Risk Assessment for Opioid Epidemic in the United States

TEAM MEMBER PARTICIPANTS

Everyone in our team participated and regularly worked on the project since the very beginning. However, the following were the major contributions by our team members:

Abhishek Hanchate: Data Correlation, Predictive Modelling, and Risk Matrix

Akshay Kadu: Data Fitting/Distribution Analysis and Fault Tree Analysis

Barbara Martinez: Background study, Bayesian Network, and Bayesian Model

EXECUTIVE SUMMARY / ABSTRACT

The purpose of this project is to quantify and evaluate specified potential risks associated with the use of opioids, which are very commonly prescribed drugs or painkillers. The value in this research is the potential mitigation of the risk due to overdose from opioid consumption, a rising epidemic in the United States. Utilizing a variety of data sources, we were able to apply different statistical and quantitative risk analysis methods to better identify patterns and therefore potential risk factors. We focused our scope on prescription, distribution, and consumption patterns, trends in overdose when compared to demographics and location, and time studies for high prescription rates. We also identified at-risk states and counties to account for the worst-case scenario. With our given results, we were able to make conclusions on how to mitigate these risks as well as recommendations for future work in better monitoring this epidemic as consumption continues to increase concurrently with mortality rates.

1. INTRODUCTION

Opioids analgesics have historically been prescribed to treat severe pain, either acute or chronic. Over the years, opioid overdose rates have steadily increased in the United States. In 2017, there have been over 47,000 deaths due to opioid overdose. While this statistic includes prescription opioids, synthetically manufactured opioids, and heroin, 80 percent of people who use heroin reported to have abused prescribed opioids at first. Therefore, while an overdose may be as a result of heroin, there is a strong probability that the user was first abusing prescription opioids and later transitioned to heroin. In the same year, it was found that approximately 1.7 million Americans had developed substance use disorders for prescription opioids, increasing the potential risk of overdosing from the prescribed drug or increasing the risk of transitioning to heroin and later overdosing from heroin misuse (NIDA).

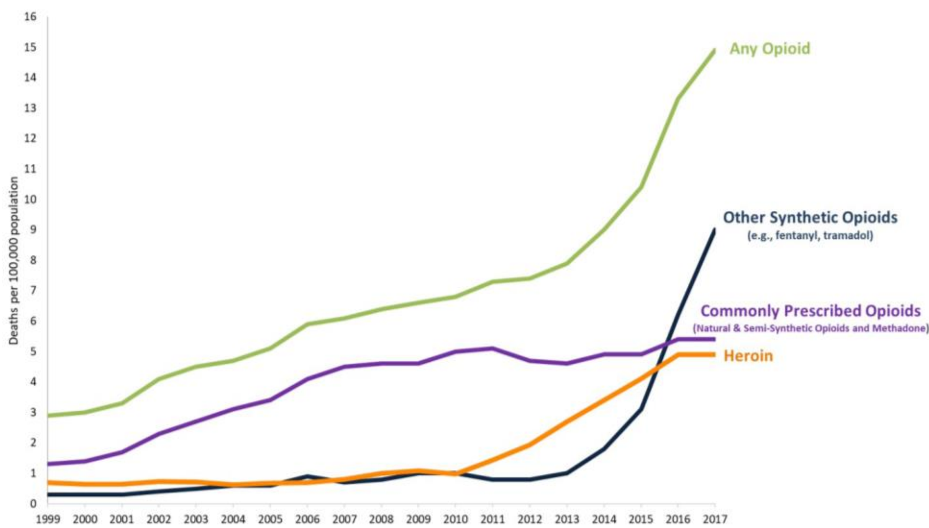


Figure 1.1. Overdose Death Rates Involving Opioids by Type in the US

While there are a variety of health risks that are caused due to opioid use or misuse, there also exist other variables that can impact the probability of these health risks. Therefore, for the purpose of this report, we looked at the risk of drug overdose deaths related to prescription pain-killers or opioids. We also narrowed the scope of relevant and impacting variables to include - dosage and prescription patterns, individual factors (i.e. age, race, sex) and location factors (i.e. urbanization, unemployment). We utilized the selected data sources (CDC, Washington Post, US Census Bureau) to guide our analysis and implemented different methods to look at the problem from different points of view and provide a variety of results and conclusions. This is particularly important because drug overdose is a multi-faceted risk that can be influenced by many variables in different combinations, therefore one method of analysis is insufficient to provide future recommendations. The objective of this research is to discover different variables that can lead to or impact death due to opioid overdose, quantify those variables that have sufficient data, and propose future recommendations on how to monitor these variables to mitigate risks.

This project was selected due to the extreme gravity of potential risks associated with the use and misuse of prescription opioids. Prescription painkillers are one of the leading causes of unintentional deaths in the United States, impacting not only the individual user but a variety of other fields as well. While we will focus on the risks related to the prescribed user, it is important to look at the problem holistically to understand the far reaches of its influence as well as its severity. Though this problem is within the medical and healthcare field, it is still relevant to engineering in the sense that it is related to a system of interconnected elements and factors. Manipulating one of the many factors can change the probability of overdose death, which can propagate across to other targets. It is a complex problem with a variety of moving variables, many of which are not included in our project in order to control the scope. The goal is to study different key factors to better help identify patients that are at a higher risk of developing dependence and potentially risky behavior, thereby minimizing the chance of life-endangering risks.

2. BACKGROUND

Since the 1990s, distribution and dispensing of opioids, commonly known as prescribed pain killers, has increased concurrently with the mortality and morbidity due to the drug (Brady et. al, 2014). Interestingly enough, this increase has not been noted in the number of patients who experience sufficient pain to require an opioid prescription. As a result, this indicates that the spike in distribution is linked not to a need for opioids for medical purposes but rather for misuse. Individual use of prescription painkillers has increased by 402% between 1997 to 2007 (Gugelmann, 2011), while the rate of unintentional overdose fatalities in the United States increased by 124% during the same timeframe, mainly due to the increase in opioid related overdoses (Bohnert et. al., 2011). In a study done specific to West Virginia drug patterns, 93% of overdose deaths were as a result of opioids and the majority of the deaths were younger individuals between the ages of 18 to 44 years (McLellan, 2008). Additionally, the risk of overdosing was significantly higher for individuals who were prescribed a higher dosage (Bohnert et. al., 2011). By 2007, opioid overdose was the second major contributor to unintentional deaths in the United States (Gugelmann, 2011).

In addition to the increasing mortality and morbidity rates, there is also an economic burden linked to prescription opioid overdoses, abuse, and dependence. In a study done in 2013, the estimated economic burden was found to be $78.5 billion. This includes costs such as health care costs, treatment costs, criminal justice costs, and lost productivity costs from a person's place of employment. Approximately one quarter of those costs come specifically from fatal cases and another quarter is linked to the loss of productivity, either from reduced time, increased disability, or incarcerated individuals (Florence et. al. 2016). These findings highlight the wide impact of opioid abuse and dependence, extending beyond the potential health risks incurred by the individual.

As a result of the identified trends, the White House Office of National Drug Control Policy published a document to highlight four major issues: patient and clinician education, drug disposal, illegitimate prescriptions, and prescription monitoring (Gugelmann, 2011). Most states have implemented electronic prescription drug monitoring programs, or PDMPs, in order to deter and minimize abuse of controlled substances. Clinicians are able to access these databases before prescribing to a patient, allowing them to make an informed decision when prescribing medication. The goal is to help reduce opioid abuse while still providing patients with appropriate pain relief. Unfortunately, a study found that implementation of PDMPs did not show a significant impact on opioids dispensed (Brady et. al, 2014). Additionally, PDMPs do not account for stolen drugs or "prescribed" opioids purchased on the internet. This can be shown by the case in Kermit, West Virginia, where drug manufacturers sent five million opioid pills to the town with only 400 people. Furthermore, the CDC reported more than one-half of patients who receive opioid treatment are still receiving opioids more than four years later.

While prescription painkillers pose a very grave and high-risk threat, it is unreasonable to completely remove them from the healthcare market. Therefore, we studied a variety of factors that can impact potential risks in order to mitigate those that are within our control and monitor those that are not, allowing healthcare providers to make more informed decisions specific to any given patient within a given location in the US. The results of our research, in combination with the CDC guidelines for prescribing opioids for chronic pain, should allow healthcare providers to understand more of the risks associated and how to potentially mitigate them.

In order to complete our research, we utilized a combination of statistical methods and quantitative risk analysis methods. Data correlation was done to find trends between prescription rate and dosage rate, as well as trends between dosage units and overdose deaths. Predictive modelling was utilized to find patterns in distribution and consumption on a daily, monthly, and yearly basis. Bayesian models were created to quantify the probability of dying due to an overdose given selected variables, which was then used to also create a Risk Matrix. Finally, a fault tree was developed to find potential events that could lead to an overdose.

3. METHODS

3.1. Data Visualization

Data visualization is the graphical representation of information and data or a form of visual art by using visual elements like charts, graphs, and maps that grabs our interest and keeps our eyes on the key message. These tools or techniques provide a friendly and easygoing way of storytelling with a purpose to see and understand the trends, patterns, and any outliers in the data. Therefore, for our study, we have implemented several of these visualization methods on platforms such as Tableau and Python. The figure below shows the number of distributed pills per person per year in an interactive way with hover feature for the trend of the same over the years in the form of a geographical heat map of the United States. The darker the color, the more is the distribution of the opioid pills in that particular region.

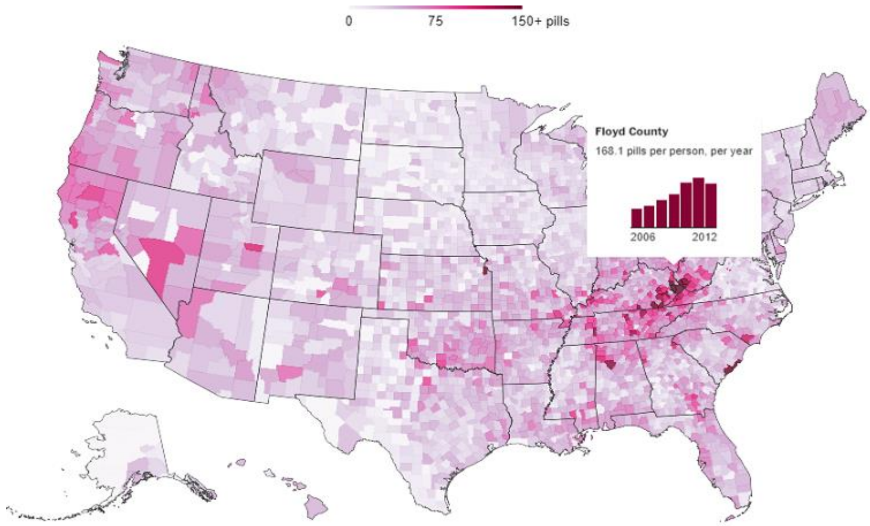


Figure 3.1.1. Number of distributed pills per person per year (from 2006 through 2012)

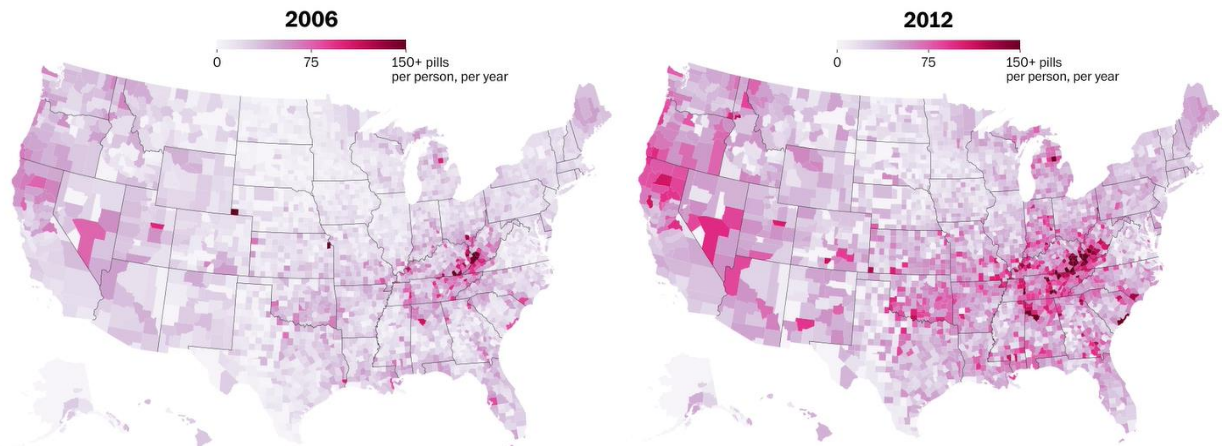


Figure 3.1.2. Number of distributed pills per person per year (2006 vs 2012)

3.2. Data Correlation

3.2.1. Comparison of Prescription Rate and Dosage Rate

Prescriptions has played an important role in the opioid epidemic in the US and has been on the rise. We investigated if the number of prescriptions given out per state increases the chances of drug abuse or if people avoid consuming pills in-spite of the prescriptions. Comparing prescription rate for the states of West Virginia and Texas, we found a strong correlation between the prescription rate and the number of pills consumed per person and although this makes intuitive sense, there is more to the story than meets the eye. To find out the number of prescriptions given out in each county, we considered the population of these counties based on the US Census Bureau Data population estimates.

We can clearly see that the dosage rate in West Virginia is much higher than the prescription rate. The same analysis for the state of Texas shows that even though the prescription rate across the state was higher, the opioid consumption rate was still much lower.

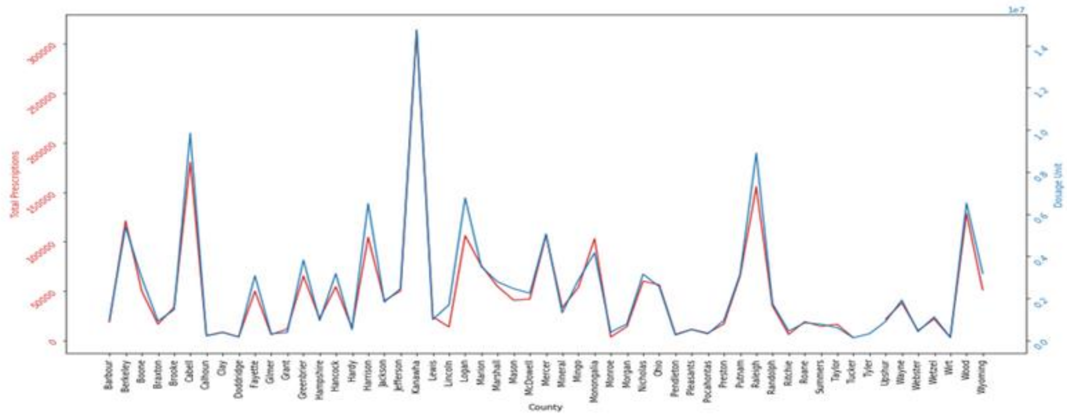


Figure 3.2.1.1 Trend of Prescription rate and Dosage rate in West Virginia

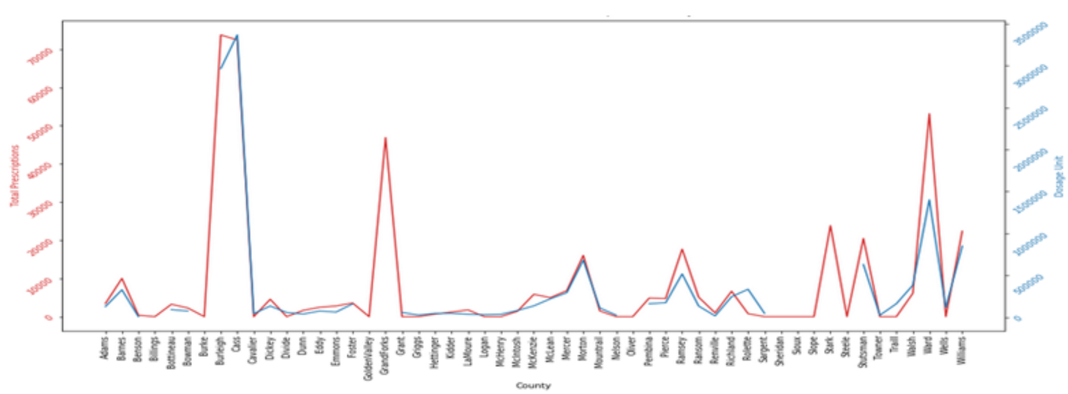


Figure 3.2.1.2 Trend of Prescription rate and Dosage rate in Texas

3.2.2. Comparison of Dosage Units and the Overdose deaths

Deaths due to opioids intoxication has been on the rise in the US. From 1999 to 2017, more than 702,000 people have died from a drug overdose. In 2017, more than 70,000 people died from drug overdoses, making it a leading cause of injury-related deaths in the United States. Of those deaths, almost 68% involved a prescription or illicit opioid.

To relate the overdose deaths to the dosage units, pills sold and the number of deaths were plotted below to infer if a correlation exists. The states are shown on the x-axis whereas the average opioid consumption and related deaths across the states are shown on the y-axes. The graph clearly showed that the highest consuming states of West Virginia and Kentucky had the highest number of average deaths while Kansas and Texas had a much lower death rate. The state of North Dakota was the least affected state.

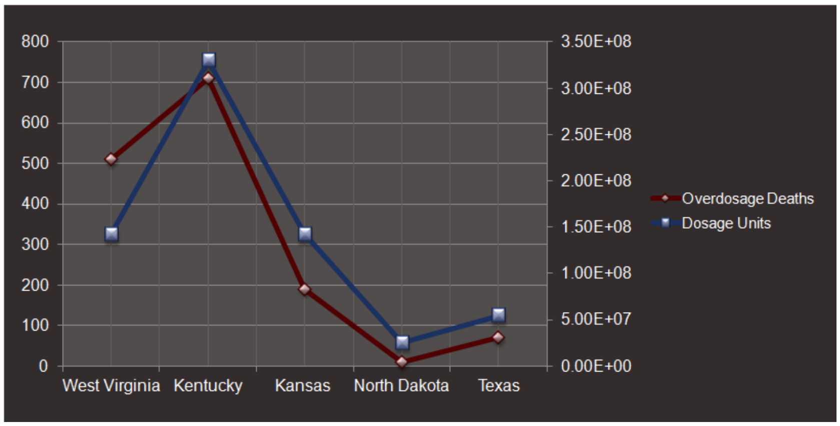


Fig 3.2.2. Average Overdose Deaths vs Average Dosage Units (2006-2012)

3.3 Predictive Modelling

Using the 'Transaction_Date' information available from the Washington Post dataset, we also studied the distribution and consumption patterns and trends on a daily, monthly, and yearly basis. Due to computing limitations of our machine, we restricted only to twenty million rows of data randomly from year 2006 through 2012. The following trends were observed during the exploratory data analysis of opioid distribution and consumption over different time stamps.

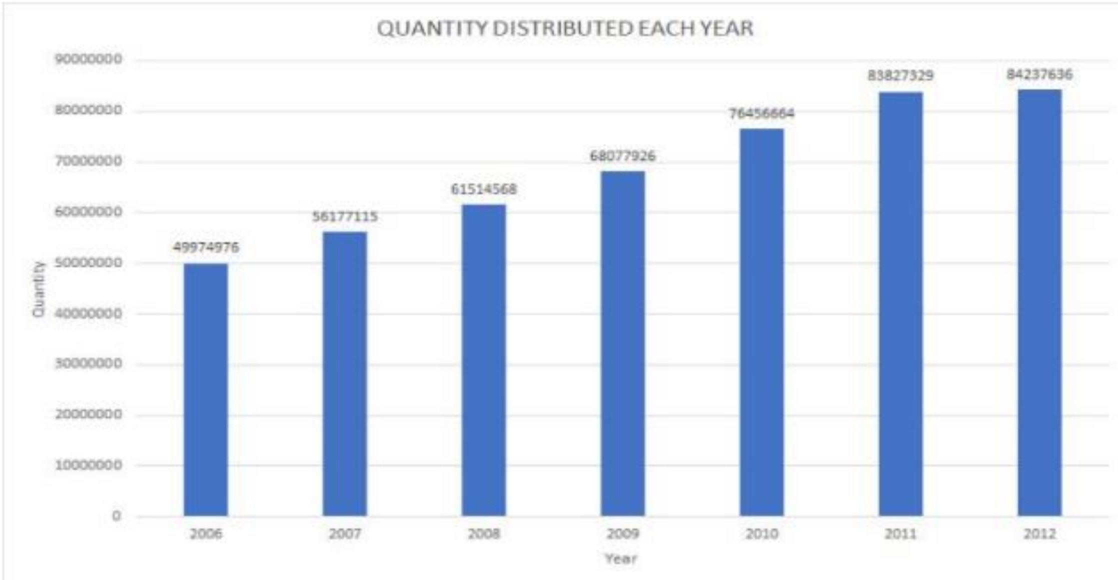


Figure 3.3.1. Trend of Opioid distribution/consumption from year 2006 through 2012

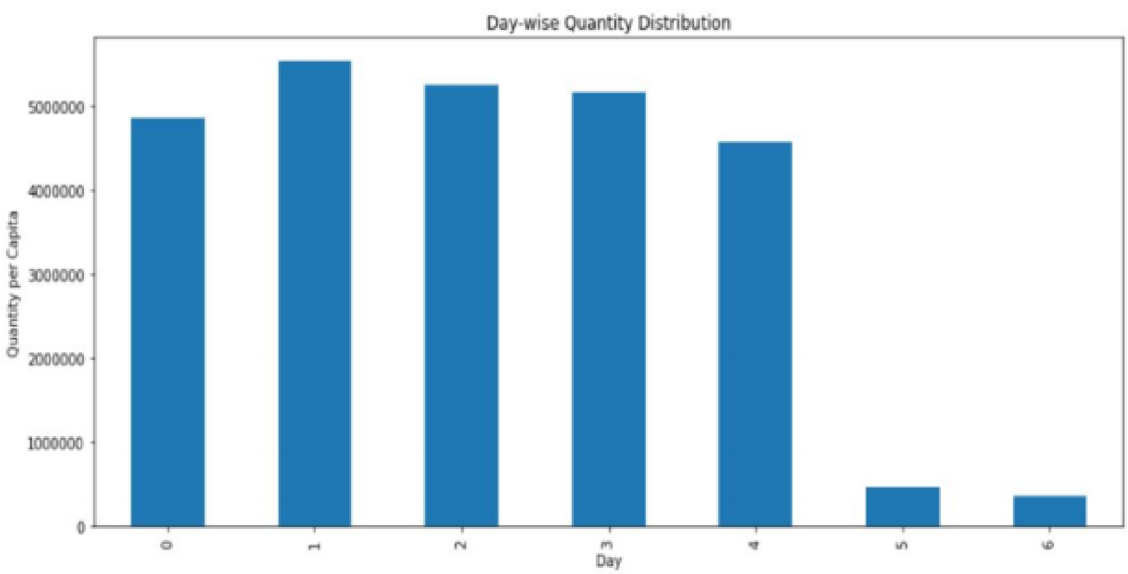


Figure 3.3.2. Day-wise trend of Opioid distribution/consumption

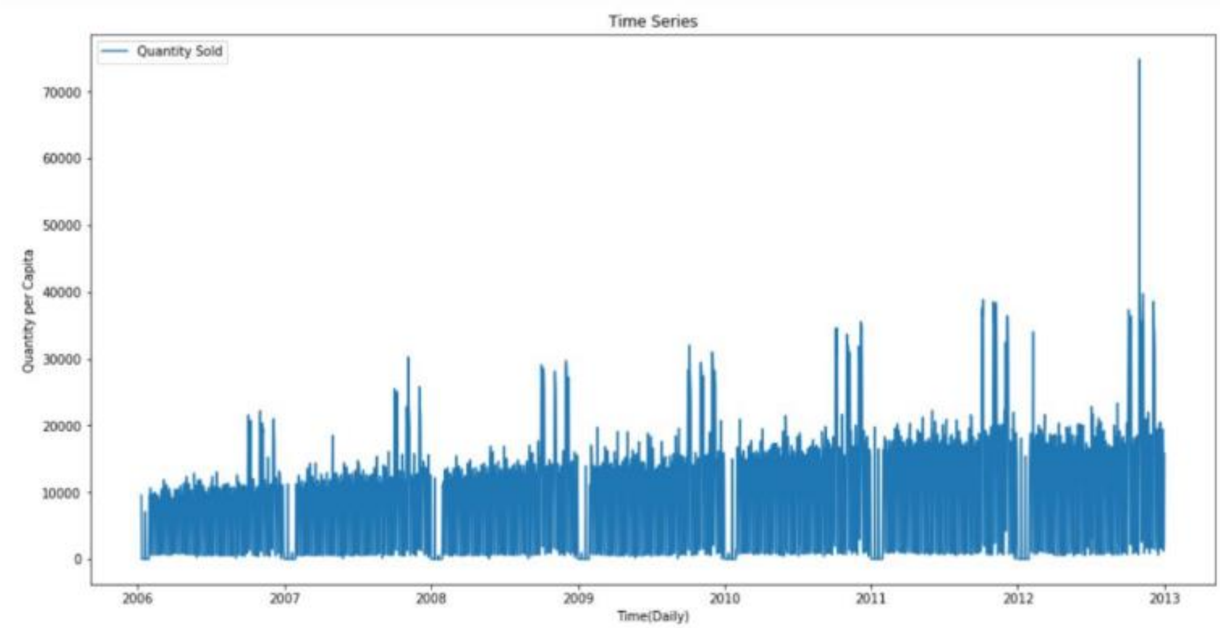


Figure 3.3.3. Yearly day-wise trend of Opioid distribution/consumption

3.4. Bayesian Models

In terms of quantifying the above-mentioned risks, we utilized Bayesian networks. Based on the data, we selected factors that had strong correlations to death by overdose. Additionally, we included other variables that are typical when considering drug use behavior and trends, such as unemployment and urbanization. The factors that we decided to include in our Bayesian networks are: (1) race, (2) age, and (3) gender of the user, (4) whether the user is being prescribed, (5) the dosage being prescribed, (6) unemployment and (7) urbanization. The dosage unit is Milligram Morphine Equivalent (MME) which is a value assigned to opioids to represent their relative potencies. Once we limited the scope of relevant variables, we constructed a Bayesian Network model as shown below to update the probability of deaths due to overdose.

From this Bayesian network, observations can be entered within each node for a patient to determine the risk of dying due to an overdose. As shown above, the individual nodes were grouped by similar classification and linked to a synthetic node that can later be connected to the top node when proper data is available. At the moment, the current data available is insufficient to calculate the conditional probabilities needed to connect the synthetic nodes to the top node. This is one of the limitations of our model but can be remedied in the future if data is collected in a certain format.

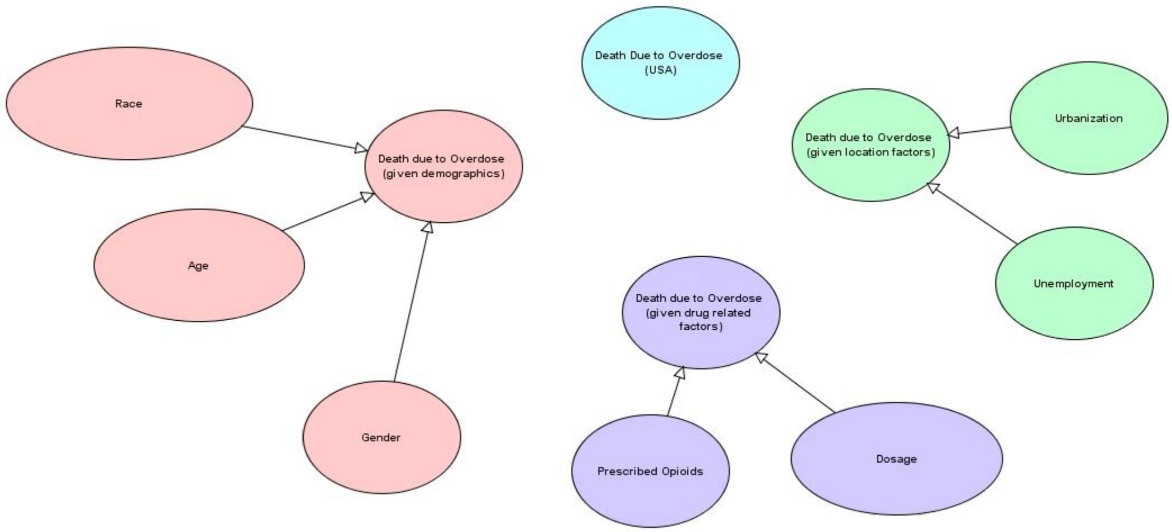


Figure 3.4.1. Building a Bayesian Network in Agena Risk

Based on the data that is available, we were able to create a model for the United States. This is another limitation of our model, given that it represents an average of the entire country. States and counties have very different probabilities for the parent nodes as well as the conditional probabilities. While the probabilities for the parent nodes were available for states and counties, the conditional probabilities were not. Again, this can be remedied in the future if data is collected in a certain format for all counties and states.

The demographics network was constructed using data from the United States Census Bureau and the Center for Disease Control and Prevention (CDC). The drug related network was also constructed using data from the CDC. The location network was constructed utilizing data from the CDC and the United Nations. The top node was constructed utilizing data from the CDC. All data sets were set in the year 2014 for consistency. Based on these values, the conditional probabilities were calculated as shown in the Tables 1-6 in the results section.

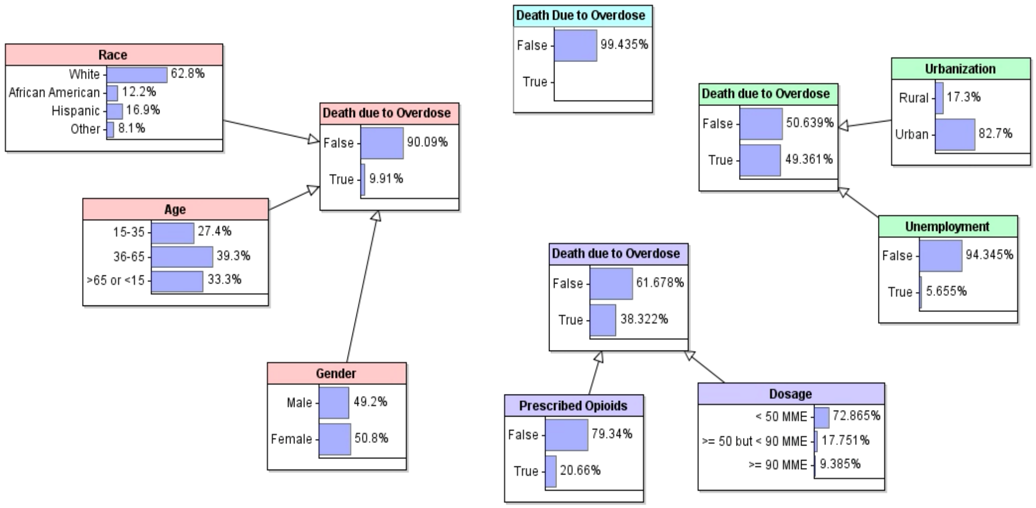


Figure 3.4.2. Bayesian Network with Probabilities in Agena Risk

It should be noted that data was not available to accurately calculate the conditional probabilities for death due to overdose given that the victim has not been prescribed opioids but is taking a given dosage. Therefore, we adjusted the probability using the number of overdoses for users without a prescription and the distribution of different prescribed dosages. Unprescribed dosages are not recorded and therefore difficult to accurately model. Additionally, those conditional probabilities do not account for other factors, such as a patient taking more than prescribed or other treatments that a patient is receiving in addition to the prescription. As a result, there are not an accurate representation of what may actually be impacting the risk of death due to overdose.

It must also be noted that overdose data in terms of unemployment classified unemployment and unpaid together. Therefore, the value that was used in the calculations can include victims who were employed but simply unpaid. Similarly, this means the employment rate is not accurate as it does not include individuals who were employed but unpaid. Additionally, there was a category for employment unknown, which can alter both employment and unemployment.

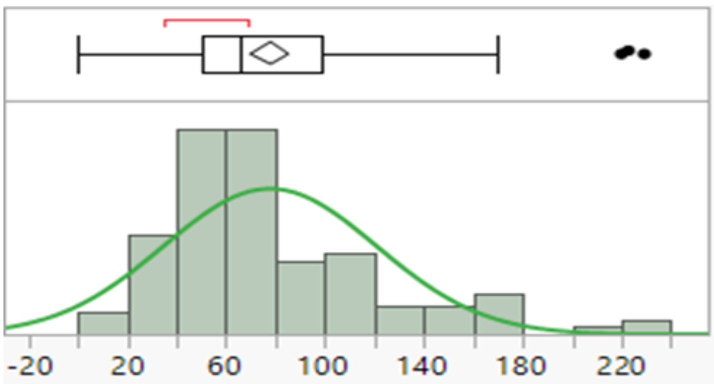
Based on the data available and our assumptions to adjust for values that were unavailable or incomplete, we developed the above models. While the current models do not connect to the top node, the top node was still included in order to compare the individual models to the averaged probability of death due to opioid overdose. The observations can be entered into the model to update the probabilities for a specific individual.

3.5 Data Fitting/Distribution Analysis

Here we fit the data of opioids dosage rate per person in JMP and using the box plots and summary statistics, we compared the distribution for the following states:

1.Kentucky (One of the states with the highest opioid consumption rates)

2.North Dakota (One of the lowest opioids consuming states)



Quantiles

100.0%	maximum	229.1612108
99.5%		229.1612108
97.5%		218.6318939525
90.0%		145.15114178
75.0%	quartile	98.988392655
50.0%	median	65.42452544
25.0%	quartile	50.1383940625
10.0%		35.053662007
2.5%		18.728136296
0.5%		0
0.0%	minimum	0

Summary Statistics

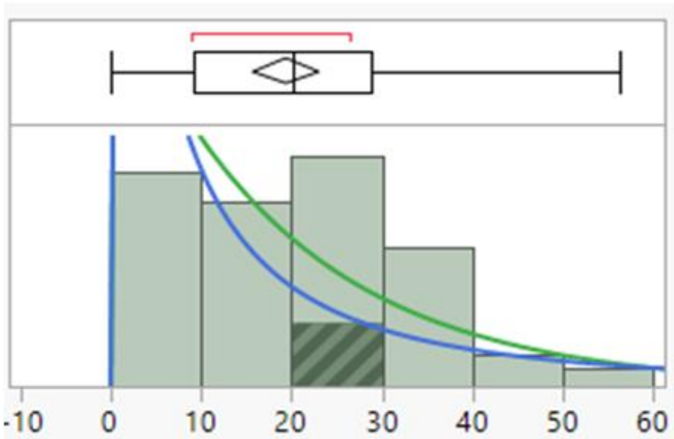
Mean	77.767842
Std Dev	43.090933
Std Err Mean	3.933646
Upper 95% Mean	85.556854
Lower 95% Mean	69.97883
N	120

Fitted Normal Distribution

Parameter		Estimate	Std Error	Lower 95%	Upper 95%
Location	μ	77.767842	3.933646	70.058038	85.477647
Dispersion	σ	43.090933	0.4264015	42.263253	43.786199

Figure 3.5.1. Analysis of Dosage Rate data across Kentucky (2012)

The graph for Kentucky resembles a Normal Distribution although it may not be the best fit for the data. On fitting the normal distribution, we see the mean is located at 77.76MME with a standard deviation of 43.09. Considering $\boldsymbol{\alpha} = 0.05$, the upper and lower 95% confidence interval for the mean value ($\boldsymbol{\mu}$) were obtained as $70.05 \leq \boldsymbol{\mu} \leq 85.47$. Looking at the box plot, we can clearly see that most of the data points are concentrated between the lower quartile of 50.13 and median of 65.42, which shows the median value of opioid consumption in Kentucky was as high as 65 MME per person per day. It is also shocking to see that the maximum value of opioid consumption surpassed 200 MME in few cases, which can be observed as outliers.



Compare Distributions

Distribution		AICc
Gamma		424.20442
Lognormal		448.88993

Summary Statistics

Mean	19.335244
Std Dev	13.489242
Std Err Mean	1.8528899
Upper 95% Mean	23.053339
Lower 95% Mean	15.617148
N	53

Quantiles

100.0%	maximum	56.29164864
99.5%		56.29164864
97.5%		53.356965483
90.0%		34.821695522
75.0%	quartile	28.90701033
50.0%	median	20.24281467
25.0%	quartile	9.232585596
10.0%		0.7192345034
2.5%		0.1921114532
0.5%		0.110497238
0.0%	minimum	0.110497238

Fitted Lognormal Distribution

Parameter		Estimate	Std Error	Lower 95%	Upper 95%
Scale	μ	2.385867	0.20288	1.9809143	2.7908196
Shape	σ	1.4769884	0.1434578	1.2348976	1.8098791

Fitted Gamma Distribution

Parameter		Estimate	Std Error	Lower 95%	Upper 95%
Shape	α	1.0017934	0.1713759	0.7052243	1.3799384
Scale	σ	19.300582	4.2328782	12.974505	30.889399

Figure 3.5.2. Analysis of Dosage Rate data across North Dakota (2012)

We also analyzed the distribution of consumption across the state of North Dakota. The results are very similar to the study that says North Dakota is considered as one of the states with lowest opioid consumption rate in the US. Looking at the distribution of the data, we can clearly figure out that probability density functions like Gamma or Lognormal could be a good fit. However, after fitting both the functions and comparing them on the basis of AIC (Akaike Information Criterion), Gamma distribution is a clear winner. The AIC value for Gamma distribution is lower than that for the Lognormal as seen above.

The box plot for North Dakota shows mean opioid consumption rate of less than 20 MME across the state, which in contrast to the analysis for Kentucky, is much lower and considered as a safe medication. The shape parameter(α) for the best fit i.e. the Gamma Distribution lies around 1 MME with the scale parameter(σ) of 19.3 MME. As before, we assumed α-value = 0.05 to determine the 95% confidence interval for the scale parameter to obtain $0.705 \leq \alpha$ (shape parameter) ≤ 1.379.

3.6. Fault Tree

A fault tree is commonly used in Risk Assessment and Reliability Analysis can be seen as a top-down graphic model using logic gates and fault events to model the chain of events/conditions leading to an undesired event. A fault tree identifies and determines significance of potential causes and contributors to failure. Once the causal factors of hazards or undesired events during system design/development are established, they can be worked on in order to eliminate or mitigate hazards. The relationship of an undesired event to basic events/causes of the fault tree are explained below:

• **Top event - the undesired event**

For the opioid risk analysis, the worst undesired event can be death due to opioid intoxication or emergency hospitalization and hence can be considered as the top node.

• **Immediate events - The causes of the top event**

Opioid Intoxication or overdose death can be classified into- 1) Opioid overdose and 2) Consumption of mixture of opioids and other substances, which are the two major causes of opioid intoxication. An 'OR' gate is used to classify these events as either events can lead to the top event.

• **Intermediate events or following events - Causes of the Immediate events**

The first immediate event i.e. Opioids overdose can occur due to either consumption of opioids to the extent of 90 MME/day or above or in some cases 50-90 MME/day could be riskier depending on the reason for consumption and method of prescription. Whereas a person may consume opioids mixed with other substances due to of lack of awareness or drug education, lack of drug monitoring programs, or simply an urge to get high. Again, 'OR' gates are used to resolve the immediate events into these following events to show either of the causes can lead to immediate event.

• **Basic events - The lowermost nodes or the causes of the intermediate or following nodes**

The cause of constantly consuming opioids to the extent of 50 MME/day can result due to no tapering in opioid consumption in spite of ordered by the doctor and taking opioids for longer than prescribed for the treatment. This can be combined by improper use of or avoiding the use of 'Naloxone' to lower down the deadly impact of opioids. A combination of all these factors or causes can lead to a person consuming more than 90 MME of dosage per day leading to overdose. The same is the case of consistently consuming a dosage of more than 50 MME/day which can be due to low level of monitoring or irregular check ups, especially in cases where people have Respiratory Depression or End-stage Renal Disease (ESRD), simply called as ‘Kidney Failure’. All these combinations of factors are represented using the ‘AND’ gate.

Once these basic events and high-risk fault paths are identified, the undesired event can be mitigated by implementing the important risk measures.

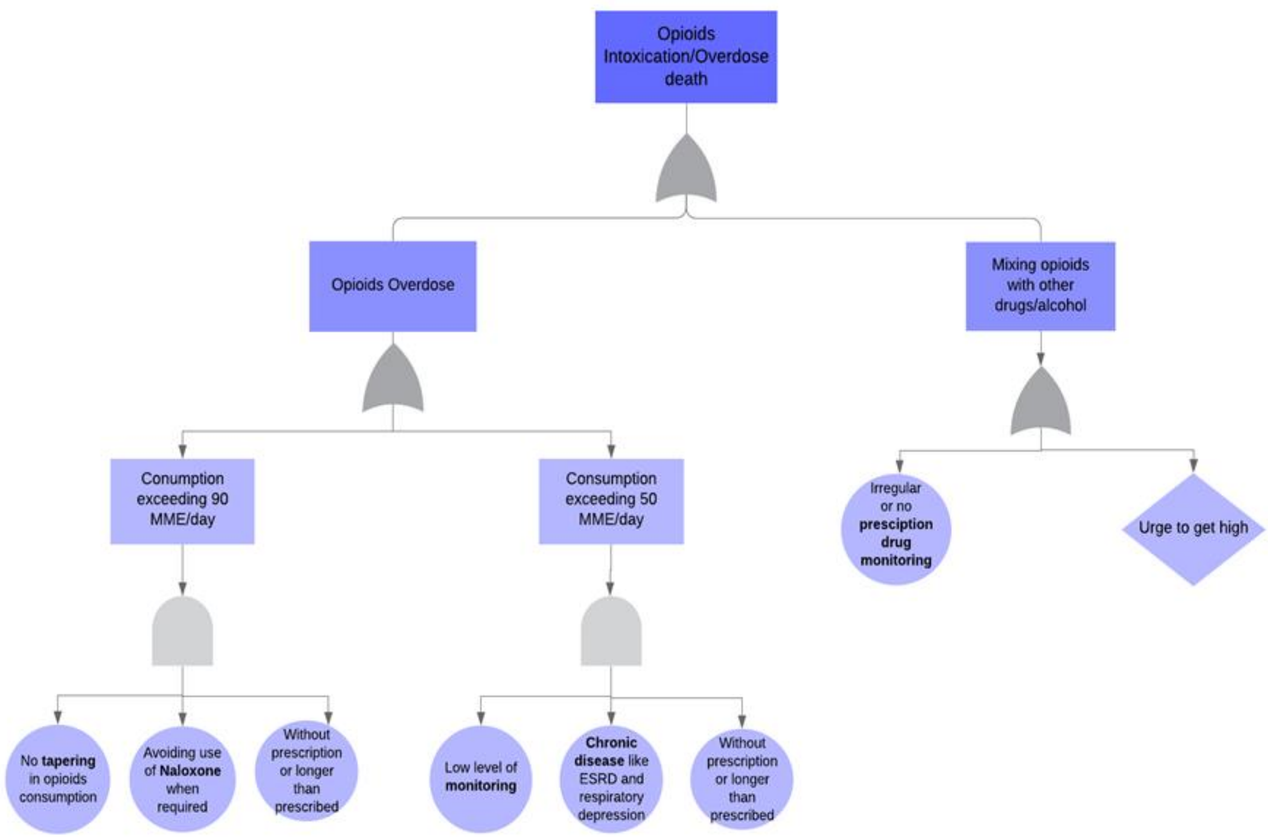


Figure 3.6.1. Fault Tree

3.7 Risk Matrix

A risk matrix is a matrix that is used during risk assessment to define the level of risk by considering the category of probability or likelihood against the category of consequence severity. This is a simple mechanism to increase visibility of risks and assist management decision making. We developed a similar risk matrix based on a combination of factors and Morphine Milligram Equivalent (MME) which is the commonly used unit for prescribed dosage of opioids. The factors include three age groups, gender, and employment status of an individual as these significantly affect the risk of developing opioid overdose or death. Obviously, several other factors can be included in the matrix but for visualization purpose, we only focused on the ones with readily available data.

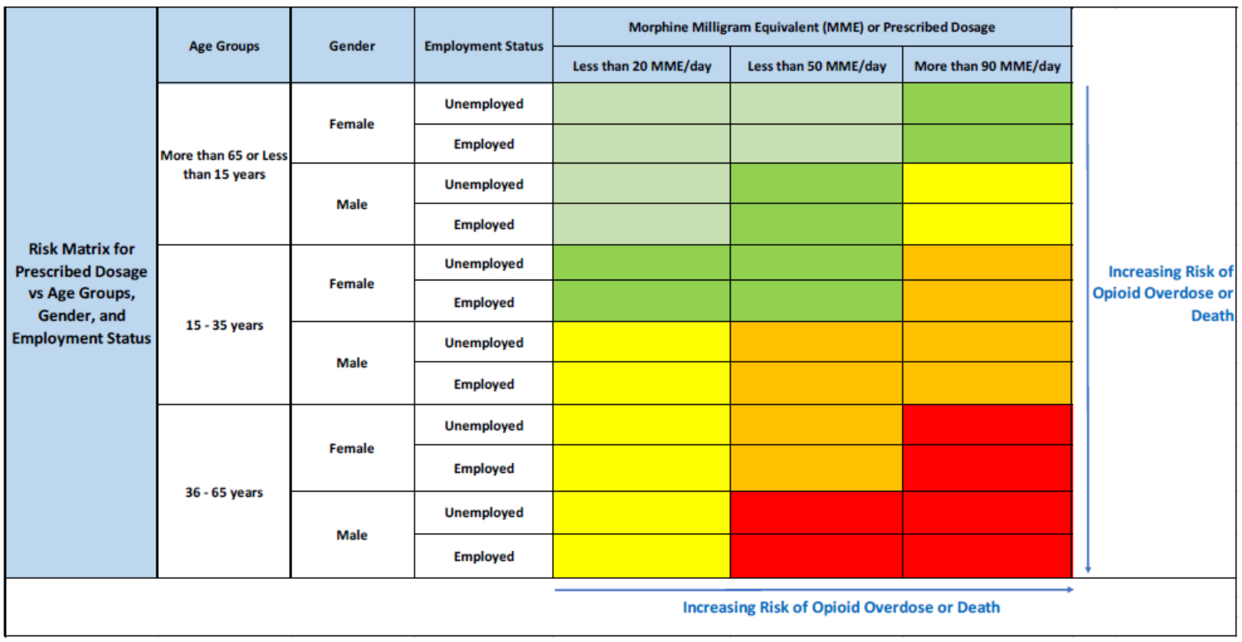


Figure 3.7.1. Risk Matrix

4. RESULTS

4.1. Data Visualization

As we can see in Figure 3.1.2, the distribution and consumption of opioids are highest in the states of West Virginia, Kentucky and a part of California whereas it is lowest in the Northern states of North Dakota, South Dakota and Nebraska. It is also comparatively lower than the national average in the state of Texas. We also visualized the same for two particular years i.e. 2006 and 2012 and the increase in opioid distribution and therefore consumption is evident from observing the below figures.

4.2. Data Correlation

The dosage rate in West Virginia is much higher than the prescription rate which is a clear indication that people have been taking opioids for longer than prescribed or even if they are not prescribed.

The same analysis for the state of Texas shows that even though the prescription rate across the state was higher, the opioid consumption rate was still much lower. The difference can be clearly seen in the approach of people in using opioids as medication tool or as a drug. The states of Kentucky and West Virginia has dominated others in the resulting deaths due to overdose and is on the rise.

Additionally, Figure 3.2.2 clearly shows that the highest consuming states of West Virginia and Kentucky had the highest number of average deaths while Kansas and Texas had a much lower death rate. The state of North Dakota was the least affected state.

4.3. Predictive Modeling

It is clear from Figure 3.3.1 that the opioid distribution has consistently increased ever since the year 2006 through 2012. The day-wise trend in Figure 3.3.2 shows approximately 80 percent lower figures for weekends compared to weekdays. An interesting pattern was also observed while looking at the time series plot in Figure 3.3.3 for the Opioid distribution/consumption on a daily basis for 7 years from 2006 through 2012. There is evidence of strong seasonality in this case as we can see three distinct spikes every year in the last quarter.

4.4. Bayesian Models

Race	White					
Age	15-35		36-65		>65 or <15	
Gender	Male	Female	Male	Female	Male	Female
False	0.881354	0.907355	0.670338	0.742585	0.973435	0.979257
True	0.118646	0.092644	0.329662	0.257414	0.026564	0.020743

Race	African American					
Age	15-35		36-65		>65 or <15	
Gender	Male	Female	Male	Female	Male	Female
False	0.990385	0.992492	0.973283	0.979138	0.997847	0.998319
True	0.009615	0.007508	0.026717	0.020861	0.002153	0.001681

Race	Hispanic					
Age	15-35		36-65		>65 or <15	
Gender	Male	Female	Male	Female	Male	Female
False	0.991434	0.993311	0.976199	0.981415	0.998082	0.998502
True	0.008566	0.006688	0.0238	0.018584	0.001918	0.001497

Race	Other					
Age	15-35		36-65		>65 or <15	
Gender	Male	Female	Male	Female	Male	Female
False	0.99654	0.997298	0.990385	0.992493	0.999225	0.999395
True	0.0034600035	0.0027020029	0.009615	0.0075070076	7.75E-4	6.05E-4

Prescribed ...	False			True		
Dosage	< 50 MME	>= 50 but < 90 ...	>= 90 MME	< 50 MME	>= 50 but < 90 ...	>= 90 MME
False	0.421896	0.859165	0.925543	0.854075	0.964451	0.981206
True	0.578104	0.140835	0.074457	0.145925	0.035549	0.018794

Unemploym...	False		True	
Urbanization	Rural	Urban	Rural	Urban
False	0.897745	0.40071	0.960447	0.808768
True	0.102255	0.59929	0.039553	0.191232

Tables 1-6. Conditional Probabilities of Bayesian Networks

Based on the conditional probabilities calculated for the model, certain trends became apparent within each sub model. In regards to deaths due to demographic factors, males had a higher probability of death due to overdose. More specifically, white males between the ages of 36-65 had a higher probability of death. African American and Hispanics had similar probabilities when compared by age and sex, although Hispanics had slighter lower probabilities. Looking at the probabilities based on location factors, there was a higher probability of death due to overdose in urban areas compared to rural areas. Additionally, the probability was higher for employed individuals than unemployed individuals in both areas. Finally, the probability of death was significantly higher if the individual was not prescribed opioids compared to those who were prescribed. Furthermore, the probability of death was higher for lower dosages.

4.5. Data Fitting/Distribution Analysis

Comparing the distribution fits for the consumption/dosage rate in the states of Kentucky and North Dakota, the mean range of the distribution ($70.05 \leq \boldsymbol{\mu} \leq 85.47$) for Kentucky lies on a higher scale than that for North Dakota ($\boldsymbol{\mu} = 19.3$). The distribution for Kentucky is highly concentrated around the median and the upper quartile of 65 MME and 98 MME respectively, which are considered as high-risk zones for opioid epidemic.

4.6. Fault Tree

After resolving the worst-case scenario or the undesired event of death due to overdose and analyzing the fault tree, the important basic events or causes identified are:

i) Improper use of Naloxone

ii) Taking opioids for longer than prescribed

iii) Low level of monitoring/check ups

iv) No tapering in the use of medication opioids

v) Chronic diseases like ESRD or respiratory depression

vi) No Drug Monitoring programs

4.7. Risk Matrix

From the risk matrix, it is evident that:

- Males are at more risk of opioid overdose and associated death than females.
- Individuals who are employed are at more risk of opioid overdose and associated death.
- The age group of 36-65 years is the most "at risk"

5. DISCUSSION/CONCLUSION

5.1 Data Correlation

After establishing a correlation between the amount of prescriptions and opioid consumption, we can conclude that:

i) The number of prescriptions in the states affected by Opioid epidemic has to be stringently brought down to a safe number.

ii) Laws should be enacted that restrict the dispensing of opioids for minor health reasons that can actually be treated with low strength medicines or sometimes exercise.

iii) States with average consumption amount of greater than 90-100 MME/day can limit prescribing opioids to 50 MME/day.

We also recommend a more stringent process for screening patients before giving out an opioid prescription and maintaining a database, to track that the person has stopped the intake of these drugs once the prescribed period is over. This will not only control the consumption-prescription discrepancy, but also mitigate the risk of overdose due to higher consumption than prescribed.

5.2 Predictive Modeling

Based on the yearly increase shown in Figure 3.3.1, we can conclude that the increasing distribution is linked to an increase in consumption of these prescribed opioids. It can also be due to an increase in doctor prescription rates as well as promotion by drug manufacturers. The day-wise trend in Figure 3.3.2 could be due to changes in routine behavior from weekdays to weekends, as well as less open business hours on weekends. Finally, the time series plot in Figure 3.3.3 can be due to seasonality differences. It is an indication that the sales of these opioids are being further pushed or promoted by their manufacturers and distributors to meet their financial goals for any particular fiscal year. This leads to more consumption and more risk of opioid overdose cases. Such hypothesis is an alarming sign from the manufacturer as it conveys their focus on profitability than on the public health and safety.

5.3 Bayesian Models

The findings from the results of the Bayesian models lead to some interesting points for consideration. The most significant is the higher probability of death for lower dosage. As stated earlier, the risk of overdosing was found to be significantly higher for individuals who were prescribed a higher dosage (Bohnert et. al., 2011). Therefore, these findings contradict prior studies and an overall a general assumption. The differences in conclusions can be due to how risk was measured in prior studies. Additionally, there could be behaviors and other factors that skew that statistics so that death probability is higher for lower doses. For example, individuals with lower dosages may not be taking the drug as prescribed, or they may be mixing with other drugs or substances. It may also be possible that there is more strict monitoring and treatment for those with higher doses due to the higher risk, while monitoring for lower dosages is not as strictly monitored with less additional treatment. There is also a possibility that due to lower dosage, patients are not as cautious with intake and take more than their daily prescription. Therefore, while their prescription dosage may be low as indicated in the data, the actual daily intake exceeds the prescription and is not accounted for when data was collected. Given the contradicting findings and potential for other factors, more research and studies must be done to closer monitor and analyze the true probability.

Another significant finding was that employed individuals were at a higher risk for death than those that are unemployed. While this may seem in opposition to stereotypes, this result makes sense given the scope of the data. Values were calculated looking at prescription opioids and therefore those with employment have easier access to these types of drugs. They can obtain prescription painkillers using healthcare insurance provided by employers, whereas unemployed individuals do not have as much access to healthcare providers. Therefore, unemployed individuals may utilize a different substance that is easier to obtain.

Finally, it was found that individuals living in urban areas had a higher probability of death. While this makes sense given the high population rates in urban areas, mortality rates were also very high in rural areas such as Kentucky and West Virginia. Since the population rates are higher in urban areas though, this skews the conditional probability in favor of urban areas and underestimates the probability of death in rural areas. This is a limitation of our model, given that it was averaged across the entire United States.

5.4 Data Fitting/Distribution Analysis

The wide variations in the mean and interquartile ranges of the dosage consumption shows the urgency of implementing laws that restrict the supply of opioid tablets for the highly affected states. The large variance between the distribution in the states of Kentucky and North Dakota is contributed not only by the consumer but the suppliers as well, who do not care about the public health for their own profits. And hence, the mean range for the state of Kentucky has to be lowered down steeply. Furthermore, few outliers on the distribution plot shows consumption of more than 200 MME/day which is shocking. A visit to these areas and study of why is consumption so high and how can it be mitigated can be significant.

5.5 Fault Tree

Considering the basic events listed above, necessary steps can be taken both by the consumer as well as the government in mitigating the risk of opioids. The government actions can include organizing

Drug Monitoring and Awareness Programs regularly and keeping a check on the hospitals if they are dispensing the right quantity of opioids for medications. Consumers can take care of dosage limits by not taking medications for longer than prescribed, avoiding the use of high dose opioids for minor injuries and using Naloxone as an alternative.

5.6 Risk Matrix

We can conclude that usually employed individuals especially males in their middle age are more prone to develop opioid misuse habits and are therefore at more risk of overdose associated deaths. The reasons such as health Insurance, having more money, etc. are some of the factors which increase the tendency of significantly more opioid use. Health insurance involves more chances of over prescription by the Doctors.

6. RECOMMENDATIONS

Currently our Bayesian model is limited given that it only accounts for the US, which does not provide an accurate representation of more specific factors that are impacted by the location of the potential user. For example, the conditional probabilities of death due to overdose in the state of Kentucky would look significantly different to that of Texas. Furthermore, our model is also limited in that some of the data used to create the model was not available and assumptions needed to be made to complete the model. As a result, the margin of uncertainty increases even more when applying this model to specific locations. Finally, our model is divided into three sub-models as there was insufficient data to combine all three to get a final output for probability of death due to overdose. As a result, we have three independent probabilities of death but no way of combining them to get a final value. In order to overcome these limitations, we propose the following recommendations for the future.

1) Data Collection: As previously noted, some assumptions were made when calculating the conditional probabilities of the output nodes due to limited or insufficient data for the US models. In the future, data should be collected in such a way that these conditional probabilities are already accounted for and can easily be extracted. For example, when a person dies due to opioid overdose, records should be kept in regards to all the parent nodes in our model. Additionally, records should also be kept in such a way

that allows for the 3 outputs nodes (or synthetic nodes) to be connected to the top node in our model. In that way, we would not have three independent probabilities in regards to death due to overdose, but rather one. Furthermore, this form of data collection should be extended to states and counties as well, not solely for the US. With this more accurate data, the model can be updated and adjusted easily to fit the needs of the healthcare provider or other users. It would remove the margin of error and uncertainty that currently exists in our model.

2) State and County Models: Provided that data is recorded in the manner mentioned above and the model can be updated to combine all 3 synthetic nodes, this model could be adapted to show the specific probability associated with a specific state and county. Probabilities would have to be altered within each node but the basic framework and concept of the model is the same regardless. Therefore, it would be easy for the model to be used in different settings. This would be extremely valuable given that specific states and counties differ in terms of both the parent nodes' probabilities and conditional probabilities, as shown in the map below.

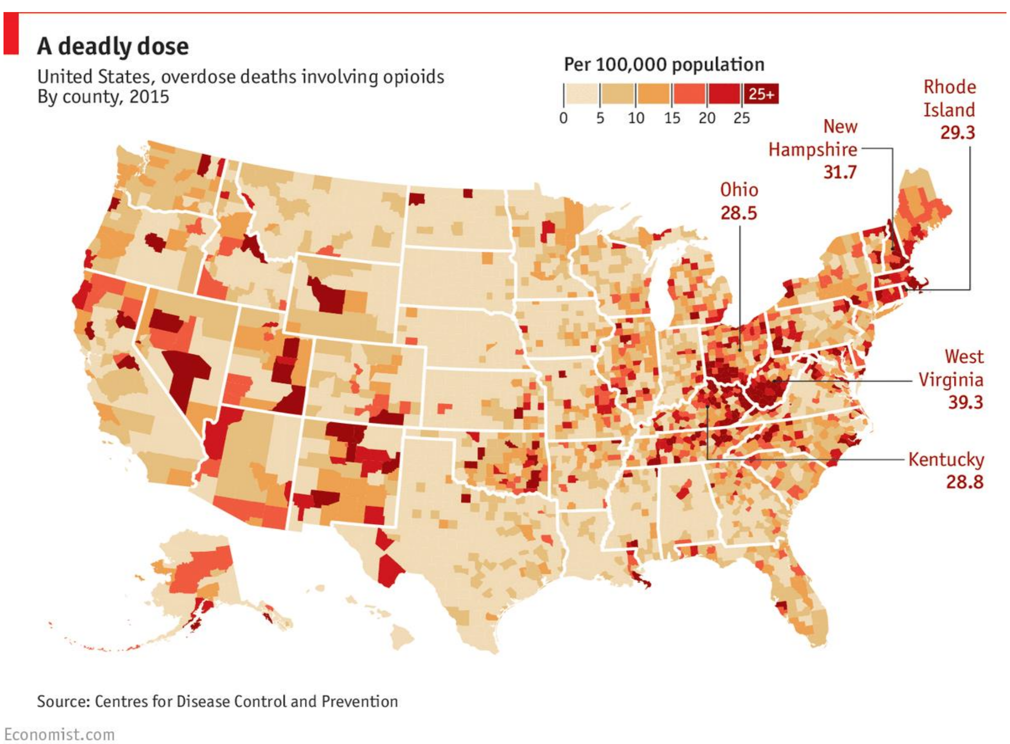


Figure 6.1. Overdose Deaths Involving Opioids by County, CDC

3) Expanded Models: Additionally, the model could be expanded to include other variables and factors that we did not include in our model. This could include factors such as illiteracy, free-and-reduced lunch rates, and income. Other factors, such as consumption behavior, mental health issues, and treatment programs could also be studied to see how they impact the probability of death due to overdose. In the event of an expanded model, data collection would have to reflect this change and account for the new variables.

4) Models for Other Risks: Though outside the scope of our project due to limited data, the CDC also records the number of hospitalization visits and ER visits for different drugs. If data was recorded for these risks in a similar fashion as mentioned previously, new models can be created using our basic framework to assess the risk of hospitalizations and ER visits as well. These models can be created on a nationwide basis, as well as by state and county.

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