A Study on Predicting Medication Adherence

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Executive Summary

Adverse drug events (ADEs) are a significant concern worldwide, impacting a substantial number of patients, leading to healthcare complications and additional costs. Our project aimed to utilize comprehensive datasets provided to predict potential adverse drug events in patients, enabling healthcare providers and stakeholders to take preemptive action and mitigate risks associated with medication therapies.

Our initial approach involved an in-depth exploration and preprocessing of the data to understand the variables and ensure the quality and integrity of the datasets used for model training. We addressed null or missing values through novel strategies tailored to each variable, ensuring no essential information was lost. Furthermore, variables were scaled using StandardScaler to normalize the data, essential for the performance of many machine learning models.

In our pursuit of precision and reliability, we employed an ensemble machine learning approach, leveraging the strengths of multiple algorithms including LightGBM, XGBoost, CatBoost, and AdaBoost. The strategy involved using Optuna for hyperparameter optimization to ensure each model's peak performance and then integrating these models through stacking, followed by bagging to reduce variance, and calibration for reliable probability estimates. Performance evaluation of our predictive model was primarily based on the ROC-AUC score, a common metric for classification tasks, especially in imbalanced datasets like those dealing with ADEs. In addition to accuracy, we examined the model's confusion matrix to understand its performance in terms of false positives and negatives, crucial for real-world applications.

The implications of ADEs are far-reaching, affecting patient safety, increasing healthcare utilization, and driving up costs. By accurately identifying patients at high risk of ADEs, interventions can be timely, which is beneficial for patient outcomes and helps in resource optimization. Current preventive measures in healthcare systems rely on manual flagging and basic rule-based systems, but the incorporation of our AI-driven model can significantly enhance prediction accuracy and early intervention.

For healthcare providers and stakeholders, the deployment of this model translates into actionable insights and the ability to allocate resources effectively, such as personalized medication plans, targeted patient education, and follow-ups, potentially reducing ADE-related hospitalizations and associated costs. By our estimates, implementing this predictive model could result in substantial cost savings due to decreased adverse drug events. For every 1,000 patients flagged as high risk and managed proactively, significant savings are anticipated, not just in monetary terms but also in improved patient safety and quality of care.

Background

In the evolving landscape of healthcare, adverse drug events (ADEs) have emerged as a profound concern, affecting a significant portion of patients globally and imposing substantial health risks and financial burdens. ADEs, defined as any harm experienced by a patient as a result of exposure to a medication, are currently one of the leading causes of hospitalizations and emergency department visits, contributing to escalated healthcare costs and, more critically, patient morbidity and mortality. Research indicates that approximately 10% of hospital admissions are related to ADEs, and a considerable proportion of these events are preventable[1]. The complexities associated with polypharmacy, particularly in the elderly and those with chronic conditions, amplify these risks[2]. Therefore, the early identification of potential ADEs is not only crucial for individual patient safety and health outcomes but also represents an opportunity for significant cost savings within healthcare systems.

The exigency of addressing ADEs is further underscored by the associated avoidable healthcare utilization, highlighting the need for more proactive and preventive approaches in medication management. Given the advancements in machine learning and data analytics, there is an unparalleled opportunity to harness these technologies to predict ADEs and initiate preemptive interventions.

Case Introduction and Business Problem

The prevailing challenge is to utilize available healthcare data to identify patients at heightened risk of adverse drug events, thereby enabling healthcare providers, including hospitals and health insurance companies, to tailor interventions and reduce associated negative outcomes. Leveraging datasets that encompass detailed patient medical histories, medication records, and other relevant factors, we aim to develop a predictive model that accurately flags high-risk individuals, delineates the variables most predictive of ADEs, and formulates actionable strategies for healthcare stakeholders.

Definition of Metrics / Key Performance Indicators

Our model's primary output is a probabilistic estimation indicating a patient's risk level for experiencing an ADE. The foremost key performance indicator for our model's efficacy is the Area Under the Curve of the Receiver Operating Characteristic (AUC-ROC). This metric is paramount because it evaluates the model's accuracy in discriminating between those patients

[1] Shehab, N., et al. (2016). "US Emergency Department Visits for Outpatient Adverse Drug Events, 2013-2014." JAMA.
[2] Qato, D. M., et al. (2018). "Changes in Prescription and Over-the-Counter Medication and Dietary Supplement Use Among Older Adults in the United States, 2005 vs 2011." JAMA Internal Medicine.

who are likely to experience an ADE and those who are not, irrespective of a skewed dataset.

Simultaneously, we recognize the importance of fairness and the potential for certain biases within healthcare data, particularly concerning demographic or socioeconomic variables that might correlate with healthcare access and quality. Thus, our secondary metric, the fairness indicator or disparity score, will assess whether our model's predictions inadvertently favor certain groups over others. This step ensures that our predictive tool is equitable and just in its risk assessments, thereby maintaining trust and reliability.

Both these metrics are integral to our modeling process and will be elaborated upon in subsequent sections, providing a comprehensive view of our model's performance and fairness in predicting adverse drug events.

Preliminary Research

Adverse Drug Events

Before delving into a machine learning-driven approach to this issue, it's imperative to deeply understand the concept and implications of "Adverse Drug Events" (ADEs). ADEs encompass any harm related to the use of medications, either prescribed or over-the-counter, including physical injury, mental health implications, or decreased quality of life[3]. ADEs are a longstanding concern worldwide, but their prevalence and complexity have surged with the increased usage of multiple medications, especially among the elderly and those with chronic illnesses.

In the context of healthcare costs and patient safety, ADEs pose a significant burden. As of 2020, approximately 10% of hospital admissions were related to ADEs, and notably, a substantial fraction of these were deemed preventable with better medication management and monitoring practices. The economic impact is also staggering, with ADEs accounting for a considerable proportion of healthcare expenditures annually[4]. The COVID-19 pandemic further complicated this scenario by disrupting routine healthcare services, potentially leading to increased medication errors or mismanagement.

Furthermore, ADEs are not uniformly distributed across all segments of the population. Vulnerable groups, including the elderly, those with multiple comorbidities, and individuals in

[3] "Adverse Drug Events in the Outpatient Setting: An 11-Year National Analysis," Pharmacoepidemiology and Drug Safety.
[4] "Economic burden of preventable adverse drug reactions in healthcare systems: A systematic review," Research in Social and Administrative Pharmacy.

lower socioeconomic strata, are disproportionately affected[5]. This disparity is often due to factors such as polypharmacy, health literacy, access to healthcare, and the complexity of healthcare systems.

Given the escalating costs, both in terms of human health and healthcare expenditures, coupled with the unequal burden of ADEs among populations, there is an urgent need for innovative, data-driven strategies to predict and prevent these events.

Data

Exploratory Data Analysis (EDA)

In our initial exploratory data analysis (EDA), we focused on the 'target_train' dataset with 1,232 records, immediately noting a significant imbalance with only 9.5% (117) instances indicating unsuccessful therapies (tgt_ade_dc_ind), underscoring the challenge of modeling with imbalanced classes. Our attention was drawn to the role of gender in therapy discontinuation, prompting a deeper analysis into potential disparities. An exploratory visualization indicated variations in therapy adherence between genders, suggesting that gender may play a role in the likelihood of an adverse drug event leading to therapy discontinuation. This insight calls for a gender-stratified approach in further analyses and intervention planning.

[5] "Impact of Adverse Drug Reactions on Hospitalizations and Emergency Department Visits in the United States: A Retrospective Analysis from 2008 to 2015," J Patient Saf.

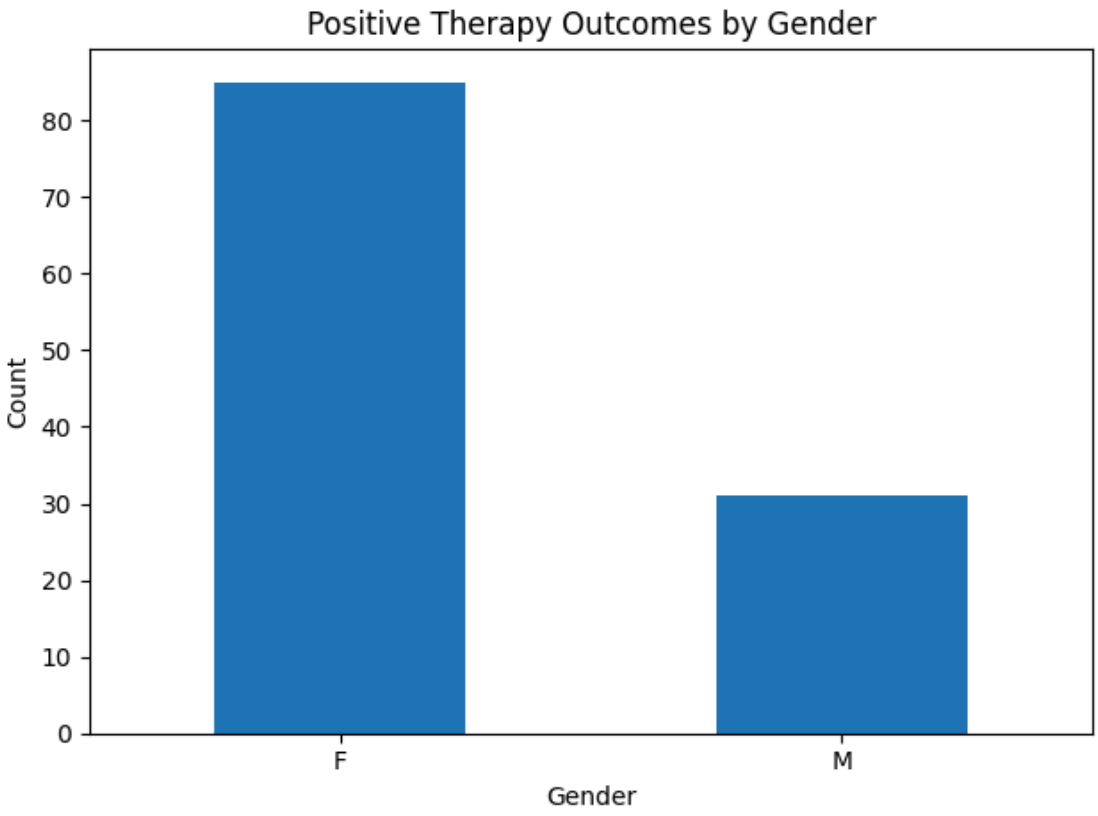

Figure 1: Distribution of positive therapy outcomes categorized by gender

Further, a deep dive into the 'medclms_train' records revealed a high occurrence of 'ade_diagnosis' (6,848 instances), emphasizing the critical role adverse drug events play in therapy adherence. Conversely, 'pain_diagnosis' and 'seizure_diagnosis' were considerably less frequent, suggesting these conditions might be under-detected or under-reported. Examining 'rxclms_train' and 'rxclms_holdout', we observed a notable average medication cost, hinting at financial barriers potentially influencing therapy discontinuation. Our analysis also extended to demographic factors, recognizing their potential impact on treatment adherence, though specific race details were anonymized. The EDA not only underscored key data facets and challenges but also illuminated the importance of demographic factors, particularly gender, in therapy adherence. This sets a solid foundation for informed data preprocessing, feature selection, and ultimately, the development of a predictive model adept at identifying at-risk individuals for therapy discontinuation.

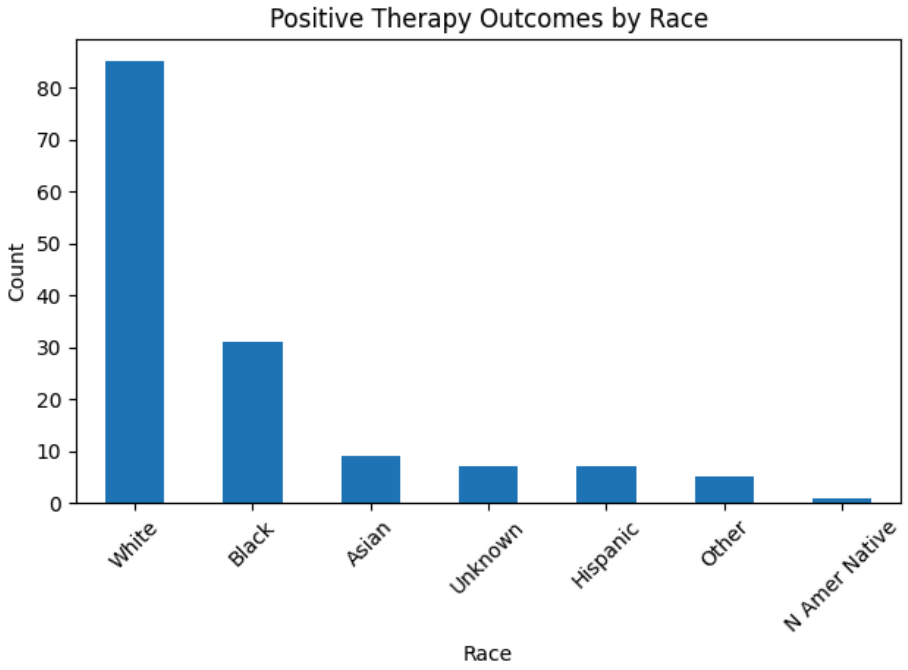

Figure 2: Distribution of positive therapy outcomes across different racial groups

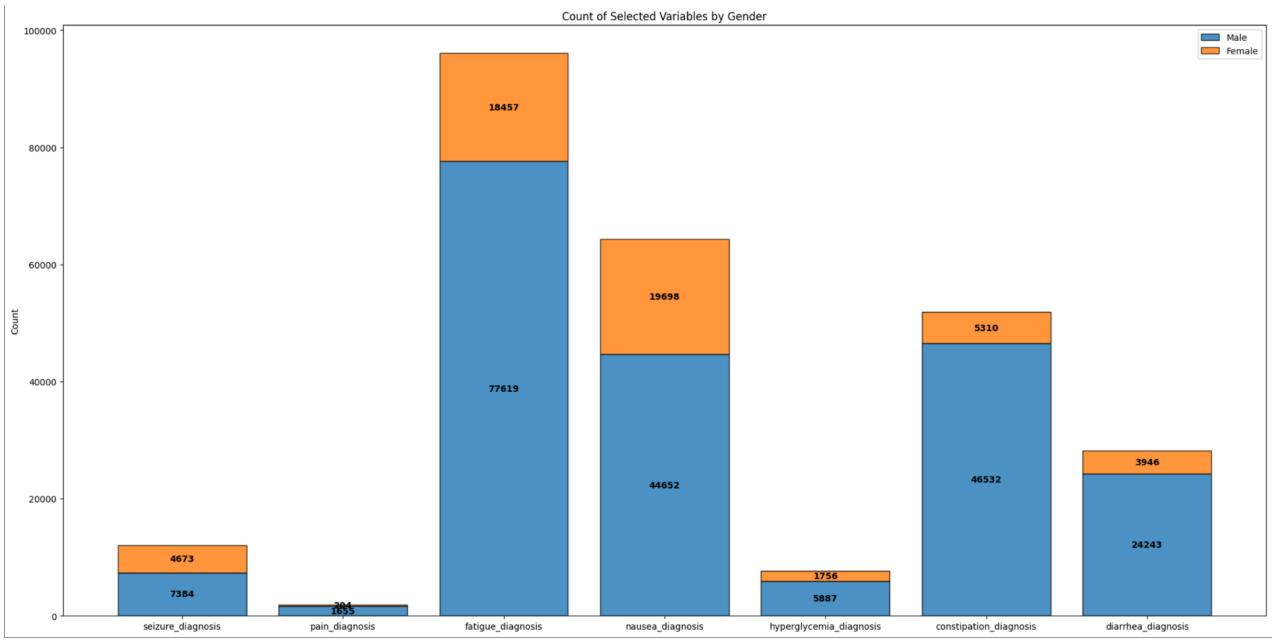

Figure 3: A comparative count of selected ADEs stratified by gender

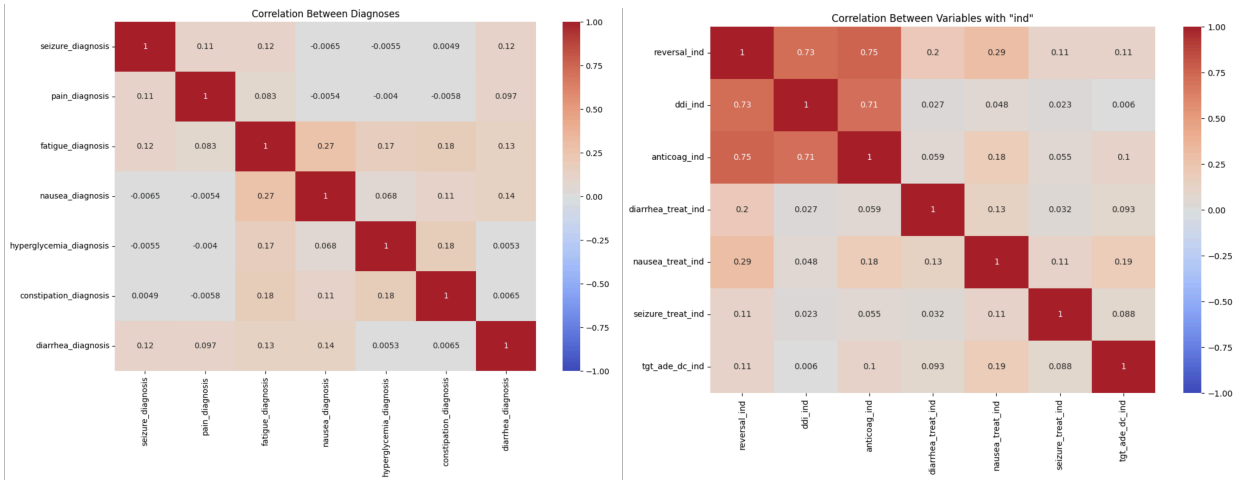

Figure 4: Correlation Coefficients Among Diagnoses. b. Correlations of Variables with 'Ind' Suffix.

Data Cleaning

Clean and reliable data is a cornerstone for creating effective predictive models. Thus, our first task was to delve deep into our datasets and pinpoint areas with missing or inconsistent values. We observed that within the 'target_train' dataset, several variables had gaps, including 'race_cd', 'est_age', 'sex_cd', 'cms_disabled_ind', and 'cms_low_income_ind'. Our review of the 'medclms_train' dataset highlighted further discrepancies, especially in diagnostic codes from 'diag_cd2' to 'diag_cd9', and in variables like 'reversal_ind' and 'util_cat'. Issues in the 'rxclms_train' dataset mainly revolved around drug descriptions and measurements, covering fields such as 'gpi_drug_group_desc', 'gpi_drug_class_desc', 'hum_drug_class_desc', 'strength_meas', and 'metric_strength'.

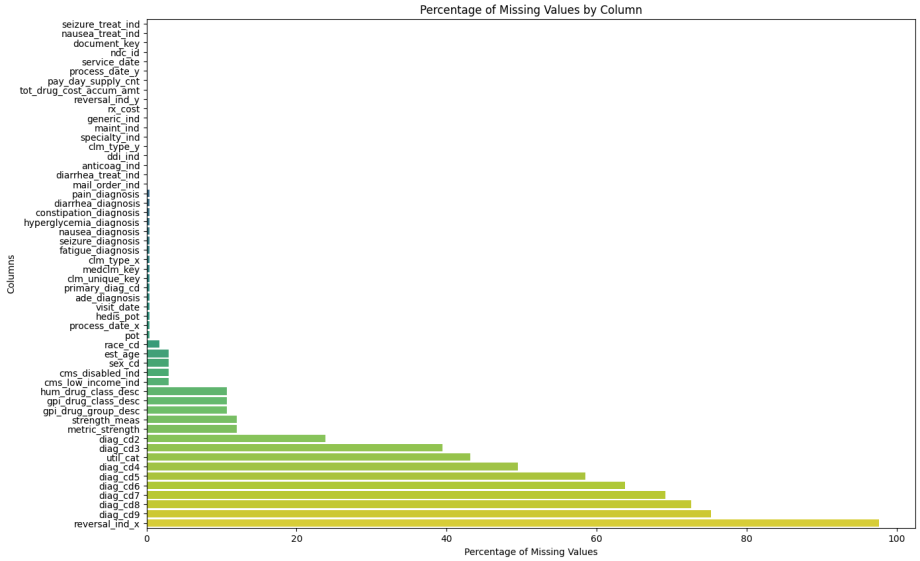

Figure 5: A bar chart illustrating the proportion of data missing in each column.

With the insights from industry best practices, we decided to drop columns where more than 75% of data was missing. For attributes displaying a strong trend (more than 90% similar entries), we filled the missing slots with the most common value or mode. This principle was applied notably to 'cms_disabled_ind' and 'cms_low_income_ind', where we presumed that the bulk of the data points were neither indicative of disabled nor low-income categories. In cases where missing values could shed light on particular patterns or demographics, we opted for a more nuanced approach. Rather than making arbitrary substitutions, we added an auxiliary category named "Unknown" for such instances. This was particularly done for 'race_cd' and 'sex_cd', keeping in mind the potential insights that such non-responses might offer.

Table 1: Strategy for Handling Missing Data

Scenario	**Method Employed**	**Columns Affected**
Over 75% missing	Column Omitted	diag_cd2' through 'diag_cd9', 'reversal_ind', 'util_cat'
Over 90% homogeneity	Mode Substitution	cms_disabled_ind', 'cms_low_income_ind'
Categorical data with missing values	Labeled as “Unkniwn”/”Missing”	race_cd', 'sex_cd'
Continuous data with missing values	Median or Mean Substitution	Median for 'est_age', 'metric_strength'; Mean for 'rx_cost'

Subsequently, we transformed textual categories into numerical values using One Hot Encoding, bearing in mind to retain any inherent order within numeric-seeming categories, like risk assessments. We took special care to maintain consistency while handling the holdout set. For instance, while filling gaps in continuous variables such as 'race_cd', 'est_age', and 'metric_strength', we used median values taken from the training dataset, ensuring a uniform approach.

By being thorough in our data cleaning and preparation process, we've established a solid base for the next steps in our project, ensuring our predictive models will be both accurate and dependable.

Additional Datasets

While we had the option to incorporate external data, we decided against it for the following healthcare-specific reasons:

1. **Anonymity & Confidentiality**: The healthcare data provided was highly anonymized, in accordance with confidentiality standards. Merging with an external dataset, given this level of anonymization, could risk patient confidentiality.
2. **Immediate Usability**: Our aim was to have a model ready for quick deployment. Relying on external sources would require continuous updates and assurance of data quality. The stringent standards of healthcare data made this approach too uncertain.
3. **Time Constraints & Project Focus**: The competition's limited timeframe meant we prioritized creating a robust model with the existing data. The challenges of sourcing external healthcare data, combined with potential NDA processes and confidentiality issues, further justified our approach.

For this project, we felt it best to solely use the provided data to ensure the model's integrity and practicality.

Modeling

Model Approach

After preprocessing the dataset, we initiated the modeling phase by focusing on tree-based ensemble algorithms. Ensemble methods aggregate predictions from multiple models to improve accuracy and mitigate overfitting. Given the data's complex relationships and possible nonlinearities, tree-based algorithms were deemed appropriate. These algorithms can model interactions between features and offer flexibility in capturing complex patterns.

The algorithms selected for exploration were:

- **Light Gradient Boosting Machine (LGBM)**: This is an advanced gradient boosting algorithm that grows trees leaf-wise, prioritizing leaves that result in greater loss reductions.
- **XGBoost**: An implementation of gradient boosted decision trees designed for speed and accuracy.
- **CatBoost**: Designed to handle categorical data, this algorithm can process numerous categories without manual preprocessing and improves its accuracy iteratively.
- **AdaBoost**: This algorithm adjusts observation weights based on the prediction errors of preceding trees, thereby emphasizing harder-to-classify instances.

Table 2: Summary of Tree-based Ensemble Algorithms

Feature/Model	LGBM	XGBoost	CatBoost	AdaBoost
Primary Strength	Leaf-wise growth	Speed & Accuracy	Categorical Data	Emphasizes on Errors
Training Time	Moderate	Fast	Moderate to Fast	Moderate
Handles Missing Data	Yes	Yes	Yes	Often requires imputation
Regularization	Built-in	Built-in	Built-in	Not Built-in
Scalability	Highly Scalable	Highly Scalable	Scalable	Scalable

For hyperparameter optimization, we utilized the Optuna framework. This facilitates an efficient search over hyperparameters by employing stratified k-fold cross-validation. This ensures that each fold retains the same distribution of categorical target values. The primary optimization metric was the AUC-ROC.

Final Model

- **Stacking Classifier**: To harness the capabilities of the individual models, a stacking ensemble method was implemented. The primary models—LGBM, XGBoost, CatBoost, and AdaBoost—generate predictions which serve as input features for a logistic regression meta-classifier, providing a final consolidated prediction.
- **Bagging**: To further enhance the model's accuracy and reduce potential overfitting, a Bagging classifier was incorporated. This method fits multiple versions of the stacking classifier on different subsets of the data and averages the predictions.
- **Calibration**: To ensure the reliability of probability predictions, a Calibrated Classifier was applied to the ensemble. This step calibrates the predicted probabilities, making them more interpretable.
- **Evaluation & Deployment**: Rigorous model evaluation was conducted on a separate validation set using key metrics such as accuracy, AUC-ROC, and a confusion matrix. For deployment purposes, the model, alongside the data scaler, was serialized using `pickle`, allowing for efficient future application on new data.

Modeling Analysis

Model Evaluation

In the context of gauging the predictive capabilities of our model concerning therapy discontinuation due to adverse drug reactions, a meticulous examination of the presented metrics is vital.

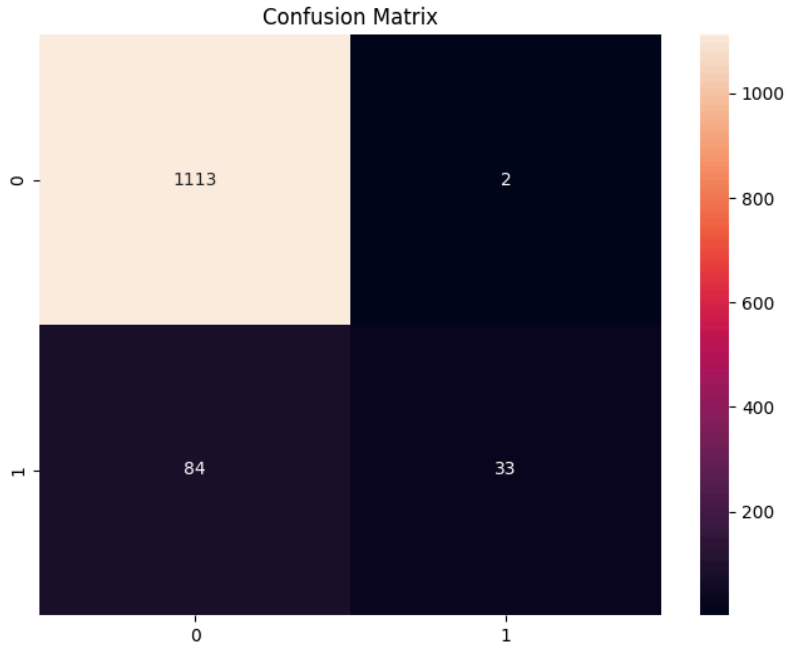

Figure 6: Confusion Matrix displaying actual versus predicted classifications

Figure 6 showcases the Confusion Matrix, which offers an insightful overview of the model's performance in categorizing patients. A notable observation is the correct categorization of 1113 instances as adherent (True Negatives) and 33 as potential discontinuation cases (True Positives). However, there exists an area of concern with 84 discontinuation cases being misclassified as adherent (False Negatives) and 2 adherent instances being wrongly projected as potential discontinuation cases (False Positives). In the healthcare domain, especially in the scope of therapy adherence, False Negatives can be particularly concerning. These instances represent missed opportunities for intervention, potentially leading to decreased patient well-being.

Table 3 highlights few key points with regards to the models evaluation:

Table 3: Classification Metrics Table

Metric	Class 0	Class 1	Average (Macro)	Weighted Average	Overall
Precision	0.96	0.95	0.98	0.97	
Recall	0.92	0.62	0.81	0.96	
F1-Score	0.98	0.77	0.87	0.96	
Support	1115	117			1232
Accuracy					0.96
AUC					0.98

- **Precision**: The high precision values of 0.96 for Class 0 (adherent patients) and 0.95 for Class 1 (predicted discontinuation) underscore the model's capability to produce trustworthy predictions. In a clinical context, such precision is crucial to ensure that interventions, resources, and time are not misallocated.
- **Recall**: While Class 0 boasts an impressive recall of 0.92, Class 1 lags at 0.62. This gap highlights potential challenges in reliably identifying at-risk patients, which, given the nature of our study, is an area warranting attention. An enhanced recall for Class 1 would translate to a more robust early-warning system, facilitating timely and effective clinical interventions.
- **F1-Score**: This metric, encapsulating both precision and recall, presents an F1-Score of 0.98 for Class 0 and 0.77 for Class 1. While the score for adherent patients is commendable, the score for potential discontinuation cases suggests there is room for refining the model's balance between precision and recall for this category.

Furthermore, the overall model accuracy stands at 0.96, reflecting its proficient performance on the dataset. Yet, the emphasis remains on the recall for Class 1. Achieving a heightened recall here is not just a statistical target but a tangible means to optimize patient outcomes and ensure the efficacious deployment of healthcare resources. Given the intricate interplay between the metrics and the real-world implications in the realm of Osimertinib therapy adherence, it is imperative to accentuate the importance of continued model refinement. The data points towards a promising direction, yet with an accent on enhancing Class 1 recall, the model can further align with the nuanced demands of healthcare analytics.

Fairness Diagnostic

Ensuring fairness in data-driven models, particularly in the medical domain, is of utmost importance. Models must be capable of providing just and equitable medical recommendations

irrespective of a patient's protected attributes, such as gender or race. The potential for bias can be heightened by uneven representation or imbalances in the training data.

Upon analyzing our dataset, it's evident that groups such as females and individuals of White ethnicity are more heavily represented than others. This disproportionate representation can influence the model's performance, potentially favoring majority groups.

To quantify fairness in our model, we use the Disparate Impact (DI) metric. The DI is defined mathematically as:

$$DI = \frac{P(Y = 1|D = \text{non-privileged})}{P(Y = 1|D = \text{privileged})}$$

Where:

- Y is the outcome variable (1 for favorable outcome, 0 otherwise)
- D represents the group status (privileged or non-privileged)

Ideally, a DI value of 1 or 100% indicates fairness, meaning both groups have the same probability of receiving a favorable outcome. Significant deviations from this value can indicate bias.

Our model yielded a DI score of 84.45%. While this suggests a reasonable degree of fairness, the 15.55% deviation from the ideal score is noteworthy. Given the imbalances observed in our dataset and the disparate outcomes across genders and racial groups, it's crucial to consider enriching the dataset with more balanced data from underrepresented groups. By addressing these disparities, we can aim for more equitable model outcomes, minimizing inadvertent biases.

Feature Importance

In predictive modeling and data analytics, understanding the significance of each feature or variable is paramount. Feature importance allows us to prioritize the most influential predictors in a dataset, enabling more effective resource allocation and decision-making. Similarly, in business contexts, Key Performance Indicators (KPIs) provide insight into an organization's health and the effectiveness of strategies over time. In this section, we analyze the feature importance from three boosting algorithms—AdaBoost, CatBoost, and LightGBM—and discuss their implications in the context of KPIs.

Feature Importance Analysis

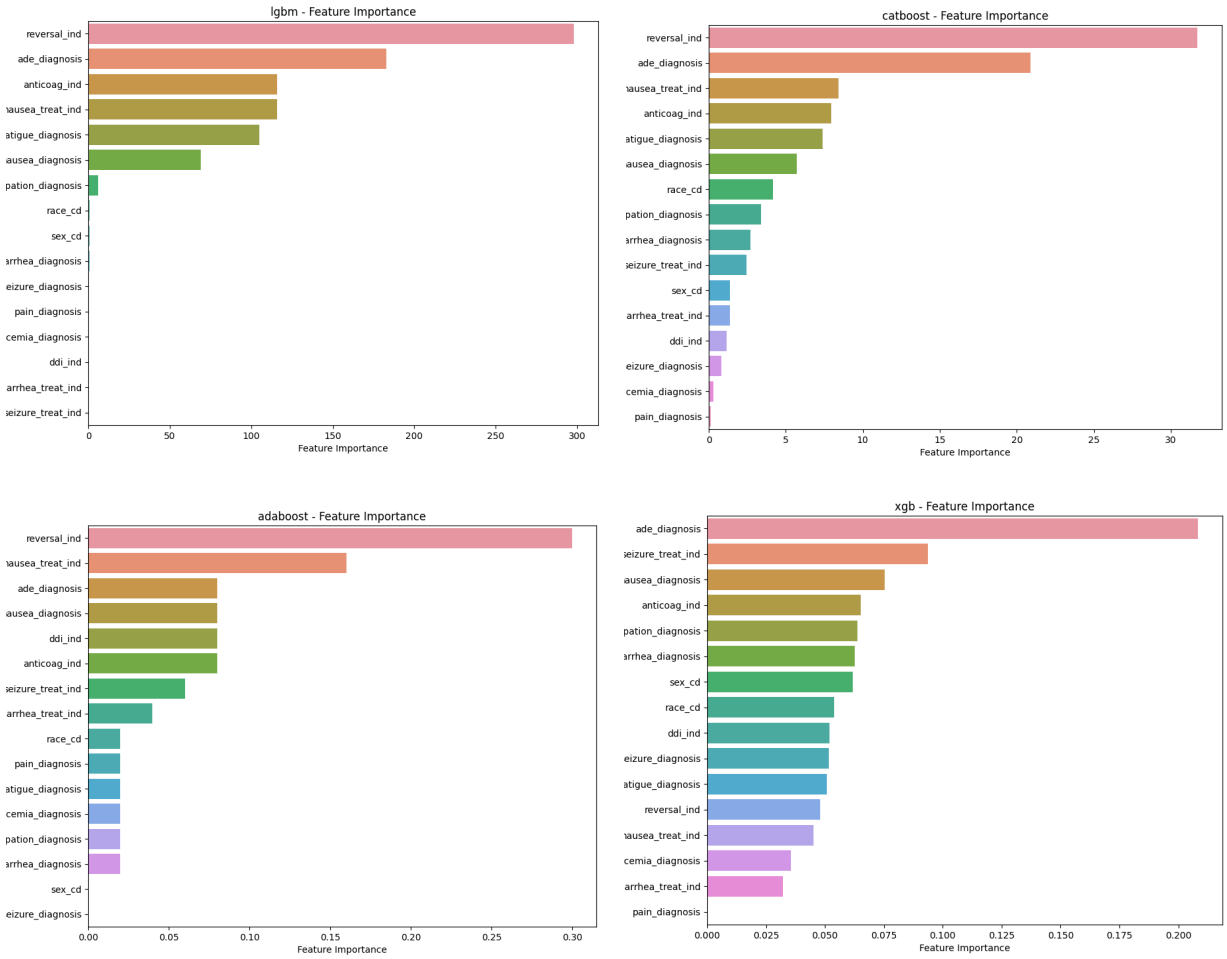

Figure 7: A) LightGBM Feature Importance. B) CatBoost Feature Importance. C) AdaBoost Feature Importance. D) XGBoost Feature Importance

- **Relevance Across Models**: The reversal_ind feature consistently ranks as the most important across all three algorithms. This consistency indicates that this feature holds significant predictive power regardless of the algorithmic nuances.
- **Variability Between Models**: While some features like ade_diagnosis and anticoag_ind maintain consistent importance across models, others show variability. Such fluctuations emphasize the benefit of ensemble methods or considering insights from multiple models for decision-making.
- **Clinical Features**: Features such as nausea_treat_ind, seizure_treat_ind, and pain_diagnosis are vital in the pharmacy claims category, suggesting the significant role of specific conditions and treatments in the predictive outcome.
- **Demographic Insights**: The features race_cd and sex_cd reflect demographic data. Their presence in the top features suggests that demographic factors also play a significant role

in the outcome. However, it's crucial to approach such features with sensitivity and ensure that models do not propagate biases.

KPI Analysis

- **Relevance to Business Goals**: KPIs such as customer retention rate, revenue growth, and customer satisfaction might be indirectly influenced by the high-ranking features. For instance, if reversal_ind relates to a claim reversal, it might impact customer satisfaction and trust levels.
- **Operational Efficiency**: If certain features indicate areas where operational improvements can be made (e.g., reduced claim reversals), these can be prioritized as KPIs. Improving on these metrics might lead to better organizational efficiency and customer experience.
- **Monitoring Over Time**: The importance of a feature or KPI can evolve. It's crucial to periodically revisit the feature importance and KPIs to ensure alignment with current business objectives and challenges.

Understanding feature importance offers a clear lens into which variables drive predictions and, by extension, business outcomes. By aligning the most influential features with relevant KPIs, organizations can make informed decisions, allocate resources more efficiently, and pivot their strategies to meet evolving challenges.

Business Analysis And Recommendations

Osimertinib, a groundbreaking medication in the realm of oncology, has provided renewed hope for patients battling a particularly aggressive form of lung cancer known as non-small cell lung cancer (NSCLC). As a targeted therapy, Osimertinib has demonstrated remarkable efficacy in treating NSCLC patients with specific genetic mutations, primarily the epidermal growth factor receptor (EGFR) mutation. This drug has not only extended the lives of countless individuals but also significantly improved their quality of life. However, amid the optimism surrounding Osimertinib's success, there exist significant challenges posed by Adverse Drug Events (ADEs). These unintended and sometimes harmful effects of Osimertinib and other chemotherapy drugs raise important concerns for both patients and healthcare providers. We identified targeted groups from the patients who suffered ADEs, risks surrounding a patient given an ADE and the underlying impacts and business challenges for Humana. We then tried to conclude optimal actions that benefit both the patient's life-expectancy and Humana's business interests.

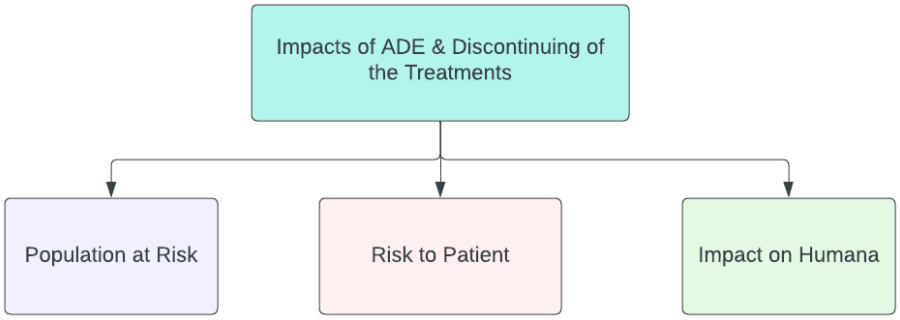

Figure 8: Areas of focus on approaching the impact of ADE and prevention of discontinuation the Osimertinib treatment

Population at Risk

In our detailed exploration of data and subsequent modeling, a specific demographic group – Caucasian females – emerged as notably high-risk for therapy discontinuation due to Adverse Drug Events (ADEs). The intricate nexus of genetic predispositions, hormonal variations, and sociocultural factors compounds the complexity of their treatment landscape. Addressing the unique needs and challenges of this demographic is not merely a statistical necessity but a moral imperative that aligns with the ethos of personalized, equitable healthcare.

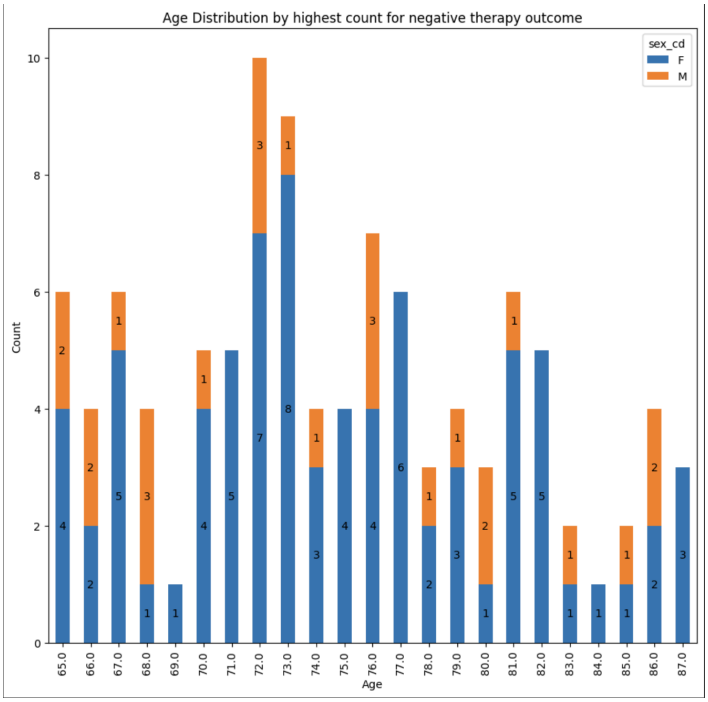

Figure 9: Most frequent age distribution between gender of therapy that were negative

Our model unveiled nuanced insights, painting a comprehensive portrait of the heightened vulnerabilities of Caucasian females to ADEs. Certain pharmacogenomic interactions and hormonal influences can potentially accentuate the intensity of ADEs, resulting in a higher propensity for treatment discontinuation. Moreover, sociocultural dynamics, including caregiving responsibilities and societal roles, can sometimes impact the prioritization of personal health and well-being.

Discontinuing the Osimertinib treatment puts patients at risk

Discontinuing osimertinib after treatment can lead to a significant drop in survival rates, as demonstrated by the 10% differential between osimertinib-treated patients and those on a placebo[6]. Moreover, discontinuing osimertinib may result in earlier disease relapse or progression. This could increase medical expenses for both healthcare systems and insurance providers, due to the intensified treatments and interventions needed for patients who relapse. Consequently, this subjects patients to potential financial strain.

Many side effects can be effectively managed. For instance, for mild rash or skin issues, patients can enhance fluid consumption, moisturize post-shower, steer clear of products that dry the skin, apply hydrocortisone for itch relief, and use mild cleansers for acne. To manage nausea, doctors can prescribe anti-nausea medications. Consuming frequent, smaller meals, embracing

[6]Phillips, Carmen. (2023, July). "*Lung Cancer Trial of Osimertinib Draws Praise—and Some Criticism*."

natural remedies, taking deep breaths, and improving ventilation can also help combat nausea. For anemia, regular blood tests are conducted for monitoring. Furthermore, healthcare experts can provide diverse solutions and recommend appropriate medications to tackle a range of side effects[7]. Abandoning the treatment due to controllable adverse effects is not recommended, especially since osimertinib has been scientifically validated to be highly effective against lung cancer.

ADEs & Discontinuing the Osimertinib treatment harms Humana

The decision to discontinue Osimertinib treatment has a direct negative impact for Humana as a health insurance company.

As previously discussed, ceasing Osimertinib treatment poses significant health risks to patients, thereby placing Humana at risk of managing a rising number of untreated insurance subscribers. This could lead to several challenges for Humana.

- **Increased Healthcare Costs:** ADEs can result in hospitalizations, additional medical procedures, or emergency care. When clients drop out of treatment due to ADEs, it can lead to higher healthcare costs for insurance companies, especially if the client's condition deteriorates, requiring more intensive and expensive interventions. It amplifies Humana's financial burden, as the company would need to cover subsequent treatments for adverse drug events (ADEs) and potential relapses. Specifically, insurance plans that include Osimertinib coverage might experience an increased utilization rate.
- **Impact on Premiums:** If there is a pattern of clients dropping out of treatment due to ADEs, it may lead to increased claims and healthcare costs for the insurance company. To cover these higher costs, Humana might need to raise premiums for all clients, potentially making insurance less affordable for everyone, hence making Humana less competitive in the market.
- **Reputation and Customer Satisfaction:** If clients experience ADEs and drop out of treatment while under Humana's coverage, it can negatively impact Humana's reputation and customer satisfaction. Clients may perceive Humana as unresponsive or uncaring if they feel they did not receive adequate support in managing ADEs.
- **Impact on Market Presence:** Furthermore, Humana invests resources in upholding its healthcare network and forging contracts with healthcare providers and pharmaceutical companies. A decline in Osimertinib treatment subscribers could compromise the efficiency of this network and erode market presence.
- **Risk Assessment and Underwriting Challenges:** A high rate of clients dropping out of treatment due to ADEs can complicate risk assessment and underwriting processes. This might bring on additional cost and labor for Humana and subsequently impact coverage terms.

[7]Omopariola, Damilola., Weiser, Patricia. (2023, May). "*Tagrisso side effects: What you should know*."

- **Potential Legal Liability:** There is a chance that patients suffering from ADEs lead to legal actions against healthcare providers or pharmaceutical companies. If Humana is involved in these legal proceedings, it can result in financial liabilities, legal expenses, and reputational damage.

Approaches to reduce discontinuation of Osimertinib treatment

We have developed available approaches for Humana to encourage patients to continue the Osimertinib treatment and prevent the risk raised by discontinuation of the Osimertinib treatment. The overall goal is to leverage our data and analytics to target members at risk, encourage medication adherence to allow oncology patients to live longer, fulfilling lives. We are also introducing risk mitigations methods that could help Humana operate at lower financial, legal and operational risks, which also ensures oncology patients with stable, competitive and high quality plans.

Encourage Medication Adherence:

- **Patient Education and Support:** Ensure patients are well-informed about the benefits of continuing treatment, the potential risks of discontinuation, and the manageable nature of many side effects[8].
- **Integrated Care Models:** Develop integrated care models that incorporate medication management into the overall treatment plan. Collaboration between insurance companies, healthcare providers, and pharmacists can improve coordination and adherence.
- **Medication Therapy Management (MTM):** Offer MTM services to patients, which involve medication reviews and consultations with pharmacists to address any concerns, side effects, or interactions[9].
- **Coverage of Symptomatic Treatments:** Expand insurance coverage to include treatments or therapies that help manage or mitigate the side effects of Osimertinib,
- **Financial Incentives:** Offer reduced copays or premiums for patients who adhere to their Osimertinib treatment regimen, providing a financial motivation to continue therapy.
- **Telemedicine and Remote Monitoring:** Offer telemedicine services where patients can quickly consult with healthcare professionals about side effects without the need for physical visits. This ensures timely advice and intervention.
- **Feedback and Follow-Up:** Continuously monitor and provide feedback to patients on their medication adherence progress. Use automated reminders or personal outreach to check in on their status and offer support when needed.

[8] Paterick, T. E., Patel, N., Tajik, A. J., & Chandrasekaran, K. (2017, January). *Improving health outcomes through patient education and partnerships with patients*. Proceedings (Baylor University. Medical Center).
[9] Ferreri, S. P., Hughes, T. D., & Snyder, M. E. (2020, April 2). *Medication therapy management: Current challenges*. Integrated pharmacy research & practice.

- **Pharmacy Networks:** Collaborate with pharmacy networks to ensure easy access to medications and promote adherence through medication synchronization, medication packaging, and adherence support services.
- **Real-Time Prescription Monitoring:** Implement systems that track real-time prescription fills and refills, allowing for early intervention when patients miss refills.
- **Data Analysis and Predictive Modeling:** Use data analytics and predictive modeling to identify individuals at risk of therapy dropouts or non-adherence. Target interventions, such as personalized reminders or additional support, to these high-risk members.

Risk mitigations:

- **Tiered Premiums or Incentives:** Introduce a tiered premium structure where patients who adhere to their treatment plan benefit from reduced premiums. This could motivate patients to continue treatment.
- **Separating the Risk Pool:** Publishing a new policy assigned to patients who are highly likely to opt out of the treatment, offering different premium and medical coverage according to their medical needs.
- **Collaborative Care Plans:** Work in tandem with healthcare providers to develop a care plan that is holistic. This might include regular reviews of the patient's progress, side-effect management, and psychological support.
- **Pharmacy and Provider Collaboration:** Foster close collaboration with pharmacies and healthcare providers to ensure a comprehensive view of a patient's medication regimen. This can help identify potential ADE risks and provide early intervention.
- **Prior Authorization Protocols:** Implement stringent prior authorization requirements for high-risk medications to ensure they are prescribed appropriately and with a focus on patient safety.
- **Medication Reconciliation:** Promote the use of medication reconciliation during transitions of care to minimize the risk of errors and ADEs. This can involve checking and verifying the patient's medication list and resolving discrepancies.
- **Legal and Regulatory Compliance:** Ensure compliance with relevant legal and regulatory requirements related to medication safety and ADE reporting.

Recommended Approach for Humana

We advocate for an integrated approach leveraging Data Analysis and Predictive Modeling to target populations at risk and implement our recommended methods to encourage medication adherence plus conducting the risk mitigations. This triad ensures that patients are both well-informed and adequately equipped to handle any Adverse Drug Events (ADEs) during their treatment, maximizing convenience and minimizing both costs and preventable ADEs.

Importantly, this approach operates autonomously, allowing Humana great agility in risk management and swift operational adjustments.

By this means, Humana can deeply embed itself within the patient's treatment journey, maintaining constant communication with those undergoing Osimertinib treatment. By providing vital information and resources, Humana not only motivates patients to persist with their regimen but also underscores its patient-first ethos, solidifying its reputation as a patient-centric insurer.

Risk Pool Segmentation ensures that insurance remains affordable, thereby reducing the financial strain on policyholders and offering Humana a competitive edge in the insurance landscape. A specialized policy catering to potential insurers who are inclined to abandon treatment can be fine-tuned to their unique requirements without affecting other policyholders. We can also target populations who are already policy holders and focus on extra care and education to minimize the probability of them opting out, offering specialized coverage or riders for ADE-related expenses to provide financial protection to clients. Policies could be tailored for those experiencing specific side effects like Nausea or Fatigue during their Osimertinib course - factors our model identifies as significant predictors of treatment cessation. Through such targeted policies, Humana can better address the health needs of its clientele while adeptly managing the risks associated with Osimertinib treatment discontinuation.

A Vision for Equitable, Informed Care

By honing in on the unique needs of Caucasian females at high risk, we transcend generic healthcare provision, entering a realm of personalized, equitable care. Each strategic initiative, rooted in comprehensive data analysis, is a stride towards a future where healthcare is not a blanket solution but a personalized journey. In this envisioned paradigm, every patient, regardless of their demographic or risk profile, receives the nuanced, informed care essential for optimal health outcomes and holistic well-being.

In this light, the data becomes more than numbers and patterns – it transforms into a catalyst for change, driving a healthcare revolution where equity, personalization, and informed care converge to redefine the patient experience. Every intervention, policy, and initiative inspired by this data is a testament to the power of integrative, informed care – where every patient is seen, heard, and valued in their uniqueness.

Expected Value for Humana

Our business proposals, designed to enhance patient outcomes and optimize operational efficiencies, are poised to deliver significant value to Humana. These initiatives, anchored in

comprehensive data analysis and predictive modeling, aim to mitigate the financial and health risks associated with Osimertinib treatment and its potential Adverse Drug Events (ADEs). Our analysis reveals that the total medical claim costs related to ADEs stand at a staggering $158,715,000, complemented by additional drug costs of $79,174,107.22, amounting to a combined potential expense of $237,889,107.22. By implementing the strategies we advocate — encompassing patient education, integrated care, real-time monitoring, and advanced data analytics — we anticipate a reduction in ADE-related therapy discontinuations by 25%. This strategic foresight is projected to yield substantial savings of approximately $39,678,750.

Here's the detailed rationale behind these values:
1. Patient Education and Support: Empowering patients with knowledge and continuous support is expected to decrease ADE-related medical visits and associated costs. Educated patients, aware of how to manage side effects, are less likely to seek emergency medical interventions, directly reducing a portion of the projected $158,715,000 in ADE-related expenses.

2. Integrated Care and Real-Time Monitoring: These initiatives are pivotal in sustaining Osimertinib treatment adherence. By averting treatment discontinuation, we prevent the subsequent and often more severe costs linked to disease progression and potential relapse, which are considerably higher than ongoing treatment expenses.

3. Data Analysis and Predictive Modeling: Leveraging these techniques enables the early identification of patients at high risk of ADEs or treatment discontinuation. Early interventions not only enhance patient outcomes but also curtail the potential $158,715,000 in medical claims costs related to ADEs.

The following table breaks down the calculated financial implications:

Table 4: Financial Overview of the Anticipated Impact of Proposed Strategies on Humana

Metric	Amount
Total Medical Claim Cost for ADEs	$158,715,000
Total Drug Cost	$79,174,107.22
Total Cost (Medical Claims + Drug Cost)	$237,889,107.22
Expected Savings (25% reduction in ADEs)	$39,678,750

These values were derived from a detailed analysis of current costs borne by Humana, including medical claims related to ADEs and the cumulative drug costs for patients. The expected savings are calculated based on a 25% reduction in ADEs, a conservative estimate grounded in the anticipated efficacy of our proposed interventions.

In essence, the value proposition extends beyond immediate cost savings. It represents Humana's strategic shift towards a holistic, patient-first model, where healthcare is not only reactive but also proactive, personalized, and preemptive. This comprehensive approach not only augurs financial prudence but also fortifies Humana's standing as a pioneer in technologically integrated, patient-centric healthcare.

Conclusion

Discontinuing Osimertinib treatment can result in challenges such as cancer recurrence, disease progression, squandered healthcare resources, and increased business costs. By learning the demographics of patients who tend to discontinue treatments, educating patients about the significance of Osimertinib treatment and the feasibility of managing ADEs, coupled with offering essential support, both Humana and its insurance subscribers can benefit. Combined, we can ensure to keep contributing to the broader medical industry and human well being.

Appendix

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