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Nurturing Excellence,
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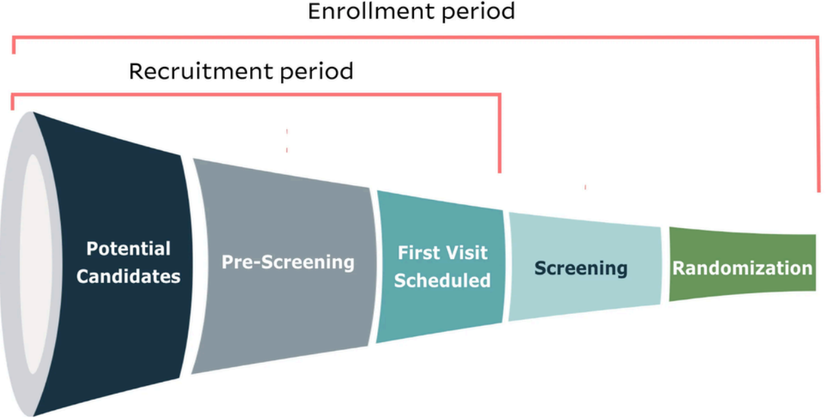
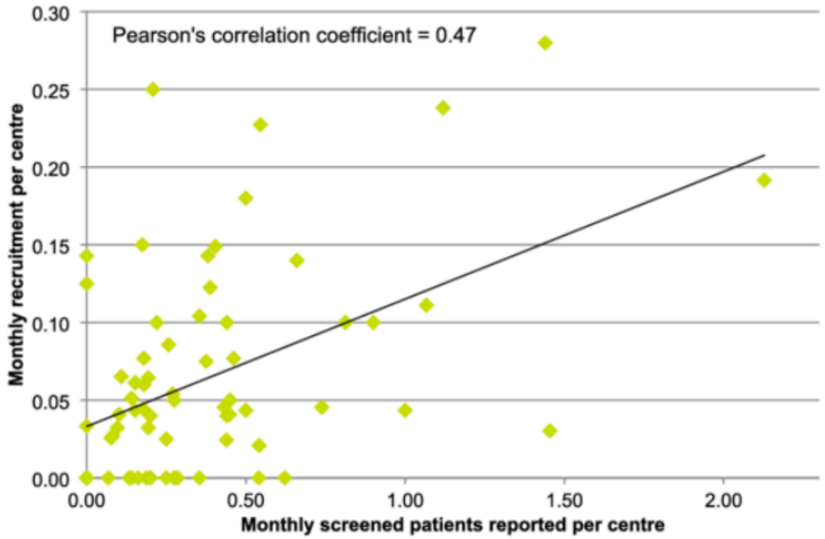
Problem Statement – 4

Utilizing data to predict recruitment rate (RR) in clinical trial for benchmarking





Clinical Trial Delays and Mortality Statistics:

- **85% of clinical trials fail to recruit enough participants on time, causing delays in completion.** Source: CenterWatch, 2021.
- **37% of trial sites fail to meet enrollment targets, and 11% fail to recruit a single patient.** Source: Biopharma Dive, 2020.
- **Recruitment rates vary by phase, with Phase I having lower rates due to smaller, specific populations.** Source: Applied Clinical Trials Online, 2019.
- **Recruitment rates differ geographically, with North America averaging 0.92 p/s/m and Europe 0.77 p/s/m.** Source: Tufts Center for the Study of Drug Development, 2020.
- **Rare disease trials have significantly lower RR, averaging 0.1–0.3 p/s/m due to limited eligible populations.** Source: Orphanet Journal of Rare Diseases, 2020.
- **Recruitment delays can cost $600,000–$8 million per day for large pharmaceutical trials.** Source: Pharmaceutical Technology, 2020.

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Approach & methodology

Overview

- The project aims to develop an AI model that predicts the recruitment rate of clinical trial participant based on historical data. The model should provide insights into which factors (e.g., conditions, age, sponsor etc.) affect the recruitment process.
- Clean and preprocess structured (e.g., study design, age, sex) and unstructured (e.g., conditions, sponsor) data.
- Use XGBoost for structured data and BERT for unstructured text data.
- Compare the outputs of different models for improved prediction accuracy.
- Evaluate model performance using RMSE, R^2, and SMAPE.
- Implement SHAP and LIME for explainability of model predictions.

Methodology

Data Collection & Preprocessing

- To handle textual data effectively, we will vectorize the text fields using BERT, TF-IDF, and TensorFlow's Text Vectorization Layer.
- Identify and handle outliers using methods like IQR (Interquartile Range) or Z-score.
- Impute missing data using statistical methods or remove rows/columns with excessive missing values.

Model Developement:

- Implement feature selection through PCA, LASSO regression, and domain expert validation.
- Deploy baseline models (Linear Regression, Decision Trees) before advancing to complex models (Random Forest, XGBoost, Neural Networks)
- Apply SHAP and LIME for model interpretation and feature importance visualization

Accuracy Metrics

- RMSE: To measure model prediction error.
- R^2: To evaluate the model's fit and explanatory power.
- SMAPE: For percentage error to ensure robustness across varying data.

Framework / tools used

scikit-learn:

- Purpose: For data preprocessing (scaling, encoding), feature selection, and model training (classification, regression).

TensorFlow/Keras:

- Purpose: To build and train deep learning models, including neural networks, for more complex patterns.

Pandas & NumPy:

- Purpose: To handle and manipulate data, perform data cleaning, and numerical operations efficiently.

NLTK/SpaCy:

- Purpose: For text data preprocessing like tokenization, lemmatization, and stopword removal.

Matplotlib/Seaborn:

- Purpose: For visualizing data distributions, correlations, and model performance (like accuracy, ROC curves).

HuggingFace:

- Purpose: For using BERT and other transformer models to create embeddings from clinical trial text data, leveraging pre-trained medical domain models like BioBERT and ClinicalBERT for improved text representation

Model choice & setup

Model Selection

Baseline vs. Advanced Models:

- **Baseline Models:** Use simpler models like Linear Regression, Decision Trees, and Logistic Regression with TF-IDF to establish a performance baseline.
- **Advanced Models:** Implement more complex models like Random Forest, Gradient Boosting (XGBoost), and Neural Networks when using BERT embeddings.

Performance Evaluation:

- Compare models using metrics like RMSE, MAE, and R-squared while ensuring proper cross-validation.

Hyperparameter Tuning:

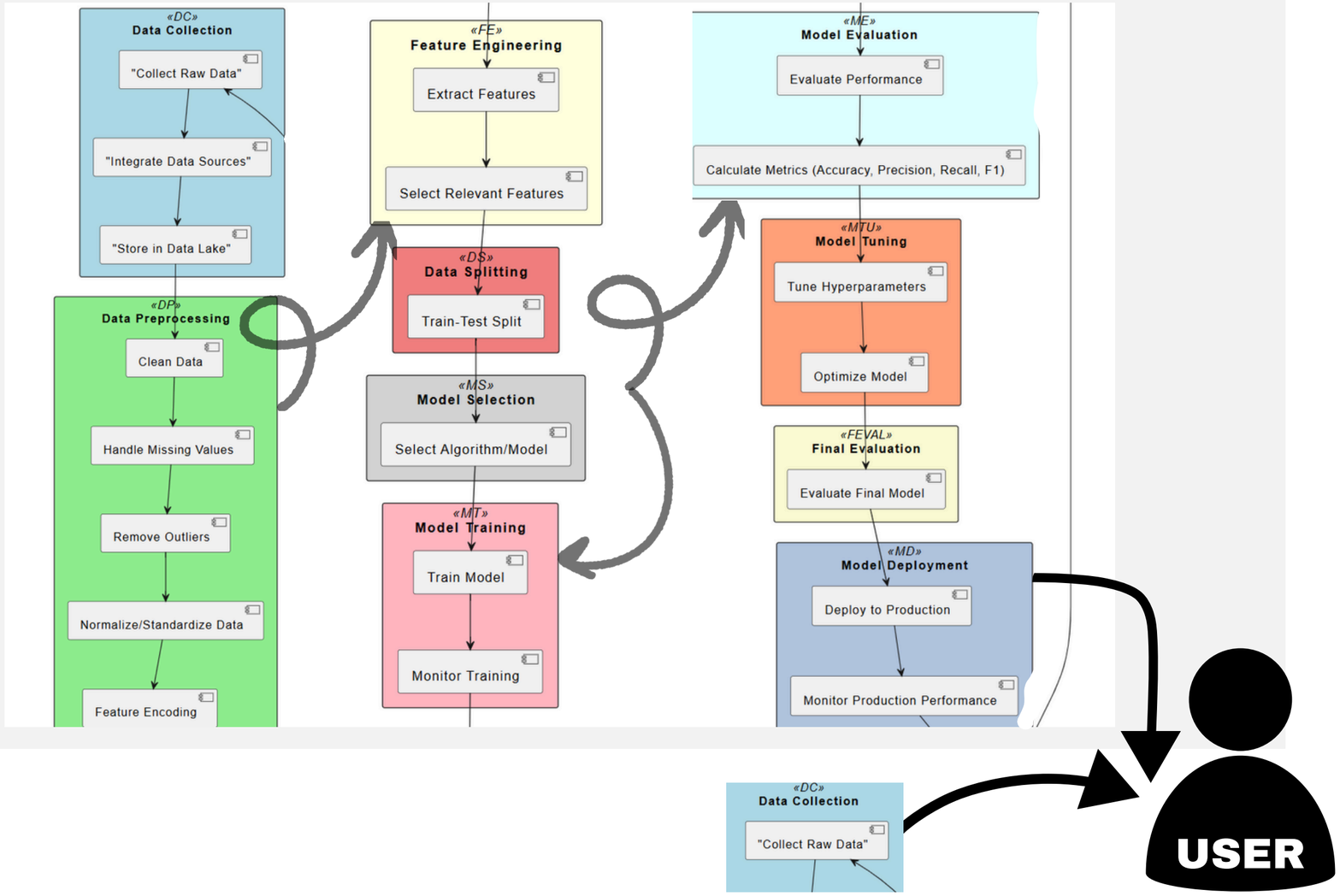
- Apply techniques like Grid Search and Random Search for optimal model configurations.

Feature explainability:

- We will use techniques like SHAP (SHapley Additive Explanations) and Permutation Importance to identify key predictors.
- We will apply tools like LIME (Local Interpretable Model-agnostic Explanations) for visualizing feature impact on predictions.

Model Architecture

Technical flow of the end-to-end ML pipeline



Model Training & Evaluation

Evaluation Metrics

Model Training Process:

The model training process will involve splitting the dataset into training, validation, and test sets to ensure unbiased performance evaluation. Both baseline models like Logistic Regression with TF-IDF and advanced models such as Neural Networks with BERT embeddings will be trained and compared. Hyperparameter tuning will be performed to optimize the model's performance.

Evaluation Criteria and Metrics:

The evaluation will focus on measuring the model's accuracy and reliability using standard performance metrics. These metrics will help assess both error magnitude and model fit to ensure effective recruitment rate prediction.

Discuss key performance metrics:

- Root Mean Square Error (RMSE): RMSE measures the standard deviation of the residuals (prediction errors) and gives more weight to larger errors due to squaring the differences.
- Mean Absolute Error (MAE): MAE measures the average magnitude of errors between predicted and actual values, making it easier to interpret.
- R-squared (R^2) Score: R^2 measures how well the model explains the variance in the target variable, with values ranging from 0 to 1 (where 1 indicates a perfect fit)

$$\text{RMSD} = \sqrt{\frac{\sum_{i=1}^{N} (x_i - \hat{x}_i)^2}{N}}$$

$$\text{MSE} = \frac{1}{n}\sum_{i=1}^{n}(Y_i - \hat{Y}_i)^2$$

$$R^2 = 1 - \frac{RSS}{TSS}$$

Results and visualization

Model Outcomes

Prediction Accuracy:

- A **low RMSE** will indicate precise prediction of recruitment rates, enabling better trial planning and cost management.
- A **high R^2 score** suggests the model effectively captures the variability in the recruitment rate due to the features considered.

Key Findings:

- Influential Factors: **SHAP analysis** will highlight influential factors like **trial location and eligibility criteria**, with findings suggesting that stricter criteria may slow recruitment, while specific locations may consistently excel in recruitment speed.

Performance Metrics:

- **RMSE, R^2, and SMAPE** will guide the model's reliability and utility.
- **Cross-validation** consistency will indicate generalizability across different trials.

Implications for Stakeholders:

- **Pharmaceutical Companies:** Optimize trial timelines and **reduce delays** to save millions in revenue.
- **Clinical Sites:** Identify **recruitment bottlenecks** and address them proactively.
- **Regulatory Authorities:** Gain insights into **recruitment trends** for better oversight.

Explainability

Techniques for Interpretation:

SHAP (SHapley Additive Explanations):

- Provides a detailed breakdown of each feature's contribution to individual predictions.
- Highlights the most **influential factors** (e.g., trial location, eligibility criteria) for recruitment rate prediction.
- Summary plots and dependence plots will illustrate the **impact and interaction of features**.

LIME (Local Interpretable Model-agnostic Explanations):

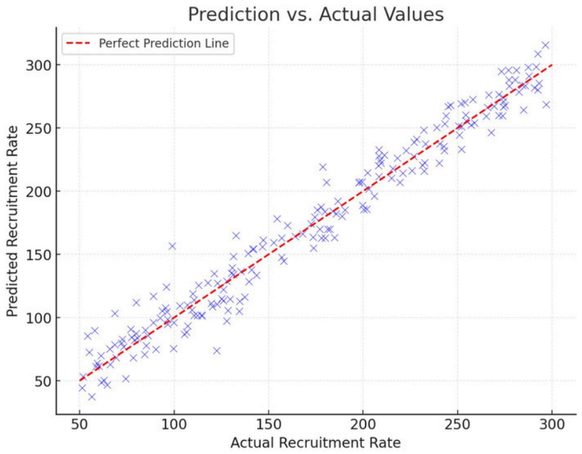
- Offers **localized explanations** for specific predictions.
- Useful for understanding how changes in input features affect individual outcomes.

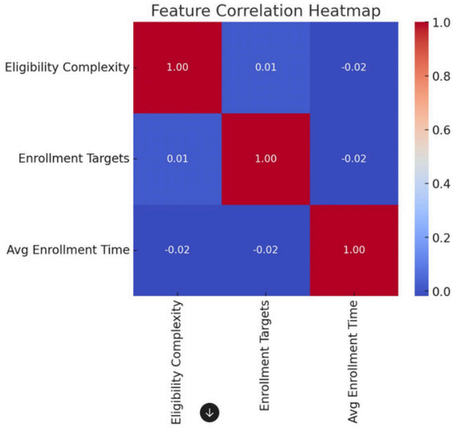
Feature Importance Analysis:

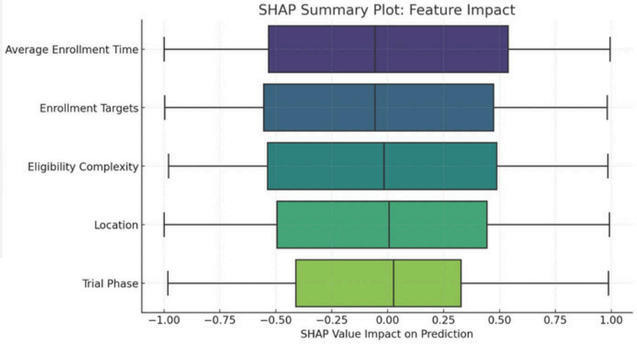
- Explains which **structured** (e.g., trial phase, location) and **unstructured** (e.g., eligibility criteria) features most impact the recruitment rate.
- Enables stakeholders to **identify actionable areas**, like optimizing trial locations or revising eligibility requirements.

Transparency and Trust:

- Ensures stakeholders can understand why the model makes **specific predictions.**
- Facilitates **actionable decision-making** by connecting predictions to real-world factors.







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Challenges & Next Steps

Limitations

Data Quality and Availability:

- Missing or incomplete records, especially for key variables like eligibility criteria and outcomes, can impact model accuracy.
- Limited data for rare conditions or less common trial phases may reduce the model's robustness in these areas.

Sampling Bias:

- Recruitment patterns vary across geographies and trial types, leading to potential over-representation of well-funded or populous regions in the data.
- Historical data may not fully represent diverse populations or under-resourced areas.

Unbalanced Data:

- Datasets with a majority of trials achieving high recruitment rates may cause the model to underperform on trials with low or no enrollment, which are critical for prediction.

Evolving Trends:

- External factors like public health crises (e.g., COVID-19), regulatory changes, or medical advancements are not fully captured in historical data, limiting the model's ability to adapt to current dynamics.

Lack of Standardized Reporting:

- Variability in how clinical trial data is reported (e.g., different formats, terminologies, or languages) can introduce inconsistencies and reduce the reliability of predictions.

Next Steps

- Include more diverse datasets, including rare conditions, global trial data, and failed trials to reduce bias.
- Incorporate data on public health events, policy changes, and demographic trends to capture evolving recruitment dynamics.
- Use advanced imputation methods and NLP techniques to clean and process missing or unstructured data.
- Use transfer learning and advanced hyperparameter tuning to increase model generalization and prevent overfitting.
- Develop dynamic models that adapt to new data and implement online learning for real-time updates.
- Combine SHAP with other interpretability methods and build user-friendly dashboards for non-technical stakeholders.
- Implement bias detection and correction, especially for eligibility criteria and geographic representation.
- Test the model on external datasets to ensure generalizability and conduct expert reviews for real-world alignment.
- Build tools to simulate recruitment scenarios and integrate the model into trial management systems.
- Investigate patient behavior and causal relationships to improve recruitment prediction accuracy.

THANKYOU

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