Recurrence Risk Assessment for Treated Cancer Patients: A Comprehensive Probability Based on Clinical and Molecular Factors

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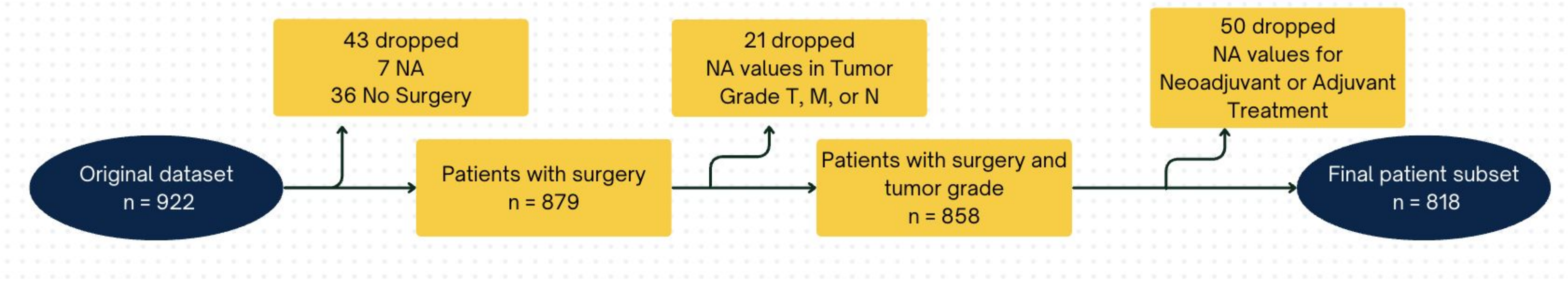
Background

Cancer Data Science

- The Oncotype Score is a genomic test that predicts recurrence risk and guides chemotherapy decisions for specific breast cancer types.
- The limitations of this score is that it can only be used for those with Luminal-A type cancer. Additionally, it only informs adjuvant chemotherapy decisions.

The Data

- Original clinical features dataset included 922 patients with 98 variables.
- The data subset used included 818 patients who underwent surgery, with features encompassing surgery type, adjuvant and neoadjuvant treatments (radiation, chemo, endocrine, anti-HER2 Neu), molecular subtype, and tumor grades (T, M, N).



Original dataset
n = 922

43 dropped
7 NA
36 No Surgery

Patients with surgery
n = 879

21 dropped
NA values in Tumor Grade T, M, or N

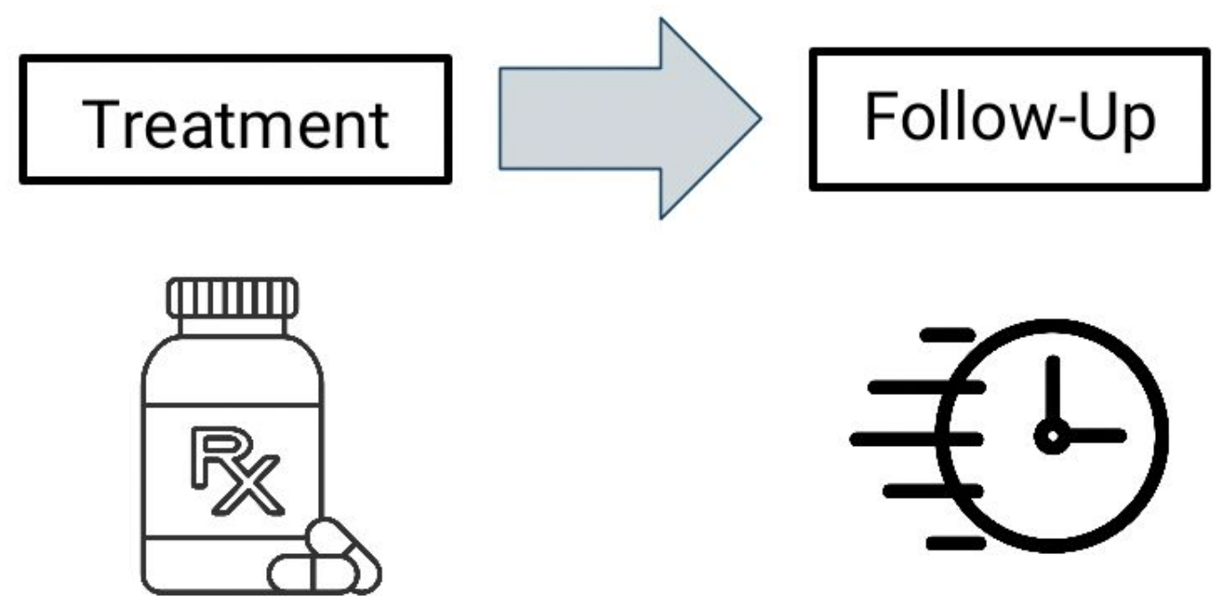
Patients with surgery and tumor grade
n = 858

50 dropped
NA values for Neoadjuvant or Adjuvant Treatment

Final patient subset
n = 818

Motivation and Goal

- Our project explores how to more effectively assess recurrence risk using a combination of clinical and molecular data for treatment planning.



Treatment

Follow-Up

- In order to address genomic test limitations (restricted eligibility, cost, chemotherapy focus), an interactive R Shiny application was developed as a tool for clinicians and patients.

Methods

Outcome Definition

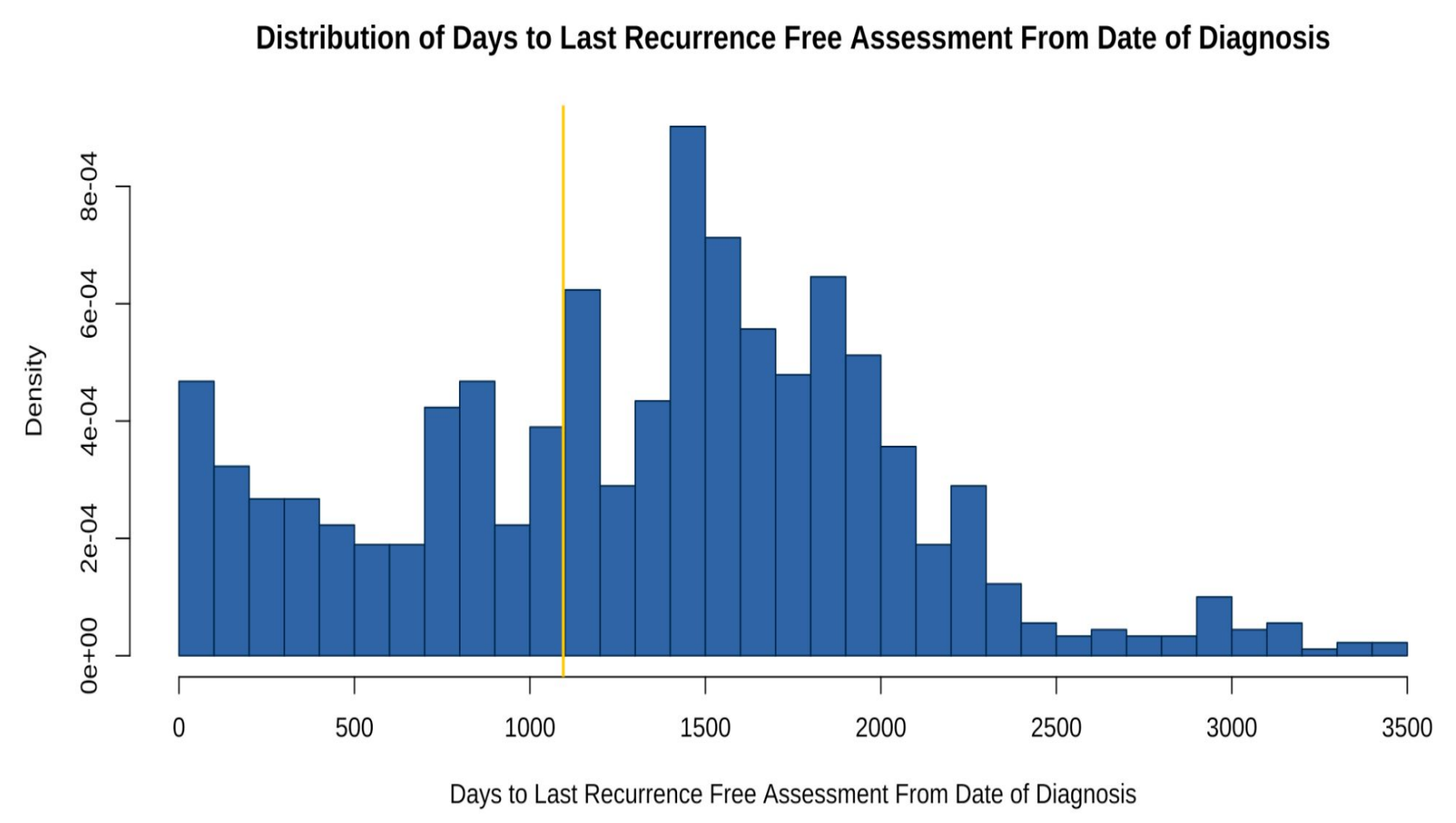


Figure 1. Distribution of patient follow-up time, with a yellow line representing the value we chose (3 years).

Figure 2. The table displays the percentage of patients followed-up at 1, 2, and 3 years. We face a trade off: more certainty in outcome versus more minority class events.

Time	Followed (%)	No Recurrence	Recurrence
1 Yr	91.6%	806	12
2 Yrs	83.5%	780	38
3 Yrs	69.4%	762	56
Total	100%	734	84

SMOTE

- Synthetic Minority Oversampling Technique
- Generates synthetic examples for the minority class, helping to balance imbalanced datasets and improve model performance.

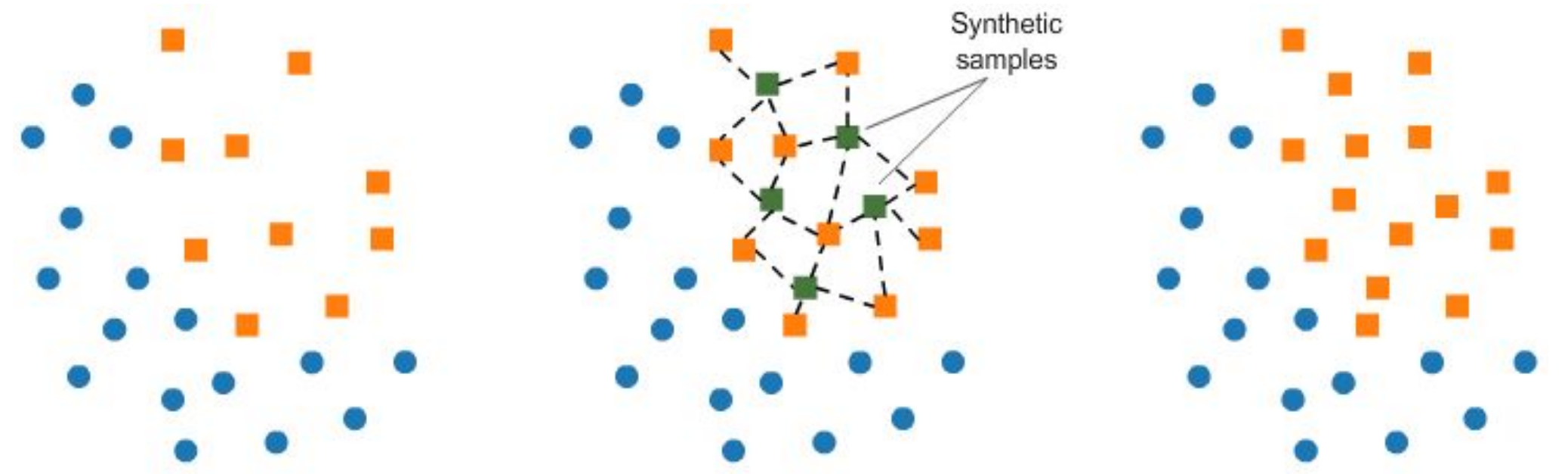


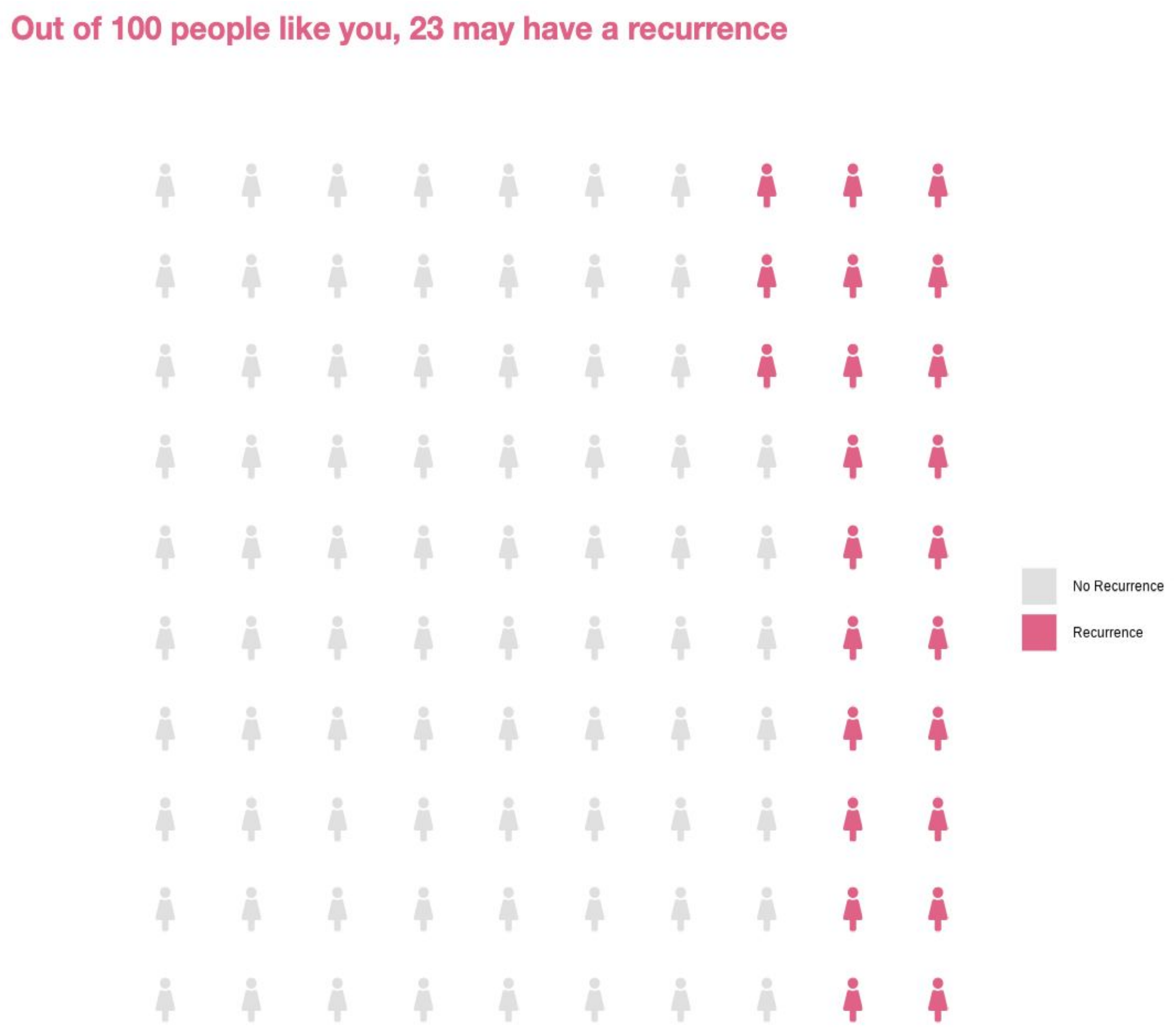
Figure 3. A visual representation of the way that SMOTE creates new synthetic instances.

XGBoost

- XGBoost is a machine learning method that builds a series of decision trees, with each new tree learning from the mistakes of the previous ones, ultimately combining their predictions to give you a probability score for classification.
- Advantages of XGBoost:
  - ○ Works well with highly imbalanced datasets, built in class weighting functions to address that issue.
  - ○ Has built in feature importance function which is helpful with interpretability and understanding the model's drivers.
  - ○ Built-in LASSO regularization. Important for preventing overfitting.
- Our model combines SMOTE with hyperparameter tuning to enhance the performance of the model.
- We performed our hyperparameter tuning using a GridSearch with a 5-fold cross validation. This method searches over every possible grid to maximize a chosen evaluation metric.

R Shiny Application

- An interactive web application was developed to provide clinicians with a tool for inputting patient diagnosis data and neoadjuvant treatments.
- Generates a recurrence risk probability.
  - ○ Clinicians can use the score to determine adjuvant treatment course.
  - ○ Patients can use the score to visualize their risk.
- Features a human pictogram display to make the recurrence risk score easy to understand for both patients and clinicians.



Out of 100 people like you, 23 may have a recurrence

Figure 4. R Shiny App Recurrence Risk Pictogram. This figure illustrates the user-friendly output of our R Shiny application, translating patient data into an easily digestible visual of recurrence probability to aid treatment discussions between clinicians and patients.

Results

Evaluation Metrics

- Calibration plot: a plot that displays the predicted probabilities on the x axis and the observed outcomes on the y axis.
- AUC: a single number that measures the area under the ROC curve. Models aim to be close to 1, as 0.5 represents random chance.
- Brier Score: measures the accuracy of probabilistic predictions for binary outcomes, calculated as the mean squared difference between predicted probabilities and actual outcomes; a lower score indicates better calibration and accuracy.

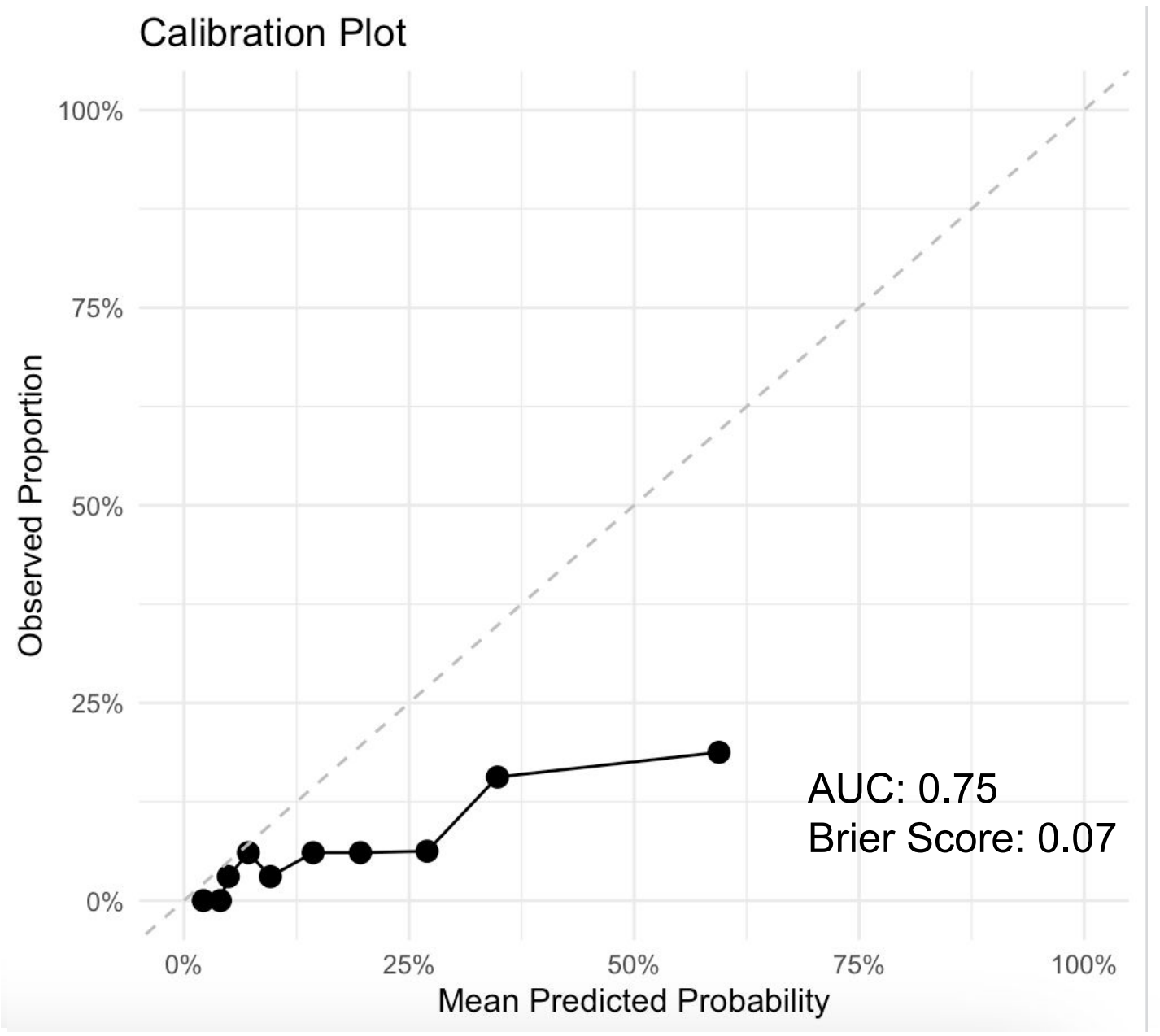


Figure 5. A calibration plot for our model with the AUC and Brier Score

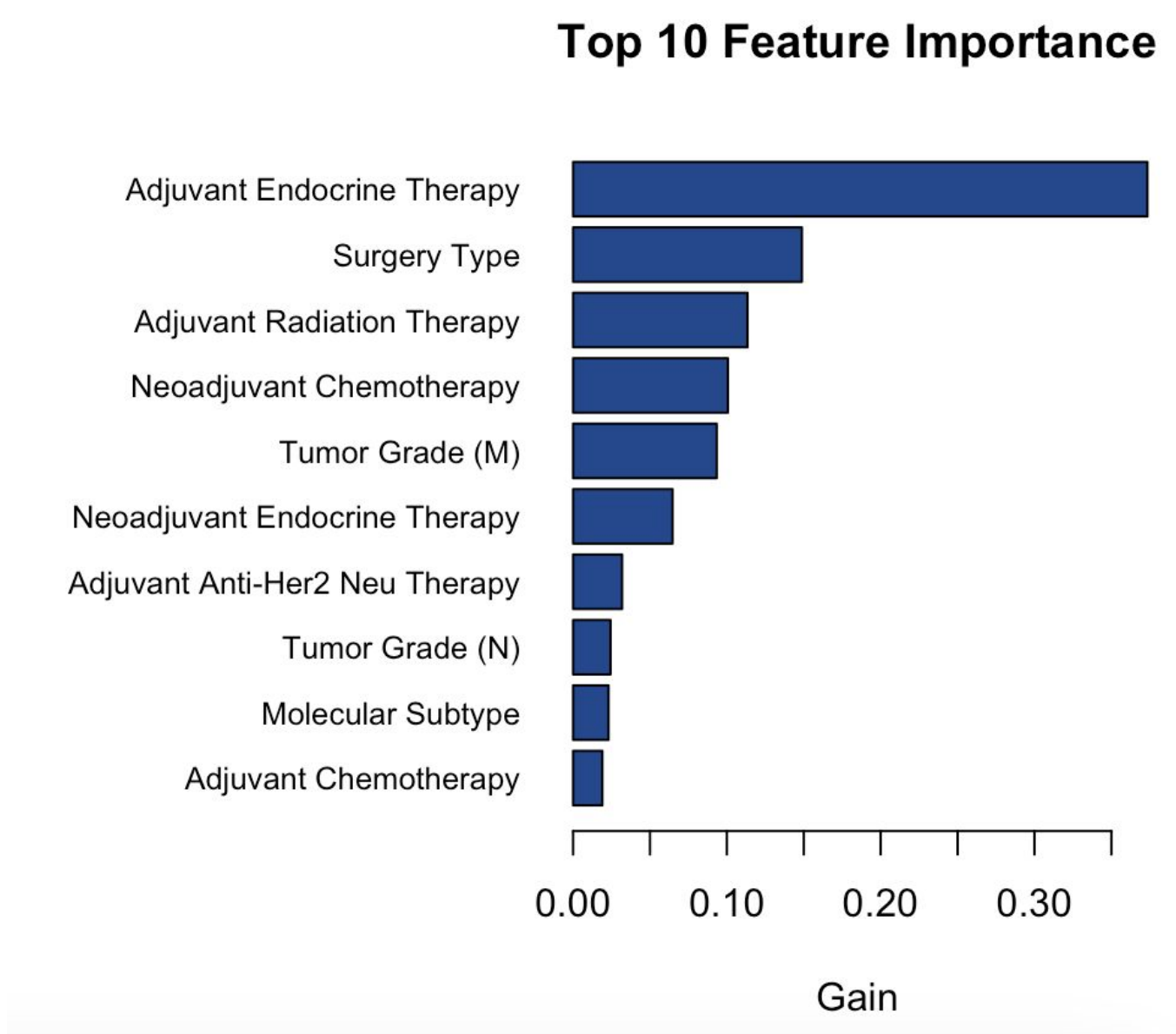


Figure 6. A bar chart displaying the top 10 most important features

Limitations

- Our model treats recurrence as a binary outcome. This is limiting because it cannot capture the details and information about when recurrence will occur which is an important factor in treatment decisions
- For clinical use, other predictors such as sociodemographic and comorbidity data should be incorporated.
- Predictions are limited to a 3-year timeline. As seen in Figure 2, we are missing events that occur past 3 years as well as potentially missing recurrence events that occur after the study was completed.
- Only 69.4% of the patients in our dataset were followed up with to the 3 year mark, representing a portion of uncertainty in their outcome.

Future Work

- To further explore the performance of our model, we could compare it to oncotype score predictability in a prospective trial.
- Expand R Shiny Functionality: Develop new features, such as the ability to compare predicted outcomes for different hypothetical treatment scenarios.
- Time-to-Event Prediction: Adapt the model to predict specific time-to-recurrence probabilities rather than just binary outcomes.

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References

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