Humana

Improving Adherence to Osimertinib in Patients with Adverse Drug Events

Humana - Mays Healthcare Analytics Competition - 2023

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1 Executive summary

While doing research for this report, we learned that cancer is a journey that is unique for every patient. Some journeys see a betterment due to the support from the health care system, whereas some journeys end abruptly with a significant loss of life. As part of this analysis, we tried to understand such journeys for patients in TAGRISSO® (Osimertinib) therapy, which is used to treat non-small cell lung cancer with EGFR + mutation. Studies have found that Osimertinib decreases the mortality risk and cancer recurrence risk for the patients significantly. However, a few patients face adverse drug events like fatigue and nausea during this therapy, and later drop out of treatment prematurely, leading to this drug becoming ineffective. But many such cases, if identified early, could have been managed with the intervention plans like the one we proposed in the recommendations section of this report.

We were given a dataset that contained mediclaims and pharma claims for 1232 Humana members in Osimertinib therapy, out of which 117 patients dropped out prematurely and had a reported ADE during the therapy. We calculated the sum of prescription costs for the Osimertinib claims (NDC IDs 310134930, 310135030) for the target group of these 117 patients and noticed that around $5 million worth of Osimertinib medicine failed to have its intended impact because of the non-adherence. As a health insurance provider for these patients, Humana bears a major chunk of this monetary loss, indicating that the impact of medicinal non-adherence extends beyond the scope of patients; it impacts the entire health care system. While non-adherence is a complex behavior which couldn't be captured in simple patterns, we gave it our best shot by analyzing the claims data to understand the patterns among the target group of patients and reviewing the supporting literature to ensure that the patterns we found from data are backed by the research.

One of the important insights we learned from this data early on was that the target group consists of two types of patients – those who drop out early due to the factors which existed before the therapy, and those who drop out after showing some initial adherence, mostly because of the difficulties in managing their complicated health conditions. This made us build two separate models at pre-therapy and therapy phases to separate the two groups and provide a tailored solution to each of them instead of a one-size-fits-all solution. To make sure that the patterns generated by these models are not influenced by the bias towards any race or gender group of patients, we implemented safeguards by including disparity score as one of the metrics for model selection at each phase.

Finally, based on the patterns learned by these models, we provided an actionable and time-based plan Humana could use to make a difference in the therapy outcomes of these patients.

2 Case Context

2.1 Case Background

The American Cancer Society reports that 1 in 16 people will be diagnosed with lung cancer in their lifetimes. This stat becomes even more concerning when considering that lung cancer has the highest mortality rate among all cancer types[1]. About 85% of these lung cancers fall into a category known as 'Non-Small Cell Lung Cancer'[2]. A distinctive feature of cancers in this category is their slow growth, often remaining hidden until they reach advanced stages. This cancer is sometimes caused due to a mutation in EGFR protein of Cancer, which makes the cells grow uncontrollably. This is named 'EGFR + mutation'[3].

Osimertinib (Tagrisso):

Osimertinib, a third-generation drug to treat the EGFR + mutation, was approved for medical use in the US in 2015 [4]and it has become a standard therapy for early-stage cancers where risk of relapse is high[5]. Osimertinib is also used to treat Stage IV cancer, which has spread beyond the original site. Studies have proven Osimertinib's efficiency in increasing the survival rate and decreasing the risk of cancer recurrence among the patients with EGFR + mutation.

Adverse Drug Events of Osimertinib:

Adverse Drug Events (ADEs) for a medication are the harmful side effects (anticipated and unanticipated) caused by the usage of that medication. Osimertinib is known to cause side effects, including but not limited to fatigue, nausea, diarrhea, constipation, and skin rashes.

2.2 Problem Understanding

As a renowned health care company, Humana is carving the path by helping cancer patients improve their treatment outcomes with various programs. But a major portion of these outcomes depend on a patient's adherence to the treatment. In the case of Osimertinib therapy, adverse drug events caused by the medicine make adherence a difficult task for the patients.

We tried to understand the prevalence of medicinal adherence problem in general, and how it affects the Osimertinib therapy, and found below problems that concern Humana directly:

1. **Failure to adhere to the treatment could increase the overall medical costs for patients in Osimertinib therapy:**

In United States, 50% of treatment failures, around 125,000 deaths, and up to 25% of hospitalizations each year[6] are attributed to the non-adherence of patients to the medication. This was estimated to have an overhead medical cost of about $100 billion per year. When patients drop out of Osimertinib therapy prematurely, it might increase the overhead expenses for that group of patients in the long run.

[1] Lung Cancer Facts 2023 https://www.lungcancerresearchfoundation.org/lung-cancer-facts/
[2] What is Luncg Cancer https://www.cancer.org/cancer/types/lung-cancer/about/what-is.html
[3] EGFR-mutated non-small cell lung cancer https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4694955/
[4] U.S. Food and Drug https://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/208065Orig1s000TOC.cfm
[5] National Cancer Institute https://www.cancer.gov/news-events/cancer-currents-blog/2023/osimertinib-lung-cancer-adaura
[6] Medication Adherence Elephant in the room https://www.uspharmacist.com/article/medication-adherence-the-elephant-in-the-room

2. Wastage of Osimertinib medicine:

Every year, medicinal drugs worth billions of dollars are wasted in the United States due to medicinal wastage, and half of it is attributed to the medicinal non-adherence of patients[7]. In addition to the financial wastage, premature discontinuation of Osimertinib therapy not only squanders the millions invested in its development but also risks the wastage of a potentially life-saving medication.

3. Increased risk of cancer recurrence:

Studies have shown that 45 to 76% of Non-Small Cell Lung Cancer patients who had surgery alone or surgery followed by chemotherapy will see their cancer return within 5 years[8]. But using Osimertinib for adjuvant therapy has proved to decrease this chance of cancer recurrence. Therefore, prematurely discontinuing Osimertinib therapy will result in a reduction of these benefits for patients and an increased risk of cancer recurrence. This will not only raise medical expenses but also worsen the health of patients.

If patients could be provided proper support to manage the adverse drug events of Osimertinib, adherence to therapy could be increased, which improves the patient's quality of life in the long run. Therefore, the main objective of this analysis is to help Humana understand the factors that go behind a patient's decision in discontinuing the therapy when they have a reported history of ADEs during their therapy duration.

3 Data Understanding

Training and holdout datasets:

We were provided with the data for 1232 Humana members in Osimertinib therapy. Each member had a flag indicating whether they stopped therapy within 6 months and had a reported ADE at some point during the therapy. We used this data to train the models for analyzing the relationship between the various patient-level variables and the flag indicator. Additionally, we had a separate holdout dataset with approximately 470 patients for evaluating the model's performance. In both the training and holdout datasets, there were three tables with different granularities, as described below:

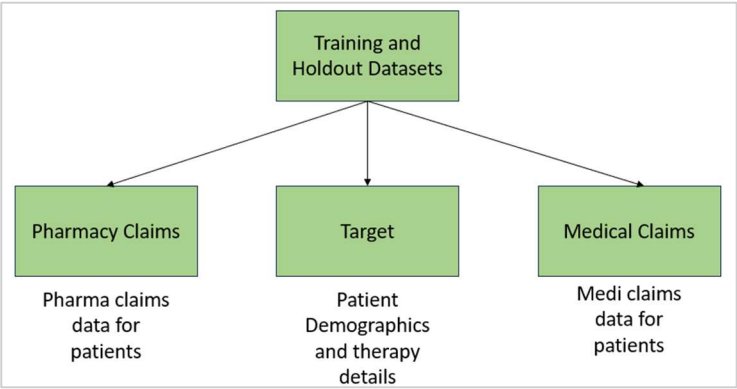

Figure 3.1.1: Three Tables in the Dataset

[7] "Don't let medicines go to waste" https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7485414/
[8] Adjuvant treatment of stage 1B (tumor is 4 cm or larger), 2, or 3A NSCLC https://www.keytruda.com/non-small-cell-lung-cancer/treatment-options/adjuvant/

Target variable for the analysis:

The flag indicator mentioned in the previous section is the main target variable for the analysis. This indicator can take values of either 0 or 1, and the below visualization gives the therapy scenarios for each of the two values for this flag indicator.

	Description	Flag indicator	Number of Patients
Target Group	**Discontinued therapy** prematurely and had an **reported ADE(s)** during the therapy	**1**	**117**
Non - Target Group	**Continued therapy** for 6 months	0	1115
Non - Target Group	**No reports of ADE(s)**, but **discontinued therapy** prematurely before 6 months.	0	

Figure 3.1.2: Therapy Scenarios for Target and Non-Target Groups

The group of patients with a flag indicator value of 1 is our primary focus, and we'll refer to them as the "***Target Group.***" On the other hand, patients with a flag value of 0 are considered the "***Non-Target Group".*** Among the 1232 patients in the training dataset, 117 were in the target group. This means there's a baseline rate of 10% in the entire dataset, which closely matches the 13% baseline rate reported in the ADAURA clinical trial for patients discontinuing Osimertinib therapy because of ADEs[9].

Target table:

The Target table is one of three tables present in both training and holdout datasets. It contains patient-level information such as therapy start and end dates, flag indicator for therapy discontinuation, demographics and indicators sourced from the CMS Federal Agency.

Race and gender variables:

The chart below shows the uneven distribution of race and gender among the patients in the dataset.

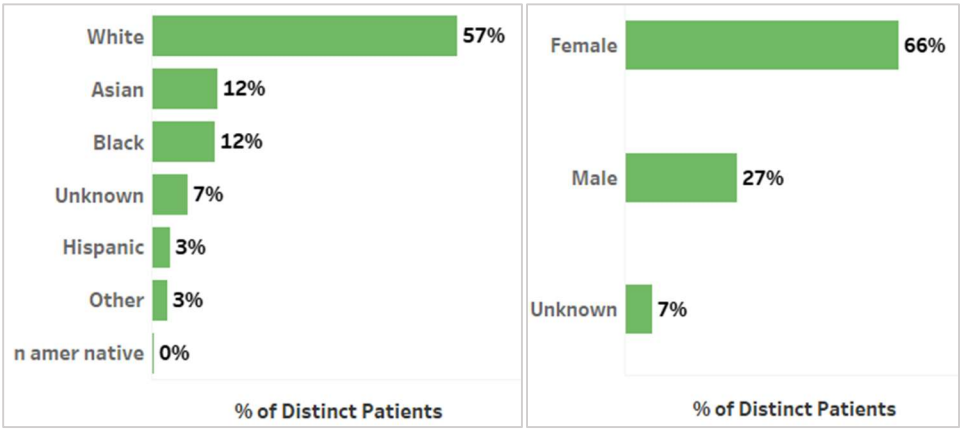

Figure 3.1.3: Distribution of Race and Gender of Patients in a Dataset

[9] The ADAURA trial investigated the use of Osimertinib (Tagrisso) as adjuvant therapy for early-stage non-small cell lung cancer (NSCLC) with specific EGFR mutations https://www.cancer.gov/news-events/cancer-currents-blog/2023/osimertinib-lung-cancer-adaura

Patterns in the Therapy Duration for Target Group:

The visualization below indicates that the highest number of therapy discontinuations from the target group happened within the first 30 days of therapy.

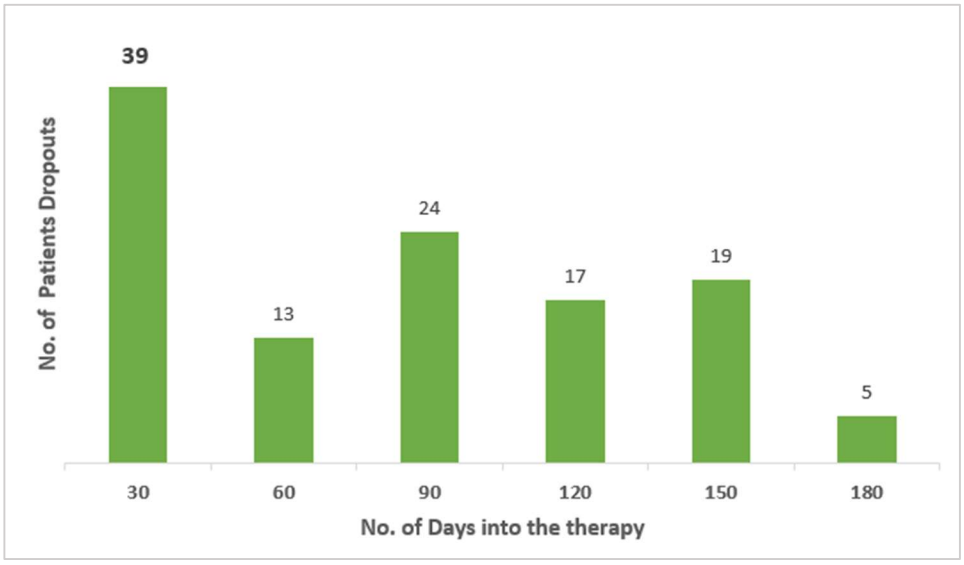

Figure 3.1.4: Number of Target Group Patients Dropping out of Therapy

Mediclaims table:

The Mediclaims table contains the medical claims data of patients, covering the period from 90 days before the start of Osimertinib therapy to the end of therapy. It contains details like ICD 10 diagnosis codes, visit dates, utilization category, and indicators for the specific ADE diagnoses of Osimertinib.

Number of medical Claims for ADE-Related Conditions:

Among all the ADE-Related claims in the data, fatigue and nausea are more common, whereas Seizure and Pain are less common.

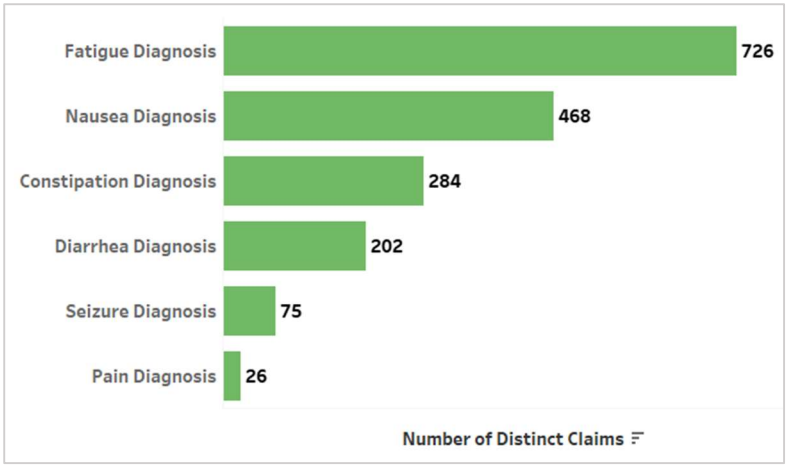

Figure 3.1.5: Distribution of ADE related Diagnoses in Medical Claims

Distribution of utilization categories among the medical claims:

Outpatient and Physician Office are the most common utilization categories as per the below distribution.

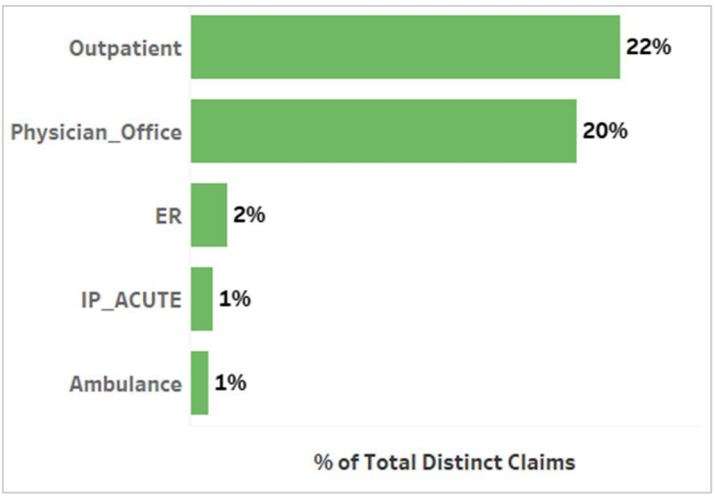

Figure 3.1.6: Distribution of Utilization categories in Medical Claims

Pharma claims table:

The Pharma claims table contains the Pharmacy claims data of patients, covering the period from 90 days before the start of Osimertinib therapy to the end of therapy. It contains details like NDC IDs for the claim, pay day supply, drug cost, and indicators for generic and maintenance drugs.

Distribution of Pay day Supply among the claims:

Payday Supply refers to the quantity of medication provided to a patient. It is measured in terms of the number of days for which the medication is expected to last. Based on the below distribution, we can see that most claims in the dataset have a Payday Supply of one month or shorter.

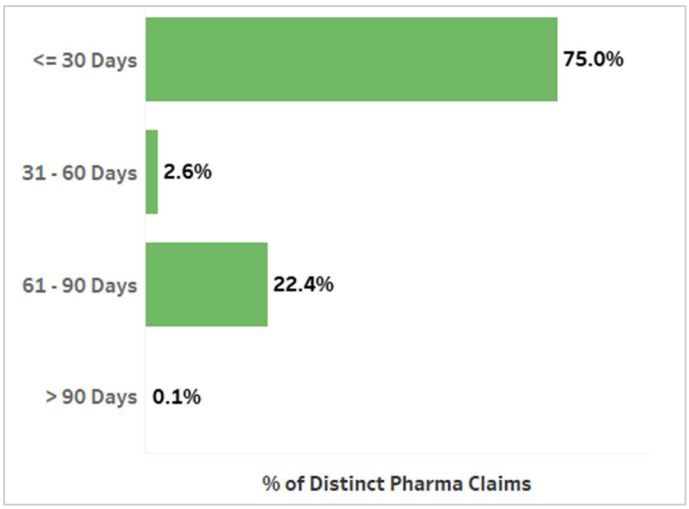

Figure 3.1.7: Distribution of Pay Day Supply of Drugs in Pharma Claims

Osimertinib in Pharma Claims:

We have identified that drugs with NDC IDs 310134930 and 310135030 represent Osimertinib. Osimertinib is the most expensive drug among all those available in pharma claims.

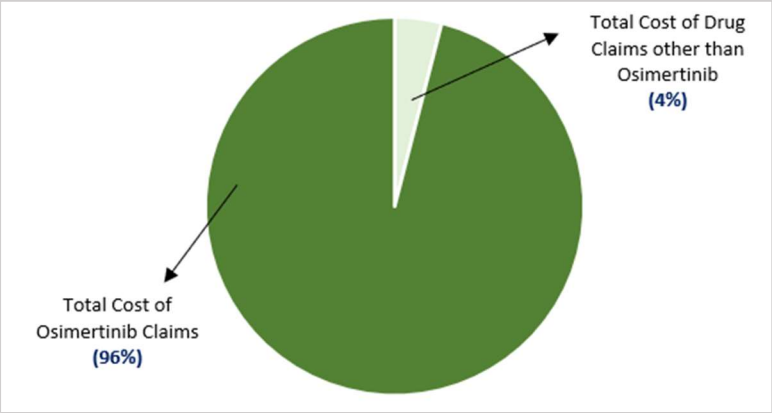

Figure 3.1.8: % Breakdown of Drug Costs in Pharma Claims

Master table:

We took the below steps for creating a single master table from the three individual tables:

1. Aggregated the mediclaims and pharmaclaims data, and changed them to be at the patient level
2. Joined the aggregated tables with the patient-level Target table using the therapy_id column.

The common link among the three tables was the 'therapy_id,' which is a combination of a unique patient identifier and the therapy name (e.g., “1115389643-TAGRISSO-1”).

Once we joined the tables, we noticed an interesting pattern in the data as shown below:

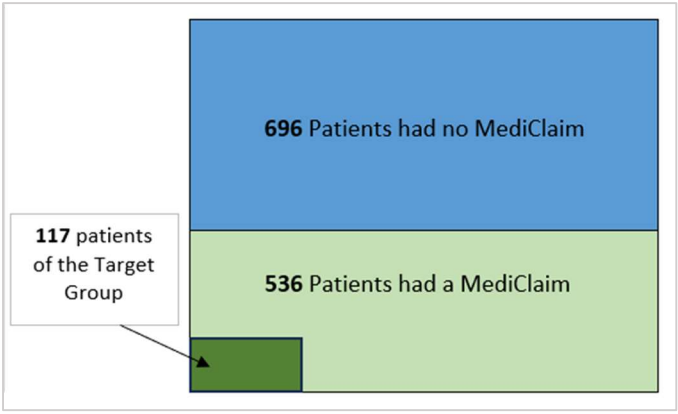

Figure 3.1.9: Patients with a Mediclaim vs Patients without a Mediclaim

We noticed that the 117 patients of target group were concentrated within a small subset of the 536 patients who had at least one Mediclaim in the data.

4 Modeling

4.1 Data Cleaning

After joining the three tables and doing some exploratory analysis, we noticed a few issues which were addressed in following ways:

1. **Data leakage in the training dataset:**

The training data provided includes complete patient journey (3 months of claims before the therapy started and 6 months of claims after the therapy started). To prevent the model from learning the therapy end date for each patient by looking at their behavior in the final stages of treatment, we removed the claims from the last few days of the dataset using the following dynamic cutoff duration rule.

Duration of claims for a patient	Cutoff duration
< 10 days after therapy start	No claims were dropped
11 - 45 days after therapy start	The claims for last 5 days were dropped
46 - 75 days after therapy start	The claims for last 15 days were dropped
> 76 days after therapy start	The claims for last 30 days were dropped

Figure 4.1.1: Dynamic Rule for cutting off the claims before Therapy End

2. **The patients with no records in both mediclaims and pharmaclaims tables:**

In the training dataset, there were 59 patients who didn't have any records in either the mediclaims and pharmaclaims tables. Since we are building models to extract patterns from the claims data, this could skew the results of the models. Therefore, we excluded them from the training data, reducing our dataset from 1232 to 1173 patients.

3. **Preventing disparity in the model due to the presence of race and gender variables in training data:**

As shown in Figure 3.1.3, we do not have an equal or at least a comparable number of records for different race and gender groups of patients. Using such variables directly to train the model could induce a bias towards underrepresented classes in the data. To mitigate this disparity problem, we initially considered the following three alternatives:

1. Oversampling the patient-level data from underrepresented race and gender groups in the training data of the model.
2. Creating separate models for the individual groups based on each combination of race and gender categories. This approach allows us to gain insights into the behaviors of the at-risk target group at a more granular level, thereby removing any potential bias.

3. Removing the race and gender data of patients from the model by dropping these variables from the training data.[10]

We attempted the first alternative of oversampling the minority classes in the training data and building the model. However, we later realized that the model overfitted to the training data, making it difficult to interpret any insights. We couldn't pursue the second alternative due to insufficient records to train a model for each group. Therefore, we determined that the third alternative of dropping race and gender variables from the training data was our best option for addressing bias in the model and proceeded with it.

However, we were aware that dropping the race and gender variables does not eliminate the problem of disparity completely. There could be underlying conditions from medical claims or drugs from pharma claims that might act as proxies for race and gender. Therefore, we conducted sanity checks on the predictions of the models by interpreting their important variables to ensure that no significant bias had crept in from the underlying claims data.

4. Missing values in the demographic variables in the target dataset:

As shown in Figure 4.1.2, the missing values across the variables age, gender, and others are highly correlated. This means that patients with missing values in one of these columns also have missing values across all the columns. We initially considered imputing the missing data in the training dataset with median (for age) and mode (for disability and low-income indicator flags). But we felt it is not the best approach in sensitive problem statements like this one because it might oversimplify the complex nature of this problem.

Later, we looked at the percentage of patients among this group who belonged to the target group and found out that there are no such patients. This assured us that the imputation won't add bias to our analysis, so we decided to impute this missing data with median and mode statistics.

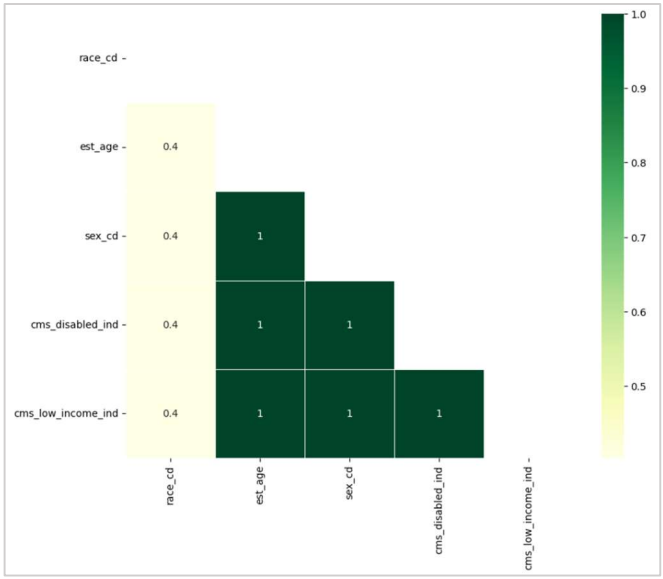

Figure 4.1.2: Correlation between Null Values among the variables in Target Table

[10] Treatment adherence and clinical outcomes of osimertinib (Osi) among ethnic-minority patients (pts) with EGFR-mutated NSCLC https://ascopubs.org/doi/abs/10.1200/JCO.2023.41.16_suppl.e18536

4.2 Model objectives and Methodology

When we began building the models for this analysis, our primary objectives were as follows:

1. Identify early-stage risk factors for patients entering the target group.
2. Ensure that the model's insights are free from bias.
3. Produce informative, meaningful insights without over-reliance on a select few variables.

Below, we outline how we adjusted our methodology to align with these objectives:

1. Early risk detection:

Based on our research, we identified two distinct patient groups who struggle to adhere to Osimertinib therapy after experiencing ADEs. The journey of these two patient groups can be seen from the below image:

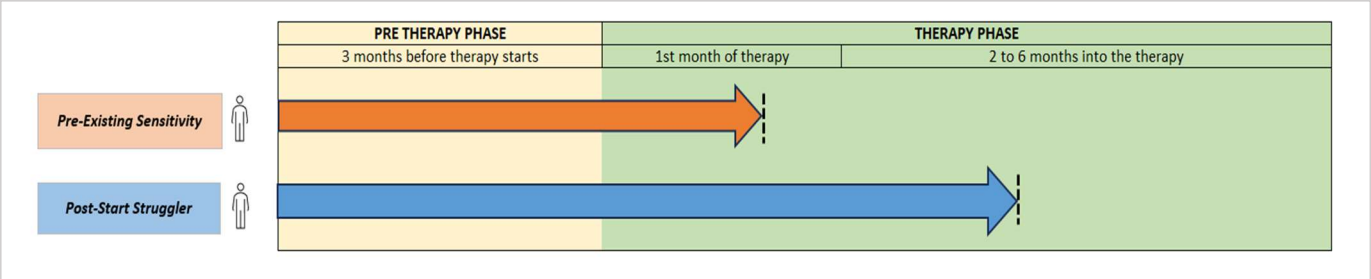

Figure 4.2.1: Two Types of Patients in Target Group

Pre-Therapy Phase: The 3-month phase before a patient's therapy starts.
Therapy Phase: The phase that follows a patient's Osimertinib therapy initiation.

Patient group 1, from the **'Pre-Existing Sensitivity'** group **(PES),** stopped therapy within the first month after facing ADEs. Their pre-therapy history likely reduced their tolerance towards ADEs and caused them to discontinue therapy.

Patient group 2, **'Post-Start Strugglers' (PSS)**, remained in therapy for over a month before dropping out. For this patient, post- therapy events were likely a key factor in their decision to end therapy. While intervening at any point before a patient ends therapy can benefit the 'Post-Start Strugglers,' the 'Pre-Existing Sensitivity' group would require support from day one.

Hence, we chose to create two models to address this difference. Model 1 is built using the data from the 3 months before the start of therapy for all patients. It focuses on identifying the risk factors during the pre-therapy phase before the therapy begins. In contrast, Model 2 uses data from both the pre-therapy and therapy phases for the same patients, enabling a re-evaluation of the risks during the therapy phase.

2. Using disparity score for model evaluation:

Our second objective is to build a model with low disparity. Initially, we excluded the race and gender variables from the training data of the model for this purpose. However, we still needed to develop a method for calculating the disparity score based on the model's predictions for each patient. This was necessary to

ensure that there are no underlying biases introduced by pharma or mediclaims data that may affect specific groups.

Based on our research, we have adopted a metric known as the 'Disparate Impact Index' (DI)[11] and customized it to suit our objectives as follows:

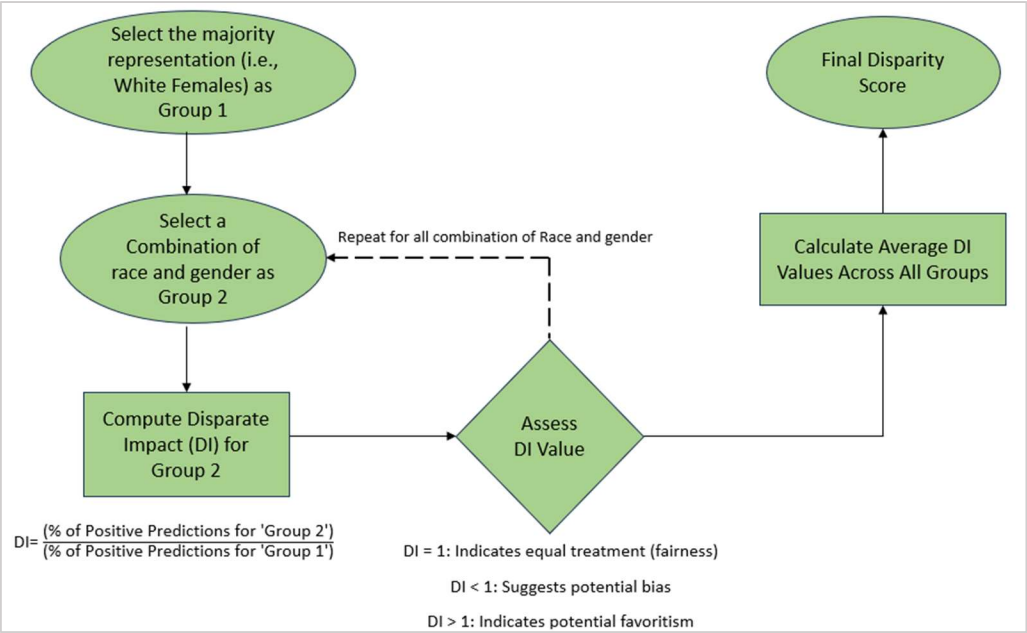

Figure 4.2.2: Disparity Score Calculation Flowchart

But it won't be a straightforward task to choose the best model just based on the lowest disparity score, as in some cases, there could be a trade-off between the model's predictive power and disparity score. Hence, we created a new metric called 'Model Evaluation Index', which is a weighted sum of disparity score, AUC, and recall scores for each model.

$$\text{Model Evaluation Index} = \text{Wd} * \text{Disparity Score} + Wa * AUC\ Score + Wr * Recall\ Score$$

Wd (weight for disparity score) = 40%
Wa (weight for AUC score) = 30%
Wr (weight for Recall score) = 30%

Using this metric to choose the champion model at each phase ensures that any drop-off in the disparity score is penalized heavily, while also maintaining good predictive power in terms of the AUC and Recall.

[11] Disparate Impact https://docs.aws.amazon.com/sagemaker/latest/dg/clarify-post-training-bias-metric-di.html

3. Building a model with more focus on "why" rather than "who":

Our final objective was to build an informative model over an accurate one to help Humana understand the risk factors for patients falling into the target group. If there was a way to capture the informativeness and explain ability of the model in a single metric, we would have included it as one of the individual components in the 'Model Evaluation Index' metric defined in this section. But since there was no such straightforward metric, we relied on building multiple iterations of models with different features and utilized the SHAP values and feature importance to interpret each of these models.

4.3 Feature engineering

The variables for our models were designed by aggregating different data points from Mediclaim and pharma claim details at the patient level. While the initial steps we took for data cleaning helped us resolve some broad issues with the data, we noticed that there were still a few considerations needed before we could use these variables as features in our model:

1. Handling duplicates in the mediclaims data:

In the mediclaims table, each record represented the details of a line item within a claim, rather than the overall details of the claim. Initially, this led to an overcounting issue when aggregating the data for patients with multiple line items within a single claim. Therefore, we decided to count the distinct visit dates for each patient when generating the variables for analysis. We conducted spot-checks to see if any patients had multiple distinct visits on a single day and proceeded only after confirming that there weren't many instances to significantly impact the analysis.

2. Standardizing the variables to account for different patient durations:

We noticed that the patients had different durations of Osimertinib therapy. While we built separate models to address this, using data from all patients during model training could give more weight to those with shorter therapy periods when identifying the target group. To address this, we standardized the variables by calculating rates, and using them as variable instead of raw counts. *

For example, if we had the count of medical visits for ADE-related diagnosis in Pre-Therapy and Therapy phases:

$$Medical\ Visit\ Rate\ for\ ADE\ related\ diagnosis\ in\ Pre\ Therapy\ Phase = \frac{\text{Number of Medical Visits for ADE related diagnosis in Pre Therapy phase}}{(Therapy\ Start\ Date - Earliest\ Medical\ Claim\ Date\ in\ Pre\ Therapy\ phase)\ in\ days}$$

$$Medical\ Visit\ Rate\ for\ ADE\ related\ diagnosis\ in\ Therapy\ Phase = \frac{\text{Number of Medical Visits for ADE related diagnosis in Therapy phase}}{(Latest\ Medical\ Claim\ date\ in\ Therapy\ Phase - Therapy\ Start\ Date)\ in\ days}$$

* Detailed formulae for all the variables we included in the model are in APPENDIX section

3. Handling Model's bias towards Mediclaim variables:

As shown in figure 3.1.9, we noticed that all the patients in the target group were in a subset of the training data where patients had Mediclaim records. Because of this, we filled in missing Mediclaim data with zeroes for patients without Mediclaim records. This led the model to rely too much on Mediclaim data in separating the target and non-target groups, making it assign higher importance to these variables. As a result, it wasn't paying enough attention to other important factors like pharma claims and demographics.

To fix this, we ran the model multiple times and removed a few Mediclaim variables. We kept doing this until the model started recognizing patterns from pharma claims and demographic variables.

4. Determining the variables to use in the final model for each phase:

We initially started with a pool of 260 variables derived from both mediclaims and pharmaclaims data to train our models for both the pre-therapy and therapy phases. However, after several rounds of model refinement and variable reduction by looking at the feature importances, we ultimately arrived at 15 variables for the final model at Pre-Therapy phase and 27 variables for the final model at Therapy phase.

15 Variables extracted from the Claims History of Patients before Therapy Starts (Pre-Therapy Phase)			
Demographic	Diagnosis Rates	Healthcare Utilization Rates	Drug Claim Rates
Estimated Age of the Patient	ADE Diagnosis Rate Before Tx	Physician Office Visit Rate Before Tx	Mental Health Drug Claim Rate
CMS disability indicator	Mental Health Diagnosis Rate Before Tx	Outpatient Facility Visit Rate Before Tx	Maintenance Drug Claim Rate
CMS Low-income indicator		ER Visit Rate Before Tx	Narcotic Drug Claim Rate Before Tx
		Inpatient Acute Care Visit Rate Before Tx	Hypertension Drug Claim Rate Before Tx
			Diabetes Drug Claim Rate Before Tx
			Anti-Infective Drug Claim Rate Before Tx

Figure 4.3.1: Variables for the model in Pre-Therapy Phase

27 Variables extracted for Patients during Therapy Phase			
15 Variables from Pre-Therapy Phase	Drug Fill Info	Drug Claim Rates	Diagnosis Rates
	Generic Drug Claim Rate in Tx	Nausea Drug Claim Rate in Tx	Fatigue Diagnosis Rate in Tx
	Mail-Ordered Drugs Rate in Tx	Diarrhea Drug Claim Rate in Tx	Nausea Diagnosis Rate in Tx
	Avg Days' Supply of Drugs in Tx	Seizure Drug Claim Rate in Tx	Constipation Diagnosis Rate in Tx
		Mental Health Drugs Claim Rate in Tx	Diarrhea Diagnosis Rate in Tx
			Pain Diagnosis Rate in Tx

Figure 4.3.2: Variables for the model in Therapy Phase

4.4 Model selection

1. Choice of the algorithm:

When deciding which algorithm to use for modeling purposes, we examined the data and observed a significant amount of non-linearity and interaction in the relationships between the feature variables and the target flag indicator. We determined that tree models would be suitable for both capturing these relationships and facilitating interpretation with tools like Shapley values.

2. Data Splitting for modeling purposes:

We decided to split our data into a 85:15 ratio. 85% of patient data was used for modeling the relationships, while the remaining 15% was used for evaluating those models. This 15% of data served as a validation set to assist in tuning our models and determining the final models that performed best based on the Model Evaluation Index metric.

3. Model Selection for the Pre-Therapy phase:

As mentioned earlier, we had 15 variables at this stage to identify the target group of patients. We built three models on these set of variables, and their performances on validation data are shown below:

Model	Disparity Score (40% weight)	AUC Score (30% weight)	Recall Score (30% weight)	Model Evaluation Index (MEI)
Random Forest	97%	73%	71%	82%
Extreme Gradient Boosting	94%	68%	52%	74%
Light Gradient Boosting	96%	74%	68%	80%

Figure 4.4.1: Model Comparison in Pre-Therapy Phase

As shown in the table above, the final model selected at this phase is a Random Forest model, which is a group of multiple individual tree models.

The main parameters we tuned and used for the final model are as follows:

1. Number of individual tree models – 220
2. Criterion for splitting the nodes – Gini Impurity
3. Maximum depth for each tree – 15
4. Minimum Samples needed at leaf nodes – 24

Model 1's ability to separate the Target group and non-target group:

The AUC score helps us understand the model's ability to differentiate between the target and non-target groups. A 50% AUC score typically suggests a model dependent on random guesses without any clear rules. In this case, an AUC score exceeding 50% signifies that the model has learned some relationships in the data and, as a result, performs better than mere random guessing in separating the two groups.

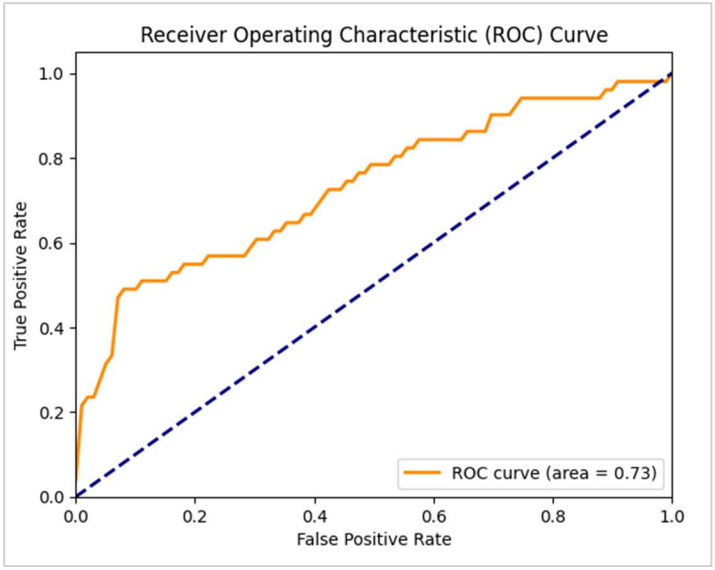

Figure 4.4.2: ROC Curve for Pre-Therapy Phase Model

Model 1's Recall on Target Group:

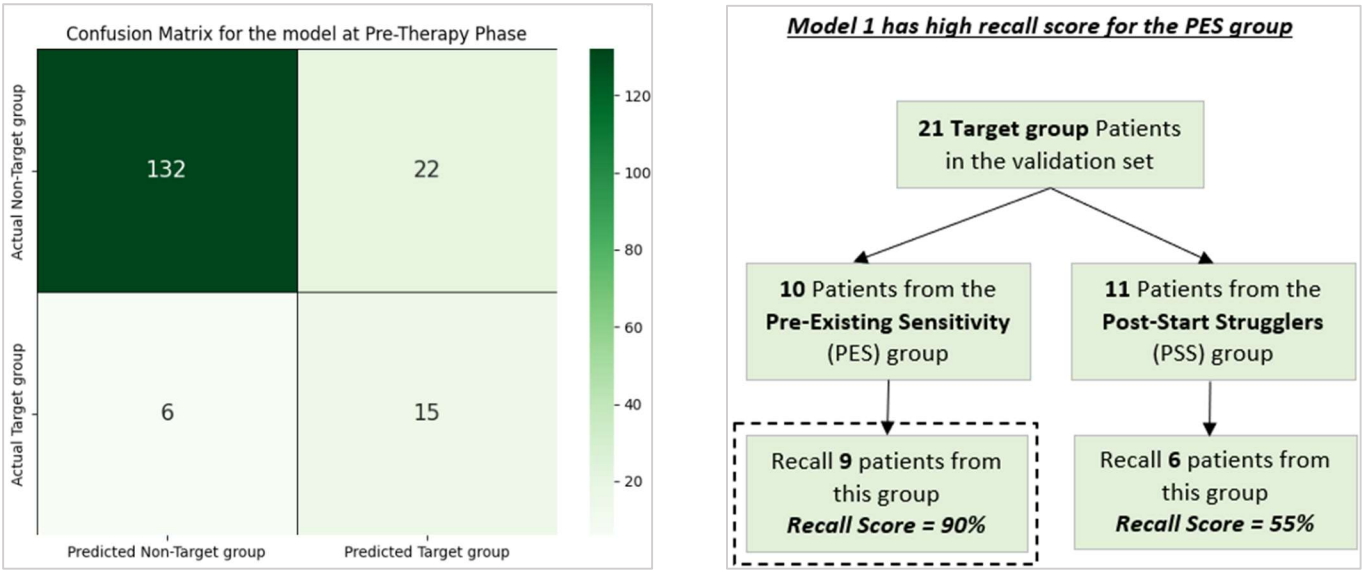

Figure 4.4.3: Confusion Matrix and Recall Scores for Pre-Therapy Phase Model

As seen from the above visualization of confusion matrix, the final model at the pre-therapy phase was able to recall 15 out of the 21 Target group patients (71% overall recall rate). This model had a good recall rate for the Pre-Existing Sensitivity group (90% recall rate), indicating that it can identify patients who might drop out of the therapy early due to their previous history. Since this model was built using only the patients'

data before they even started their Osimertinib therapy, the insights we derived from this could help Humana understand which patients would need attention right from day 1 of their Osimertinib therapy.

4. Model Selection for the Therapy phase:

In this stage, we had a total of 27 variables. Once again, we employed the same approach of constructing three models using this set of variables and compared their performances on validation data.

Model	Disparity Score (40% weight)	AUC Score (30% weight)	Recall Score (30% weight)	Model Evaluation Index (MEI)
Random Forest	96%	85%	76%	87%
Extreme Gradient Boosting	95%	82%	68%	83%
Light Gradient Boosting	96%	84%	72%	85%

Figure 4.4.4: Model Comparison in Therapy Phase

Even at the therapy phase, Random Forest model performed the best based on our evaluation. The parameters we used for the model at this phase are as follows:

1. Number of individual tree models = 400
2. Criterion for splitting the nodes = Gini Impurity
3. Maximum depth for each tree = 23
4. Minimum Samples needed at leaf nodes = 21

Model 2's ability to separate the Target group and non-target group:

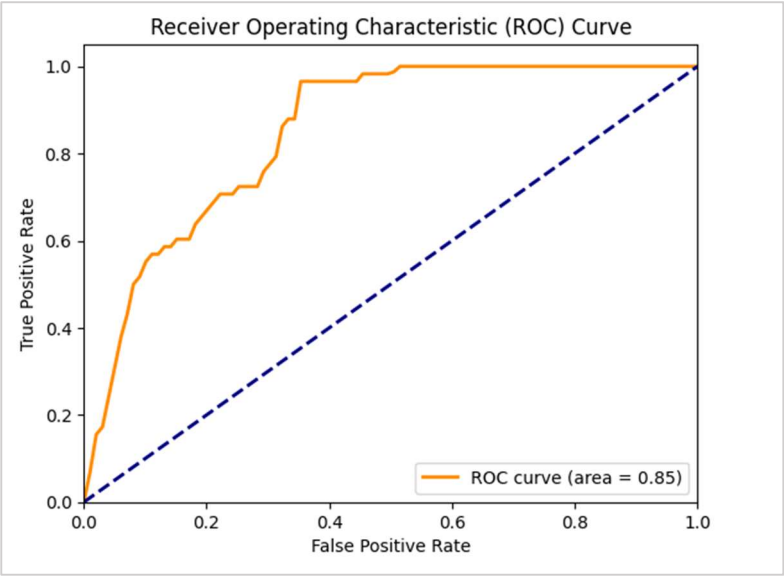

Figure 4.4.5: ROC Curve for Therapy Phase Model

As seen from the above image, AUC score is greater than 50%, proving as a sanity check to ensure that model has learned a few patterns from the data in separating the target group from the non-target group.

Model 2's Recall on Target Group:

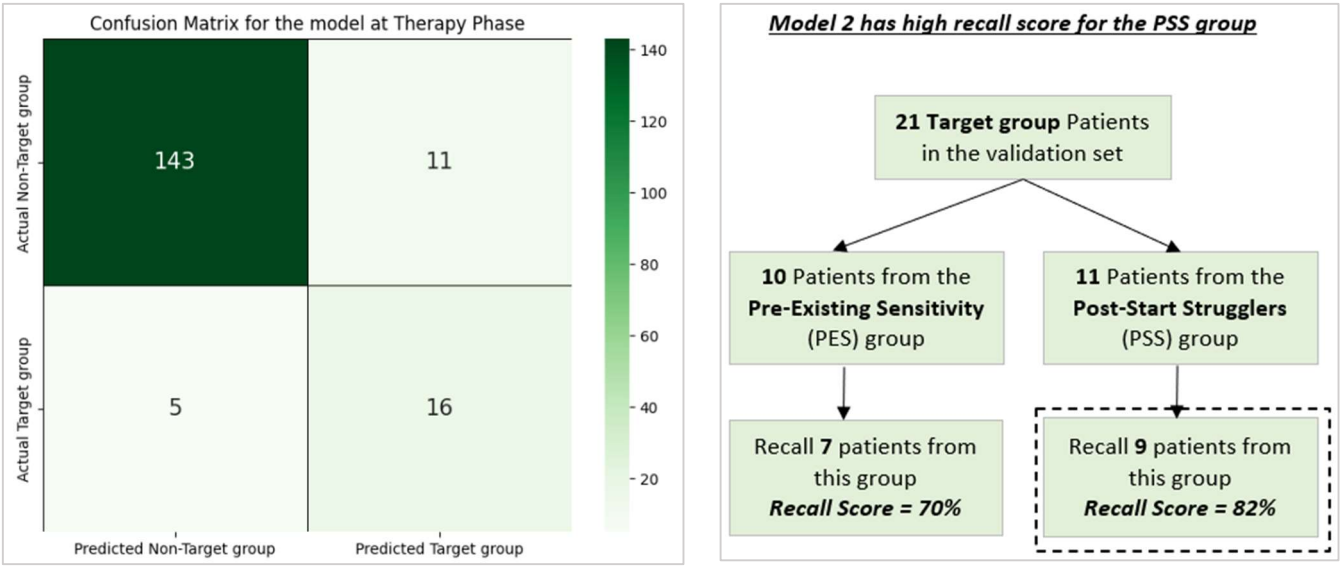

Figure 4.4.6: Confusion Matrix and Recall Scores for Therapy Phase Model

As seen from the above visualization, Model 2 was able to recall 16 out of the 21 Target group patients (76% overall recall rate). This model had a good recall rate on the Post-Start Strugglers (82%), indicating its ability to identify people who are struggling to manage their ADEs during the therapy.

This model could also provide a way for Humana to re-evaluate the therapy discontinuation risk for the PES group patients who were identified by Model 1 in the pre-therapy phase.

5 Important Risk Factors Derived from Model (KPIs)

We used the Model Evaluation Index as a metric to make sure our models learned some patterns from the data without being biased towards any demographic group of patients. To understand the patterns learned by these models, we used Shapley values, a concept from game theory. If Shapley values are positive for a certain group of patients, it means the model's predictions for them are closer to the target group. We used this information to identify the top five risk factors for patients in the target group during both the pre-therapy and therapy phases.

The top five risk factors from model 1 at Pre-Therapy Phase:

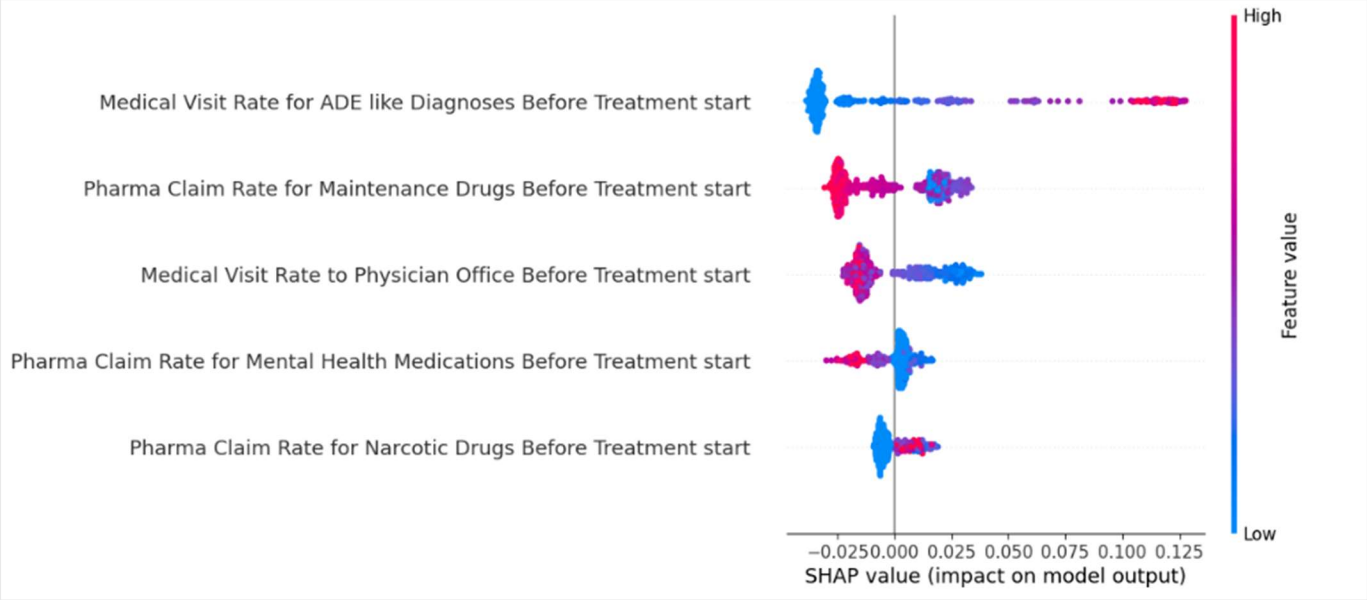

Figure 5.1: Shap values for imp variables of Model 1 at Pre-Therapy Phase

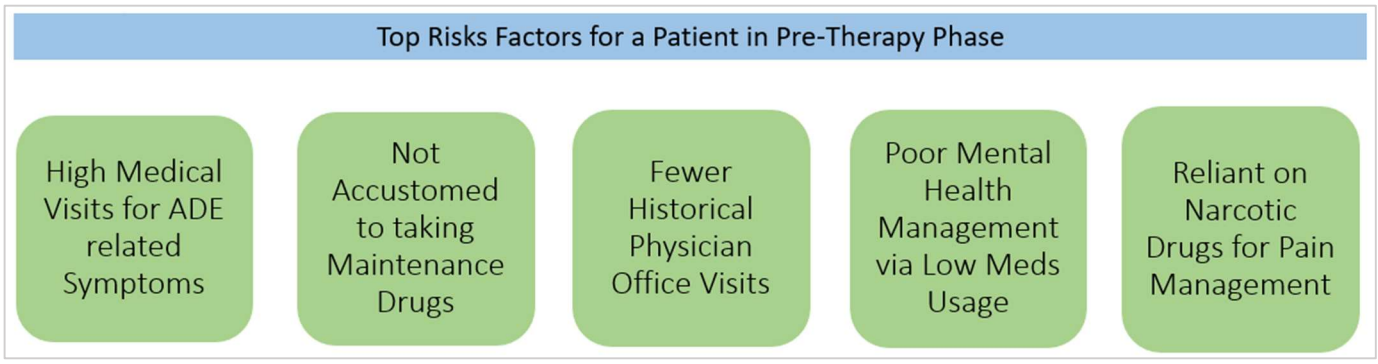

Figure 5.2: Key Factors at Pre-Therapy Phase

The top five risk factors from model 2 at Therapy Phase:

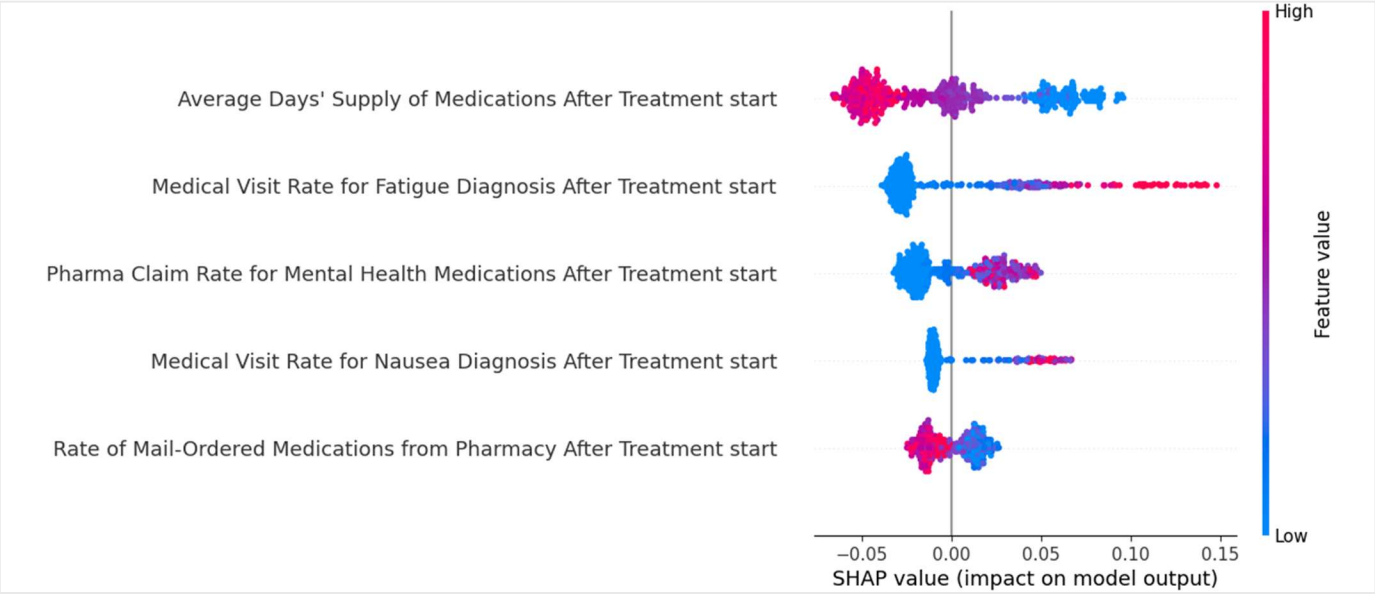

Figure 5.3: Shap Values for imp variables of model 2 at Therapy Phase

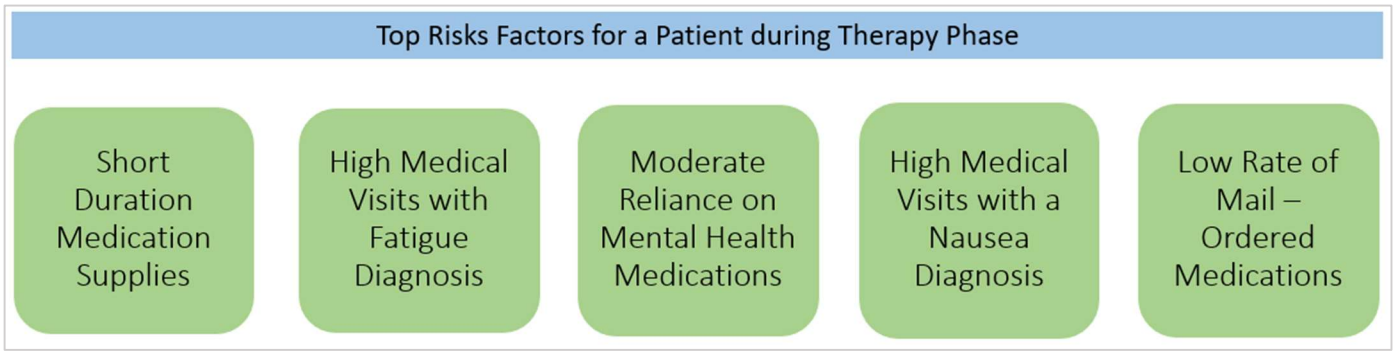

Figure 5.4: Key Factors during Therapy Phase

6 Analysis, Implications and Recommendations

Medication adherence is a complex behavior that cannot be improved through a single method. The World Health Organization shares a similar perspective, leading them to propose a multi-dimensional model for examining medication adherence, known as WHO-MAM[12]. WHO-MAM identifies five dimensions that can influence adherence: patient-related factors, social/economic factors, therapy-related factors, condition-related factors, and healthcare system/healthcare team-related factors. The current problem statement for this study, which directly pertains to ADEs for Osimertinib therapy, falls under the therapy-related factors dimension. However, our analysis results revealed that these five dimensions do not operate in isolation; there is a significant degree of interaction among them. This insight allowed us propose recommendations that touch multiple dimensions and could provide substantial business value to Humana, as discussed below:

[12] World Health Organization Dimensions of Adherence https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6625256/

1. Improving the Patient's relationship with healthcare system

Building a good Patient-Healthcare relationship can have a positive impact on how patients perceive their treatment and improve the treatment outcome despite the adverse drug events.

Key Insights:

Our analysis indicates that patients who make fewer visits to the physician's office before starting therapy are at an increased risk of discontinuing the treatment [Fig 5.2]. This may be due to these patients lacking a trusted and reliable physician or could result from a general mistrust of the healthcare system. It hinders the patients from learning how to manage Osimertinib therapy with its adverse drug events.

In the traumatic journey of a patient following a cancer diagnosis, healthcare workers including doctors, nurses, and pharmacists, can play a significant role as difference-makers. They have the capacity to directly influence the patient's behavior during therapy and their adherence to it. As patients process this life-altering news mentally, the primary source of support from their physicians is crucial in helping them remain resilient and motivated.

Based on a study, 63% of patients with cancer expressed that the physician should take the primary responsibility in decision-making[13]. This indicates that patients establish trust with their physicians and value their opinions when making important decisions. Therefore, a doctor or pharmacist who can clearly explain the available treatment options, educate patients about the impact of Osimertinib, and guide them on how to manage the side effects could help patients adhere to the therapy. Research has shown that patients tend to be more worried about the side effects that are not cautioned to them in advance by healthcare professionals[14].

Proposed solution:

We suggest that Humana should take initiatives to encourage a good bond between the physicians and the patient right from day zero, when a patient gets diagnosed with cancer. For this purpose, doctors, nurses, and the pharmacists that interact with patients in Osimertinib therapy would need to be trained in the following areas:

1. How to show compassion with the patients intending to start their Osimertinib journey?

2. How to educate the patients on the less complications and reduced cancer recurrence rate of Osimertinib compared to Chemotherapy?

Humana could develop new training materials for cancer patient interaction on the two topics mentioned above and incorporate them into their existing library of Provider Compliance training materials[15]. These training sessions should be mandated for healthcare workers who are involved in Humana's insurance plans and directly interact with patients undergoing Osimertinib therapy.

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[13] The enigma of doctor-patient relationship https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6482679/
[14] Patient Medication Adherence - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3191684/
[15] Provider Compliance Training Material - https://www.humana.com/provider/news/provider-compliance

Also, Humana could think about adding its Medicare members who are on Osimertinib therapy to its Medication Therapy Management (MTM) program[16]. Many patients taking this treatment already fit the MTM criteria because they have high medication costs, use opioids for pain relief during treatment, or have existing conditions like hypertension. Since MTM involves one-on-one reviews with pharmacists, it could help build a good relationship between patients and pharmacists.

2. Synchronized Prescription refill program

Synchronizing the refill dates of a patient's various prescription medications such that they can be picked up or delivered on the same day each month could prove beneficial to the patients in Osimertinib therapy. This could simplify the medication management process for the patients, reduce the number of trips to the pharmacy, thereby improving the medication adherence[17].

Key Insights:

One of the important considerations to establish a better healthcare system is to have a patient-centric approach. While patients face multiple barriers to adhere to treatment, Humana has always aimed to reduce these barriers for them. Two such barriers Humana can remove for patients are:

1. The complexity when patients are on multiple medications.
2. The logistical obstacles of visiting the pharmacy to purchase medications or using mail-order services.

Humana could utilize its existing infrastructure of synchronized prescription refilling for this purpose.

Based on our analysis, a low mail-order prescription rate for patients during the therapy phase is a risk factor that may lead to non-adherence to Osimertinib treatment after reported ADEs [Fig 5.4]. This means that the Humana members who have chosen mail-order delivery for prescribed medicines show better adherence to Osimertinib treatment compared to their counterparts.

In addition to this logistical barrier, our analysis shows that people with a higher number of hospital visits for ADE-like symptoms before starting therapy have a higher probability of non-adherence [Fig 5.2].

There are three possible reasons why these patterns are associated with high non-adherence rates:

a) Patients who already have experienced conditions that resemble ADE before therapy may develop a fear and avoid Osimertinib just to stay away from that pain again

b) Their existing condition might worsen the side effects associated with Osimertinib treatment.

c) Patients are concerned about the additional financial burden if they purchase medications to ease the symptoms.

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[16] What is MTM https://www.humana.com/medicare/medicare-programs/medication-management-adherence-mtm
[17] P A Synchronized Prescription Refill Program Improved Medication Adherence- http://assets.fiercemarkets.net.s3.amazonaws.com/public/004-Healthcare/external/Doshi-FF.pdf

Solution:

We firmly believe that improved access to medications can help patients manage their side effects and enhance adherence to Osimertinib therapy. Therefore, in addition to mail-order and auto-refill services for Osimertinib, Humana can leverage patients' medical history to offer synchronized prescriptions, addressing preexisting conditions that may be exacerbated when they start their therapy. When patients experience adverse drug events, access to medications can eliminate logistical and behavioral barriers, increasing their likelihood of adhering to Osimertinib treatment while managing side effects.

The existing Centerwell services for Auto Refill, medication synchronization, reminder, and tracking services can be enhanced and upgraded to recommend medications based on a patient's medical history. Humana should also provide clear training on how patients in Osimertinib therapy could use the Centerwell Pharmacy mobile app, and offer tele-support to guide and activate these services.

Also, since most medications used to treat fatigue, tiredness, and similar conditions are categorized as Tier 1 and Tier 2 generic medicines, the financial burden on patients will also be significantly lower since Humana offers a zero-dollar copayment for these drugs[18].

We believe Humana can implement this solution for two main reasons:

i) Centerwell Pharmacy's platform and infrastructure are already in place to implement these solutions
ii) Humana has access to the patients' historical medical records.

3. Active Support Calls

Patients who are diagnosed with cancer often have mental disorders in the form of comorbidity with depressive and anxiety symptoms being the most common. Providing support to these patients with their mental health management could improve their adherence.

Key Insights:

Based on research, mental health disorders in cancer patients are directly related to the level of disease progression, the presence of pain, accompanying ADEs associated with drugs, sadness due to current or expected losses, and fear of death[19]. It was no surprise when we identified mental health-related variables showing up as important in our analysis for both the pre-therapy phase and therapy phase of a patient's treatment lifecycle. This made us realize that mental health offers an important perspective in understanding the patient's adherence behavior to Osimertinib.

We conducted a detailed analysis within the data to understand the behavior of Humana members with a focus on how mental health plays out in their treatment journey. We found clear trends which give out the message 'mental health is a real concern.' Let's walk through our findings about the patterns in mental health-related problems Humana members face while they are going through Osimertinib therapy.

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[18] Humana Medication Adherence https://docushare-web.apps.external.pioneer.humana.com/Marketing/docushare-app?file=3793790
[19] Mental health care in oncology - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7214708/

a) Mental health patterns in pre-therapy phase (before the therapy starts):

We observed that a significant number of patients are diagnosed with mental health-related illnesses, possibly as they try to process the news of cancer, even before therapy begins. However, about one-third of these patients in the data used for this analysis did not take any medication during the pre-therapy phase to address their mental health. A primary reason behind patients not taking any medication could be a lack of awareness. However, within this group, we noted that over 30% of these patients discontinued the Osimertinib therapy.

b) Mental health patterns in therapy phase (after the therapy starts):

The situation is quite different once the patients start their therapy. The patients develop severe mental health related concerns which could be accounted for Osimertinib intake. So, we see that around 172 patients who didn't have mental health prescriptions before therapy started taking psychiatric drugs during the therapy. The problem at this point is that patients could develop a reliance on using these drugs to manage their conditions, which was shown to be a major concern in research papers. We suspect that this could again be a result of patients' lack of awareness on how to manage their mental health issues.

We could clearly see from both phases that poor mental health management increases the risk of non-adherence in the patients undergoing Osimertinib therapy.

Solution:

We propose that all patients should receive education and training on how to manage their mental health-related issues effectively. Additionally, a controlled substance agreement plan should be developed to help patients avoid substance abuse. While cancer and Osimertinib treatment can cause mental distress in patients, proper education and prescription of appropriate medications can assist them in managing their mental health while dealing with adverse drug events.

We have observed that Humana offers a virtual visit program[20], which provides patients with access to behavioral health specialists upon scheduling appointments. This program could be extended to Humana's existing Cancer program[21], allowing behavioral health specialists to work alongside oncologists, providing counseling to patients experiencing adverse drug events and helping them avoid substance abuse to manage pain. This can enable Humana to establish a dedicated team of experts who can deliver comprehensive care to cancer patients and support their therapy adherence.

4. Medicine adherence packaging

Many patients in Osimertinib therapy may face challenges in recalling the prescriptions they need to take regularly to manage their conditions. Employing medication adherence packaging that simplifies the medication schedule for these patients could enhance adherence[22].

[20] Primary Preventive Care https://www.humana.com/home-care/primary-preventive-care/telehealth
[21] Humana Cancer Program - https://www.humana.com/provider/medical-resources/clinical/health-programs/cancer-program
[22] Impact of a Medication Adherence Packaging Service - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7838800/

Key Insights:

Nonadherence related to a person's ability to take their medication, such as forgetfulness, confusion over medication dosage, and difficulty opening a prescription bottle, can be classified as unintentional nonadherence. As discussed earlier, the adverse drug events (ADEs) associated with the Osimertinib drug have a significant impact on the mental and physical health of the patients, rendering them vulnerable and unstable in making correct decisions or maintaining clear thoughts.

When we investigate the risk factors discussed earlier, such as hospital visits related to fatigue, nausea, and mental health concerns, extensive reliance on mental health prescriptions like Trazodone (NDC ID: 60505-2653-1), and logistical or physical barriers that limit a patient's access to medicines, we understand that these factors collectively can have a great effect on patients' adherence to Osimertinib.

Additionally, based on our analysis, we also found a strong association between adherence and a patient's prior experience with maintenance drugs [Fig 5.2]. The insight we have gained from this analysis is that patients who have previously taken regular maintenance drugs, such as Linagliptin (NDC ID: 0597-0140-30), for pre-existing conditions like type-2 diabetes, have already developed the habit of taking medicines daily without fail[23]. However, for patients who have not taken long-term medications before starting Osimertinib, they may struggle to follow the medication regimen.

Solution:

We conducted extensive market research to understand how unintentional nonadherence can be reduced among Humana members. Within the healthcare system, certain services and products can be utilized by Humana to address this issue for patients undergoing Osimertinib therapy. Medicine adherence packaging is one such effective tool that can simplify the medication-taking process for patients.

1. Numerous companies offer such services, including RxMAP. Alternatively, Humana can leverage its existing partnership with Curanthealth, which provides services like CuraPak® Adherence Packaging. This packaging method involves sorting medicines into easy-to-open pouches with color coding and labels to help patients know precisely which medicine to take and when to take it.
2. Implementing such a service can make the entire process of medication-taking seamless and eliminate the barriers we discussed earlier.

5. Increase the Payday supply for medicines other than Osimertinib:

We noticed that patients that ordered medicinal supplies for short duration had high non-adherence rates [Fig 5.4]. Studies have proved this pattern where 88% to 89% of members who fill 90-day prescriptions adhere to their medication regimens, compared to 73% of 30-day fills[24].

[23] Patient Medication Adherence - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3191684/
[24] Humana Medication Adherence - https://docushare-web.apps.external.pioneer.humana.com/Marketing/docushare-app?file=3793790

Key Insights:

Generally, medications prescribed for managing long-term health conditions are provided through the 'repeat prescribing' system, enabling patients to request additional supplies without requiring an additional doctor's appointment. This has proven to be an effective method for promoting patient adherence to their medication regimen.

Solution:

In our analysis we noticed that Osimertinib is predominantly prescribed for a 30 day period which is understandable, given the cost of the medicine and to control the wastage of such an important drug. However, Humana can run a pilot program to increase the pay day supply for other drugs which are associated with the patient's historical conditions and see if we witness a better adherence among the members. It could be a worthwhile study because we can underline the impact of pay day supply with Osimertinib users and eventually extend the scheme to Osimertinib drug as well from 30 days to 60 days.

6. The need for an online forum that helps patients in Osimertinib therapy connect with others going through the same journey.

When we began working on this project, we had limited knowledge about cancer. However, as we delved into the data and conducted our research, we came to realize the intensity and pain experienced by cancer patients in their journey. We read numerous stories shared by cancer patients, detailing their path from the initial shock of diagnosis to the challenging treatments and their side effects, and the highs and lows of their journey toward recovery or acceptance. While their stories were profoundly moving and difficult, they equally served as a source of inspiration for us to become fully immersed in this analysis.

One particularly inspiring story came from a resilient lady named Ivory from the Philippines. She initiated a video log on YouTube documenting her cancer journey, starting from her diagnosis of non-small cell lung cancer, through Osimertinib treatment, and her experience with associated side effects for more than two years, until she left us in May 2023[25]. Her video logs not only helped her connect with other patients experiencing similar journeys but also kept her motivated. The most significant lesson we learned was that enabling the patients in the Osimertinib therapy, a platform to share their experiences and connect with other individuals who are going through a similar journey could greatly benefit them.

Cancer support groups usually offer numerous advantages to those impacted by cancer. While many individuals receive support from their friends and family, the primary reason for their participation in such groups is the opportunity to connect with others who share similar cancer experiences. Research indicates that joining a cancer support group can enhance both the quality of life, both mentally and physically, and potential survival rates [26].

[25] Ivory's Diary - https://www.youtube.com/@ivorysdiary2361
[26] Belonging to a peer support group enhance the quality of life and adherence rate -https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3214378/

Solution:

Humana already has cancer support groups, which have been tremendously helpful for its members. However, such broad groups have a few disadvantages; even though patients connect with other cancer patients, the journey might be different for these individuals, which can act as a barrier for them to connect to a full extent.

We propose 'Ivory' – an online peer-to-peer (PTP) support group moderated by Humana, for patients dealing with Non-Small Cell Lung Cancer (NSCLC). Establishing an online support group that is open to all NSCLC patients worldwide will facilitate connections among people with very similar demographics, life experiences, and side effects. This approach can be more effective and convenient than traditional support groups. The group can be moderated and hosted by Humana as part of their Humana Cancer Program for each type of cancer patient. The success of Ivory's YouTube channel gives us the confidence that such a program will attract a significant number of cancer patients and help them stay motivated and adherent to the Osimertinib treatment.

This program could also have a long-term benefit for Humana, which we will discuss in the Future Scope section.

Multi-Dimensional Assessment of Recommendations:

As mentioned in the previous section, WHO looks at medicinal adherence in terms of five dimensions. Below, we tried to follow a similar approach by creating a matrix to understand how each of our recommendations could interact with the five dimensions.

Based on the number of dimensions affected, we believe Recommendation 1, 'Improving the patient's relationship with the healthcare system,' should be Humana's priority to improve adherence to Osimertinib.

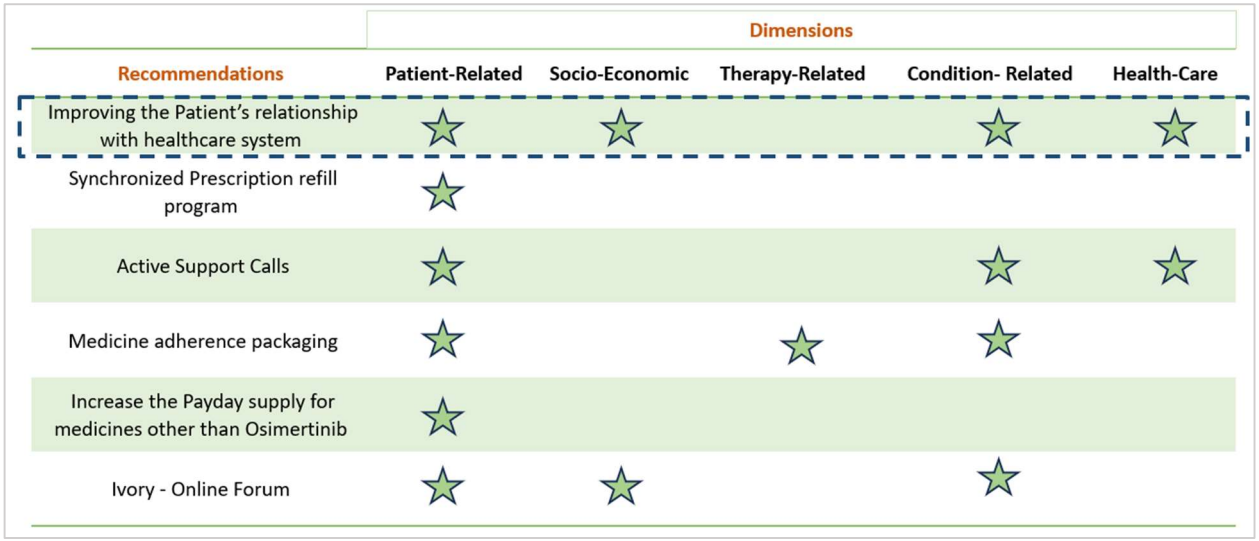

Figure 6.1: Recommendations vs Dimension Matrix

7 Osimertinib Adherence Improvement Plan

The below flowchart provides a clear timeline-based plan for Humana on how to implement the recommendations discussed in previous sections. It could also be cost-effective, as the focus group is reduced at specific phases in the timeline, which will bring down the overall cost of implementing this plan.

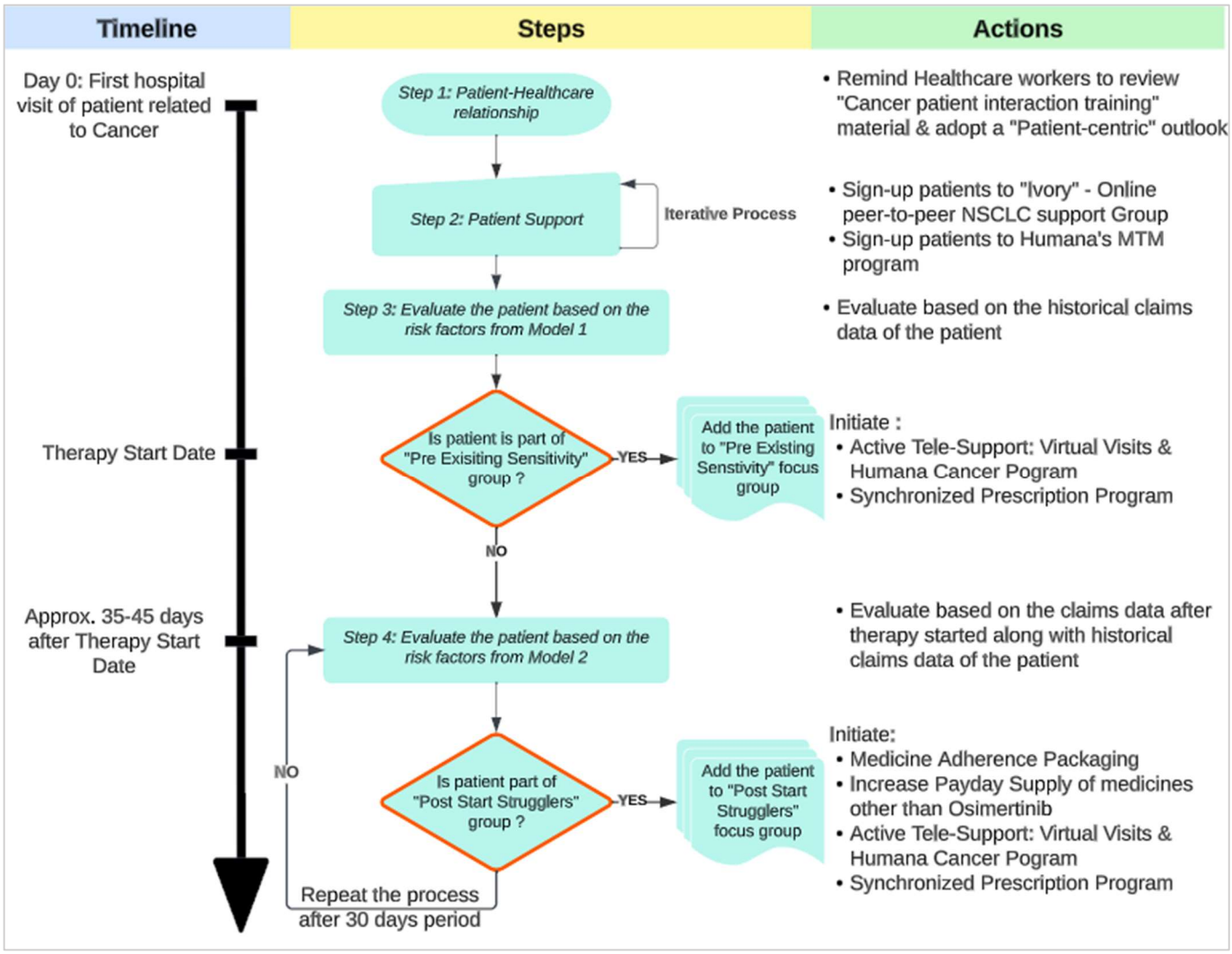

Figure 7.1: Implementation Plan

8 Expected value for Humana

By helping patients adhere to Osimertinib, Humana can make a difference in the journeys of several cancer patients in terms of improved health outcomes. While this is the primary value of implementing the above program for Humana, it could also prove to have substantial business and financial benefits. Below, we have provided some estimated figures for the financial benefits:

Cancer Recurrence Cost:

Index	Subject	Number	Formula
A	6 months of Chemotherapy [I]	$12000 * 6 = $72,000	
B	Increase in Medical costs[II]	$6,300 * 6 = $37,800	
C	Increase in Pharma costs [III]	$27,450	25% * (A+B)
D	Total costs due to cancer recurrence	$137,250	A+B+C

Patient Fails to Adhere to Osimertinib (After 3 Months duration):

Index	Subject	Number	Formula
E	Osimertinib Cost for 3 Months [IV]	$16000 * 3 = 4,800	
F	Total Cost for Patient not adhering to the Therapy [V]	$123,488	E + (55% * D)

Patient Adheres to Osimertinib for 6 months:

Index	Subject	Number	Formula
G	Osimertinib Cost for 6 Months	$16,000 * 6 = $96,000	
H	Total Cost of Patient Adhering to the Therapy [VI]	$111,098	G + (11% * D)

Expected Savings for Humana when a Patient Adheres to the Therapy:

Index	Subject	Number	Formula
I	Expected Savings [VII]	$12,390	F - H
J	Net Profit for Humana per Patient [VIII]	$7,500	

[I] Assumed recurrent cancer is Spread away from the original tumor site, which means patient would need chemotherapy - https://www.webmd.com/cancer/when-cancer-comes-back-recurrence
Cost of chemotherapy drug - https://www.asbestos.com/featured-stories/high-cost-of-cancer-treatment/
[II] Increase in medical costs due to recurrence - $6300: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10050774
[III] Assumed increase in Pharma costs other than chemotherapy drugs due to the cancer's recurrence is 25% of other costs due to recurrence.
[IV] The patient dropped out of Osimertinib therapy after an initial 3-month usage.
[V] For one patient, failure to adhere could mean a 45 to 76% risk of cancer recurrence. Assuming the average risk of recurrence in non-adherence to be 55%. For one patient, failure to adhere could mean a 45% to 76% risk of cancer recurrence - https://www.keytruda.com/non-small-cell-lung-cancer/treatment-options/adjuvant/
[VI] Adhering to Osimertinib reduces recurrence risk by 80%. Therefore, assuming risk of recurrence in adherence to be 11%.
[VII] 80% of $12,390 = ~ $10,000 per patient.
[VIII] If Humana invests $2,500 per patient on the implementation program, Net profit for Humana per patient = $10,000 - $2,500.

9 Future Scope

As we close our extensive analysis, we intend to address certain ways in which we can improve our analysis and offer a holistic view of patient experiences, potentially deriving even better understanding of medication adherence and patient care.

Mediclaim data

It was interesting to see that 100% of the 117 patients in our target group were patients who had Mediclaim data [Fig 3.1.9]. As our predictive models are primarily based on the claim variables, wearing a curious hat, we built an experimental model using just the 536 patients who had Mediclaim information. While, the idea seemed valid, the dataset size was too small to build a model with meaningful insights. If Humana can share more data of patients in Osimertinib therapy, we could have extracted insights where both Mediclaim and pharma claims data is equally weighted.

Data collection using 'Ivory' support group

The recommendation we provided in terms of the online peer-to-peer support group has a long-term advantage. During our extensive research and analysis, we realized that the problem of medicine adherence in the case of cancer patients is as much a behavioral trait as it is hidden in patients' demographics and medical claims data. As we move forward, we believe that capturing behavioral variables of the patients can help Humana in understanding non-adherence better.

Our proposed support group can be a great opportunity to reach out to thousands of global patients going through Osimertinib therapy and collect valuable data from patients in form of surveys to understand their journey. Examples of few such variables could include but not limited to – education level of patients, diet, and exercise habits, and their self-assessment scores on the grit scale[27].

10 Conclusion

There is one type of patient whose journey our analysis didn't do a good job of capturing - those who adhere to the Osimertinib therapy despite all the risk factors from all models flagging them red. They endured all the adverse drug events and had the courage to beat the odds of their therapy progression. Ivory, a Philippine woman who shared her Osimertinib therapy journey via YouTube, was one such paragon who managed to leave a deep impact on us. We admire and take inspiration from the journeys of these courageous individuals and acknowledge that they motivated us to put forth our best effort in working on this problem. We would consider our efforts on this report rewarded if even one of such patients sees a successful outcome from their Osimertinib therapy because of this report.

[27] Angela Duckworth - https://angeladuckworth.com/grit-scale/

11 Additional References

1 What Causes Constipation and Fatigue – https://www.healthline.com/health/digestive-health/constipation-and-fatigue
2 Miantenance Drugs Adherence – https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3191684/
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12 Appendix

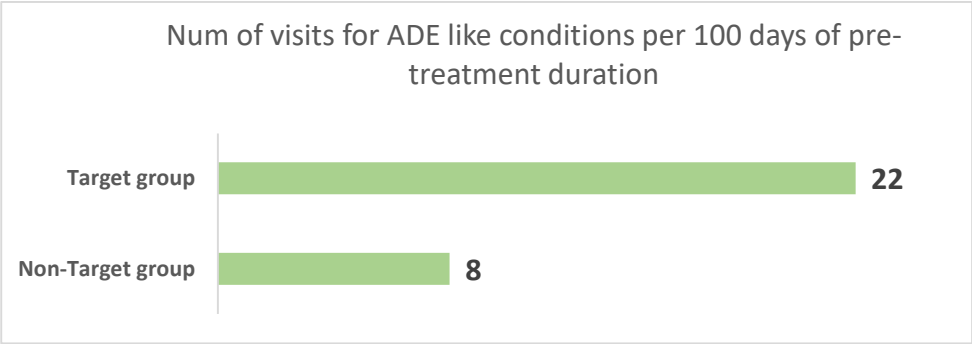
Feature Name	Description	Phase
Age	Estimated age of the patient	Both Phases
cms_disabled_ind	CMS classification as disabled	Both Phases
cms_low_income_ind	Receives low-income subsidies from CMS	Both Phases
ADE Diagnosis Rate Before Tx	ER visits for ADE symptoms / Duration of Claims before Tx	Both Phases
Mental Health Diagnosis Rate Before Tx	Mental health-related visits / Duration of Claims before Tx	Both Phases
Physician Office Visit Rate Before Tx	Visits to Physician Office / Duration of Claims before Tx	Both Phases
Outpatient Facility Visit Rate Before Tx	Visits to Outpatient facilities / Duration of Claims before Tx	Both Phases
ER Visit Rate Before Tx	ER visits / Duration of Claims before Tx	Both Phases
Inpatient Acute Care Visit Rate Before Tx	Inpatient Acute Care visits / Duration of Claims before Tx	Both Phases
Mental Health Drug Claim Rate before Tx	Mental health Drug claims / Duration of Claims before Tx	Both Phases
Maintenance Drug Claim Rate before Tx	Maintenance Drug claims / Duration of Claims before Tx	Both Phases
Anti-Infective Drug Claim Rate Before Tx	Anti-infective Drug claims / Duration of Claims before Tx	Both Phases
Diabetes Drug Claim Rate Before Tx	Diabetes Drug claims / Duration of Claims before Tx	Both Phases
Hypertension Drug Claim Rate Before Tx	Hypertension Drug claims / Duration of Claims before Tx	Both Phases

Narcotic Drug Claim Rate Before Tx	Narcotic Drug claims / Duration of Claims before Tx	Both Phases
Avg Days' Supply of Drugs After Tx	Avg days' supply post-treatment start	Therapy Phase
Fatigue Diagnosis Rate After Tx	Fatigue diagnoses / Duration of Claims after Tx	Therapy Phase
Nausea Diagnosis Rate After Tx	Nausea diagnoses / Duration of Claims after Tx	Therapy Phase
Constipation Diagnosis Rate After Tx	Constipation diagnoses / Duration of Claims after Tx	Therapy Phase
Diarrhea Diagnosis Rate After Tx	Diarrhea diagnoses / Duration of Claims after Tx	Therapy Phase
Pain Diagnosis Rate After Tx	Pain diagnoses / Duration of Claims after Tx	Therapy Phase
Nausea Drug Claim Rate After Tx	Nausea Drug claims / Duration of Claims after Tx	Therapy Phase
Diarrhea Drug Claim Rate After Tx	Diarrhea Drug claims / Duration of Claims after Tx	Therapy Phase
Seizure Drug Claim Rate After Tx	Seizure Drug claims / Duration of Claims after Tx	Therapy Phase
Mail-Ordered Drugs Rate After Tx	Drugs ordered via mail / Duration of Claims after Tx	Therapy Phase
Mental Health Drugs Claim Rate After Tx	Mental health Drugs claims / Duration of Claims after Tx	Therapy Phase
Generic Drug Claim Rate After Tx	Generic drug claims / Duration of Claims after Tx	Therapy Phase

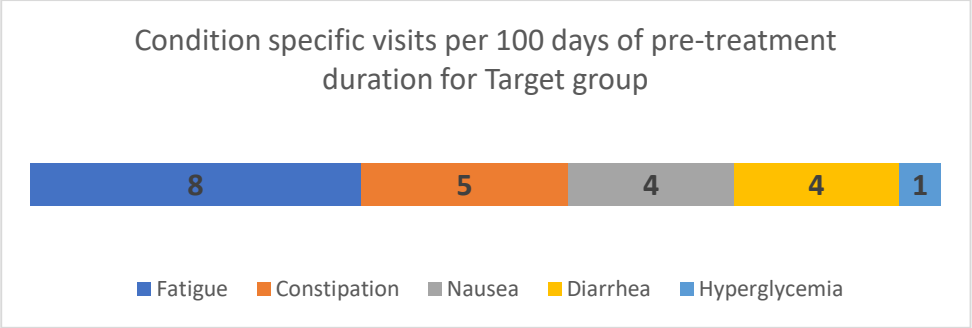
Analysis on patients with ADE-related conditions before the therapy start:

We had an ADE indicator in mediclaims when patients are diagnosed with one among the five conditions that resemble the ADEs of Osimertinib – fatigue, nausea, hyperglycemia, constipation, and diarrhea. In the stages before Osimertinib therapy started, these conditions were not caused by Osimertinib. But, an interesting pattern we noticed is that patients having a high visit rate for conditions that resemble the ADEs of Osimertinib are at an increased risk of discontinuing the therapy after facing ADEs.

Below visualization shows the difference between the target and non-target groups for number of visits for ADE like conditions per 100 days of pre-therapy duration:



Below visualization shows the breakdown of those 22 days around specific conditions, and we could see that fatigue and constipation are common conditions among target group before therapy starts.



Fatigue and constipation are common side effects for many existing conditions of patients,

Patients with low mental health medication usage before therapy start:

Cancer diagnosis is not an easy news for any patient. Research shows that around 30% of cancer patients suffer from Psychiatric disorders during some phase of the therapy.

Low mental health medication rate before therapy start could be because of poor mental health management from patient's end

1. 188 patients had at least one primary or secondary diagnosis related to mental health (diagnosis code F00 – F99) before treatment. Out of these patients, 68 patients did not have any mental health drug claim before treatment start, signaling poor mental health management. There is 30% drop out rate among these patients with a median therapy duration of 1 month.

2. 470 people have a claim for mental health drugs before the therapy start. Out of this group, there is roughly a 10% rate of patients experiencing an ADE and dropping out of therapy within 6 months. Whereas 172 people have used mental health drugs for the first-time post therapy start, and out of this group there is a 15% rate of patients experiencing an ADE and dropping out of therapy within 6 months.