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Exploring high opioid prescriptions among nephrologists in the United States using machine learning algorithms

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ABSTRACT

Background and aims: The opioid pandemic has contributed to deaths globally, and prescription opioids have played a crucial role in these deaths. Addressing overdose requires understanding the reasons behind prescription, especially in cases of chronic diseases. Several factors play a role in the increased prescription of opioids, relating to patients' lifestyle, characteristics, and disease. As these factors are complex in nature, understanding them requires machine learning approach. This study explored overprescribing opioids among nephrologists in the US using unsupervised machine learning algorithms.
Design: Two types of unsupervised clustering were applied to the Medicare Provider Utilisation and Payment Data Part-D Prescriber Summary.
Setting: The dataset had 50,134 records with 85 features relating to opioids prescription per US state. Univariate and bivariate analysis were applied first to gain understanding of the data followed by K-mean clustering and Gaussian Mixture Models.
Findings: Unsupervised clustering showed that prescription issued to males were three times higher than those issued to females. Moreover, male nephrologists were higher prescribers than female nephrologists, and a third of male nephrologists were high prescribers of opioids. The highest rates of prescriptions were seen in California.
Conclusions: Unsupervised machine learning algorithms enabled understanding of high opioid prescription across gender and US state by analysing multiple features. Both K-mean clustering and Gaussian Mixture Models achieved the same outcomes. Future work will benefit from applying deep learning in order to understand in-depth patterns in prescription and contributing factors related to over-prescribing.

1. Introduction

The opioid pandemic has contributed to major morbidities and mortalities at global levels. In 2017, 40,600 out of 70,237 deaths aids due to opioid overdose (Hedegaard et al., 2021). The situation did not ease up after 2017 where the CDC reported 645,000 deaths linked to opioid overdose between 1999 and 2021 (CDC, 2021).

In addition to non-prescription opioids, prescription opioids contribute to the risk of the opioid pandemic. Previous studies have identified that opioid prescriptions are among the major causes or opioid overdose (Guy et al., 2017; Nataraj et al.2019). Prescription opioids have been identified as a major cause for opioid abuse in the US (Mallappallil, 2017). Hence, in 2017 35 % of opioid overdose death were linked to prescription opioids (Scholl et al., 2019). However, these guidelines did not prevent physicians from overprescribing who were still not sure how to act in chronic pain management (McCann-Pineoet al., 2021).

In chronic diseases, e.g. kidney disease, opioids are prescribed for pain management; however, they can be toxic due their metabolites' accumulation in the kidney (Richards et al., 2018). Moreover, the increased prescription of opioids has contributed greatly to the opioid academic (McCann-Pineoet al., 2021). The US Department of Health and Human Services (HHS) declared a public health emergency in response to opioid crisis proposing a 5-point strategy including: Better

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Table 1
Description of the dataset.

Feature abbreviation	Feature description
npi	National Provider Identifier (NPI) for the provider
nppes_provider_state	Geographic state of the provider
nppes_provider_gender	Gender of the provider: Value 'M' denotes male, value 'F' denotes female providers, value 'blank' denotes organisation.
nppes_provider_country	nppes_provider_country = 'US' represents provider is registered in US territory and for foreign countries, nppes_provider_state = "ZZ".
specialty_description	Denotes the Medicare provider/supplier specialty code. For providers that have more than one Medicare specialty code reported on their claims, the Medicare specialty code associated with the largest number of services is reported.
total_claim_count	The number of Medicare Part D claims. This includes original prescriptions and refills. Aggregated records based on total_claim_count fewer than 11 are not included in the data file
opioid_claim_count	Total opioid drug claims, including refills. When the opioid_claim_count is between 1 and 10, it is suppressed. A blank denotes a suppressed value.
opioid_day_supply	The total number of day's supply for opioid drugs. When the opioid_claim_count is suppressed, opioid_day_supply is suppressed. A blank denotes a suppressed value.
opioid_prescriber_rate	The percent of the total_claim_count represented by the opioid_claim_count. When the opioid_claim_count is suppressed, opioid_prescriber_rate is suppressed. A blank denotes a suppressed value.
la_opioid_claim_count	Total long-acting opioid drug claims, including refills. When the la_opioid_claim_count is between 1 and 10, it is suppressed. A blank denotes a suppressed value.
la_opioid_day_supply	The aggregate number of day's supply for long-acting opioid drugs. When the la_opioid_claim_count is suppressed, la_opioid_day_supply is suppressed. A blank denotes a suppressed value.
la_opioid_prescriber_rate	The percent of the opioid_claim_count represented by the la_opioid_claim_count. When the la_opioid_claim_count is suppressed, la_opioid_prescriber_rate is suppressed. A blank denotes a suppressed value.

Prevention, Treatment; Better Data; Better Pain Management; Better availability of Overdose-Reversing Drugs; and Better Research (US Department of Health and Human Service, 2022). Other organisations released guidance to decrease prescription of opioids (CDC, 2016).

Understanding the scale of the problem is important prior to addressing it. Thus, many factors contribute to increased prescription of opioid as reported in the literature. These factors are related to patients' health, lifestyle and characteristics. Studies have reported that marginalised groups, females as well as patients with private insurance are more likely to receive more opioid prescriptions (Hoppe et al., 2017; McCann-Pineoet al., 2021). Considering the multiple factors that play a role in prescription, machine learning approaches are crucial in order to understand the degree these factors influence opioid prescriptions as they can feedback on multiple factors simultaneously and the relationship between these factors (McCann-Pineoet al., 2021; Mulainathan and Spiess, 2017).

The present study explored the high prescription of opioids among nephrologists using machine learning algorithms (MLAs). More specifically, the study utilised unsupervised clustering algorithms being K-mean clustering and Gaussian Mixture Models (GMM) that were applied to the 'Medicare Provider Utilisation and Payment Data Part-D Prescriber Summary'. The study aimed to identify patterns high opioid prescriptions among different genders and across different states.

2. Methods

2.1. Study design

The present study was a retrospective study applied to an open access dataset obtained online from the CMS (CMS, 2019). The dataset was collected by the CMS for 'Medicare Provider Utilisation and Payment data Part-D Prescriber Summary' between the years 2013 - 2018. The dataset had 50,134 records with 85 features each. It consisted of six comma separated files (.csv); such that each file consisted of 1 million prescription drug event (PDE) records that had been provided by healthcare practitioners.

Table 2
Number of missing values per features.

Variables/Features	Number of missing values or null values or blanks	Percentage of Missing Values
npi	0	0
nppes_provider_gender	0	0
nppes_provider_state	0	0
nppes_provider_country	0	0
specialty_description	0	0
total_claim_count	0	0
opioid_claim_count	17,294	34.5
opioid_day_supply	17,294	34.5
opioid_prescriber_rate	17,294	34.5
la_opioid_claim_count	7499	14.96
la_opioid_day_supply	7499	14.96
la_opioid_prescriber_rate	17,329	34.57
year	0	0

2.2. Ethical approval

The study used retrospective dataset from CMS that had no identifiable information for patients thus no ethical approval was required.

2.3. Data collection

Patients registered in 'the Medicare Part D Prescription Drug Programme' pay for prescription medications issued by specific doctors and/or other healthcare practitioners. This data has been collected as part of the dataset alongside the prescription drug plans and the PDE. Prescription drug plans consisted of Medicare Advantage Prescription Drug (MAPD) and stand-alone prescription drug plans. All this data has been summarised in 'Part D Prescriber Summary Table (PDP)'. Table 1 summarises the key features of the dataset that were included in the study.

2.4. Inclusion and exclusion criteria

Data included from the Medicare dataset were the prescription issued by nephrologists for opioid prescription patterns. NPI value served as unique identification number for each provider and no identifiable information was extracted in this study. Only opioid claims were considered where non-opioid claims were excluded from this study. Moreover, data outside the US represented < 0.1 % of the dataset so were excluded from further analysis. Moreover, gender categories other than 'M' or 'F' were below 0.1 % so were excluded. Table 2 Shows the number of missing values for features considered in this study. Missing values were seen for six variables and were excluded.

2.5. Data analysis

Univariate and bivariate analysis were applied prior to application of machine learning algorithms in order to gain initial understanding of the dataset. Then, unsupervised clustering was applied to the dataset in order to identify high opioid prescription among nephrologists across different genders and states. In this respect, two unsupervised clustering analytics were applied being K-mean clustering and Gaussian Mixture Models (GMM).

For K-mean clustering, two methods were used being the Elbow-Curve with SSD and Silhouette Analysis methods. Using the Elbow

Table 3
Number of opioid prescriptions by nephrologists across states between 2013 and 2018.

Opioid prescriptions' range (2013–2018)	N	State(s)
3000–4000	2	CA, TX
2000–3000	1	NY
1000–2000	7	FL, PA, OH, GA, IL, NJ, MI
500–1000	12	NC, MA, MO, VA, AZ, WA, TN, MD, LA, IN, WI, MN
250–500	11	SC, KY, AL, CT, CO, PR, OK, OR, MS, AR, IA
100–250	11	NV, DC, KS, WV, NM, UT, RI, NE, ID, HI, DE
50–100	5	ME, SD, ND, MT
<50	5	VT, AK, WY, VI, GU

method, a range of potential K-values was chosen then K-clustering was applied with each of the potential K-values. this was followed by calculating the distance between each cluster and its centroid prior to plotting this information. The lower the distance is, the better is the value of K. Silhouette coefficient indicated the degree of similarity between each datapoint and its own cluster as well as other clusters. The Silhouette plot enables visualising this similarity showing the distance between clusters. The score is between −1 to +1 where a value of −1 indicates that the model allotted to the wrong cluster, a value of 0 indicates that the model is very close to decision boundaries between neighbouring clusters as a clue of +1 indicates that the model is far from the neighbouring clusters.

For GMM clustering, the Elbow-Curve was used with Akaike information criterion (AIC) and Bayesian information criterion (BIC) alongside Silhouette Analysis. AIC determines how much information the model has lost. More accurate models lose less information. BIC is based on Bayesian function and is related to AIC. A lower BIC indicates a more accurate model.

3. Results

Univariate analysis showed that prescription issued to male gender was higher than female gender where both had 24,610 and 8230 records respectively. Likewise, male nephrologists' number (n = 6888) was higher than female nephrologists' number (n = 2572). Moreover, 1907 nephrologists were frequent prescribers of opioids between 2013 and 2018. In addition, 1801 nephrologists prescribed opioids only once between 2013 and 2018. Regarding the states where opioids were prescribed, opioids prescriptions were reported in 54 US states with a median prescription rate of 382 (IQR 124–726). The highest number of opioids prescriptions was seen in California (n = 3601) and Texas (n = 3105) over the five years (2013–2018) (Table 3). On the contrary, only four prescriptions were reported in Guam. Number of nephrologists who prescribed opioids in California and Texas were 1010 and 842 respectively.

N: number of states; AK: Alaska, AL: Alabama, AR: Arkansas, AZ: Arizona, CA: California, CO: Colorado, CT: Connecticut, DC: District of Columbia, DE: Delaware, FL: Florida, GA: Georgia, GU: Guam, HI: Hawaii, IA: Iowa, ID: Idaho, IL: Illinois, IN: Indiana, KS: Kansas, KY: Kentucky, LA: Louisiana, MA: Massachusetts, MD: Maryland, ME: Maine, MI: Michigan, MN: Minnesota, MO: Missouri, MS: Mississippi, MT: Montana, NC: North Carolina, ND: North Dakota, NE: Nebraska, NJ: New Jersey, NM: New Mexico, NY: New York, NV: Nevada, OH: Ohio, OK: Oklahoma, OR: Oregon, PA: Pennsylvania, PR: Puerto Rico, RI: Rhode Island, SC: South Carolina, SD: South Dakota, TN: Tennessee, TX: Texas, UT: Utah, VA: Virginia, VI: Virgin Islands, VT: Vermont, WA: Washington, WI: Wisconsin, WV: West Virginia, WY: Wyoming.

Across all states, opioid prescription rate had varying range between 0 and 100 (mean = 2). Likewise, the opioid day supply varied massively between 0 and 125,272, and the opioid claim count varied between 0 and 4329.

Bivariate analysis indicated the relationship between 'gender and opioid use' or 'state and opioid use'. For gender, opioid use showed to be higher in males that were more likely to be prescribed opioids than females. Hence, the opioid claim count, day supply and prescriber rate values were 52.6, 1253.9 and 2.1 respectively in male. Nevertheless, the latter three values were 30.6, 759 and 1.7 respectively in females. For both males and females, there was a drop in opioid claim count between from 2013 to 2018 (Fig. 1). The same drop was seen in opioid day supply and opioid prescriber rate for males and females. For state, the highest opioid prescription rate was seen for nephrologists from Arizona and the lowest was for Guam. For all of opioid claim count, day supply and prescription rate, there was a continuous decrease from 2013 – 2018 similar to the pattern seen for gender.

3.1. K-mean clustering

For K-mean clustering using the Elbow method, a range between 2 and 12 clusters was assigned to each point K, prior to calculating the mean distance of each point K to its centroid. This was followed by

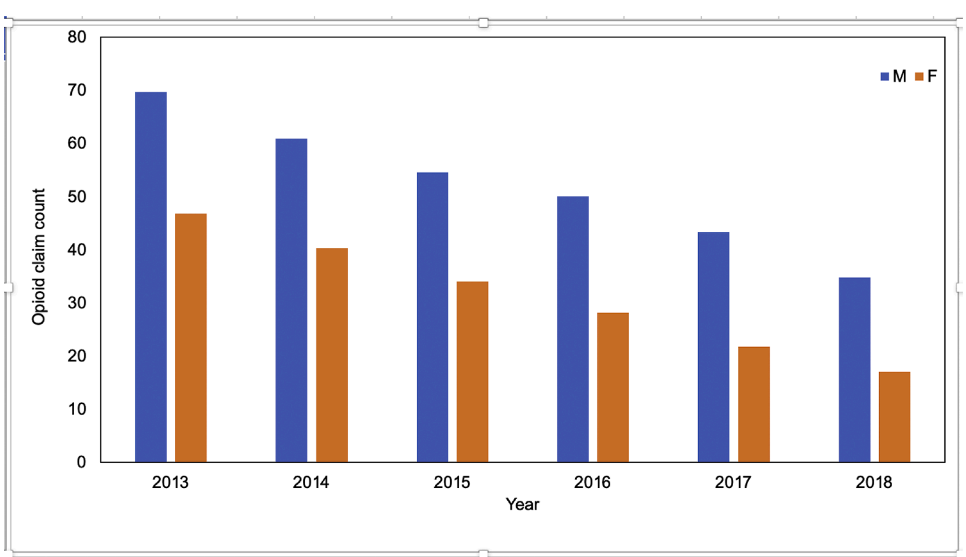

Fig. 1. Reduction in opioid claim count between 2013 and 2018.

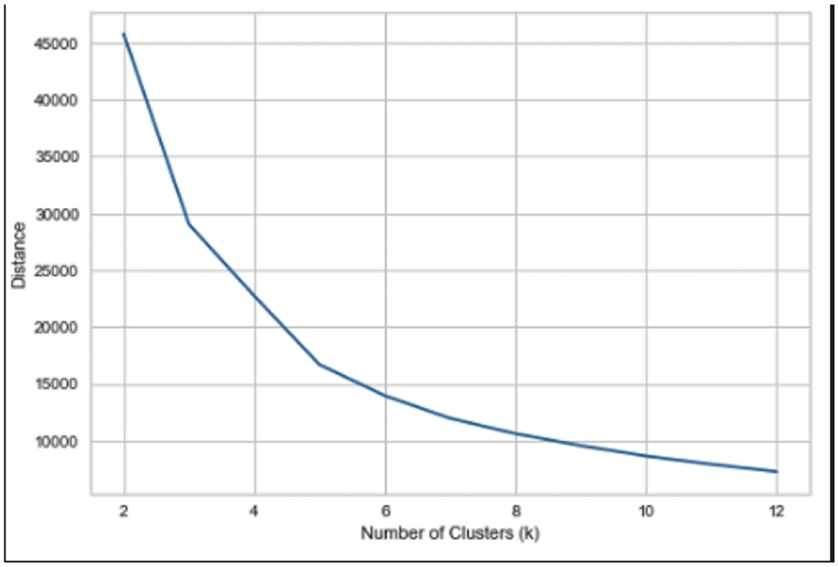

Fig. 2. Elbow Method to find optimal k for k-means cluster.

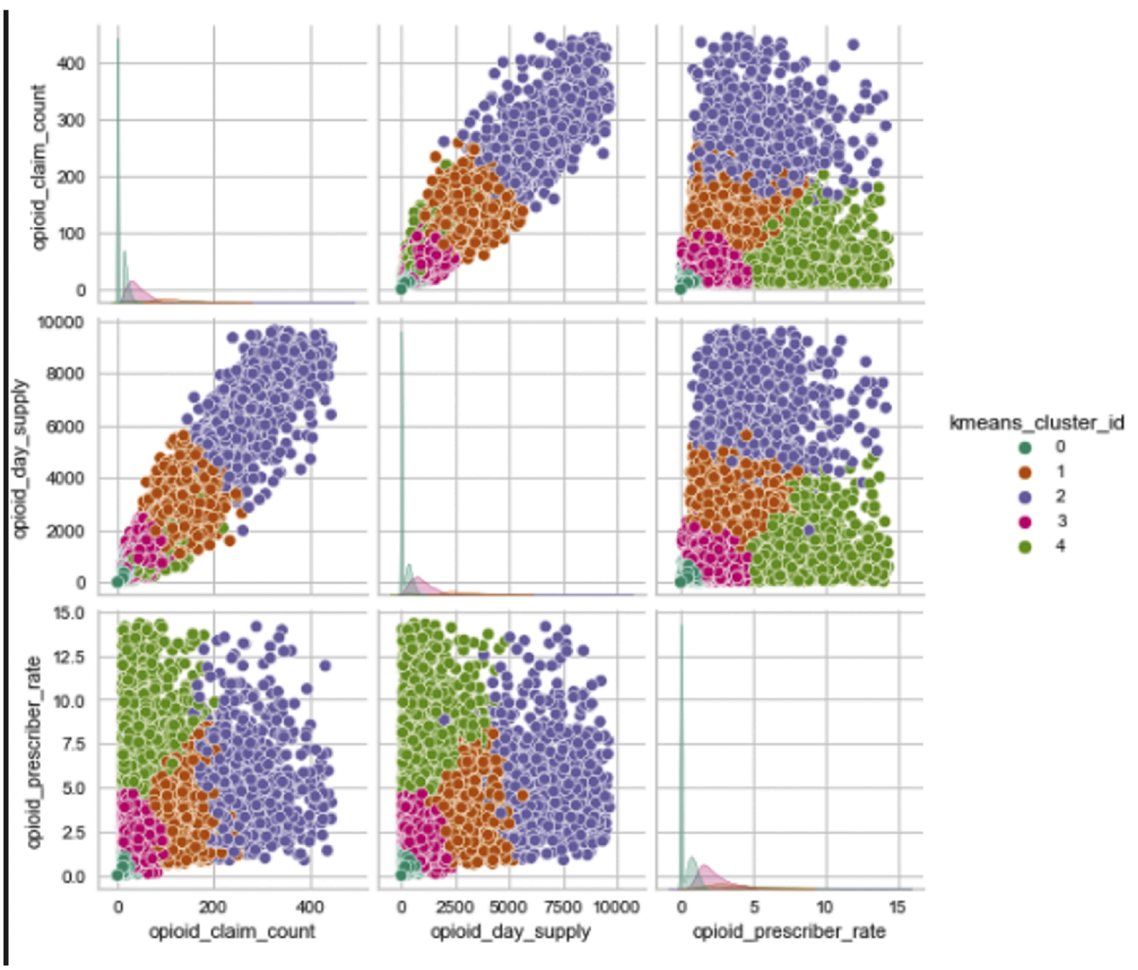

Fig. 3. Pair plot representation of k-means_cluster_id for opioid parameters.

plotting the mean distance against the number of clusters (Fig. 2), where the optimal number of clusters is the one achieved with a sudden distance drop. Fig. 2 shows that the optimum number of clusters was 5 after which the line decreased in a linear manner. In this respect, choosing number of clusters above 5 would result in overfitting. K-mean clustering using the Silhouette method was chosen for higher-dimensional data. An average Silhouette score was given to each cluster for clusters 2 - 12. The cluster that is close to 1 before which the score become

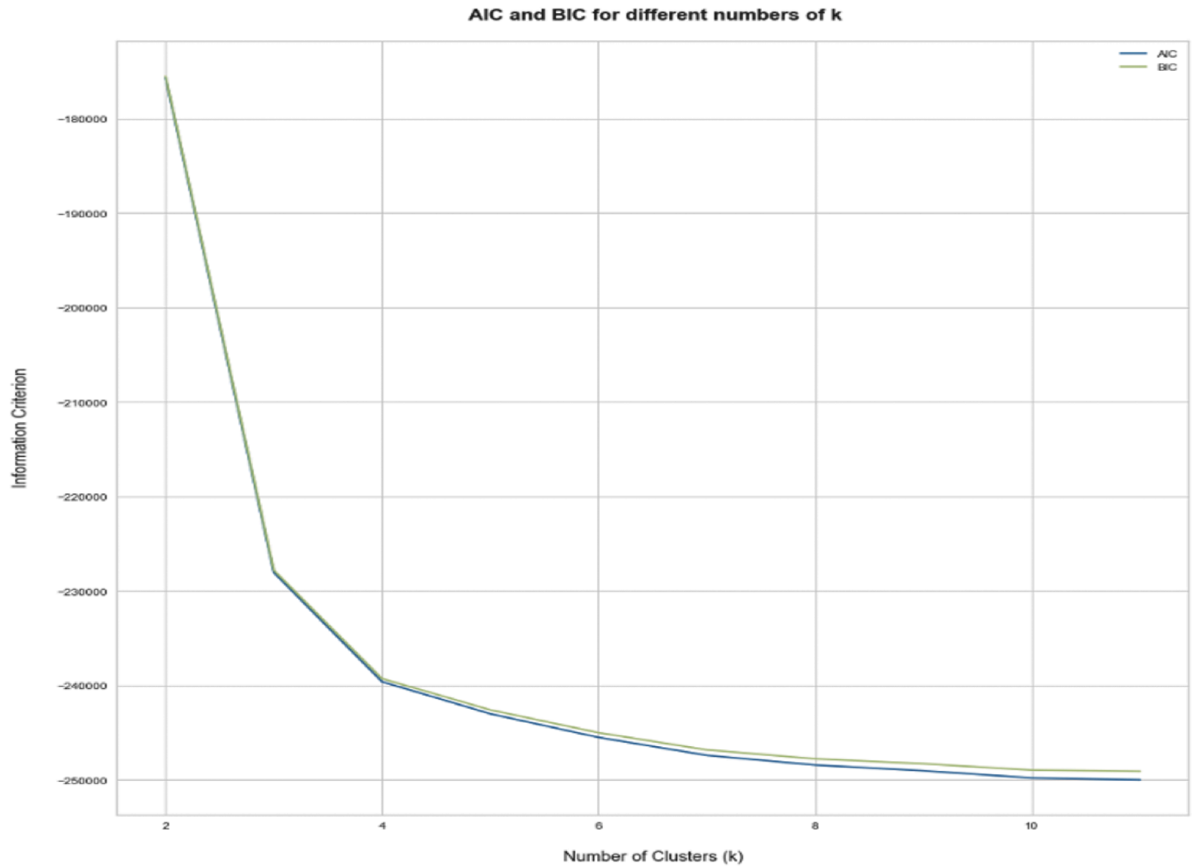

Fig. 4. Elbow Method with AIC and BIC to find optimal k for GMM method.

steady is the optimum cluster. This was achieved for cluster 5 that showed a score of 0.51. Therefore, cluster 5 was chosen as the optimum number of clusters. Fig. 3 shows the five clusters with the highest cluster values for opioid claim count and opioid day supply of 2 followed by 4. Therefore, it was considered that cluster id of 2 was the optimum number. Considering K-mean cluster of 2, nephrologists prescribing more opioids between 2013 and 2018 were identified considering gender and state. In this respect, the highest prescribers who constantly issued opioids per state was seen for California nephrologists ($n = 4$) followed by Montana ($n = 3$). Each of Alabama, Louisiana and Oregon had one nephrologist that prescribed constantly. Whereas, Arizona, Florida, Illinois, Tennessee, Virginia, Washington and Wisconsin had only one nephrologist that prescribed constantly. In relation to gender of nephrologists, it was seen that male nephrologists ($n = 17$) prescribe more than female prescribers ($n = 4$).

3.2. GMM clustering

For GMM clustering, the AIC and BIC elbow curve showed two parts where the first part was uniform and smooth and the second part had varying slopes (Fig. 4). Fig. 4 showed that the AIC and BIC stopped decreasing after six clusters. When Silhouette was applied, cluster six showed a score of 0.5362 after which the score became steady. Fig. 5 shows that 'Opioid_Prscrbr_Rate', 'Opioid_Tot_Suply', and 'Opioid_Tot_Clms' were higher in cluster 4 compared to other clusters. Therefore 4 was chosen as the optimum number. Using four clusters the highest opioid prescriptions were seen in California ($n = 2$), followed by Alabama, Florida, Montana, North Dakota, South Carolina and Wisconsin ($n = 1$ each). Moreover, all prescriptions were issued from male nephrologists.

4. Discussion

The novelty of this study underlies in the application of ML algorithms in understanding prescription of opioids and patterns of opioid prescriptions. Previous similar studies have focused on measuring the volume and rate of prescriptions using descriptive statistics or regression analysis (Chang et al., 2018; Klimas et al., 2019; Meisenberg et al., 2018; Ponton and Sawyer, 2017). Moreover, the latter studies mainly focused on single health setting.

The present study built on the findings of previous studies by considering characteristics of patients, including gender and geographical location, when assessing the volume of prescriptions. This was done by using ML models that showed strong performance in classification. ML models demonstrated patterns in increased opioid prescription by nephrologists in the US in terms of gender and geographical state. Several factors could be linked to increased opioid prescription including: severe pain experienced by patients in kidney disease (Ishida et al., 2018), high potency of opioids against pain (Jani et al., 2020) and the prevalence of chronic severe pain that is not treatable with benzodiazepines (Jani et al., 2020).

Patterns in prescription were explored using descriptive statistics and unsupervised ML analytics namely K-mean clustering and GMM. Identifying patterns and trends in opioids prescription enables making recommendations for improving medical practice related to opioids and to decrease the harm linked to opioid use and/or misuse (Pezalla et al., 2017). In this study, unsupervised clustering identified patterns in opioid prescription and showed that prescriptions were more prevalent in male gender and mainly issued by male nephrologists. Previous studies have also shown higher prevalence of opioids' use in men and this could be linked to men talking more openly about their drug use. Nonetheless, women face more stigma in cases of drugs use disorders e.

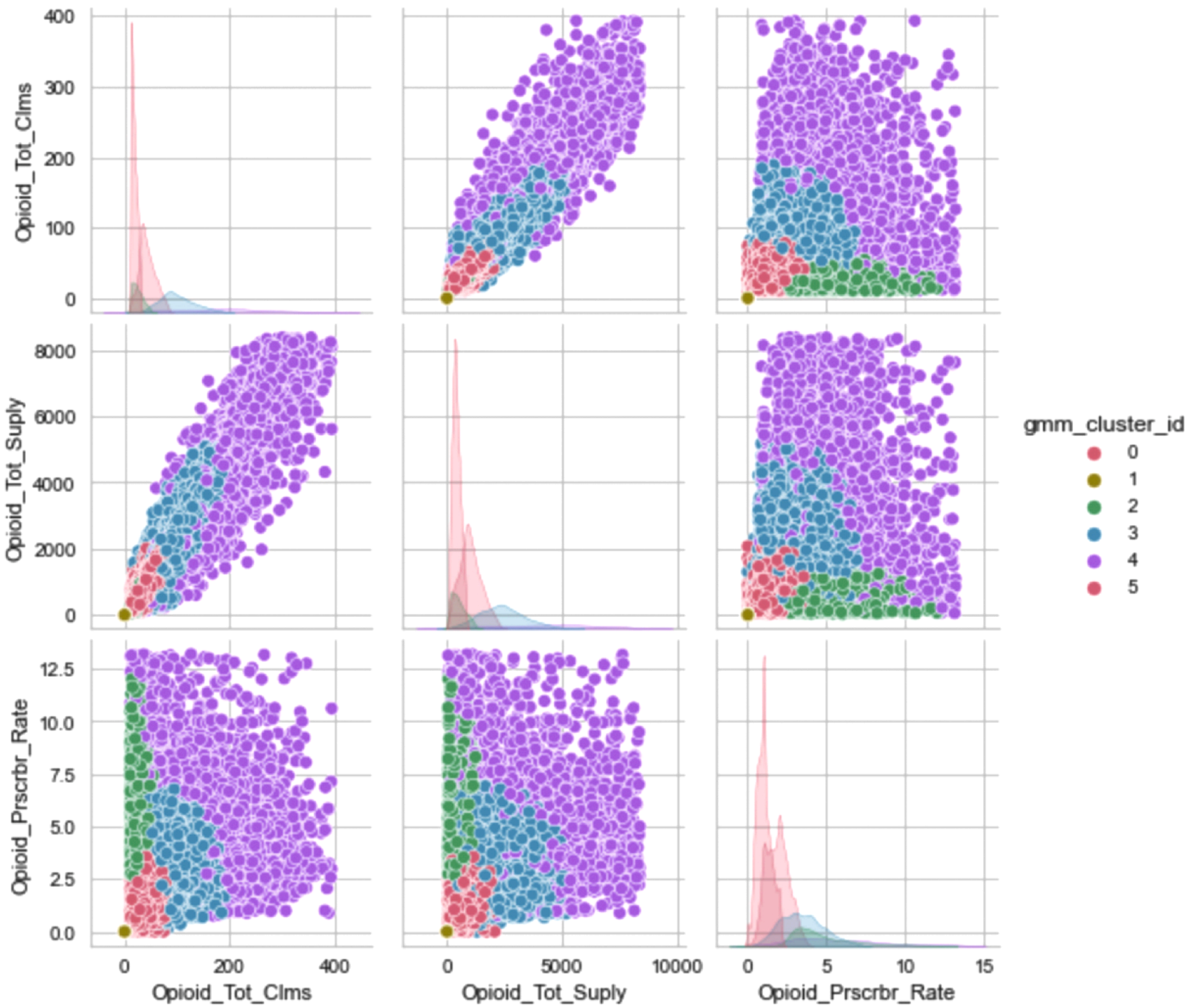

Fig. 5. Pair plot to visualize GMM clustering on the projected data.

g., opioid use disorder (Huhn and Dunn, 2020). In such cases, AI algorithms are essential as they can predict opioid misuse and overdose in patients before they occur. Early prediction allows providing targeted interventions such as counselling, referral to support groups, or medication-assisted treatment.

Regarding geographical state, California and Texas were at the top states prescribing opioids. This finding contradicted studies in the literature that showed lower opioid prescribing and use in both the aforementioned states after implementation of regulations (Paulozzi et al., 2011; Strickler et al., 2020). Yet, these studies were related to general opioid use whereas our study was more specific to patients with kidney diseases. In future, researchers could develop personalised opioid treatment plans for patients with chronic pain. These plans can consider a patient's individual pain profile and/or risk factors for increased opioid prescription. Moreover, AI could be used to develop new treatments for chronic pain that are less likely to lead to addiction or overdose. These treatments could include new drugs, devices, or therapies.

This study had few limitations. The first was that the study utilised retrospective data with many variables related to the patients so we could not exclude the possibility of potential confounding factors. There was no way to authenticate whether patients have taken the medicines' prescribed or if they have missed doses or taken overdoses. Not following the medicine regimen in terms of dosing and frequency could result in adverse outcomes (Vermeire et al., 2001). In addition, it was not possible to know which specific opioid was prescribe and for what type of pain. Also, patients may have taken street opioids not through prescription and this may have been missed in the study. However, the study had large sample size collected from several states and that enabled observing patterns on large sample sets. This is important in case of patients with kidney diseases who often suffer from severe pain.

5. Conclusions

This study evaluated prescription of opioids among nephrologists in the US through a dataset accessed online from Medicare population. The study had two objectives that were met. These objectives included understanding frequency of opioids' prescription across different states and across different genders. These objectives were answered by exploring the clustering patterns in opioids' prescription using two clustering algorithms being K-mean clustering and GMM, that informed about patterns in high opioids' prescription. Across different states, California had the highest rate of prescribers with four nephrologists constantly prescribing opioids. This was followers by Montana, Oregon, Alabama and Florida who had three nephrologists each that constantly prescribed opioids.

Across different gender, male nephrologists were prescribing more opioids than female nephrologists consistently between 2013 and 2018.

K-mean clustering identified 21 male nephrologists and only four female nephrologists that were high prescribers. Similarly, GMM identified 23 male nephrologists and four female nephrologists that were high prescribers. This results for both clustering algorithms varied slightly yet both identified that male nephrologists over prescribe opioids.

These findings will in turn contribute to the understanding of the opioid pandemic. Moreover, centres in high prescribing states can be targeted with proposing plans for alternative treatments with non-opioid medicines. Future work based on these findings include understanding opioid prescription based on different datasets such as hospital datasets and social media. In addition, it will be beneficial to apply deep learning models with explainability in order to understand in more depth the high prescription rate, reasons behind it and key contributors to it.

Ethical approval

This article only used open access data and did not contain any studies with human participants.

CRediT authorship contribution statement

Shivashankar Basapura Chandrashekarappa: Writing – review & editing, Writing – original draft, Visualization, Investigation, Conceptualization. **Sulaf Assi:** Writing – review & editing, Writing – original draft, Investigation. **Manoj Jayabalan:** Writing – review & editing, Supervision, Methodology, Investigation. **Abdullah Al-Hamid:** Writing – review & editing, Visualization. **Dhiya Al-Jumeily:** Writing – review & editing, Visualization, Validation, Supervision, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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