Reducing the Gap from SCZ Relapse Episode to LAI Initiation

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Delays in LAI Use After Relapse: Why It Matters

Despite the availability of effective long-acting injectables (LAIs) for schizophrenia, there is often a significant delay between a patient's relapse episode and the initiation of LAI treatment. This gap may lead to **preventable hospitalizations**, **poorer patient outcomes**, and **increased healthcare costs**.

Data Source Overview

Data Source

Data source: CMS 2008-2010 Data Entrepreneurs' Synthetic Public Use File (DE-SynPUF)

6+ million patients

Key Approval Dates

Oral Antipsychotics:
- Risperidone (Risperdal) – 1993
- Paliperidone (Invega) – 2006

Long-Acting Injectables (LAIs):
- Risperidone (Risperdal Consta) – 2003
- Paliperidone Palmitate (Invega Sustenna) –2009

Potential Problems & Biases

- **Limited to medicare patients**
  - Older population
  - Patients under 65 with disabilities
  - Unable to see healthier younger patients, or adults with private insurance
- **3 year cut (2008-2010)**
  - Can't see entire patient journey
  - Unlikely to capture patient's initial SCZ dx
- **Drug information suppressed** (no NDC11 codes)
  - Unable to understand the treatment landscape

Cohort Identification and Preprocessing Steps

01 **Define Schizophrenia** - ICD9 diagnosis for Schizophrenia (SCZ) in either outpatient (OP) or inpatient setting (IP) (using admission date for IP, claims from date for OP encounters)

02 **Define Relapse Episode** - Inpatient encounter with a behavioral health related ICD9 code (Physiological Malfunction Arising from Mental Factors, Paranoid States, Disruptive Behavior Disorders, etc.)

03 **Explore Included Features** - Sex, race, state, comorbidities, insurance coverage, provider identifiers

04 **Create features** - Days to relapse episode, age at SCZ dx, history of substance abuse indicator, maximum follow-up date/censor date, number of inpatient & outpatient encounters prior to “initial” SCZ dx

Key Data Features and Population

Cohort Size & Relapse Rate

Cohort size: **86,023** patients with a Schizophrenia ICD9 diagnosis (in either IP or OP setting)

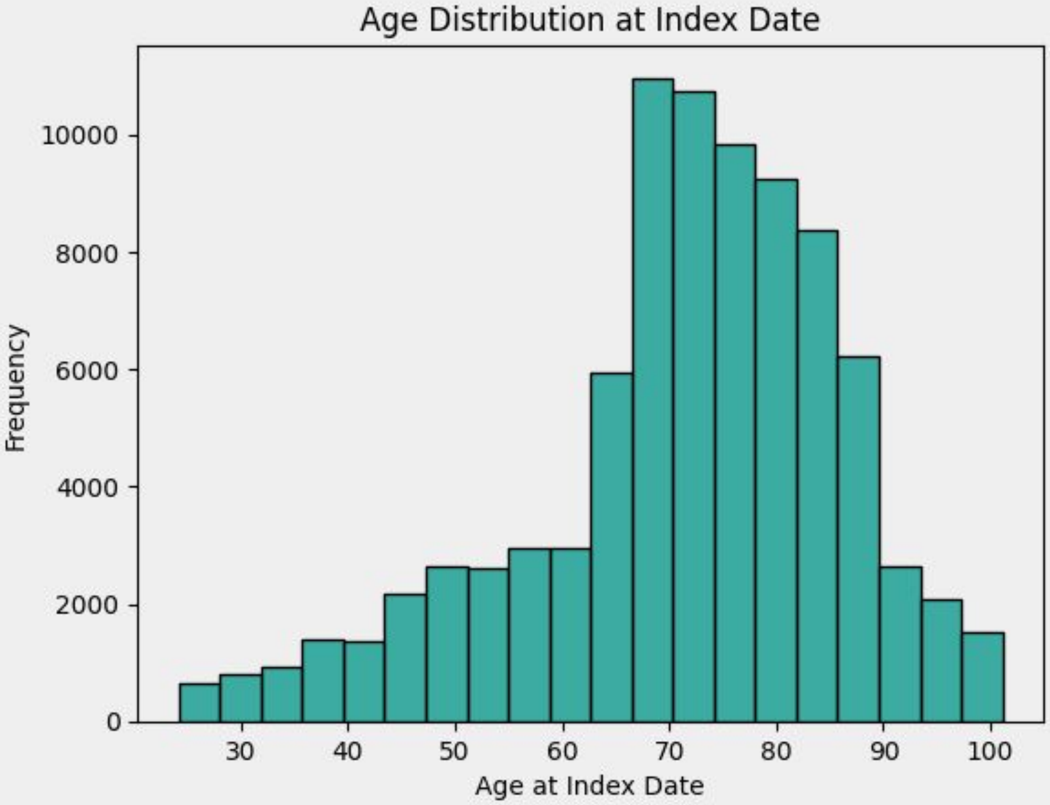
Relapse rate: **17.4%** (n=14,984)

Selected Features for Modeling and Exploration

Patient Identifier
Index date (SCZ dx)
Age at index date
Relapse date
Initial SCZ diagnosis in OP/IP setting indicator
Sex
Race
Region

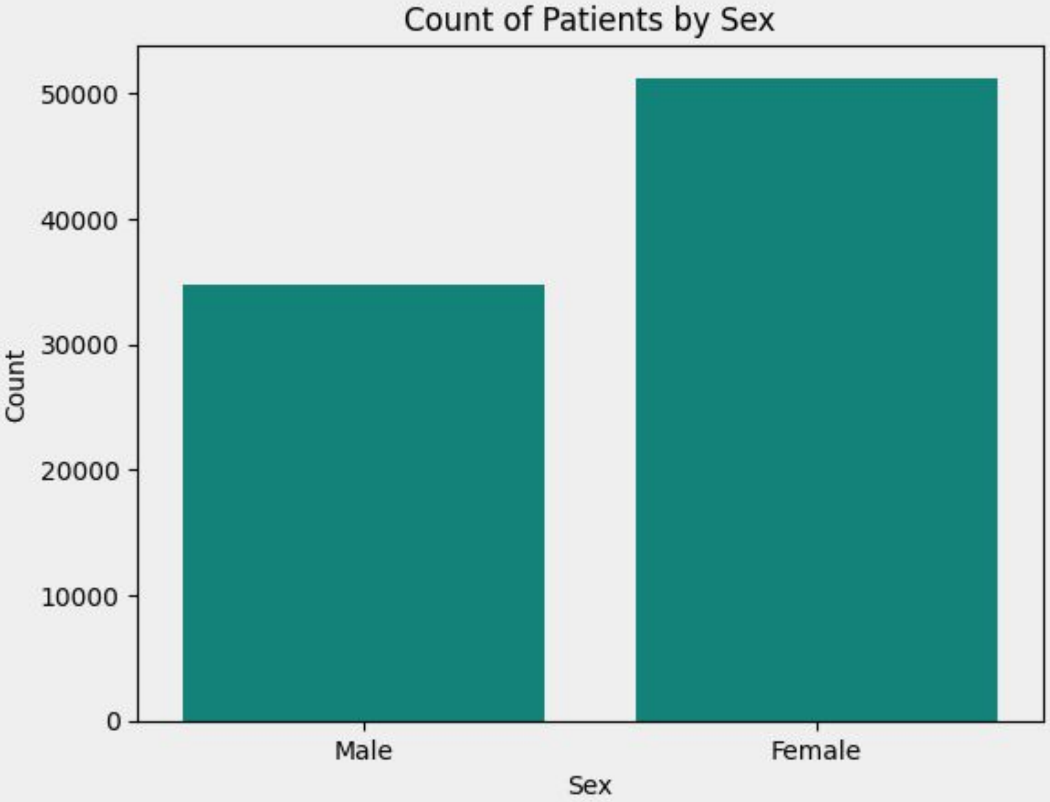
# of IP events prior to index
# of OP events prior to index
Insurance coverage (months)
Provider identifier
Prior substance abuse indicator
12 Comorbidities (cancer, diabetes, CKD, etc.)

Exploratory Data Analysis (Age at Index Date)



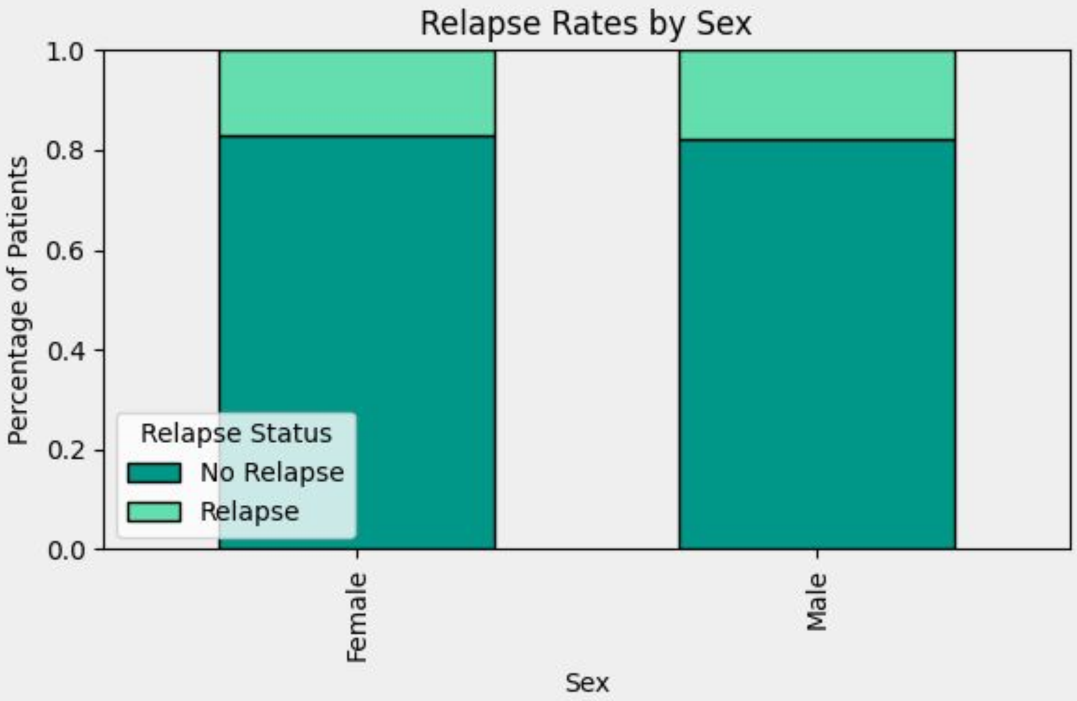
- Aligns with expected older Medicare population
- Still some young patients, but predominantly 65-85 years old

Exploratory Data Analysis (Sex)

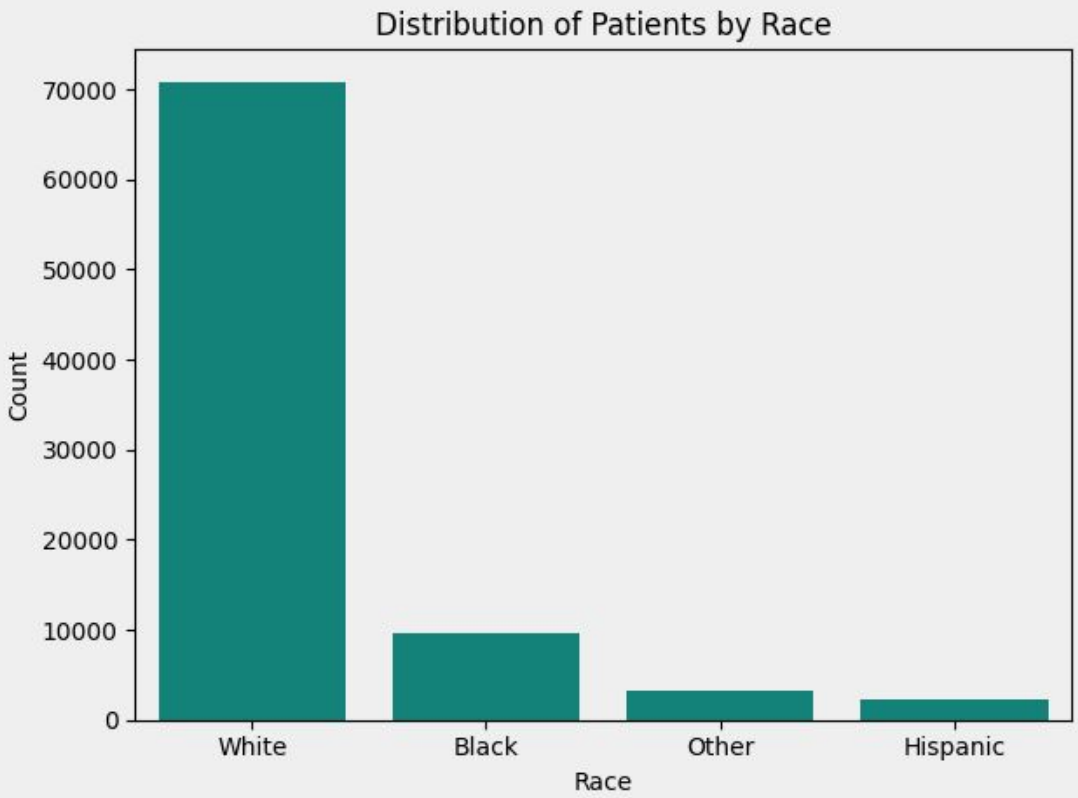


- Life expectancy in women longer than men
- Women generally use more healthcare services than men

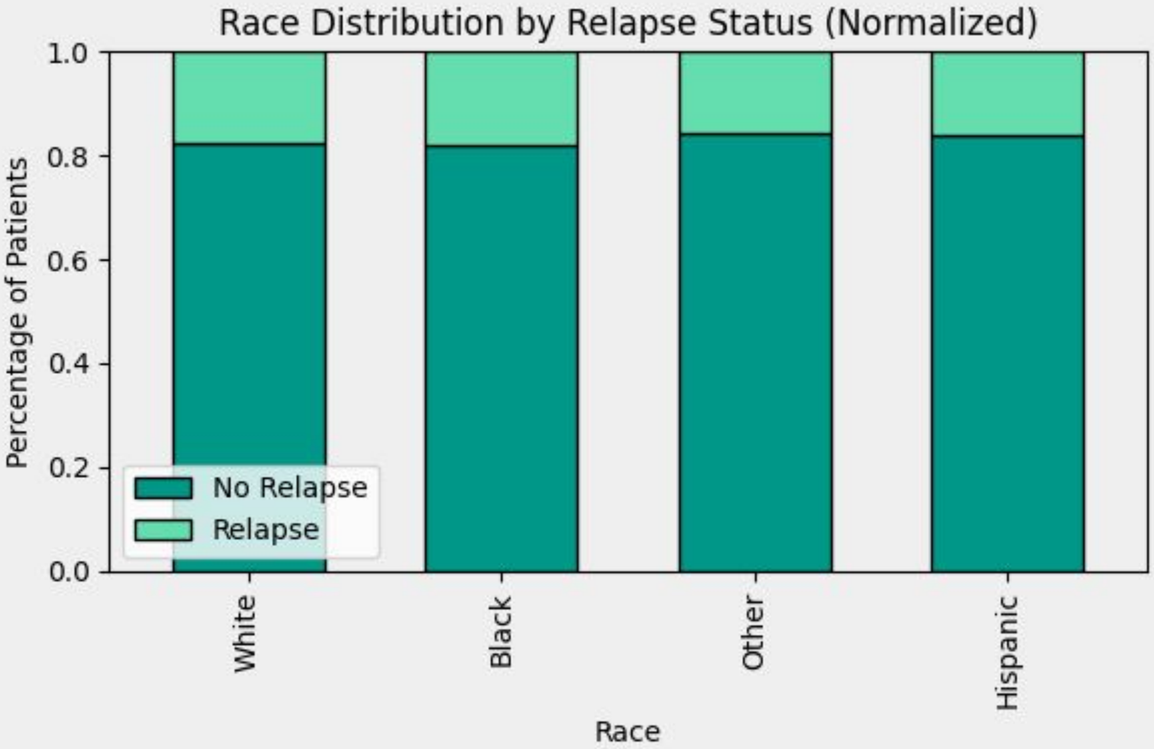
Exploratory Data Analysis (Sex vs. Relapse)



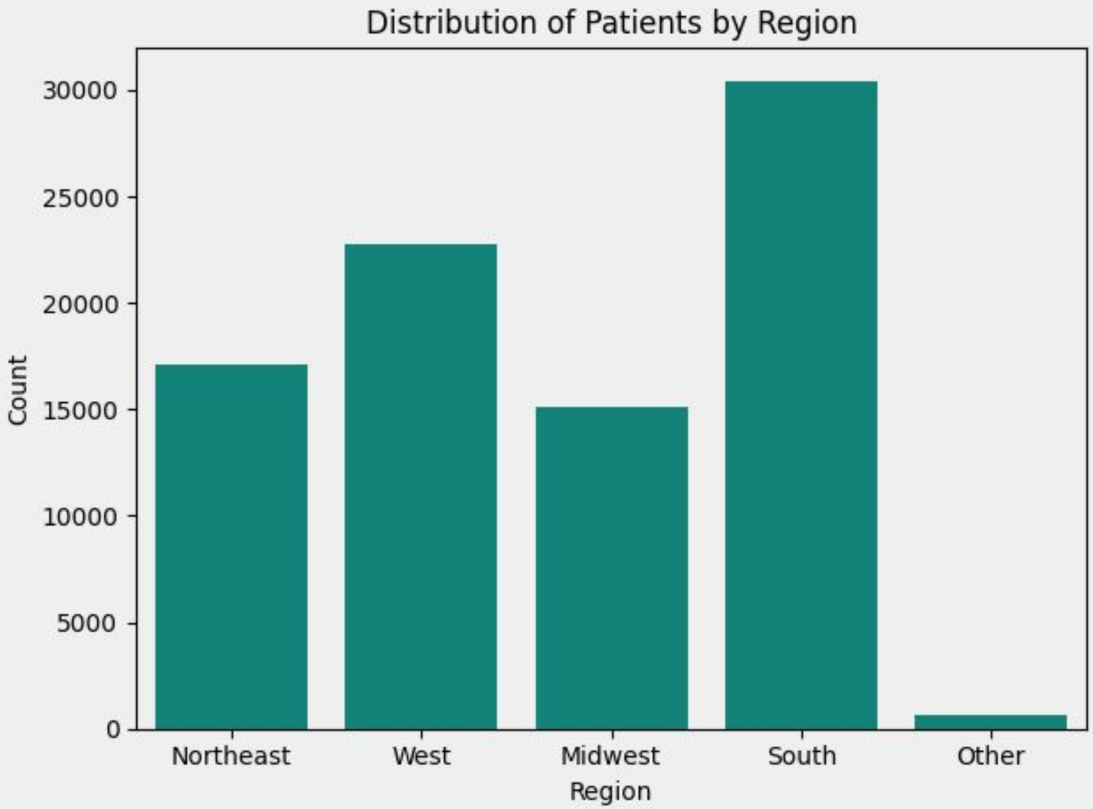
Exploratory Data Analysis (Race)



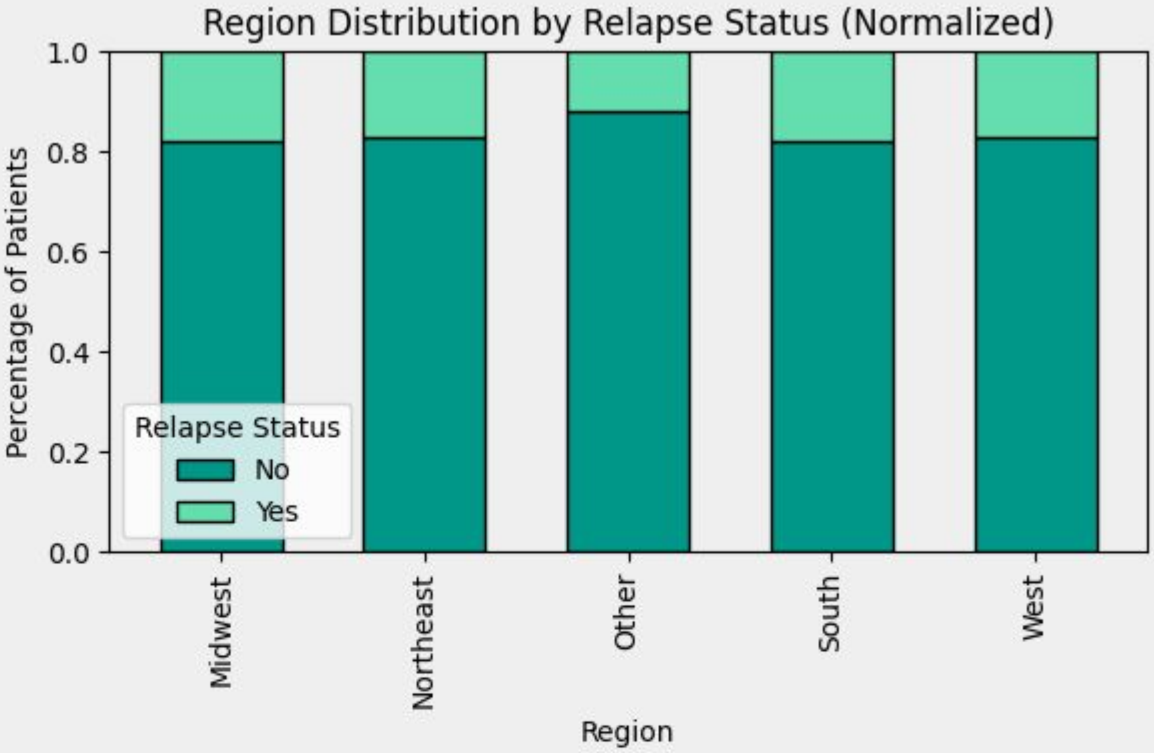
Exploratory Data Analysis (Race vs. Relapse)



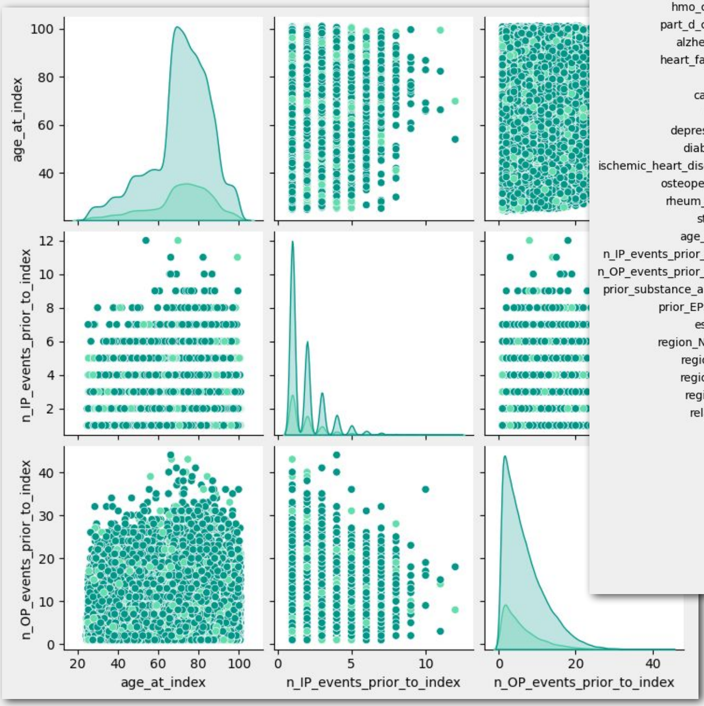
Exploratory Data Analysis (Region)

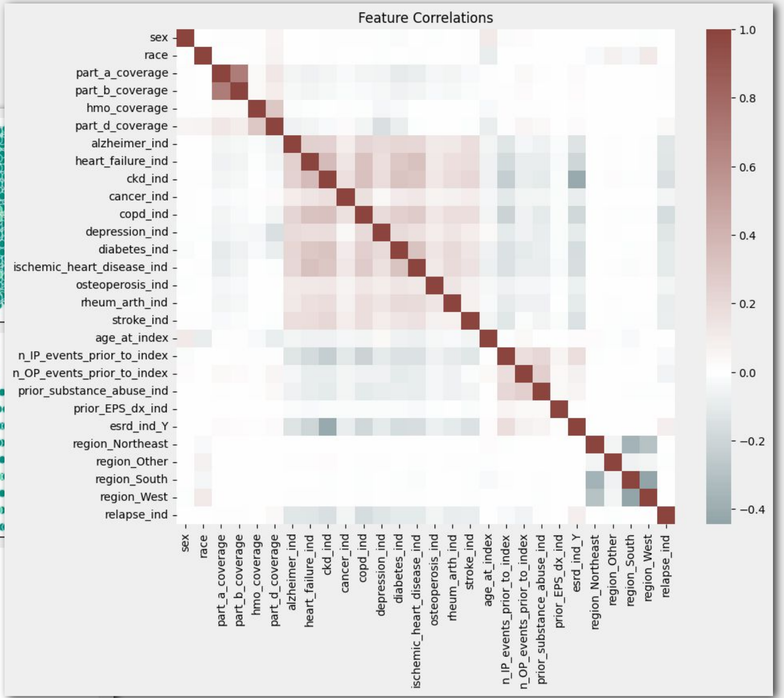


Exploratory Data Analysis (Region vs. Relapse)

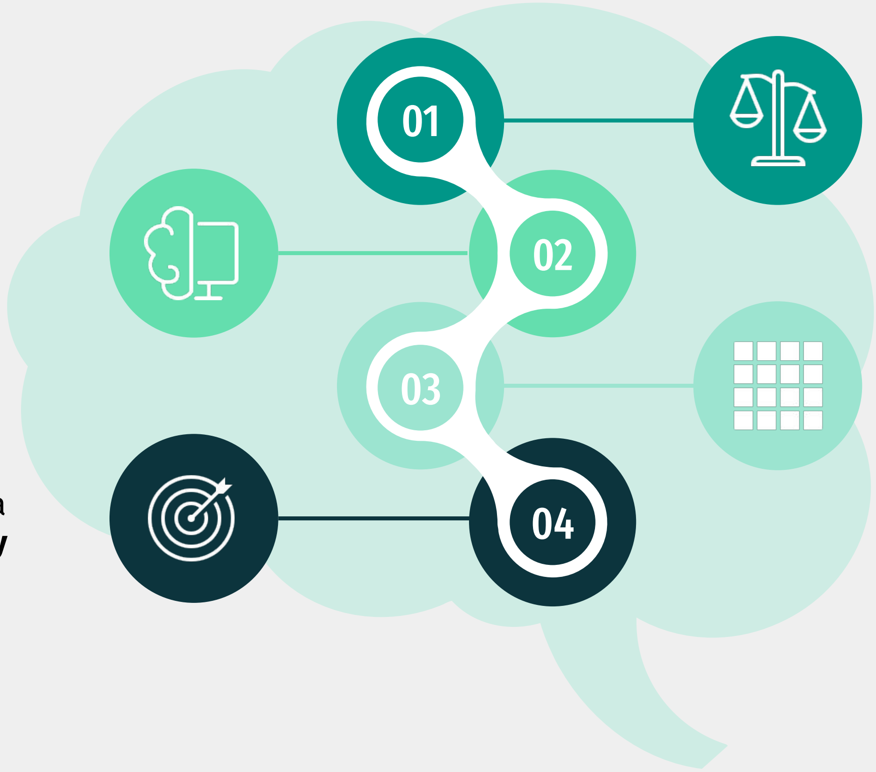


Exploratory Data Analysis (Others)





Reducing the Gap = Predicting Relapses?



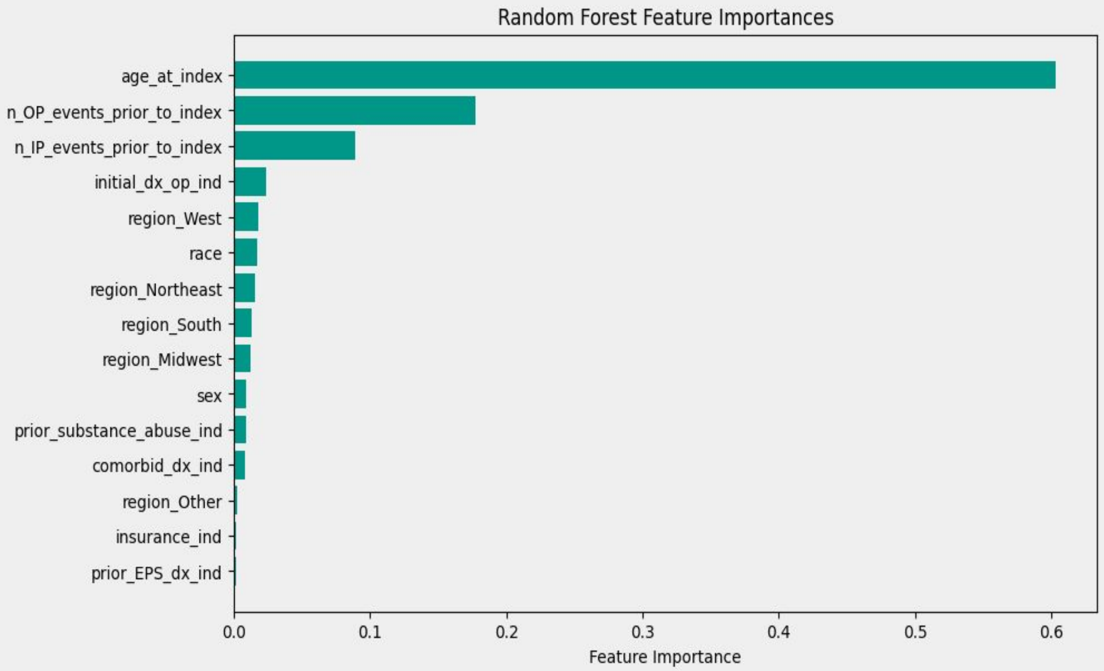
Used SMOTE (Synthetic Minority Over-sampling Technique) to balance dataset into 50/50 split between patients who did and did not relapse

Ran various ML models (Random Forest, XGBoost, SVM)

Used GridSearchCV to find the best model & parameters.

Successfully developed a model with **79% accuracy**

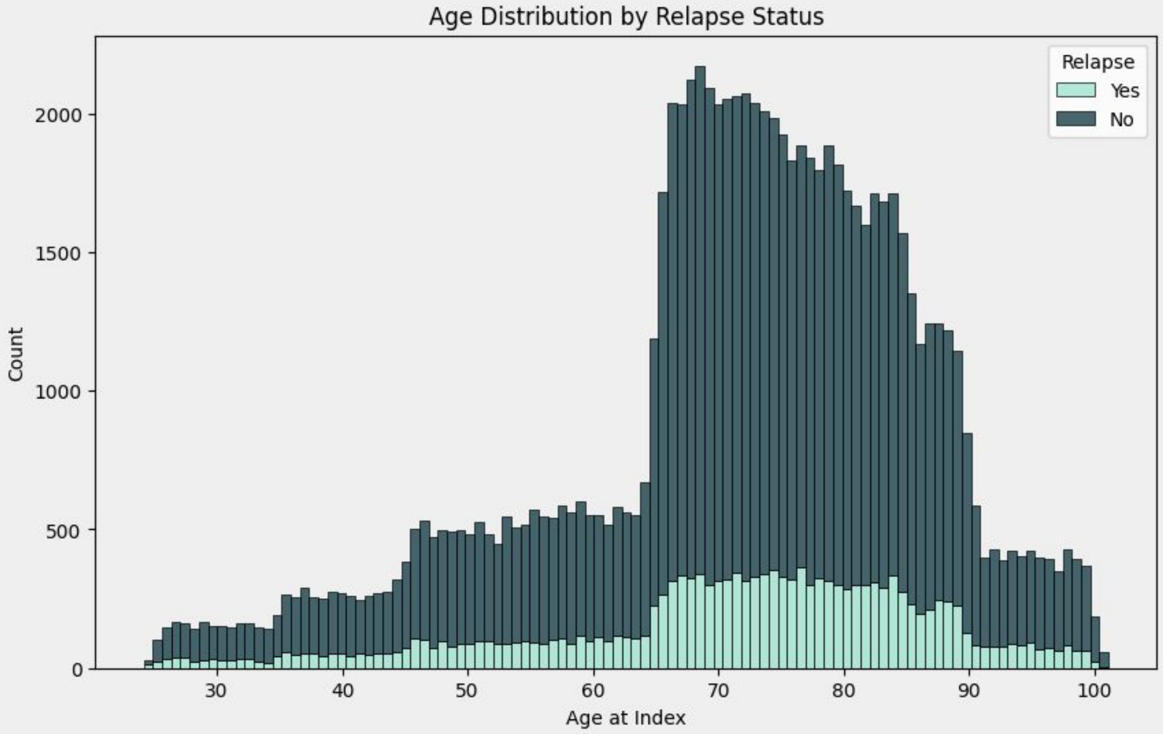
Model Outputs (Feature Importance)



- Age at index is the significant feature
- # of inpatient & outpatient events are also major factors

Note: Age was intentionally left imbalanced to highlight differences in interpretability between traditional statistical methods and machine learning models in a clinical research context.

Age vs. Relapse Episodes



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Challenges and Limitations of ML Models

Noisy Data

Even though ML can find patterns, experts in the field are needed to make sure those patterns are actually useful and meaningful.

Black Box

Machine learning models can make predictions without explaining *why* they make those decisions, making it hard to understand their reasoning.

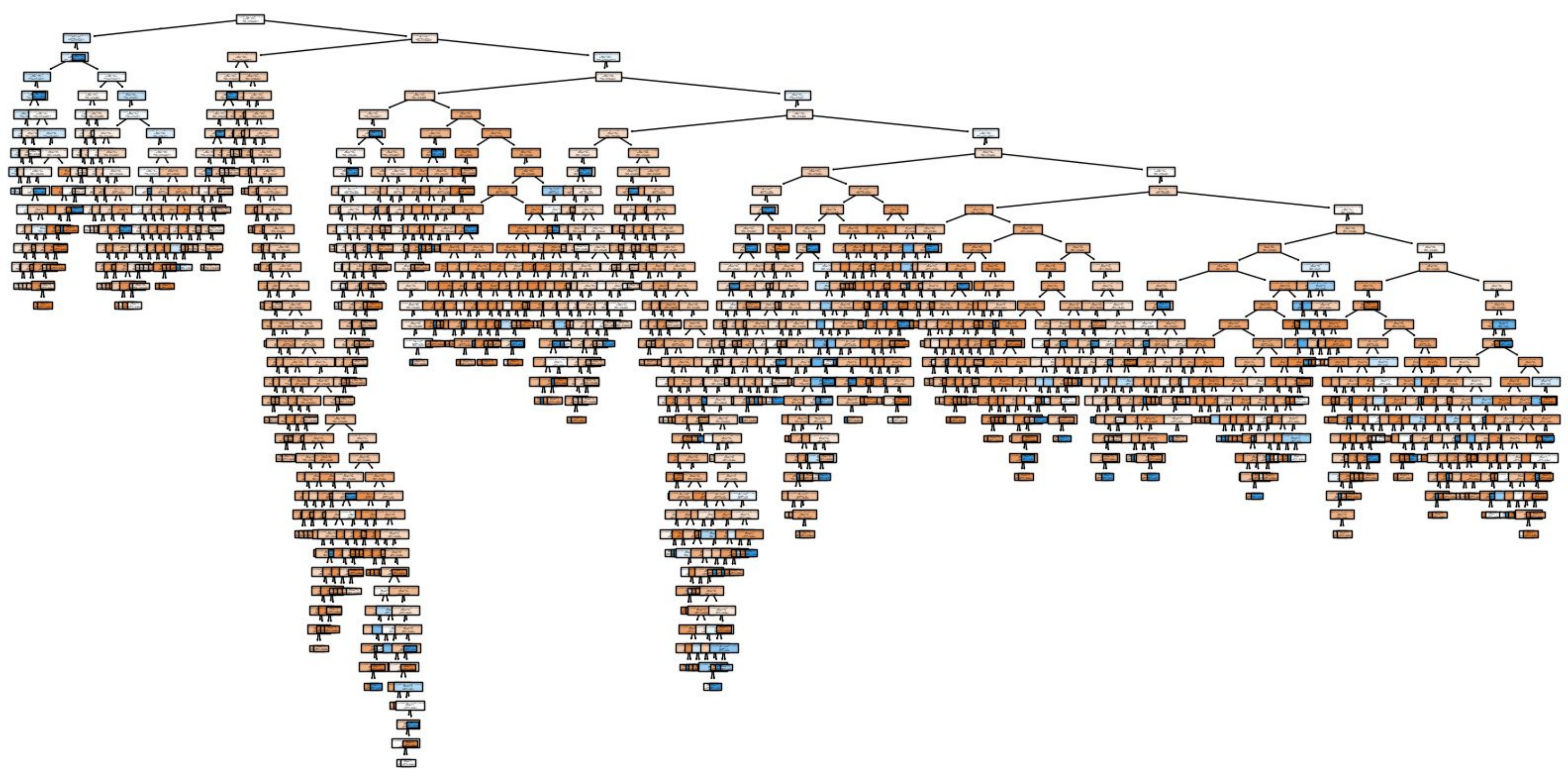
Domain Expertise Needed

Even though ML can find patterns, experts in the field are needed to make sure those patterns are actually useful and meaningful.

Overfitting

Sometimes a model can be too focused on the data it was trained on, making it good at predicting past events but bad at predicting future ones.

Random Forest Model Visualized



From Machine Learning to Statistical Models: Kaplan-Meier & Cox for Predicting Relapse

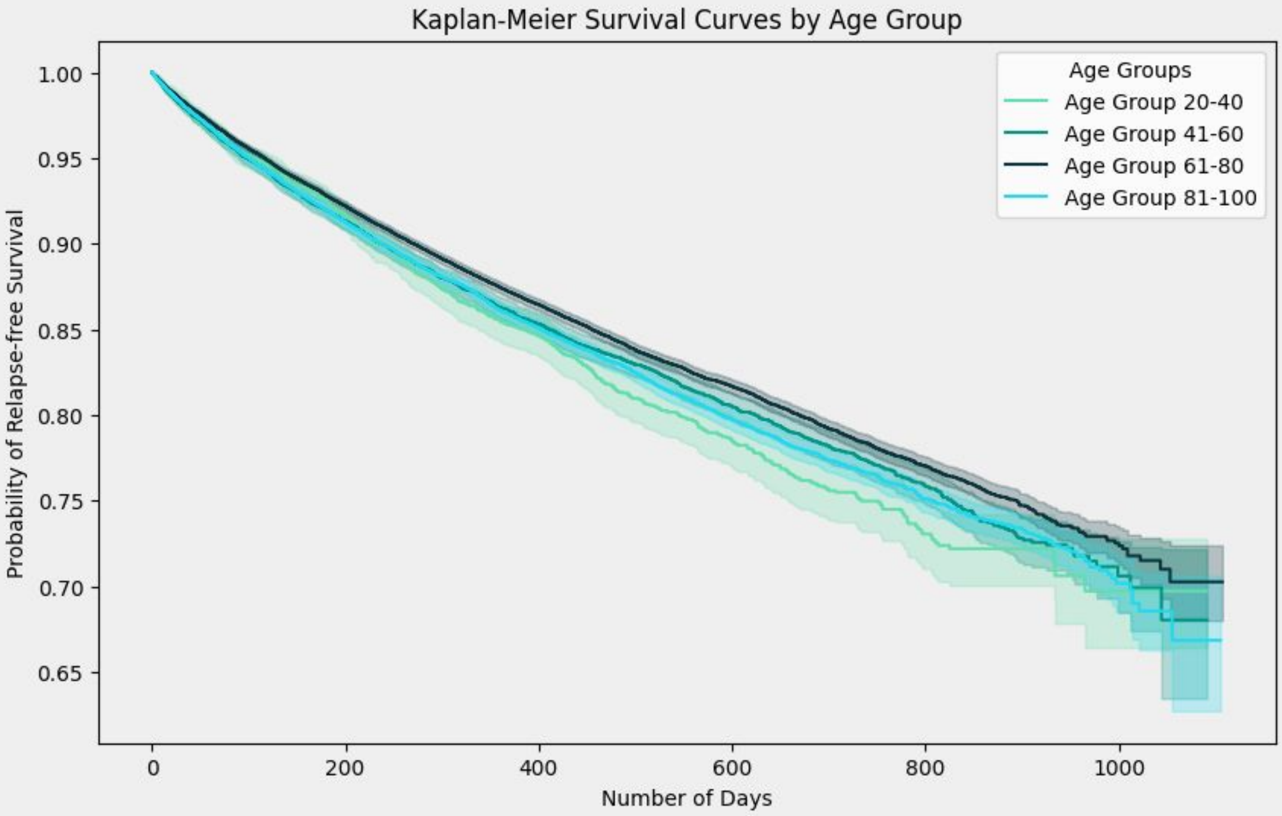
Kaplan-Meier Curves: A Clearer Picture of Time to Relapse

- Visualizes the probability of relapse over time for different groups, highlighting high-risk periods without needing complex models.
- Allows us to easily identify when relapses are most likely to occur, helping clinicians prioritize interventions.

Cox Proportional Hazards Model: Understanding Risk Factors

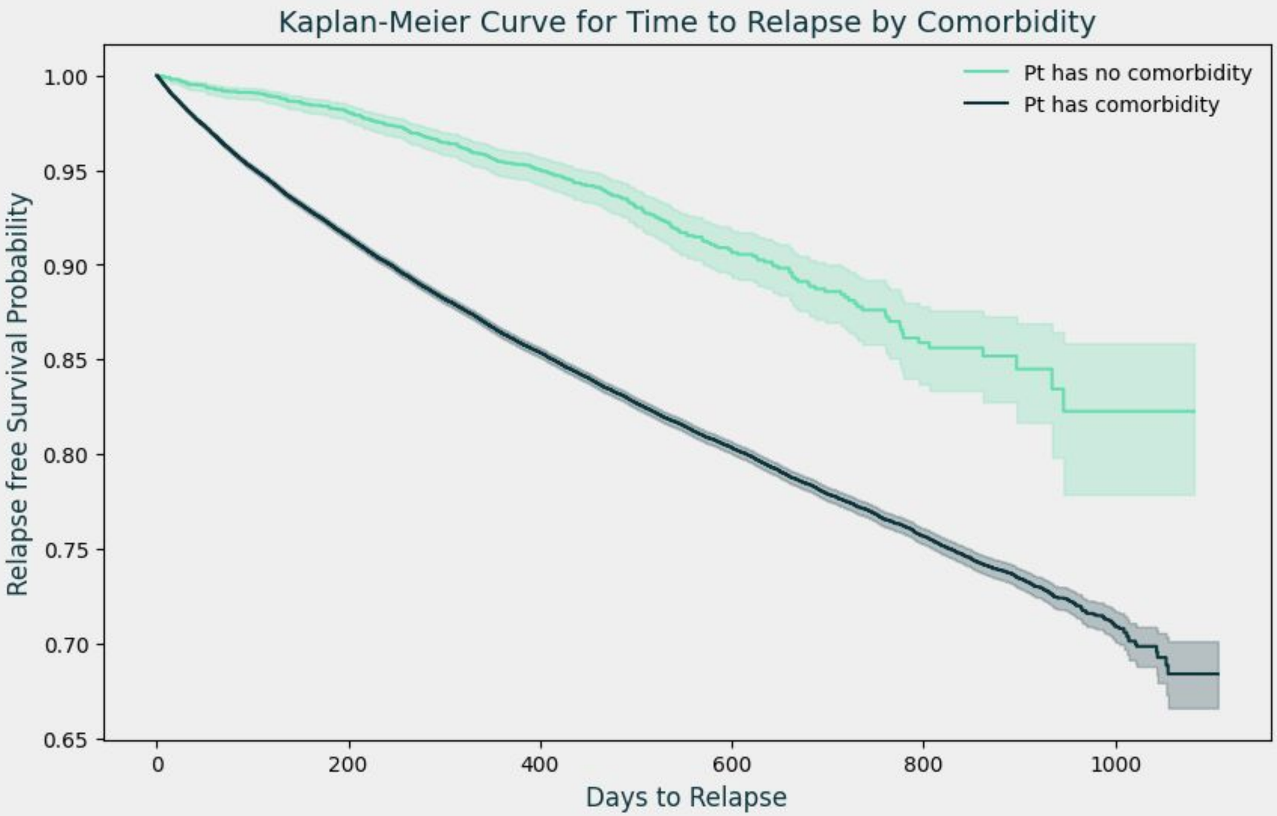
- Assesses how multiple factors (age, comorbidities, etc.) impact relapse risk, providing a clearer understanding of relapse drivers.
- Quantifies the relationship between relapse and potential risk factors, offering actionable insights for clinical decision-making.

Interpreting the Impact of Age on Relapse Risk



- The coefficient for Age at index is 0.00. This means that the effect of age on the hazard of relapse is very small, close to zero. (P = 0.08)

Interpreting the Impact of Comorbidities on Relapse Risk

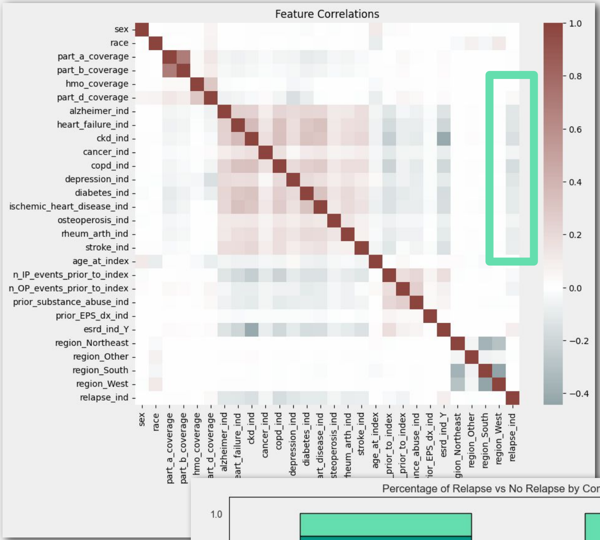


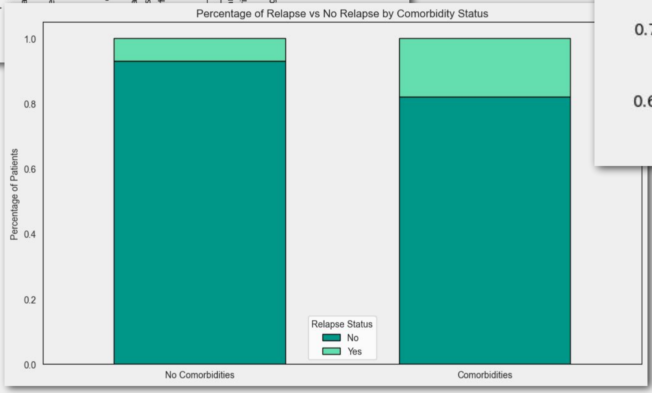
- The coefficient for Comorbidity (yes/no) is 0.93. This means that having a comorbidity increases the risk of relapse, as indicated by a higher hazard ratio.

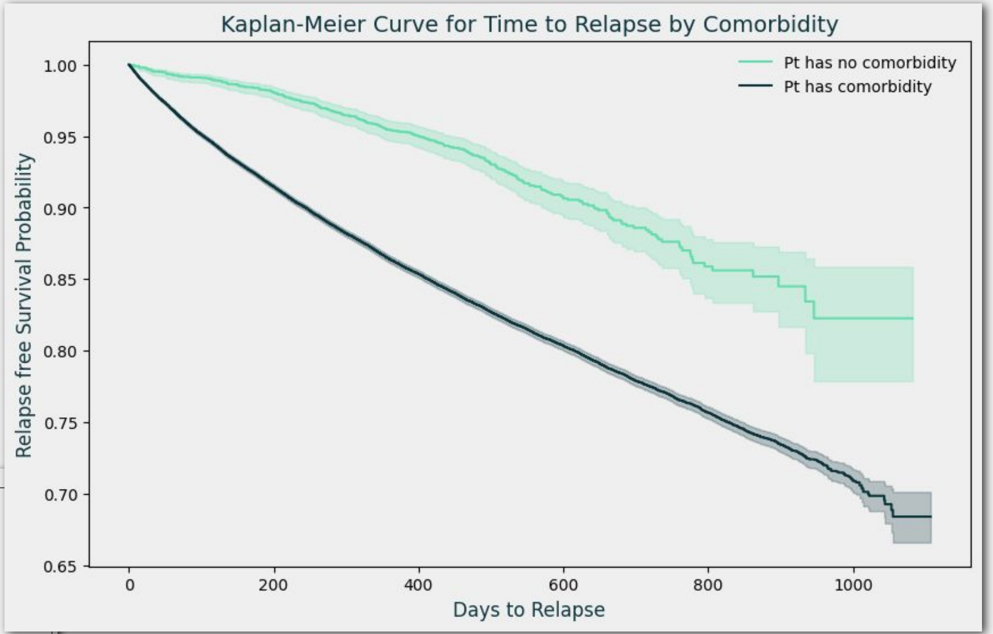
- Exponentiated value of the coefficient, also known as the Hazard Ratio (HR) is 2.52. It means that, for individuals with comorbidity, the risk of relapse is 2.52 times higher compared to those without comorbidity, assuming all other variables are held constant.

- p (<0.005) indicates that the effect of having a comorbidity on relapse is statistically significant.

Shaping Decisions Through Data Analysis & Visualization





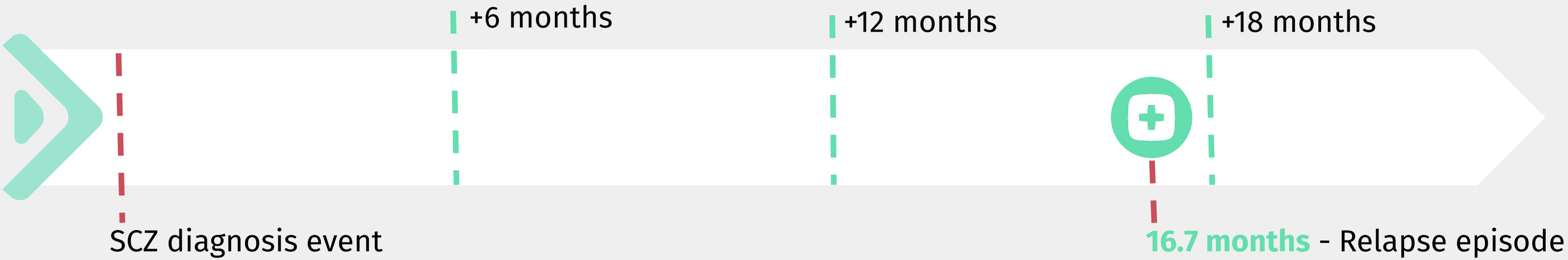


Median Time to Relapse: With vs Without Comorbidities

Patients **with comorbidities** relapse more than **twice as fast** (median 7.1 months vs. 16.7 months). Comorbid patients are **2.52 times more likely** to relapse (Cox HR = 2.52).

Patients with Comorbidities

Patients without Comorbidities



Driving Impact Through Medical Affairs Strategy

Support Earlier LAI Consideration

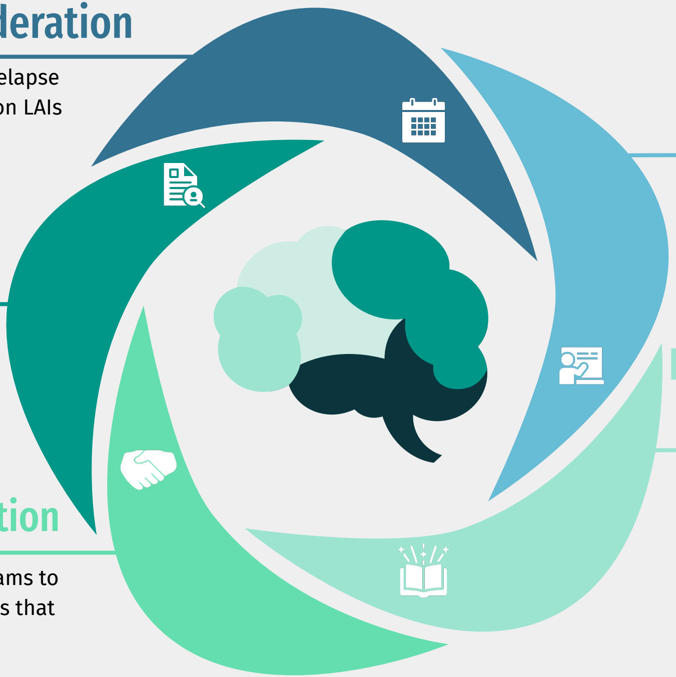
Educate HCPs on initiating LAIs prior to first relapse for patients with comorbid conditions. Position LAIs as a proactive strategy rather than reactive.

Support Outcomes Research

Propose studies to assess outcomes of early LAI initiation in comorbid SCZ patients to strengthen the value proposition.

Cross-Functional Collaboration

Partner with commercial, HEOR, and payer teams to align messaging and support access initiatives that prioritize early LAI use.



Enhance Clinical Guidelines & Materials

Use this data to inform updates to clinical education, field medical tools, and advisory board discussions. Consider real-world case examples to drive the narrative.

Equip KOLs with Compelling Storytelling Tools

Collaborate with and give Key Opinion Leaders (KOL) impactful visualizations (like the relapse timing charts) they can use at conferences or in peer-to-peer settings.