Case Study 1 Writeup

Introduction

The goal of this project is to investigate the heterogeneity of price per milligram of morphine by location and its relationship with other factors in a data set collected from `streetrx.com`. StreetRx is a study that has been collecting citizen-reported street price data of diverted pharmaceutical substances, such as morphine, since 2010. Since the price of morphine provides information about the demand, availability, and potential drug abuse, the investigation of this project could reveal insights of the morphine price over various locations and other indicators that are helpful in health surveillance for drug abuse and other health-related issues.

To this end, we used the StreetRx data set to build a hierarchical model on morphine price with a location grouping variable as well as other predictors. First, we processed the raw crowd-sourced data to eliminate noise and inconsistent coding. Second, we performed exploratory data analysis to better understand the variables' distributions and their relationships. Third, we assessed price heterogeneity with respect to the hierarchy of location data to determine which location variable(s) best predicted the outcome variable. Then, we iteratively added other predictors, including possible interaction effects, by identifying logically sound relationships and then performing diagnostics on the resulting models to assess validity.

Through this process, the best performing model we identified used dosage strength, purchase size, and a random effect for state of purchase to predict price per milligram of morphine. We determined that city was a poor predictor of purchase price due to the significant heterogeneity and thus limited data available from each city, and that region did not convey any additional predictive power that was not already captured by state. The effect of location was limited relative to the effects of dosage strength and purchase size. Variables such as purchase reason, source of information, and date were not significantly predictive of price and reduced the Bayesian Information Content of the model.

Data Cleaning

By inspecting the data set entries and the structure for each variable, we found the several issues with noisy, corrupted, or poorly formatted data. Here is a summary of the issues and the corresponding solutions to clean the data set.

First, we filtered the dataset to eliminate data from other drugs besides morphine. Some entries were ambiguously labeled, such as having drugs specified as 'morphine/oxycodone', and we eliminated these as well because we could not be certain which drugs they reported. This filtering process resulted in a new data set with 9268 records.

Second, we reformatted the **date** data. The original data had two fields representing date information: `yq_pdate` and `price_date`. The first field coded the year and quarter as a pseudo-continuous range (e.g., '20151' for first quarter 2015). This is not suitable for assessing the data on a true continuous scale because it portrays quarters within the same year as being closer together than adjacent quarters from different years (i.e., fourth quarter 2019 is closer to third quarter 2019 than it is to first quarter 2020 in this coding scheme). Therefore, we used R's string parsing methods to segment 'price_date' into the *month*, *date*, and *year*, and then created a new field for each record that counted the *number of elapsed days since a reference date*. In this case, we set *January 1, 2010* as the starting date, since the Streetrx data collection began in 2010. In addition, we found 14 entries prior to the year 2010, including 3 from the 1960s, and removed them from the dataset, resulting in 9254 observations. We did this because there was legitimate concern that the entered data might not be accurate if it was supplied long after the drug purchase event.

Third, we assessed the reported data for city in which the drugs were purchased, and the data set contained

city aliases and ambiguous references to some cities other than the formal names of cities. We saw that there were 1690 unique "city" values among the 9254 observations. However, when we inspected visually we could see that there were numerous entries with **different listed names that clearly refer to the same city**. Some users used different entries for reporting names, such as using either "Fort Lauderdale" or "Ft Lauderdale" to refer to the same city, resulting in two different values. We saw a range of other common data discrepancies, such as using city nicknames (e.g., "Philly" for Philadelphia), airport codes (e.g., "ATL" for Atlanta), or the abbreviation used by major sports franchises within the city (e.g., "JAX" for Jacksonville). Various other issues were observed frequently, such as users providing redundant state information (e.g., "Des Moines, IA" instead of just "Des Moines"), referring to a city by the specific neighborhood or borough (e.g., "Brooklyn" instead of "New York") or including single character typos (e.g., "Holywood" instead "Hollywood"). We employed the following two approaches to address this issue.

First, we imported US census data which defined the official city abbreviation used by each city and cross referenced it with the listed data. Fortunately, this process covered the majority of the entries, but there were still about 300 city values supplied that were not on the list. In the cases where the correct city could be unambiguously identified, we created a dictionary mapping the original value to its corrected value applied this mapping to the original data to correct those entries which were non-compliant. During this process we also identified and preserved records referencing unincorporated areas and townships which were excluded from the original census data, which were nonetheless legitimate.

In other cases, the original city could not be unambiguously identified from the data given. For example, some users listed their zip code, which often crossed city lines. Others listed their county, which included multiple cities, and others listed the general metropolitan areas (e.g., "Lehigh Valley" or "Dallas - Fort Worth"). We did not want to guess, so in these cases, we replaced any remaining city names with **Other/Unknown**.

One pitfall that we had to avoid was inappropriately aggregating city data that were not related. For example, the data set contained both "Hollywood, FL" and "Hollywood, CA". If we ultimately built a hierarchical model with both state and city grouping variables, we did not want to mistakenly label data from those two places as being from different states but the same city. Therefore, we augmented our coding of the city name by appending the state as well so that each city was uniquely encoded, even if it shared its name with another city in a different state.

Next, we inspected data defining the **source** of the price transaction data. There were over 50 unique entries, too many to do rigorous grouping on. However, there were common themes among the unique values, such as similar sources being referred to in slightly different ways. In particular, we observed that each of the sources was one of the following: (A) personal information, (B) word of mouth, (C) a web forum, (D) an online black market, (E) a legal online market, (F) a web search, or (G) other/unknown. We thus mapped each unique source listed to one of those seven categories, using sub-string searches on a variety of common source keywords such as "silkroad", "bluelight", "reddit", "opiophile", "forum", "pharmacy" and others.

Finally, we addressed missing values in the data. For most fields, we simply replaced the missing value with the categorical label "other/unknown". However, we had to eliminate data points that had missing values for the response variable. This resulted in a final dataset with 8712 observations and 9 predictor variables as shown below:

- `ppm`: response variable, price of morphine per milligram, numeric value. (Notation in code: `ppm`)
- `city`: cities, where the transaction took place, 1654 unique factors. (Notation in code: `City_final`)
- `state`: states, where the transaction took place, 56 unique factors. (Notation in code: `state`)
- `region`: regions, where the transaction took place, 5 unique factors. (Notation in code: `USA_region`)
- `primary reason`: reasons for purchasing morphine, 11 unique factors. (Notation in code: `Primary_Reason`)
- `source`: sources of such transactions, 8 unique values. (Notation in code: `Source_class`)
- `days ellapsed`: number of days passed since 01/01/2010, which is the time when the data collection process started, discrete numerical value. (Notation in code: `Days_since_010110`)
- `dosage strength`: dosage strength of the purchased morphine, discrete numeric value, ranging from 1 to 200. (Notation in code: `mgstr`)
- `bulk`: indicator for purchased 10+ units, factor with levels 0 and 1. (Notation in code: `Bulk`)

The data analysis and modeling were performed upon the cleaned data set with the above predictors.

Exploratory Data Analysis

In this part, we explore distributions of the variables, potential relationships, and potential interactions that we might include in the model.

1. Response Variable

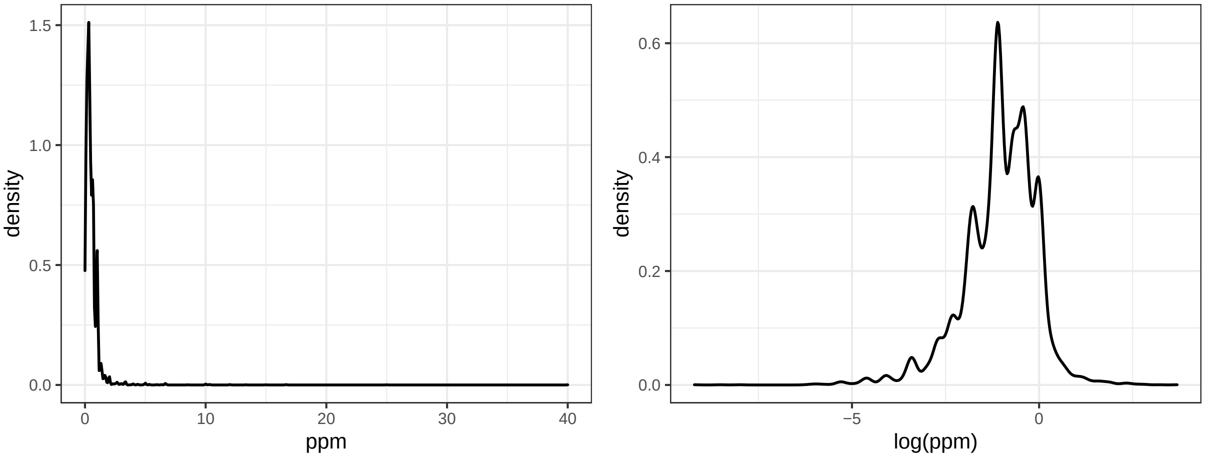


Figure 1: Log Transformation on Response

First, we examine the ppm variable (price per milligram), our primary outcome variable. Even though the values don't vary over many orders of magnitude, it has extreme right skew. Taking the log of these values appears to dramatically improve various indicators of normality while the data still fails a Shapiro-Wilk normality assessment this transform appears reasonable for the data.

2. Group Variables

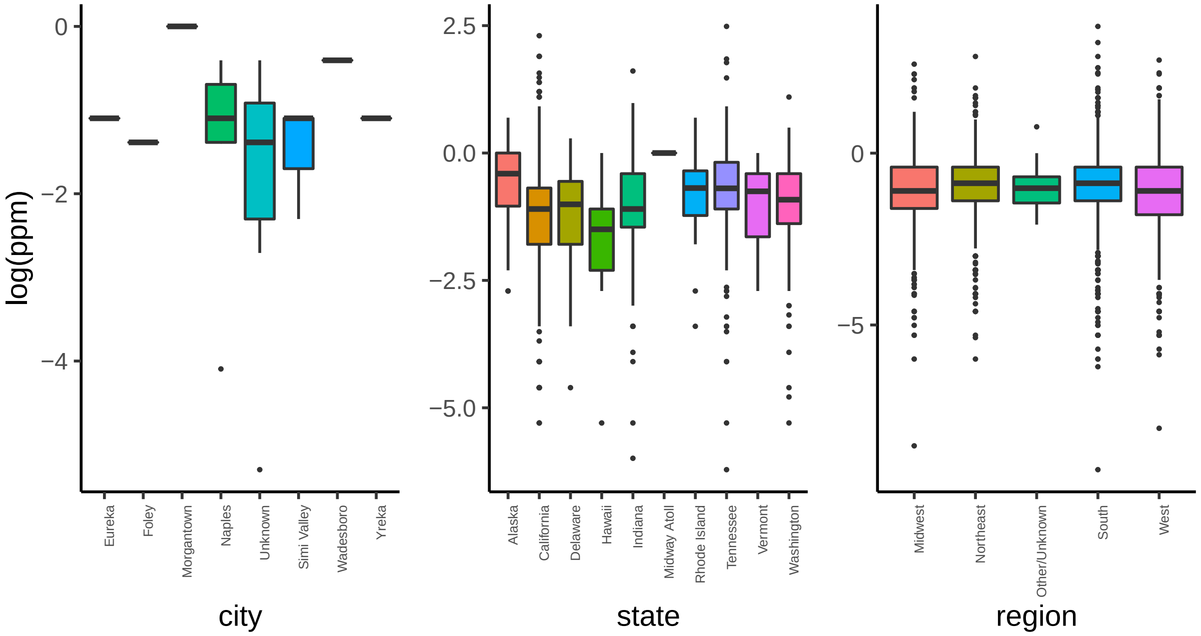


Figure 2: log ppm versus different location grouping variables.

City There are 1654 unique levels of `City_final`, which indicates the unique cities recorded in our data set. To explore whether there is a relationship between the cities and the log price per milligram of morphine, we make a box plot of randomly chosen 25 cities. The log price per milligram of morphine seems to differ by cities.
State

Next, we explore the relationship between log ppm and state. We can observe that the log ppm differs by the states.

Region Finally, we observe that the log ppm also differs by USA regions, but such difference is not quite obvious.

However, to determine which one of these grouping variables should be included in the model, we need to perform formal tests and analyses. Preliminarily, we make three models with cities, states, and regions as the only predictors respectively, and perform ANOVA tests. The results show that log ppm differs significantly by states and regions, but not that much by cities.

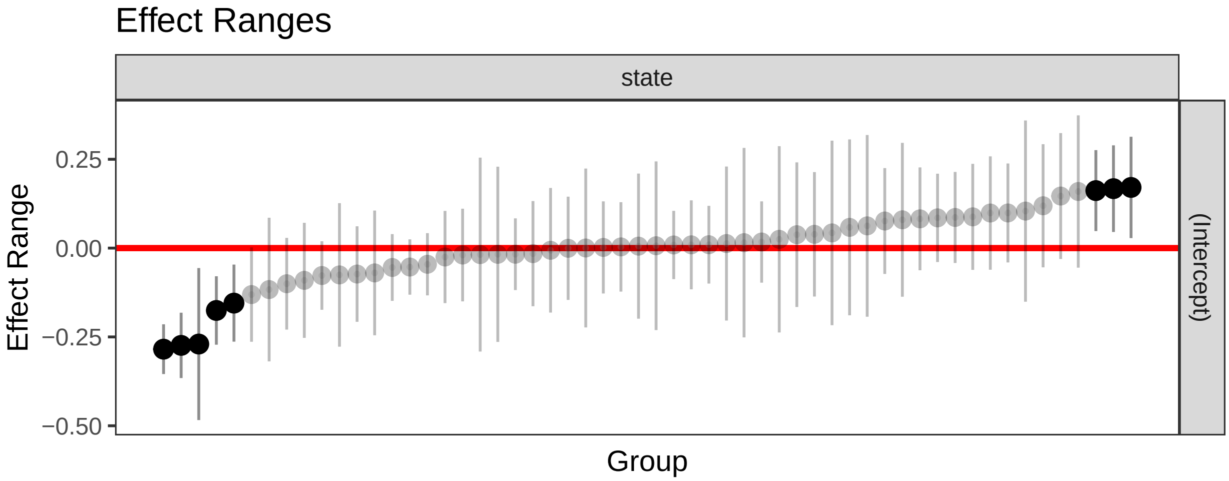


Figure 3: Distribution of State Random Effects

We then build three random effects anova models with only cities, states, and regions as predictors respectively. The plots of random effects show that state might be the best to included individually as our grouping variables, it indicates reasonable amount of information to demonstrates the heterogeneity of log ppm across locations.**(See Appendix for random effect plots for cities and regions)** A series of nested tests for including multiply grouping variables will be performed in the Model section.

3. Fixed Effect Predictors

Days The first variable we consider is the linear temporal variable we created, which is number of days since Jan 1, 2010. This lets us encode time in a semi-continuous manner. Despite the discrete encoding, the data actually functions quite well as a numeric predictor since there is high resolution relative to the overall time scale. The only apparent thing is that when we plot the price data against over time, the data is clearly sparser earlier in streetrx's history. However, with the appropriate parameter selection, this should not be a significant issue in the overall models we will create.

However, by only looking at the relationship between this variable and the log ppm, we do not observe obvious linear association.**(See Appendix Fig.7)**

We then consider the effects of days in each group, presumably by state. We randomly sample 8 states. In some states, the log ppm seems to change across the days elapsed. Such change may not be very obvious as the data points are sparse. Still, it might be worth trying to add random slopes of days by state to the model.

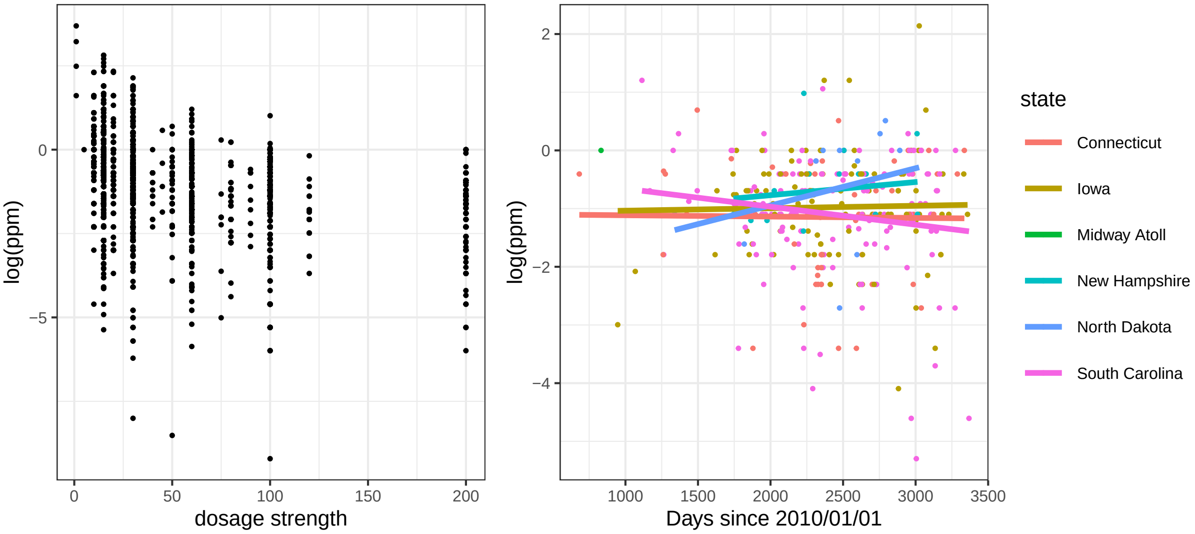


Figure 4: log ppm versus dosage strength overall, and log ppm by time in different states.

Dosage Strength Although `mgstr`, the dosage strength, is numeric, values are reported at discrete intervals, perhaps due to standard packaging sizes or users rounding off the values that they reported. All told, there are 16 unique values ranging from 1 to 200. We have two options: treat this as a categorical variable or accept the sparse numeric coding. If we do ultimately evaluate `mgstr` in our model, it does not seem that we would be interested in categorical relationships. In other words, we don't have any reason to believe there is something unique about individual package size levels. Instead, we are concerned with the general trend in how different volumes affect price. Since 16 points is more than adequate to fit a line in most applications and since the data we've collected has multiple volume sizes at each order of magnitude, it seems reasonable to continue with the numeric encoding.

There is a slightly negative linear relationship between dosage strength and log ppm. We also considered adding a random slope by dosage strength by state.**(See Appendix Fig.14)**

Primary Reason (See Appendix Fig.8 and Fig.9) It seems that, in general, log ppm does not differ too much across different primary reasons for purchasing morphine.

With-in each state, the log ppm differs according to different primary purchase reasons. Therefore, it is possible to include random slopes of primary reasons by state in the model.

Source (See Appendix Fig.10 and Fig.11) It seems that in general, the log ppm varies according to the values of the sources class, which indicates the source of each transactions recorded in the data set.

By examining the associations between source class and log ppm in a random sample of states, we can see that such associations vary across states. It might be worth considering random slopes of sources class by states in the model.

Bulk (See Appendix Fig.12 and Fig.13) The indicator for purchasing 10 units at once, Bulk, does not seem to have an obvious relationship with log ppm. We will not include a random slope of bulk by state either as the plot does not show that such association vary by states.

Model design

Grouping Variable Selection

Our first step was to determine which level(s) of location hierarchy were most appropriate for grouping observations. Prior to building any models, we examined the EDA figures (**Figures Needed Here**) and observed that log(price) did not vary much across different regions, but there was more variation across cities and states. We also observed that the sample size for most cities was very small. As a result, our suspicion was that neither 'region' nor 'city' would be good predictors in the eventual model.

We then tested a series of hierarchical models predicting price from location, with random effects on every possible combination of the three location variables (each individual variable, each pair of variables, and the combination of all three). We compared these seven models using BIC values as criterion based on the principle that, in each comparison, the two models differed by at most one variable. For example, we could compare the BIC score of the model of random effects in `city` and `region` with the BIC score of the model of random effect in `city`. But we could not compare the model of random effects in `city` and `region` with the model of random effects in `city` and `state`. This principle could also be observed in the model comparison results, which are shown below and ranked by BIC values.

1. (`state`) < [(`state`, `city`), (`state`, `region`)] < (`state`, `city`, `region`) < (`city`, `region`).

2. (`state`, `city`) < (`city`).

3. (`state`, `region`) < (`region`).

Here are some explanations of the notations. (`state`) indicates the model with random effect in `state` only, without any other predictors. (`state`, `region`) indicates the model with random effects in both `state` and `region`, no any other predictors involved. And if model1 < model2, it means that the BIC score of model 1 is smaller than the BIC score of model2. The BIC scores of the models mentioned above are shown in the table below.

Table 1. The BIC score of the models with location group variables only.

Name	Degree of Freedom	BIC Score	Random Effects
re m1	5	24141	`city+state+region`
re m2	4	24192	`city+region`
re m3	4	24132	`state+region`
re m4	4	24133	`city+state`
re m5	3	24207	`city`
re m6	3	24124	`state`
re m7	3	24209	`region`

From the above evaluation, we determined that the most likely model for predicting price from location relied only on random effects for state, and excluded city and region. This was consistent with our expectations given the EDA. Therefore, we chose to use `state` as the only group variable in locations with random effect.

Selection Among Other Variables

We built a more substantial model around our base model, which predicted log(price) using random effects for state only, by using forward stepwise selection of the remaining predictors.

Table 2. The BIC scores of the models with specified random effects and fixed effects. For convenience, we used `mgstr` to represent `dosage strength` here.

Name	DF	BIC Score	Random Effects	Fixed Effect
base	3	24124	`state`	None
m1	4	23105	`state`	`mgstr`
m2	4	23100	`state` + `mgstr` (by `state`)	`mgstr`
m3	5	23098	`state`	`mgstr` + `bulk`
m4	6	23105	`state`	`mgstr` * `bulk`

Name	DF	BIC Score	Random Effects	Fixed Effect
m5	12	23134	state	mgstr + source + bulk
m6	47	23442	state + source (by state)	mgstr + source + bulk
m7	19	23182	state	mgstr + source * bulk
m8	15	23182	state	mgstr + primary reason + bulk
m9	80	23140	state + primary reason (by state)	mgstr + primary reason + bulk
m10	6	23104	state	mgstr + bulk + days ellapsed
m11	8	23117	state + days ellapsed (by state)	mgstr + bulk + days ellapsed

First, from the **(mgstr EDA graph)**, we could see that there was a slightly negative relationship between the `log(ppm)` and the `dosage strength` variable. Since the `ppm` was log-transformed, a slightly negative coefficient between `log(ppm)` and `dosage strength` might be enlarged after exponentiation. Therefore, we considered the `dosage strength` as a quite important predictor and added it to the model. By comparing with the base model, the model with the addition of `dosage strength` as a fixed effect had much lower BIC score (Table 2. m1 vs base model). Therefore, we decided to include `dosage strength` in the model. Now, the model contained random effects for `state` and fixed effects for `dosage strength`.

From the **EDA plots**, `dosage strength` seemed to have different effects on the `log(ppm)` response variable across the sampled states. Therefore, we also considered adding random slopes of `dosage strength` by `state` to the model. Not to our surprise, the BIC score of the model decreased compared to the model without random slope of `dosage strength` by `state` (Table 2 m2 vs m1). However, the model failed to converge, so we did not include the random slope of `dosage strength` by `state`. Therefore, `dosage strength` was added to the model only as a fixed effect.

Second, from the **EDA Figure bulk**, the `log(ppm)` seemed not to vary across different `bulk` sizes, both in general and across sampled states. Therefore, we considered `bulk` as an unimportant variable. However, adding `bulk` to the model slightly lower the BIC score (Table 2. m3 vs m2). We preferred not to add random slopes of `bulk` by `state` to the model since `bulk` variable did not have different effects on the `log(ppm)` across the sampled states. Thus, we decided to add `bulk` to the model as fixed effect only. At this point, the model included random effect of `state`, and fixed effects of `dosage strength` and `bulk`.

There was a potential interaction between `dosage strength` and `bulk` variable since such interactions might imply a potential discount in the drug sale. We added the interaction to the model, but the BIC score increased. (Table 2. m4 vs m3) Therefore, the interaction term was excluded from the model.

Third, we considered adding `source` and `primary reason` to the model. From the **EDA graphs**, within sampled states, the `source` predictor seemed to have different effects on `log(ppm)` across different states. Therefore, we considered to add random slope of `source` by `state` and fixed effect `source` to the model, however, the BIC score of the model increased a lot after adding either fixed effect of `source` or both random effect and fixed effect of `source` to the model (Table 2. m5 vs m3, m6 vs m5). Therefore, the `source` variable was excluded from the model. We also excluded the `Primary Reason` from the model. From the **(Figure Primary)**, we could see that the response variable, `log(ppm)`, did not change across different `Primary Reason` categories. And across the sampled states, `Primary Reason` did not have different effects on the `log(ppm)` response variable. Therefore, we would like to exclude `Primary Reason` from the final model. In addition, the model with `primary reason` as fixed effect or both random effect and fixed effect increased BIC values a lot, which further confirmed our decision not to include it in the model. (Table 2. m9 vs m8, m8 vs m3)

We also tried to include the interaction between `source` and `bulk` as fixed effect in the model, but this interaction increased the BIC score a lot, so it was finally excluded from the model. (Table 2. m7 vs m5)

Finally, based on the **EDA Figures**, it seemed that there was no obvious relationship between the `log(ppm)` and `days ellapsed`. However, we could observe slightly different slopes of `days ellapsed` of the sampled states. In the meantime, we thought that as the local economy or regulation changed over time, the price of the morphine might also change over time as well, which also made us believe that the `days ellapsed` should be added to the model. And since each state had different development histories, the `days ellapsed` variable might have different relationships with `log(ppm)` in different states, which led us to add random slope of `days ellapsed` by `state` to the model. Therefore, we added `days ellapsed` with random slope by `state` to the model along with its fixed effect. However, either adding fixed effect `days ellapsed` only or adding both random effect and fixed effect would increase the BIC score of the model. (Table 2. m11 vs m10, m10 vs m3) Therefore, we finally excluded this variable from the model.

Model Summary

From the above reasoning and testing results, our final model could be summarised as the following formula.

$$y_{ij} = \beta_{0,j}\ \text{State}_j + \beta_1\ \text{Bulk}_{i,j} + \beta_2\ \text{Dosage Strength}_{i,j} + \epsilon_{i,j}$$
$$\beta_{0,j} = \beta_0 + b_j;\ b_j \sim \text{Normal}(0, \tau^2)$$
$$\epsilon_{i.j} \sim \text{Normal}(0, \sigma^2)$$

In the above formula, b_j represents the random effects of `state`, and $\epsilon_{i,j}$ is the error term. $i = 1, ...n_j$, where n_j represents the number of observations in group j. $j = 1, ..., J$, where J represents the number of groups.

We have neither information about nor strong belief regarding the random effect parameter τ^2 and error term variance σ^2, we would like apply a non-informational prior on these parameters. Under this condition, the information from the data set has a quite large weight estimating the model parameters, which is similar to fit the model without pirors. Therefore, considering the time cost of running the models, we decided to use the normal hierarchical model, which is specified as above.

Findings and Conclusion

Our model only includes three variables: State, mgstr, and Bulk. Mgstr and Bulk are fixed effects and State has a random effect.

Table 3. Model Coefficients Summary.

Coefficient	Fixed Effect	Lower Bd	Upper Bd
`Intercept`	-0.590	-0.639	-0.541
`Dosage Strength`	-0.010	-0.010	-0.009
`Bulk`	-0.103	-0.154	-0.052

Let's first check the fixed effect in this model. As we can see form the fixed effect table, the intercept for this model is -0.59, which means the price of the drug would be $e^{-0.59} = 0.554$ while the dosage strength is 0 and Bulk is also 0. For mgstr, its coefficent is -0.01, which means a 1 unit increase in dosage strength will lead to a 0.01 decrease in log price per mg while holding all other coefficients constant. That is to say, a 1 unit increase in mgstr will lead to original price increase by a factor of $e^{-0.01} = 0.99$ times. For Bulk, if we switch the category of bulk from 0 to 1 while holding all other coefficients constant, then the intercept of the log price will decrease 0.103, which means the original price per gram will incrase by a factor of $e^{-0.103} = 0.902$ times.

For random effect of the state, it means in different states, the base price of Morphine will be a little bit different. The across-state variation is 0.015 and the within-state variation is 0.82, which means the across-state random effct is not strong compared to within state variation. As we can see from the graph, there is certain degree random effect in the model although their contribution is small. For states like Tennessee, Virginia, and Oklahama, the price of Morphin would be higher. However, for states like Arizona, California, and Neveda, the price of Morphine would be lower.

Above plots are the diagonistic plots for the model. In the first plot, all of the points are nearly randomly distributed around the 0 line except there is a small pattern. However, that pattern is acceptable. The QQ plot shows the target variable is deviated fromm the normal distribution. That deviation is expected because

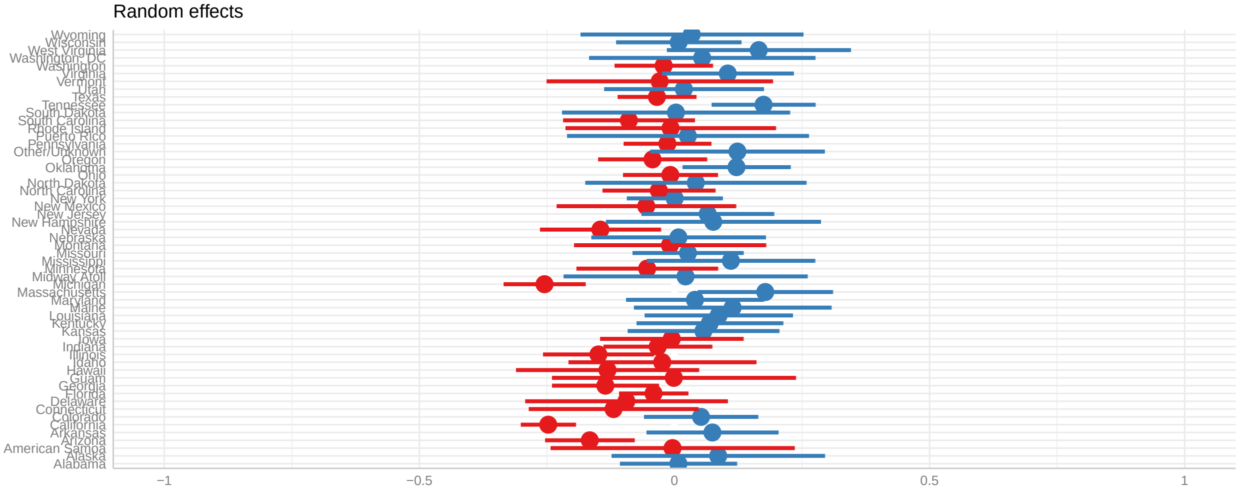


Figure 5: Random effect by state from the model.

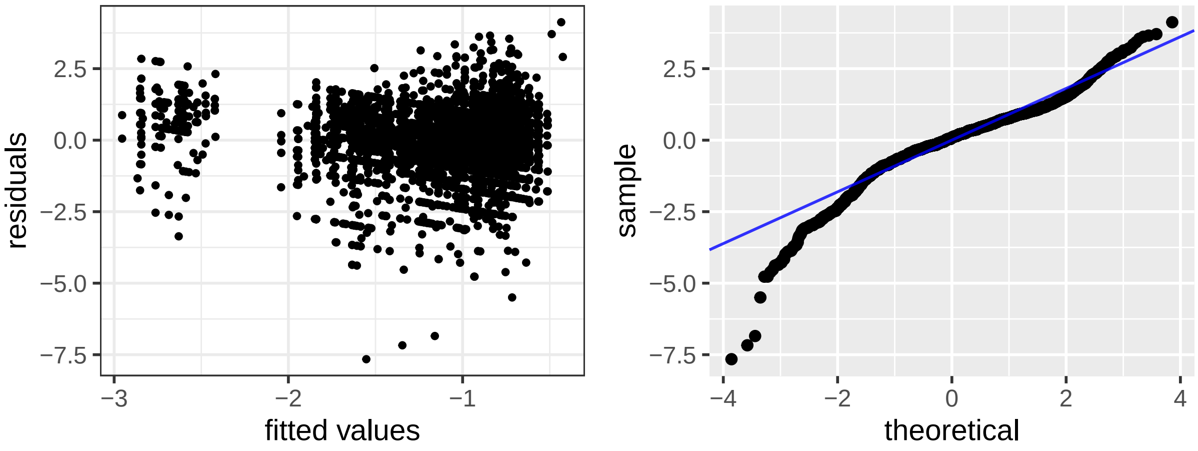


Figure 6: Diagnostic Plots, residual plots and normal qq plot.

the distribution of the $log(price)$ is not that normally distributed as shown in the EDA. For the scale-location plot, there is not an obvious pattern in the graph, which means the variance of the residual is constant across all level of predictions. In the last plot, there are also not any influential outliers exist. Thus our model is good. At this point, we successfully train a mdoel that can predict the Morphine price.

Limitations

First, when we are exploring the models, we use the forward stepwise selection with the order based on logical reasoning of the relevance between the predictors and the response variable. Since it is forward stepwise selection rather than a method which exhausts all the possible subsets of the predictors, we might miss the optimal combination of the predictors. However, this approach does protect against overfitting since we only consider models which are plausible, so it is a necessary tradeoff. When we built the model, we also cared about the interpretability of model, so we actively avoid the meaningless interactions like the interaction between the `primary reason` and `source`, whose physical meanings were hard to interpret how it was related to the price of the morphine.

Appendix

Below are the relevant figures and tables to the project.

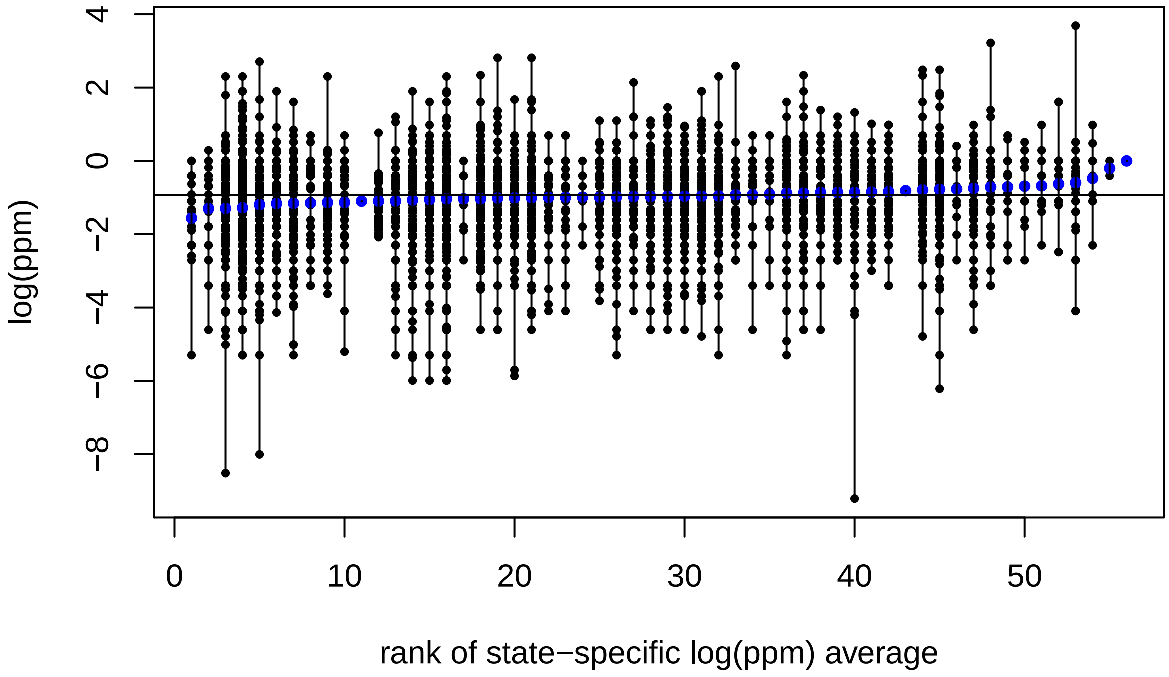
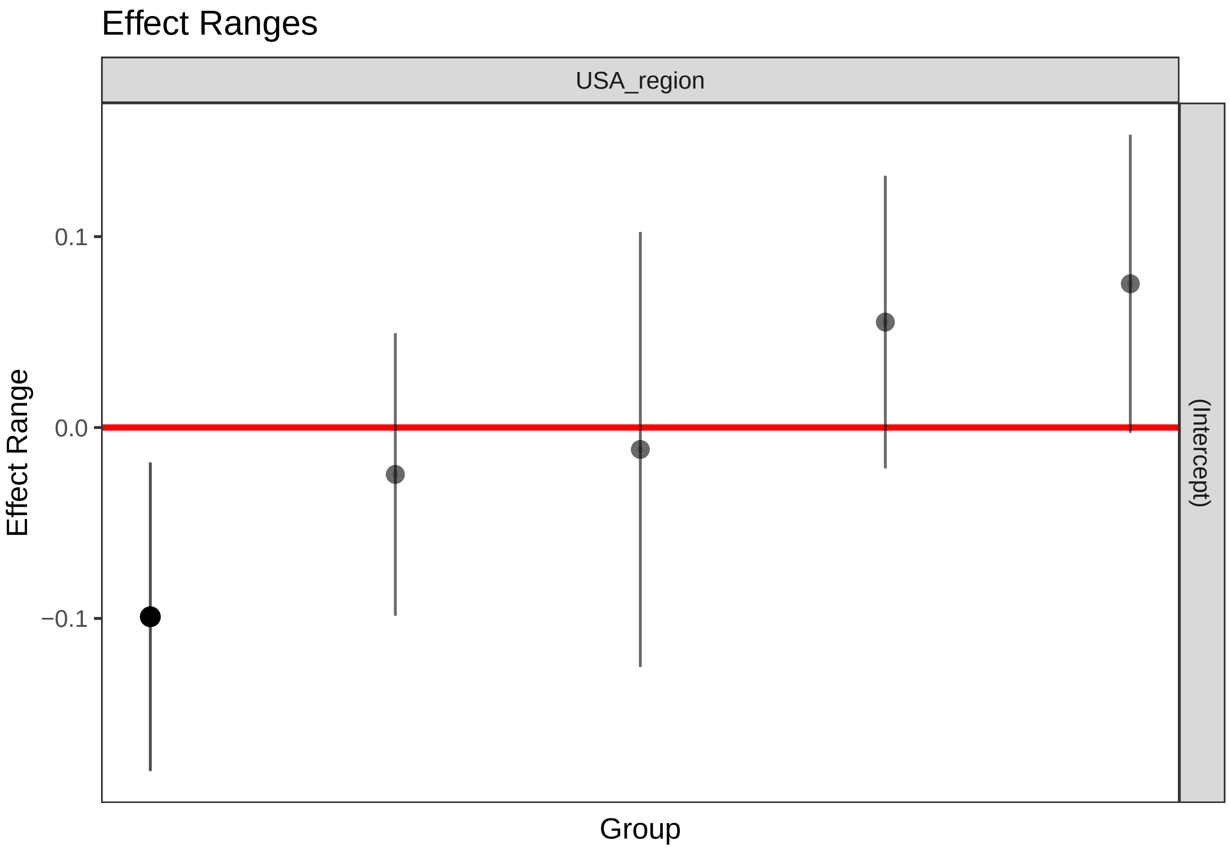
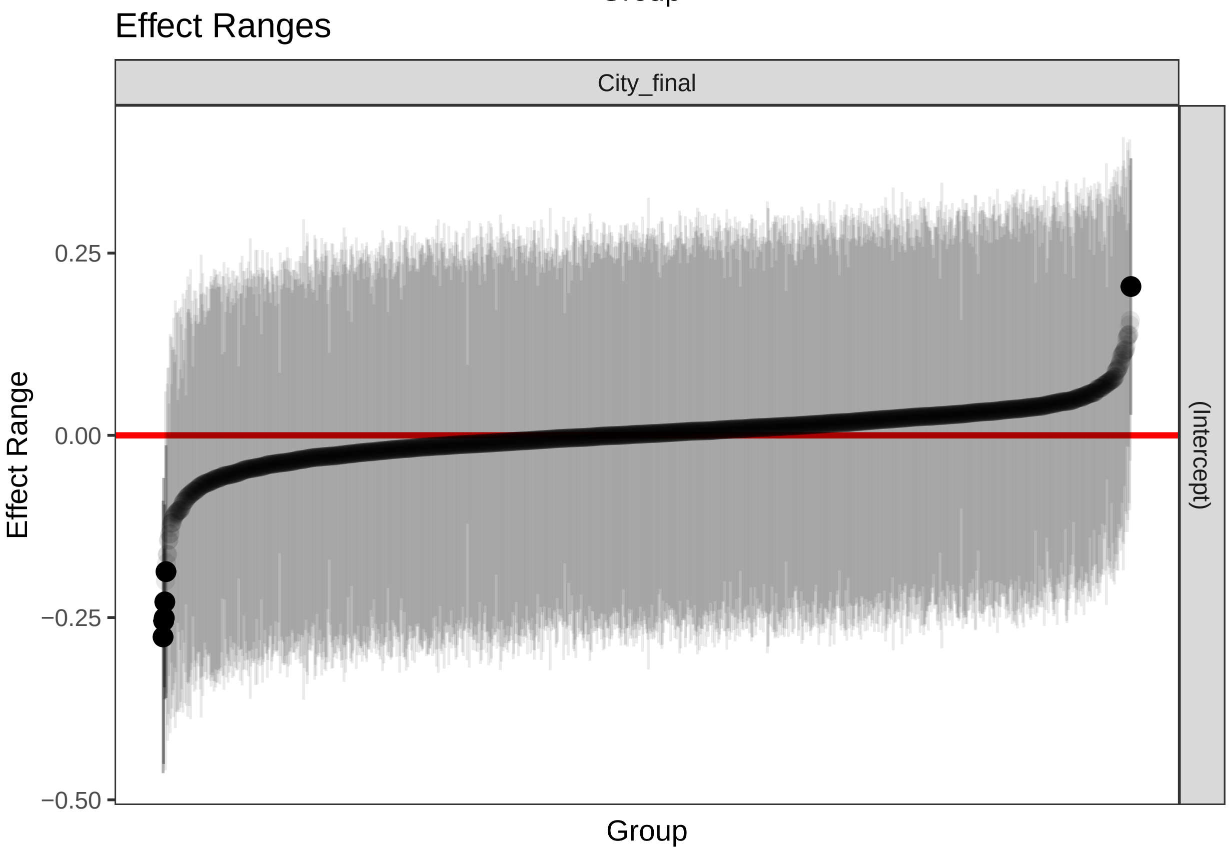


Figure 7: log ppm differs by state


Effect Ranges
USA_region
0.1
0.0
−0.1
Effect Range
Group
(Intercept)


Effect Ranges
City_final
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0.00
−0.25
−0.50
Effect Range
Group
(Intercept)

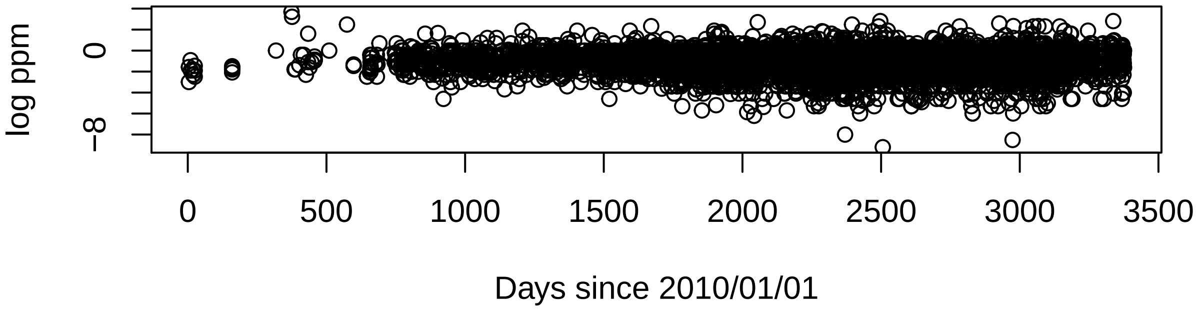


Figure 8: Relationship between log ppm and Days Elasped

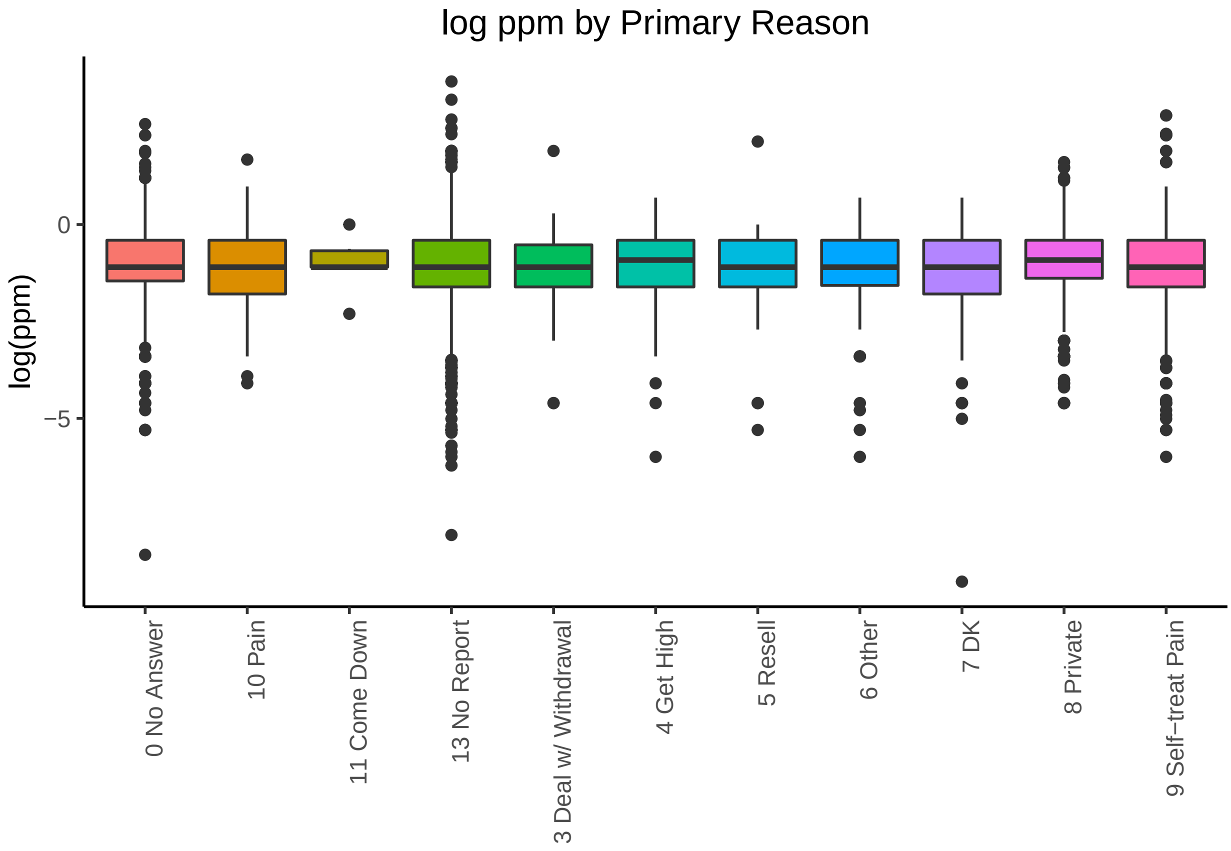


Figure 9: Relationship between log ppm and Primary Reasons

Table 4: Fixed effect

	coef	Low CI	Up CI
Intecept	-0.590	-0.6390000	-0.5410000
mgstr	-0.010	-0.0105943	-0.0094057
Bulk	-0.103	-0.1539600	-0.0520400

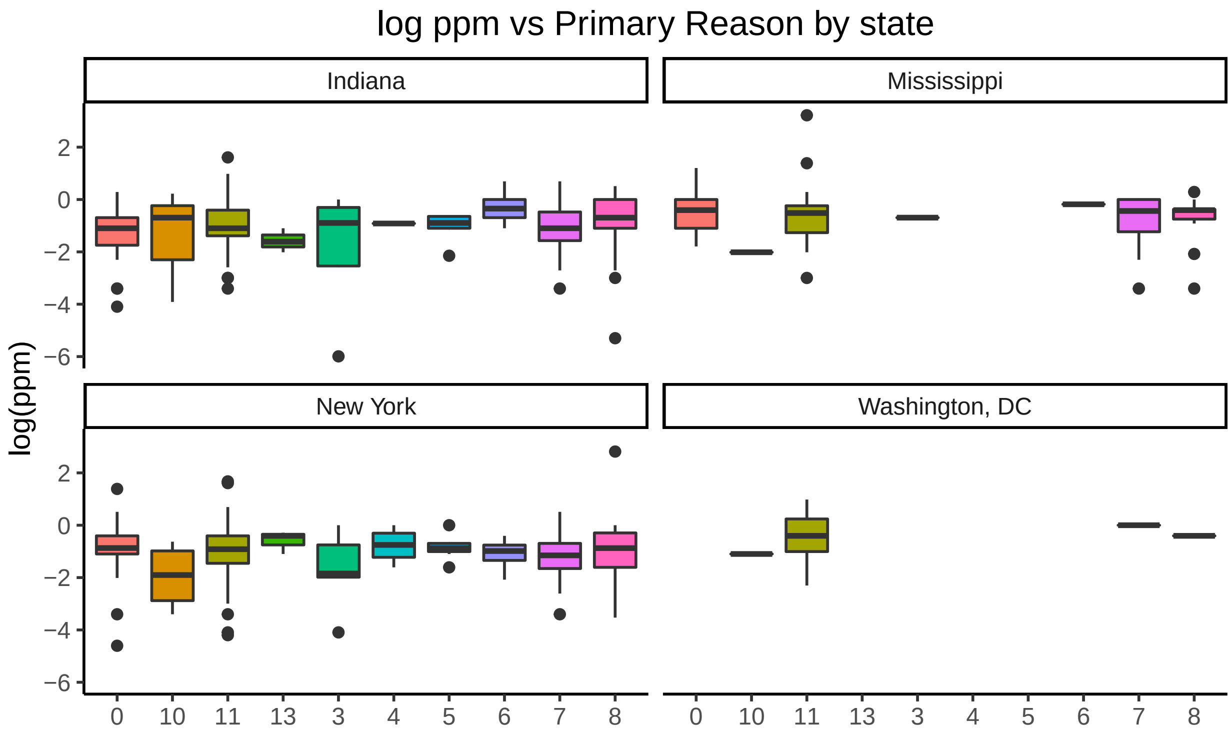


Figure 10: Analysis: random slopes of Primary Reasons by State

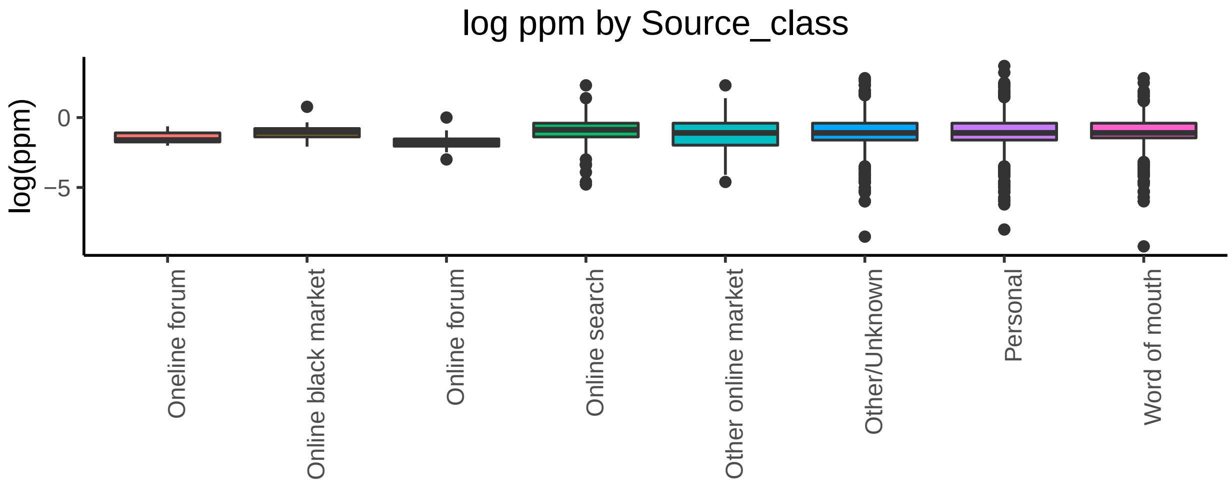


Figure 11: Relationship between log ppm and Source Class

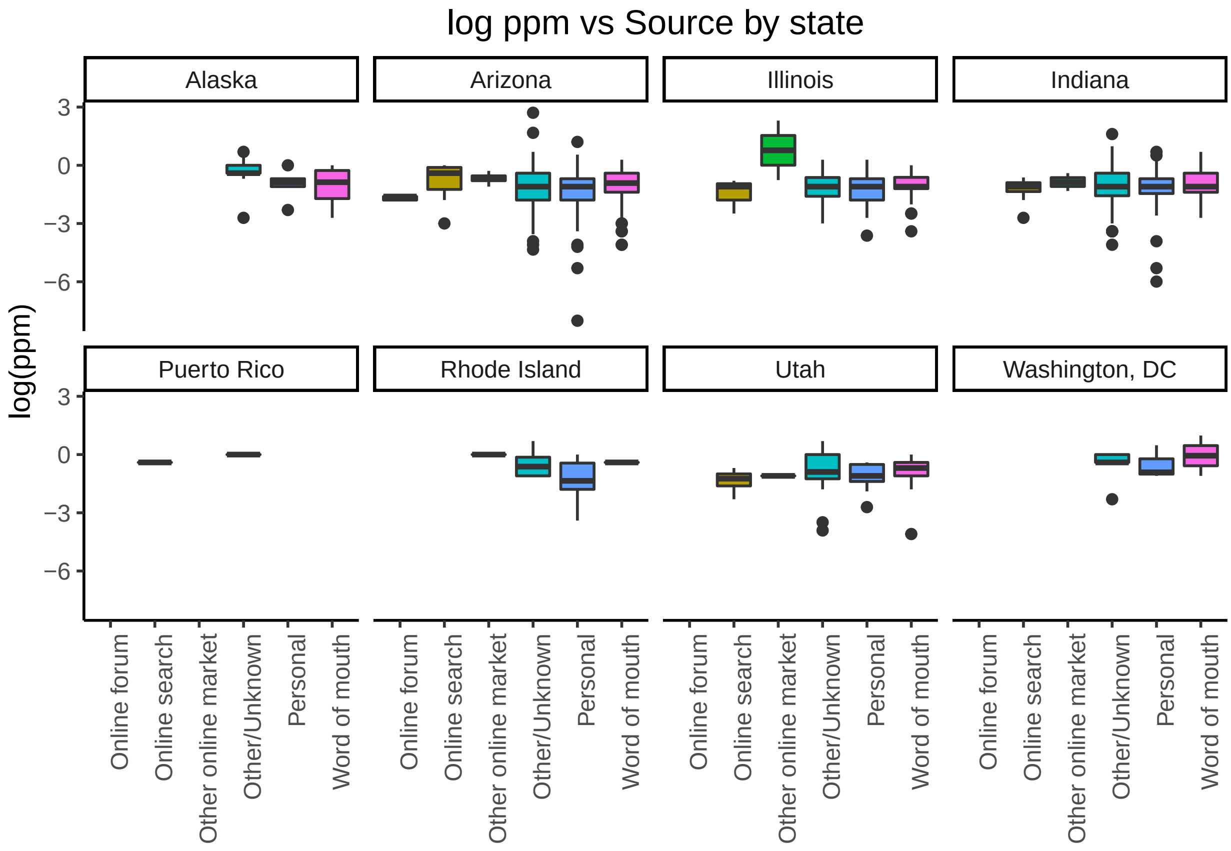


Figure 12: Analysis: random slopes of Source class by State

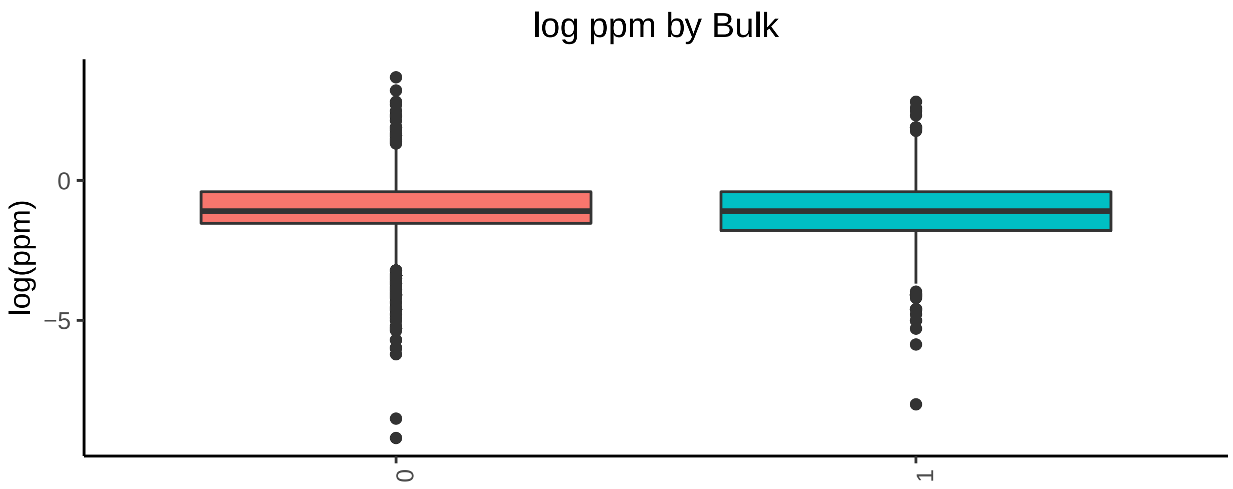


Figure 13: Relationship between log ppm and Bulk

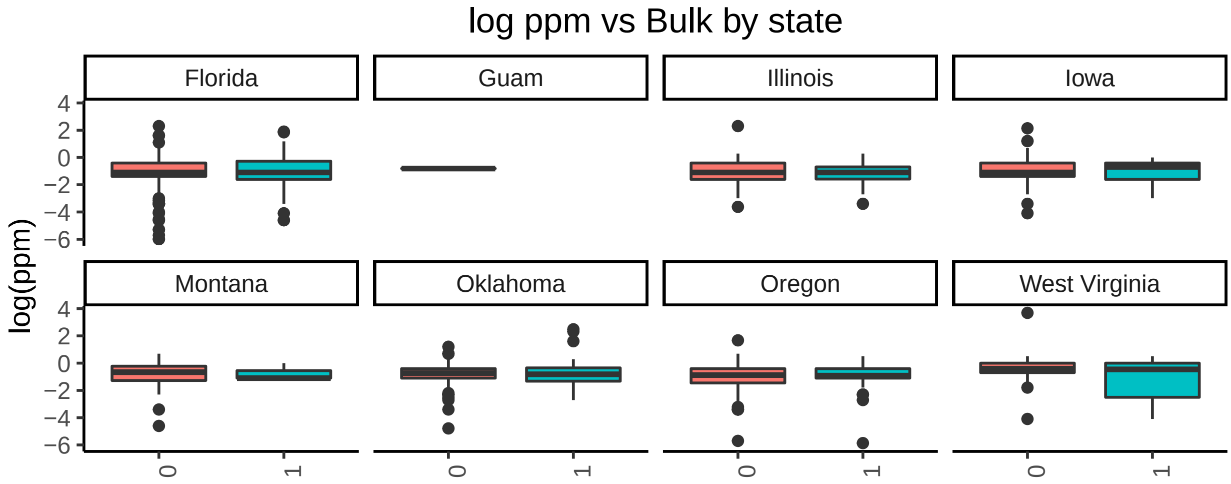


Figure 14: Analysis: random slopes of Bulk by State

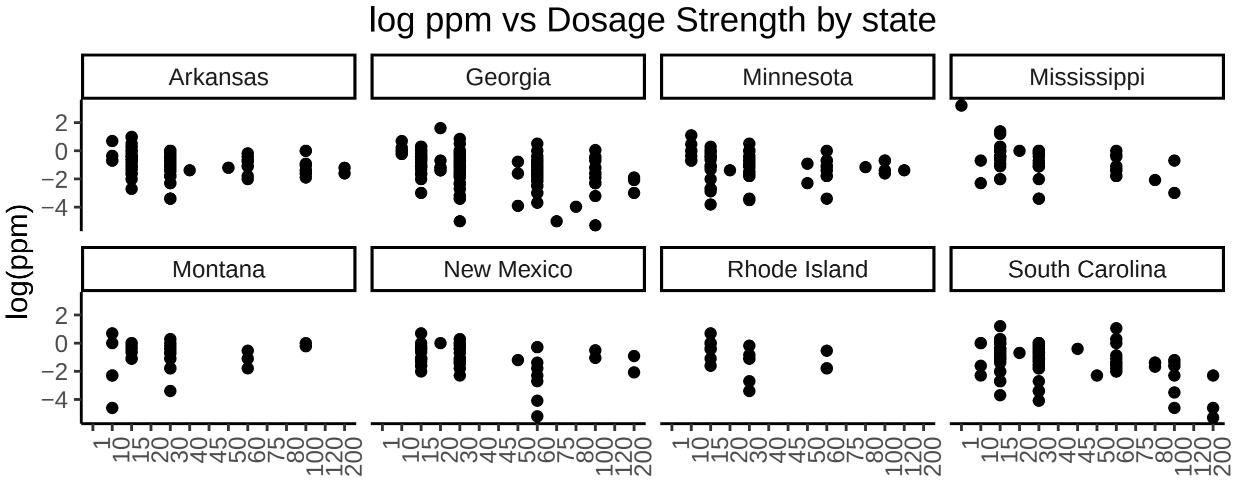
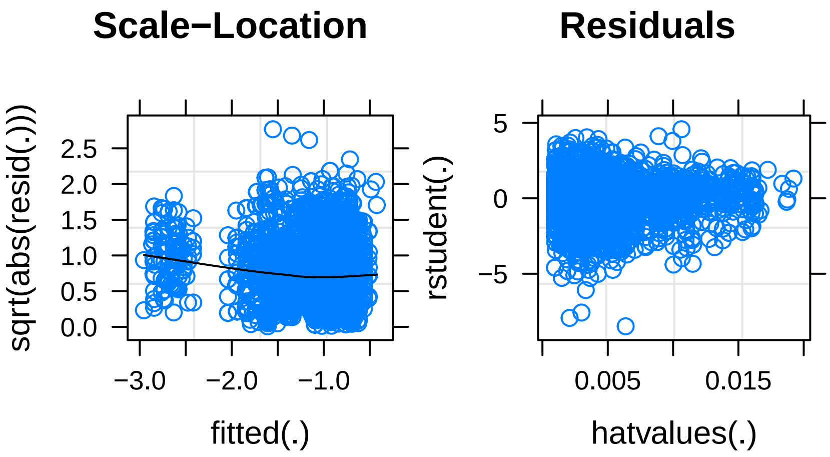


Figure 15: Analysis: random slopes of Dosage Strength by State


Scale−Location
Residuals
sqrt(abs(resid(.)))
2.5
2.0
1.5
1.0
0.5
0.0
−3.0
−2.0
−1.0
fitted(.)
rstudent(.)
5
0
−5
0.005
0.015
hatvalues(.)