Predicting Opioid Prescriptions based on Patient Demographics in MIMIC-IV

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***Abstract*—Opioids are widely used analgesics because of their efficacy, mild sedative and anxiolytic properties, and flexibility to administer through multiple routes. Understanding the demographics of the patients receiving these medications helps provide customized care for the susceptible group of people. We conducted a demographic evaluation of the frequently prescribed opioid drug prescriptions from the MIMIC IV database. We analyzed prescribing patterns of six commonly used opioids with demographics such as age, gender, ethnicity, marital status, and year predominantly. After conducting exploratory data analysis, we built models using Logistic Regression, Random Forest, and XGBoost to predict opioid prescriptions and demographics for those. We also analyzed the association between demographics and the frequency of prescribed medications for pain management. We found statistically significant differences in opioid prescriptions among the male and female population, married and unmarried, various ages, ethnic groups, and an association with in-hospital deaths.**

***Index Terms*—opioids, racial bias, mimic-iv, machine learning**

I. Introduction

"Pain is an important public health problem in the United States," as per the National Institute of Health (NIH) and the Institute Of Medicine (IOM). The average annual costs for treating chronic pain ranges from $560 to $635 billion [1]. As per the American Academy of Pain Medicine (AAPM), pain affects more individuals in the US than complicated diseases such as diabetes, heart disease, and cancer together. Chronic pain affects various aspects of a patient's life, including physical and emotional function, potentially decreasing the financial income. A record linkage study suggests that severe chronic pain causes an increased risk of mortality, independent of sociodemographic factors [2].

Techniques for pain management include the following modalities [10]. Intermittent or continuous systemic opioids. Multimodal techniques (administration of 2 or more drugs that act by different mechanisms to provide analgesia). Central regional (i.e., neuraxial) opioid analgesia; and peripheral regional analgesic techniques, including intercostal blocks, plexus blocks, and local anesthetic infiltration. Opioids are majorly used as analgesics because of their potency. Opioids have useful properties such as being mildly sedative and anxiolytic properties, and can be administered through various routes. Specifically, Morphine, Fentanyl, and Hydromorphone are widely used opioids in inpatient settings [3].

Quite a bit of research has been done on Opioid prescription differences by sociodemographic characteristics of patients. More women were identified as chronic pain sufferers among all counties and all age groups over ten years in Maine [1]. Race influences the treatment of pain. In a study, 27 percent of African Americans and 28 percent of Hispanics above 50 years reported having chronic pain, whereas non-Hispanic whites were 17 percent [4]. Another study showed that drug-related deaths were highest among non-Hispanic white people. Whites receive better pain therapy when compared to African Americans and Hispanics [5]. A study reported that the chronic pain population's percentage increases with age, with a significant increase at age 65 and more in both males and females. Between the ages of 70-74, the female chronic pain population was 50%, whereas the male chronic pain population was 50% at 85 years and greater [1]. Schieber et al. [4] have studied the variation in adult outpatient opioid prescription dispensing by Age and Sex. Like the other studies, they also found significant number of opioid prescriptions given to women than men among all age groups. Nair et al. [5] applied machine learning approaches to predict postoperative opioid requirements in ambulatory surgery patients. They used Multinomial Logistic Regression, Naive Bayes, Neural Networks, Random Forest, and Extreme Gradient Boost to predict postoperative opioid requirements in ambulatory surgery patients. Along the same lines, we attempt to see if

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sociodemographic information can help predict the type of Opioid.

In this paper, we identify associations between sociodemographic characteristics and opioid type, and then apply machine learning approaches to predict the prescriptions of the six opioids (Morphine, Codone, Hydromorphone, Fentanyl, Tramadol, and Methadone). We used Binomial Logistic Regression, Random Forest, and Extreme Gradient Boost. These models helped us to predict opioid prescriptions in various sociodemographic patients and understand their significance from the MIMIC-IV data.

II. Methodology

A. Database & Data Description

The MIMIC-IV [6] database consists of ten years of data from 2008 to 2019 of Beth Israel Deaconess Medical Center, separated into five modules: core (contains demographics, hospital admissions, and in-hospital ward transfers), hospital (EHR data with laboratory measurements, microbiology, medication administration, and billed diagnoses is stored), ICU (intensive care unit module has intravenous administrations, ventilator settings, etc.), ED (emergency department stores reason for admission, triage assessment, vital signs, and medicine reconciliation), CXR (patient chest x-rays with the associated clinical data). Mimic 'core' module consists of patients' stay information like admissions and transfers. We extracted columns such as subject id, hadm_id (hospital admission id), gender, anchor age (the age of the patient in the admitted year), anchor year group (a range of years the patient visited), ethnicity, marital status, hosp expire flag (binary flag indicating whether the patient died within the given hospitalization), insurance, admission type (classifier of the urgency of the admission) from the mimic core module. Similarly, to identify the pain prescriptions, the 'hosp' module containing hospital-level information like lab events, microbiology events, medication information, etc., is utilized. We obtained the subject_id, hadm_id, and the drug from the prescriptions table in the mimic hospital module. We do not analyze clinical notes [7] using natural language processing approaches in our study, which might provide some additional explanation for the opioid type prescribed, but is outside the scope of our approach.

We first selected the pain medications starting from the most commonly prescribed opioids such as morphine, hydromorphone, fentanyl, tramadol, methadone, and Codone [8] [9]. Non-opioid analgesics like acetaminophen, ketamine, dexmedetomidine, and NSAIDs, including ibuprofen, diclofenac, ketorolac are prioritized next [10]. We included µ2-agonists that are clonidine, tizanidine, guanfacine, and benzodiazepines like midazolam, lorazepam. Gabapentinoids such as gabapentin and pregabalin are further used in the study [11]. We combined all these drugs (19) under one 'all_pain_flag' column. We compared the commonly used six individual opioid drug prescription trends concerning overall pain medication prescriptions and demographics taken from the patients and admissions tables from the mimic core module. Hence, patients who received these prescriptions are included in the study matching the names of these drugs, 'all_pain _flag' for the overall pain prescriptions of the selected nineteen drugs, and specific flags for the chosen six opioid medications from the prescriptions table. We further joined the tables with the demographic and prescription data using subject_id and hadm_id.

B. Data Interpretation & Statistics

Pain medication prescriptions are taken from the comprehensive in-patient data for all the years included. A prescription flag is given if there's a match with the given drugs' keywords through the connection made from the database in PostgreSQL to jupyter python notebook using the cursor. After creating a pandas dataframe matching the keywords and obtaining various specific drugs, the demographics are joined to this drug information using the primary keys in those tables. We conducted exploratory data analysis by analyzing the demographic features and assessing the attributes' relations considering these features. Furthermore, we performed feature engineering cleaning by removing redundant features. For the categorical column 'anchor age', we segregated the ages into five groups such as $>16\leq32$, $>32\leq48$, $>48\leq64$, >64 and created Age bands 1, 2, 3, 4 respectively, thereby dropping the unnecessary anchor age column. We then checked for correlations among attributes with the help of a heatmap. After creating the dataframe with the required columns, we generated dummies for the columns 'gender', 'anchor year group', 'ethnicity,' 'admission type,' 'insurance,' and 'marital status. We first performed ANOVA to check if the difference between the groups is significant enough or not to proceed with the analysis. As the data is imbalanced between the prescribed and not-prescribed groups, we downsampled the specified data to match the other group. Later, we performed a logistic regression model taking the demographics in 'X' and studying the drug in 'y' as the target variable. We analyzed the classification report, score, confusion matrix, and essential features from the model. Machine learning in healthcare has been used to predict important patient characteristics such as for mental health issues [12], sedation management [13], or length of stay prediction [14]. However, machine learning approaches are fraught with biases [15] [16], and data in-itself might have biases that should be explored before machine learning models can be trained [17]. Our analysis identifies such sociodemographic biases in opioid prescription data. Thus, we performed random forests as a basic algorithm besides the logistic regression. We validated the outcomes through a confusion matrix. The ensemble technique we used to enhance the model is boosted by XGBoost (XGB), followed by plotting the feature importance [10]. Similarly, we predicted the individual opioid drug prescriptions (Morphine, Codone, Hydromorphone, Methadone, Tramadol, Fentanyl) among the overall pain medication prescriptions taken.

III. Results

We observed several exciting results from this study. When we looked at the numbers of all medications overall prescriptions from the data, we found that the 12 frequently prescribed pain medication prescriptions are 1.35% more in female patients than males. This difference majorly comes from Black/African American, Hispanic/Latino, and Asian ethnic groups. The count of these 12 drug prescriptions has risen in age groups $>16\leq48$, lowered up to 10% in patients over 48 years than overall medication prescriptions given for various diagnoses. The average age of the patients with pain drug prescriptions is 55 years eldest being 91-year old patients. We segregated the findings of individual drugs below. Table 1 shows the spread of prescriptions across age groups and genders. The frequency of opioid prescriptions are Morphine (n=17,509), Codone (n=345,594), Hydromorphone (n=309,986), Fentanyl (n=69,845), Tramadol (n=47,725), Methadone (n=17,509). The split of the prescriptions between the genders and among the age groups is given in Table 1.

TABLE I
EXPLORATORY DATA ANALYSIS OF OPIOIDS THROUGH AGE GROUPS AND GENDERS

		Age groups				
Drug	**Sex**	**16-32**	**33-48**	**49-64**	**64+**	**All**
Morphine	F	54.8%	52.7%	47.1%	52.9%	51.0%
	M	45.2%	47.3%	52.9%	47.1%	49.0%
Codone	F	63.4%	54.2%	44.4%	50.0%	50.4%
	M	36.6%	45.8%	55.6%	50.0%	49.6%
Hydromorphone	F	54.9%	55.1%	47.9%	50.9%	51.5%
	M	45.1%	44.9%	52.1%	49.1%	48.5%
Fentanyl	F	40.7%	44.5%	41.2%	45.4%	43.4%
	M	59.3%	55.5%	58.8%	54.6%	56.6%
Tramadol	F	63.9%	57.2%	53.4%	59.5%	57.8%
	M	36.1%	42.8%	46.6%	40.5%	42.2%
Methadone	F	54.6%	47.6%	34.5%	45.3%	43.3%
	M	45.4%	52.4%	65.5%	54.7%	56.7%

A. Morphine

Morphine comprises 1.1% of prescriptions overall. Morphine prescriptions are more in females (2%) than males. This difference is mainly from the Black/African American (10%) race. In-hospital deaths in patients with prescription are slightly more in 'Males.' Considering the marital status, widowed, divorced, and single women received more pills than men. In contrast, married men got more morphine than married women. Patients from the emergency ward, same-day admission, and urgent admission type received more drug orders. Prescription count reduced by 82% from 20082019. Females got more prescriptions from 2008-19. Upon dealing with the imbalances between the medication and no-prescription numbers in the data by downsampling, value counts of morphine are 1-196778 and 0-192346. The MANOVA test confirms the significance of the morphine prescriptions difference among the sociodemographic groups. The p-value is 0.0000, while the F Value is 519.5452 for factor variables ethnicity, gender, marital status, and hospital expire flag. The top 5 features by importance from XGB are gender F, anchor year group 2011-13, hospital expire flag, marital status married, and ethnicity white.

B. Codone

Codone comprises 2.0% of prescriptions overall. Women received 0.8% more Codone in their orders than men. Races Black/African American (11%), Hispanic/Latino (6%), Asian (6%) are the differentiators. Whites have received more numbers of Codone drugs. More medications for females from 20-40 years of age and the ratio of prescriptions were almost similar in both the genders from 40+years of age. Pills of Codone were less compared to overall pain prescriptions among ages 0-15, 70+ years. The medicines were more at 60-65 years of age. 2008-10: Overall Codone prescriptions were more in males when compared to females. Males belonging to the white race were prescribed more, and American Indian/ Alaska Native males were prescribed less Codone during these years. Also, the overall Codone prescriptions were reduced in the following years, and Codone was prescribed more to the male patients when compared to female patients. Like these years, the males belonging to the white race were prescribed more Codone when compared to other races. During 2014-16, Codone was not prescribed to males and females belonging to the American Indian/Alaska native race. Value counts of morphine after downsampling the data are 1-345594, 0-332060. The MANOVA test confirms the significance of the difference in Codone prescriptions among groups by rejecting the null hypothesis as the p-value is 0.0000 and the F-value is 1738.4481. The top 5 features from XGB are gender F, Insurance Medicare, Hospital expire flag, Age band 2, Age band 1, ethnicity Black African American.

C. Hydromorphone

Hydromorphone comprises 1.8% of prescriptions overall. Prescriptions in female patients are higher (3%) when compared to male patients, and the difference can be seen from Fig.1. Whites have received more numbers of Hydromorphone prescriptions. There were more prescriptions for females over 30 years of age. Pills of Hydromorphone were less compared to overall pain prescriptions among ages 0-5, 70+ years. The medications were more in 50-55 years of age. 2008-10: Overall, Hydromorphone prescriptions were more in females when compared to males. Females belonging to the white race were prescribed more, and American Indian/ Alaska Native males were not named Hydromorphone during these years. In the following years from 2011-19, the prescription count was reduced by more than half of 2008-10. Females are prescribed more Hydromorphone pills than males. Value counts of morphine after downsampling the data are 1-315681, 0-304291. The MANOVA test confirms the significance of the difference in Hydromorphone prescriptions among the demographic groups, and the null hypothesis is rejected as the p-value is 0.0000 and F-value is 1877.2970. The top 5 features by importance from XGB are gender F, Hospital expire flag, Insurance Medicare, ethnicity Black African American, anchor year group 2008-2010.

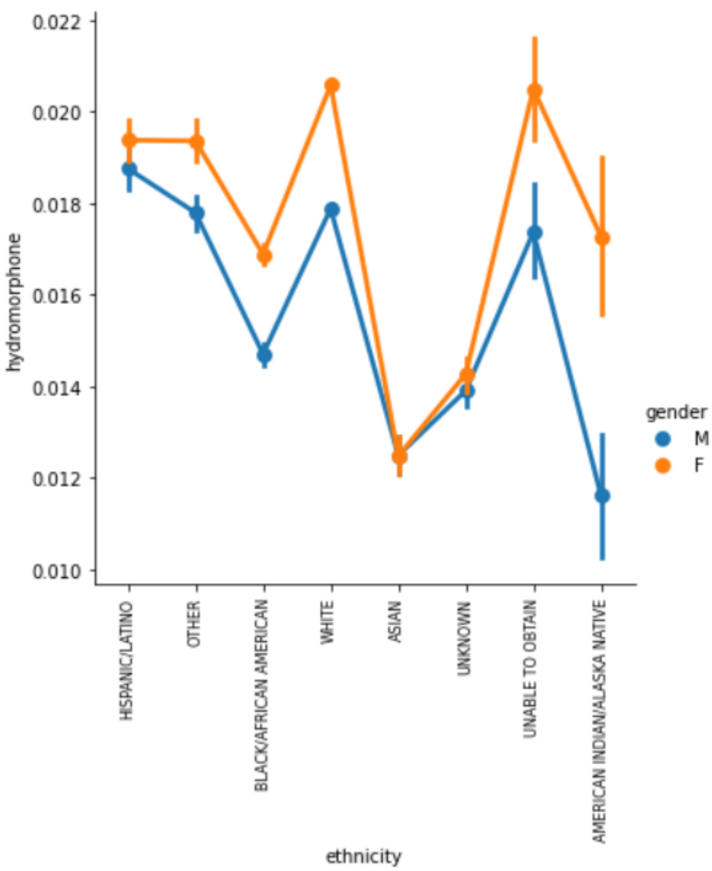

Fig. 1. Ethnicity, gender, and Hydromorphone prescriptions .

D. *Fentanyl*

Fentanyl comprises 0.4% of prescriptions overall. Prescriptions in male patients outnumber female patients by 13%. Younger Indian/Alaskan native ethnic group patients received more Fentanyl prescriptions. Females over 60 years received more medications than males. Pills of Fentanyl are higher compared to overall pain prescriptions among ages 0-5,30-35 and 55-60 years. A fall in the same is observed in patients over 90. 2008-10: Overall, Fentanyl prescriptions are more in males. This contrasts with the ethnic group Black/African American, where females have more medications than males. 2011-13: Overall, Fentanyl prescriptions are reduced to half, and male patients got more pills than females among all ethnic groups. 2014-16: Prescriptions further reduced by 10-15%, and males received more prescriptions than Black/African American females. 2017-19: There is a fall additionally; both females and males received a similar no, of pills. The average age of the patients with pain drug prescriptions is 55 years eldest being 91-year-old patients. We observed that medicines in both genders rise at 20 years of age peaked at 60 years.Medications in infants are higher in males. It's seen that prescriptions in the Hispanic/Latino group are higher from age 25 to 60. When it comes to the overall age of the patients with pain medication prescriptions, we observed that ages 55-60, 65-70, 60-65, 45-50, 50-55 got more pills while ages 15-20, 20-25 and infants received least no, of drugs respectively. In the year group 2008-2010, Prescription of pain medications in women is more than in men. It's around 50% more than men in Black/African American women, which is quite noticeable. While by 2017-2019, Black/African men have more pain prescriptions than women. We observed a significant fall (over 60%) in overall drugs and pain medicine prescriptions from 2008-2019. The results of individual ANOVA tests showed that there is a significant difference in pain prescriptions between the genders, all the age groups and all ethnic groups except between unknown-white, Black/African American-Unable to obtain, and unknown and American Indian/Alaska native ethnic groups. Value counts of morphine after downsampling the data are 1-69845,0-69231. MANOVA tests confirm the significance of the difference in Fentanyl prescriptions among demographic groups by rejecting the null hypothesis. The p-value is found to be 0.0000, and F-value is 914.8928. The top 5 features by importance are gender F, ethnicity white, Insurance Medicaid, anchor year group 2008-2010, and Age band 2.

TABLE II
PERFORMANCE RESULTS ON DEMOGRAPHICS AND OVERALL FREQUENTLY PRESCRIBED PAIN MEDICATIONS:

Drug & metric	LR		RF		XGB	
	Dem.	All_rx.	Dem.	All_rx.	Dem.	All_rx.
Morphine:						
F1-Score	0.61	0.95	0.63	0.94	0.61	0.95
Precision	0.59	0.90	0.61	0.89	0.61	0.90
Accuracy	0.55	0.94	0.61	0.94	0.61	0.94
Codone:						
F1-Score	0.61	0.95	0.63	0.95	0.62	0.95
Precision	0.59	0.90	0.61	0.91	0.60	0.91
Accuracy	0.54	0.95	0.60	0.95	0.60	0.95
Hydromorphone:						
F1-Score	0.64	0.94	0.68	0.95	0.67	0.94
Precision	0.64	0.90	0.65	0.90	0.65	0.89
Accuracy	0.54	0.95	0.66	0.94	0.65	0.94
Fentanyl:						
F1-Score	0.57	0.95	0.62	0.94	0.67	0.95
Precision	0.63	0.90	0.63	0.89	0.65	0.90
Accuracy	0.61	0.94	0.62	0.94	0.63	0.95
Methadone:						
F1-Score	0.71	0.94	0.80	0.94	0.78	0.93
Precision	0.72	0.89	0.77	0.89	0.74	0.88
Accuracy	0.55	0.93	0.79	0.93	0.77	0.94
Tramadol:						
F1-Score	0.61	0.94	0.62	0.94	0.62	0.94
Precision	0.58	0.89	0.59	0.88	0.60	0.88
Accuracy	0.59	0.94	0.59	0.93	0.61	0.93

E. Tramadol

Tramadol comprises 0.3% of prescriptions overall. Prescriptions in female patients are higher when compared to male patients over 15%. Whites have received more numbers of Tramadol prescriptions. There were more prescriptions for females from 50+ years of age. Tramadol prescriptions were less when compared to overall pain prescriptions among ages 0-15, 70+ years. The pills were more from 60+ years of age. 2008-10: Overall, Tramadol prescriptions were more in females when compared to males. Ethnic group white females were given more prescriptions, and American Indian/ Alaska Native males have not been prescribed Tramadol during these years. In the following years until 2019, Tramadol prescriptions were reduced by more than 60%, just like other pain medications, and women received more drugs than men in all these years. Value counts of morphine after downsampling the data are:1-47725,0-47501. The MANOVA test confirms the significance of the difference in Tramadol prescriptions among groups by rejecting the null hypothesis since the p-value is 0.0000 and the F-value is 309.0261. The top 5 features by importance from XGB are gender F, anchor year group 2011-13, insurance Medicaid, Age band 2 and ethnicity White.

F. Methadone

Methadone comprises 0.1% of prescriptions overall. Prescriptions in male patients are higher when compared to female patients. Asian ethnic group patients have received more methadone prescriptions. There were more prescriptions in males over 60 years of age. Prescriptions of methadone were less compared to overall pain prescriptions among ages 0-5, 65+ years. The medications were more in 50-55 years of age. 2008-10: Overall, Methadone prescriptions were slightly more in females. 2011-13: Overall, Methadone prescriptions were reduced to half, and methadone was prescribed more to male patients in these years. 2014-16: Total prescriptions were reduced when compared to the previous years. Methadone was prescribed more to males when compared to females. American Indian/Alaska native and Asians have received no Methadone prescriptions. 2017-19: Total prescriptions were again reduced when compared to the previous years. Like the last years, males were prescribed more Methadone prescriptions when compared to females. Females of the Black/African American race were prescribed more Methadone prescriptions when compared to others. Value counts of morphine after downsampling the data are: 1-17509, 0-17463. The significance of the difference in methadone prescriptions among sociodemographic groups is reinforced by the MANOVA test's p-value being 0.0000 and F-value being 342.1481. The null hypothesis is rejected. The top 5 features by importance are gender F, anchor year group 2011-13, ethnicity white, marital status married and Age band 3.

In Table 2, the three developed models returned the given F1 scores, precision, and accuracy to predict the six opioids among the overall prescriptions and demographics. It is evident that all the models (Logistic regression, Random Forest, and XGBoost) performed well (around 90%) to predict the prescriptions of the six drugs from the overall medications. Simultaneously, the models performed reasonably well (approximately 60%) to predict the combined demographics for the chosen drugs.

IV. Discussion

As far as we know, this is among the first studies trying to identify biases of significance in the opioid prescription in MIMIC-IV data. Prescription opioids are used to treat mild to extreme pain and are often administered after surgery or injury, as well as for some medical conditions. These drugs may be a vital part of treatment, but they also carry significant risks. As per several articles, the number of opioid prescriptions has decreased [11]. According to our report, the number of patients who got opioid prescriptions dramatically reduced over the years across ages, ethnic groups, and genders. This may be attributed to the Centers for Disease Control and Prevention's (CDC) recommendations to prescribe alternatives to opioids and opt for opioids during active cancer treatment and provide end-of-life care [10]. When opioids are used for chronic pain, the recommendations suggest using non-opioid therapies first, then using opioids only when the benefits are more than risks, then prescribing the lowest effective dose [18]. We observed statistically significant variations in the prevalence of receiving opioid prescriptions by gender, consistent with previous research [19] [8]. We discovered that women had a higher chance of receiving opioid prescriptions than men after controlling for other covariates. Women received more Morphine, Codone, Hydromorphone, and Tramadol prescriptions than men. Men got more Fentanyl and Methadone than women, which is in contrast with a study by Susannah et al. in Cancer patients [20]. Although several studies have shown that women report more health issues than men, our findings may seem counterintuitive as the prescriptions' comprehensive data is higher in men [21] [22]. In both ANOVA and MANOVA tests, age was substantially and positively correlated with receiving opioid medications. From the machine learning models, age was identified as a highly weighted feature for most opioid prescriptions for prediction. Similar findings were discovered and published by several other researchers [12, 22] [2] [23]. Lemke [8], Kelly, et al. [24], and Luo et al. [25] all observed a statistically significant difference in opioid usage by race or ethnicity. Our findings revealed that White patients had the highest prevalence of receiving opioid prescriptions. We discovered that they were greatest among divorced, separated, or widowed individuals, consistent with previous studies [26]. Future research should look at these sociodemographics, the number of opioid prescriptions, and the strength and duration of such drugs. Furthermore, data on older adults, Black/African women and divorced, or widowed women taking opioid prescriptions should be examined more closely. Clinicians and pharmacists could gain more insights to provide optimal care to the patients who are likely to receive opioid prescriptions. This data would be instrumental in understanding the opioid epidemic. This study can be further improved by selecting the pain diagnoses with ICD codes and analyzing the most prescribed pain management drugs. This analysis helps to address the needs of the patients who are frequent sufferers of pain with effective medical management. There is scope to understand the deaths associated with prohibited drugs in the ICU and predict the drugs that lead to those deaths.

V. Conclusion

To our knowledge, this is the first study that analyzes the prevalence of specific opioid prescriptions among the various demographic groups in Boston. Our results predict the difference between the genders in receiving the selected Opioid prescriptions in MIMIC IV data. Women will receive more medications than men across the selected drugs. Another important feature while determining the pills is 'age.' There's a difference in the varied age groups observed in almost all the opioids chosen. Surprisingly, three vastly prescribed opioids (Morphine, Codone, Hydromorphone) showed 'in hospital deaths' association with their prescriptions. Black/African American ethnic group is predicted to receive more Codone and Hydromorphone, which are the two majorly prescribed drugs among the selected drugs. Understanding the disparities among the race and ethnicity concerning opioid prescriptions can help identify these patients, introspecting the reasons, and providing exceptional care accordingly.

VI. Abbreviations

ANOVA: Analysis of Variance, CDC: Centers for Disease Control and Prevention, CXR: Chest x-rays, ED: Emergency Department, EHR: Electronic Health Record, Hadm_id: Hospital Admission id, ICD: International Classification of Diseases, ICU: Intensive Care Unit, LR: Logistic Regression, MANOVA: Multivariate Analysis of Variance, NSAID's: Nonsteroidal Anti-Inflammatory Drugs, RF: Random Forest, XGB: eXtreme Gradient Boosting.

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