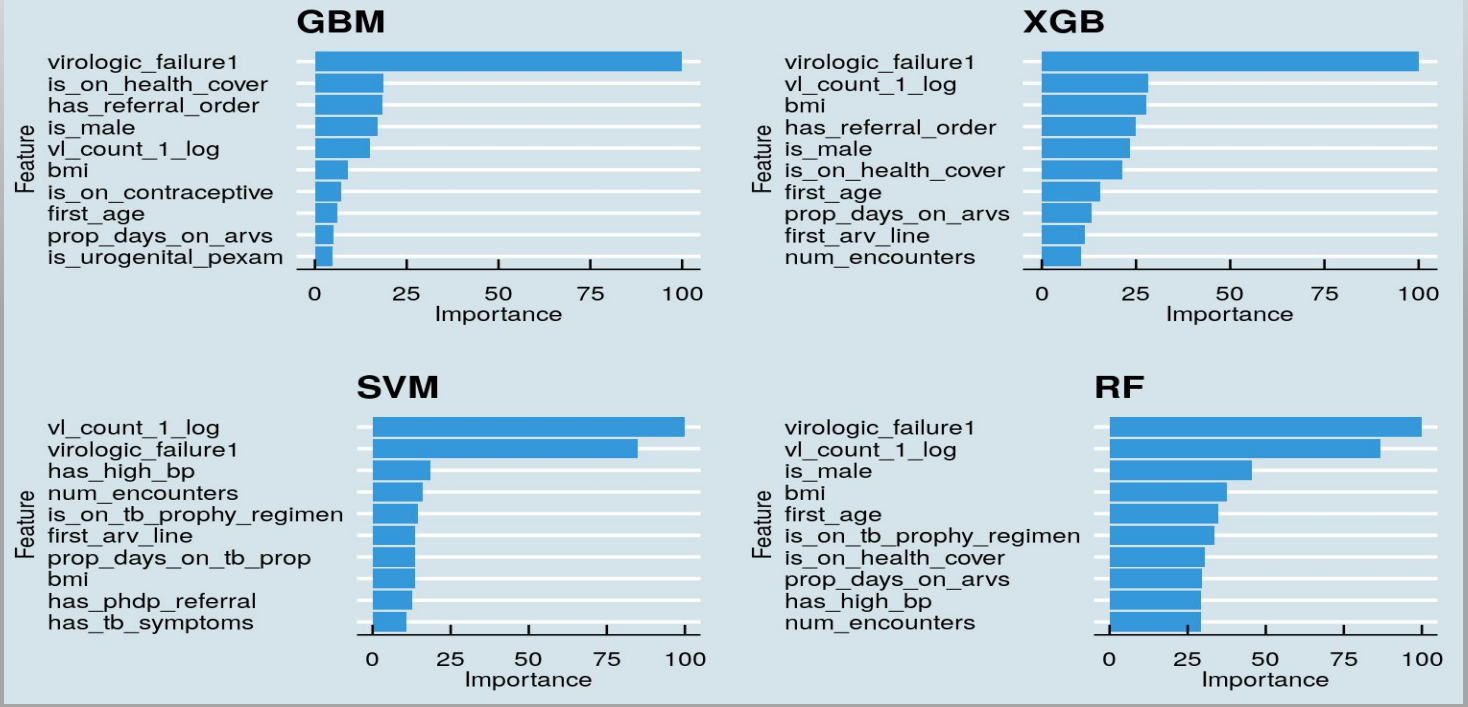

Previous virologic failure turned out to be the most important predictor. Other notable important predictors consisted of BMI, the proportion of days on ARVs, baseline ARV Line, number of clinical encounters, gender, age, referral order status, health cover status and TB-related variables e.g symptoms.

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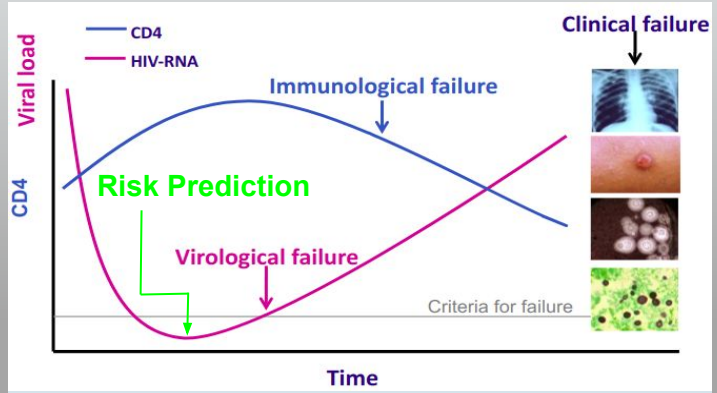

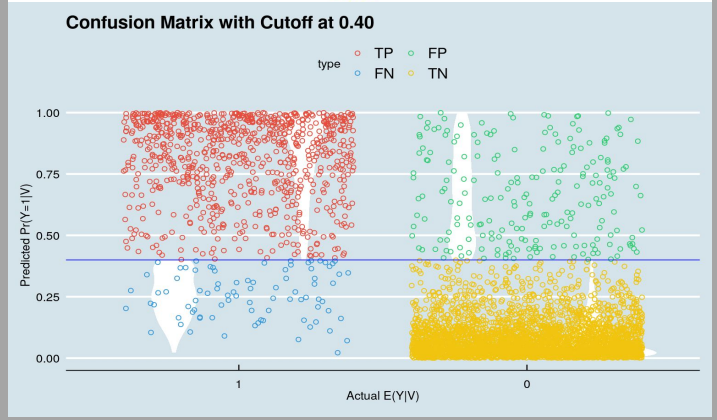

As a step towards personalized healthcare in HIV care, prospective virologic assessments can be utilized in clinical settings with rich EHR data to potentially anticipate and mitigate risk of virologic failure early enough before adverse clinical trajectories manifest. Thus, as a preventative strategy, high-risk patients identified using accurate & well-calibrated risk predictive model will benefit from targeted holistic intervention such as:

- **Intensified adherence counseling**
- **Rigorous nutrition monitoring**
- **Timely psychosocial counseling**
- **Early ordering of lab orders such as viral load tests**
- **Appropriate next-line therapy switching**
- **Enhanced drug toxicity/drug resistance/adverse drug-drug interaction monitoring**