Case Study 1 Writeup

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knitr::opts_chunk$set(echo = FALSE)
```

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 have built a hierarchical model on morphine price with location grouping variable through a data analysis and modeling process performed in the following orders. First, since the data set relies on crowdsourced and noisy free-text data, we performed various data cleaning processes to generate a data set ready for modeling. Second, we performed exploratory data analysis to understand the distributions of variables and their potential relationships. Third, we looked into the heterogeneity of the response variable by different scales of locations and chose the proper location variable as the grouping variable with random effect. Then, we iteratively added other predictors, including both grouping variables and covariates, by identifying logically sound relationships and then performing diagnostics on the resulting models to assess validity. Possible interactions among predictors, which could be either fixed effects or random slopes, were also investigated in this step. Finally, after the final model was built using the results from the previous steps, we checked the validness of the model assumptions, interpreted the model results, and drew the conclusion.

Here are the findings from the modeling process. In summary, dosage strength and unit of drugs purchased are the two most important factors affecting the price of Morphine. Location factor such as state has a limited random effect on the price of the Morphine.

Data Cleaning

The original data set contains reports of transactions of various types of drugs. By inspecting the data set entries and the structure for each predictor, 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, in the original data set, `api_temp` variable specifies the active ingredient of the drug for each observation, and we need to filter the entire data set to obtain the morphine transactions according to the drug type specified by this variable. However, there were ambiguous labels of the `api_temp` variable entries, For example, there were categories specified as `morphine/oxycodone` rather than `morphine` only. Since we did not want to include observations that were related to other drug types to interfere the morphine price modeling process, we only kept the entries that were exclusively stated as "morphine". This filtering process resulted in a new data set with 9268 records.

Second, we reformatted the **date** data in the data set. There were two fields representing date information: `yq_pdate` and `price_date`. The first field coded the year and quarter as a pseudo-continuous range. However, it was not suitable for assessing the data on a true continuous scale because it portrayed quarters within the same year as being closer together than adjacent quarters from different years (i.e., fourth quarter 2019 was closer to third quarter 2019 than it was to first quarter 2020 in this coding scheme). Therefore, instead of using `yq_pdate`, we used the `price_date` to construct a true continuous scale for measuring the date of purchase. Using R's string parsing methods we parsed the date into its individual *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, upon inspecting the date data we found that 3 entries were from the 1960s and another 11 entries were from the 2000s, which were years before the data collection was active. In this case, there was legitimate concern that the entered data might not be accurate if it was supplied long after the drug purchase event. Since a relatively small number of data were affected, we filtered out the 14 entries with dates prior to 2010, leaving us with 9264 observations.

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 almost immediately that there were numerous entries with **different listed names that clearly refer to the same city**. This was because users might have used different conventions when supplying city names. For example, users might have listed 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 using 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 borrough (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.

In most cases, the original city could be unambiguously identified and corrected. 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. Therefore, we manually created a new dictionary mapping the noisy values to the corrected values, in the cases identified above where the data could be definitively determined. Then, we applied this mapping to the original data to correct those entries which were non-compliant. During this process we also identified legitimate names of unincorporated areas and townships which were excluded from the original census data, so that we would not be unnecessarily throwing out data from real cities.

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.

Then, we inspected data defining the **source** of the price transaction data. Most entries were labeled with "Personal" or "Heard it" as the source, but there were still over 50 unique entries, too many to do rigorous grouping on. However, when we inspected each unique entry, we saw some common themes. First, many users entered the specific URL for various web pages they searched, and several web pages were represented repeatedly with different URLs. But more importantly, there were clear patterns in the types of sources listed. In particular, we observed that each of the sources was one of the following: (A) personal, (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. In fact, we could very easily convert the raw data to these categories by using sub-string search to find particular keywords, such as "silkroad", "bluelight", "reddit", "opiophile", "forum", "pharmacy" and various other terms. As a result, we bundled each source into one of those seven categories, making for much simpler and more informative grouping. This data cleaning step did not change the size of the data set.

Our final data cleaning step included many minor issue corrections and basic cleaning of other predictors. First, we noticed that the `state` field included both the entries "USA" and " ". We converted these values to"Other/Unknown" category since they did not provide any meaningful information. Second, we saw that

`bulk_purchase` was coded as a string, which wasn't helpful, so we converted it to a factor (0 = False, 1 = True). Third, we observed that there was nothing listed under the `Primay_Reason` field when the user did not enter the reason for the purchase. We marked such entries with missing values as "Other/Unknown" as we have with the other fields.

In summary, after the data cleaning process, we obtained a data set with 8712 observations and 9 predictors, which are shown below.

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

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

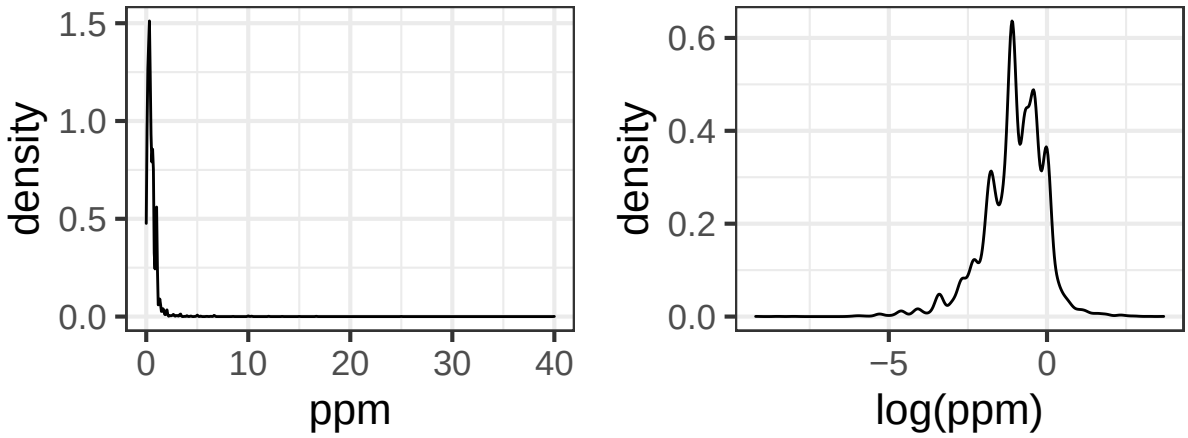


Figure 1: Log Transformation on Response

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

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.

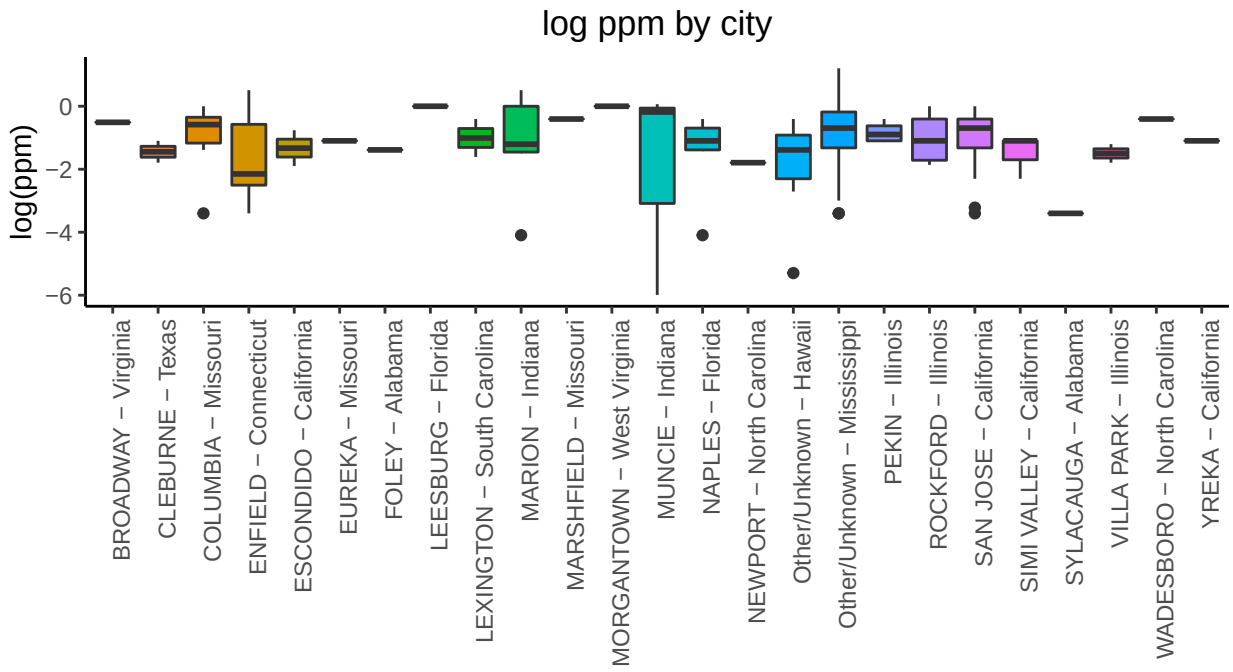
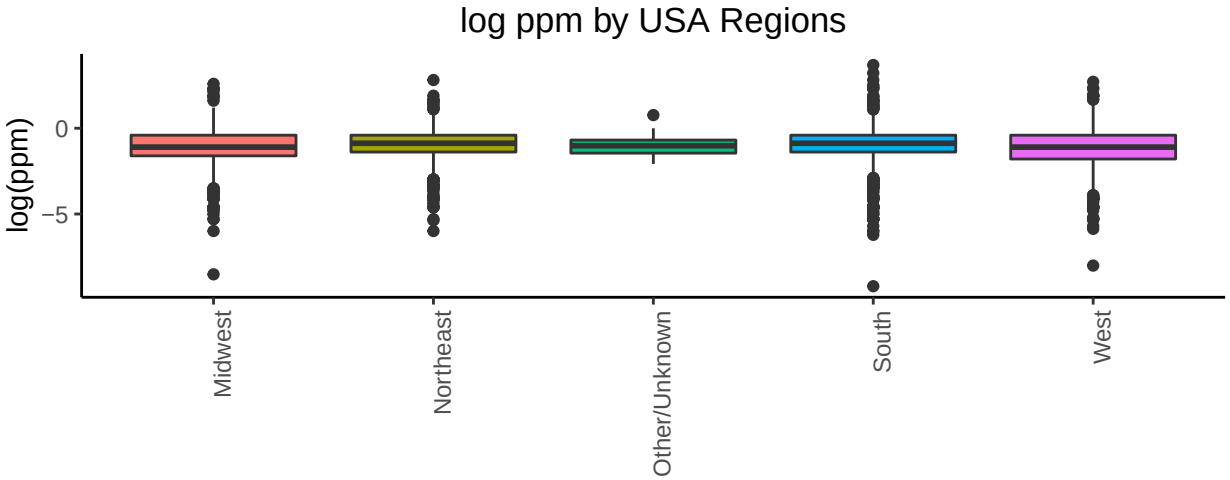


Figure 2: log ppm differs by cities

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.

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

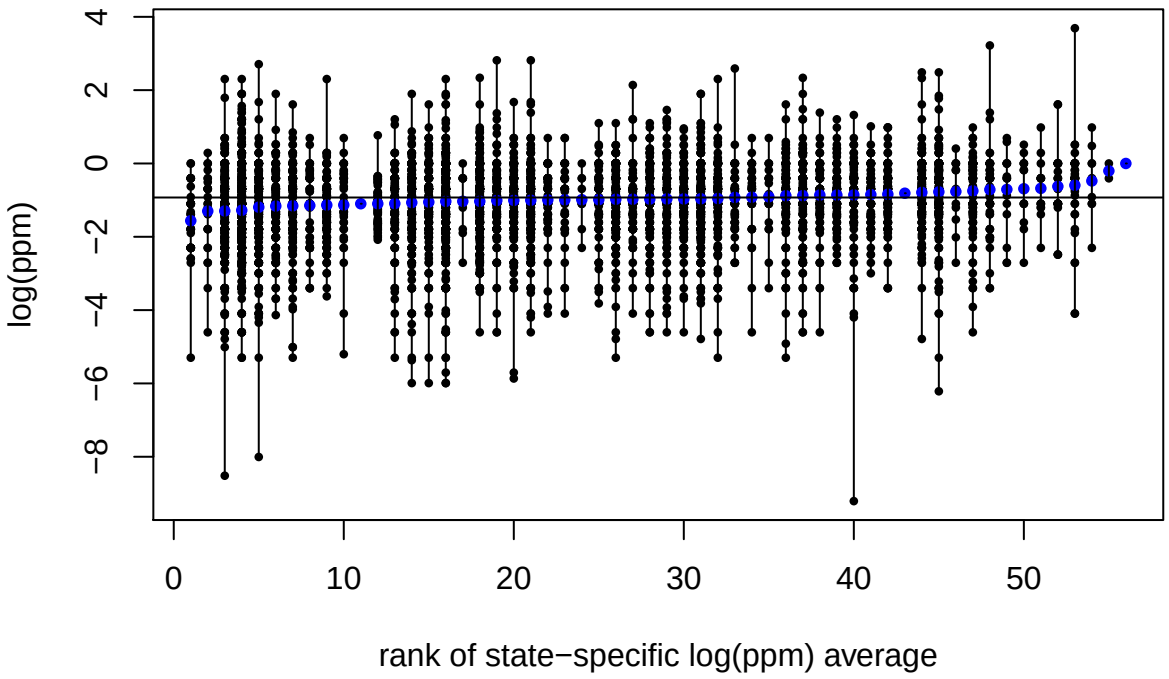


Figure 3: log ppm differs by state

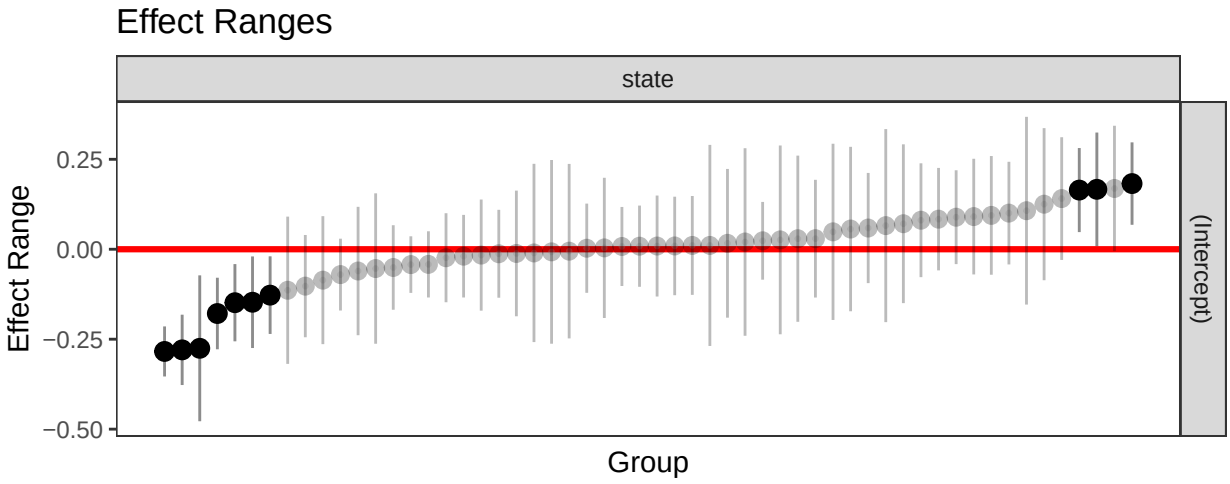


Figure 4: Distribution of State Random Effects

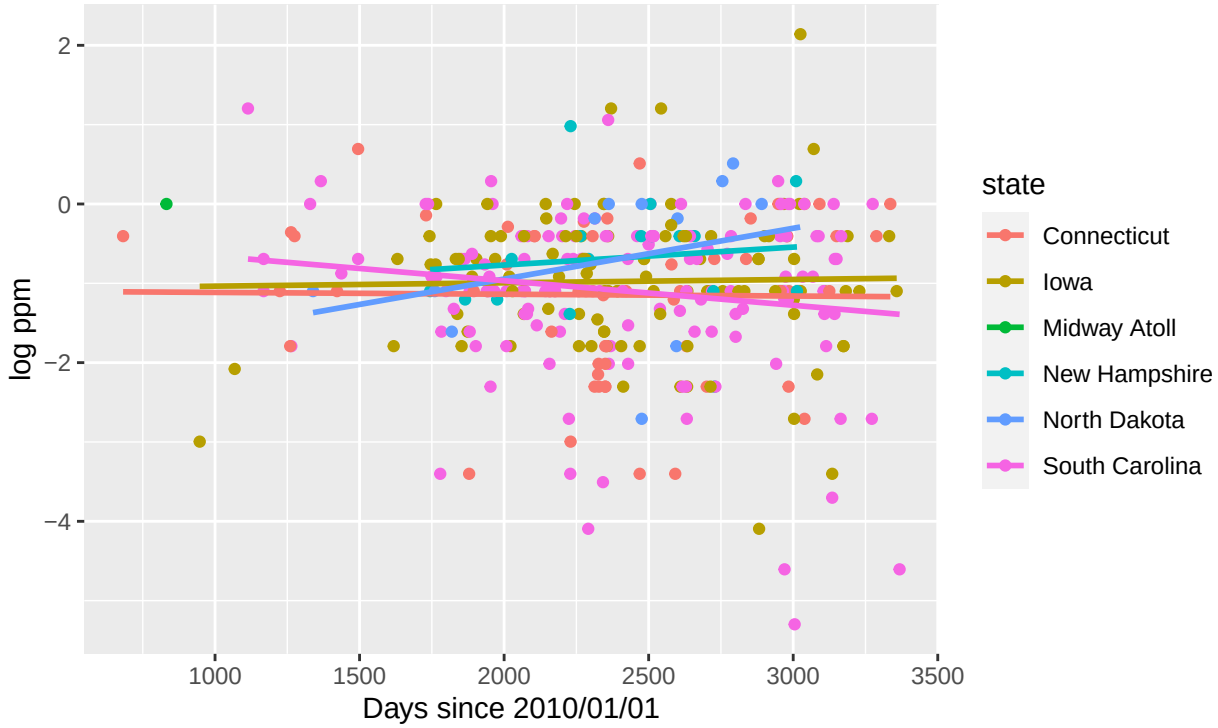
including multiply grouping variables will be performed in the Model section.

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.



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 would not consider a random slope by dosage strength by state.**(See Appendix Fig.14)**

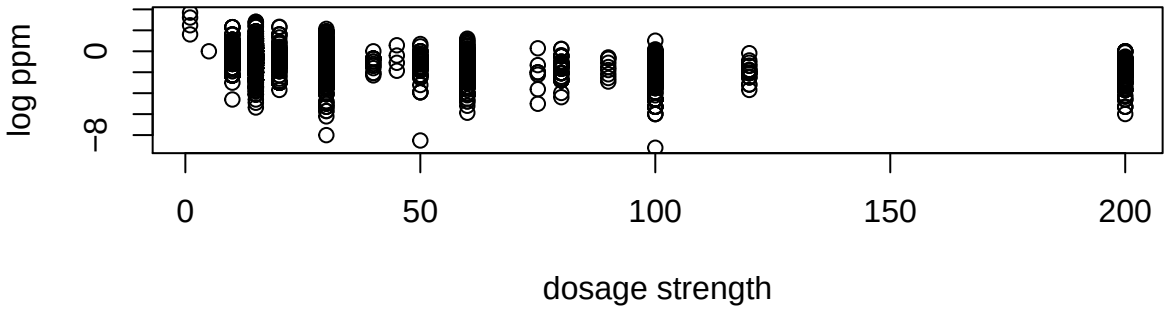


Figure 5: Slightly negative association between log ppm and dosage strength

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

Group Variable Selection

Before determining other predictors to be included in the model, we would like to first select the best location group variable which explained the heterogeneity of morphine price over that location level. We used two approaches to achieve this end. First, by inspecting the EDA figures, (**Figures Needed Here**), we could observe that the `log(ppm)` did not differ too much across different `region` categories, but there were some variations in `log(ppm)` across the sampled cities and sampled states. Therefore, we suspected that `region` might not be a good predictor explaining the heterogeneity across locations. As for `city` variable, the sample sizes within most cities were very small, so the `city` variable was probably not optimal to be included as the only location group variable in the model. The `state` variable seemed to be optimal for location group variables. In addition, we also would like to consider including more than one location group variables in the final model.

With these suspicions and ideas in mind, we built hierarchical models with random effects on every possible combination of the three location variables, which were `city`, `region`, and `state`. There were seven models in total, which were composed by 3 hierarchical models including each location variable only, three hierarchical models each including a unique pair of the three location variables, and finally the last hierarchical model including all three location variables. Then, we compared these seven models using BIC values as criterion based on the principle that, in each comparison, the two models differed in 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 results, it was easy to see that, according to the BIC scores, the model with random effect in state only was the best. Therefore, we chose to use state as the only group variable in locations with random effect.

Selection Among Other Variables

Now, the base model only involves the location variable state with random effect. We built the rest part of the model using forward stepwise selection of the predictors.

Table 2. The BIC scores of the models with specified random effects and fixed effects.

Name	Degree of Freedom	BIC Score	Random Effects	Fixed Effect
base	3	24124	state	None
m1	4	23105	state	dosage strength
m2	4	23100	state + dosage strength (by state)	dosage strength
m3	5	23098	state	dosage strength + bulk
m4	6	23105	state	dosage strength * bulk
m5	12	23134	state	dosage strength + source + bulk
m6	47	23442	state + source (by state)	dosage strength + source + bulk
m7	19	23182	state	dosage strength + source * bulk
m8	15	23182	state	dosage strength + primary reason + bulk
m9	80	23140	state + primary reason (by state)	dosage strength + primary reason + bulk
m10	6	23104	state	dosage strength + bulk + days ellapsed

Name	Degree of Freedom	BIC Score	Random Effects	Fixed Effect
m11	8	23117	`state` + `days ellapsed` (by `state`)	`dosage strength` + `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` (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 effect of `state` and fixed effect of `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 was not converged, 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 to add `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 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 economy 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

Table 3: Fixed Effect

	x
(Intercept)	-0.5892355
mgstr	-0.0100367
as.factor(Bulk)1	-0.1031110

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

Table 3. The fixed effect coefficients from the final model shown above.

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

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, 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.

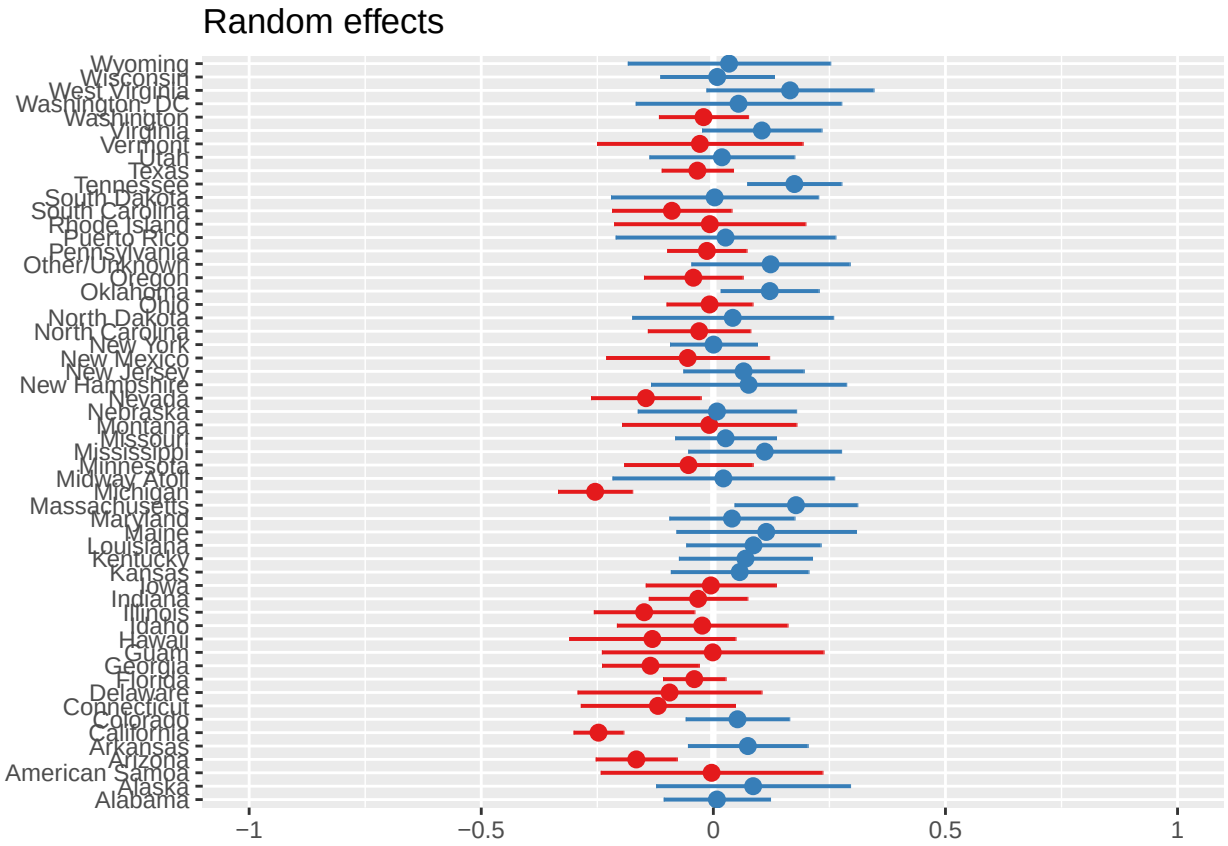
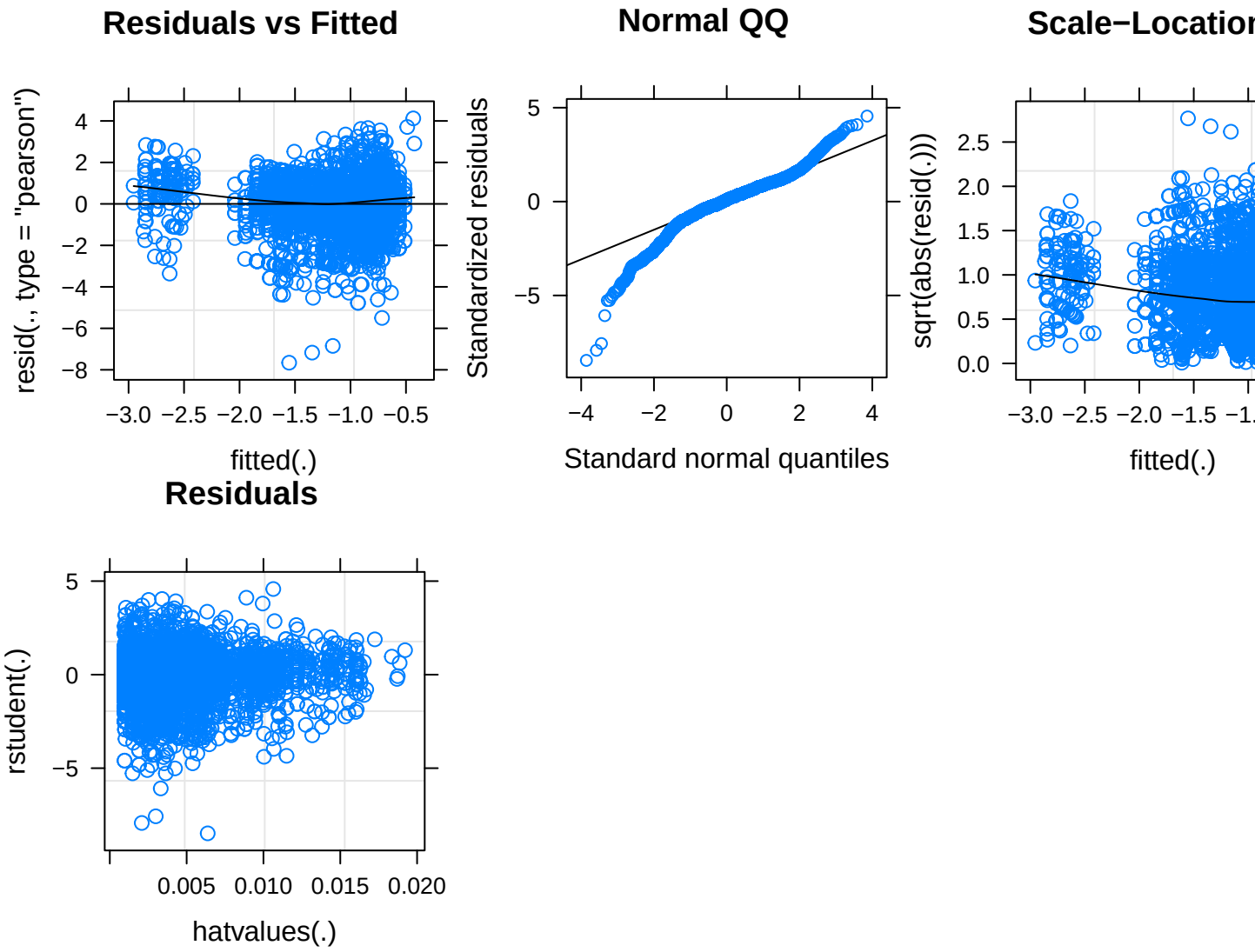


Figure 6: Random Effects of the hierarchical model.



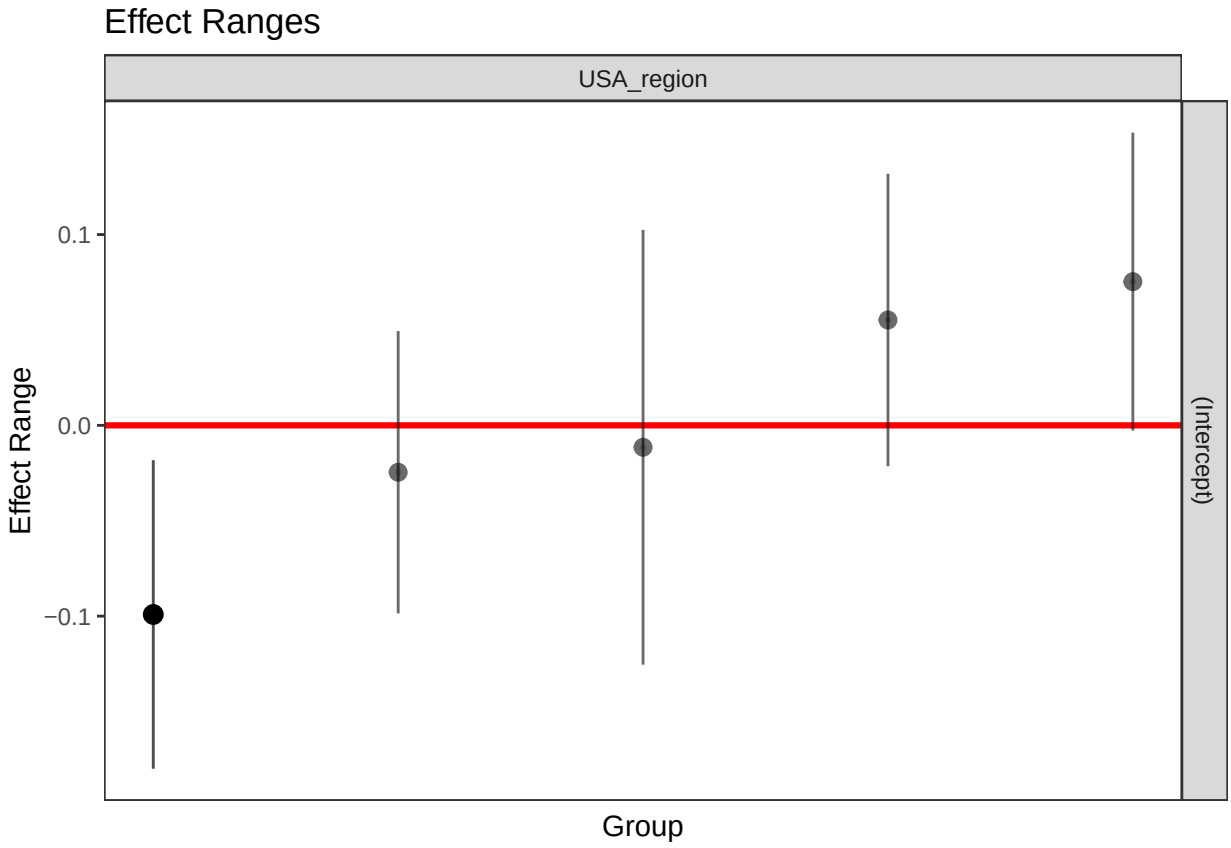
Above plots are the diagonistic plots for the model. In the first plot, all of the points are nearly randomly distributed around the 0 line except there is a small pattern. However, that pattern is acceptable. The QQ plot shows the target variable is deviated fromm the normal distribution. That deviation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

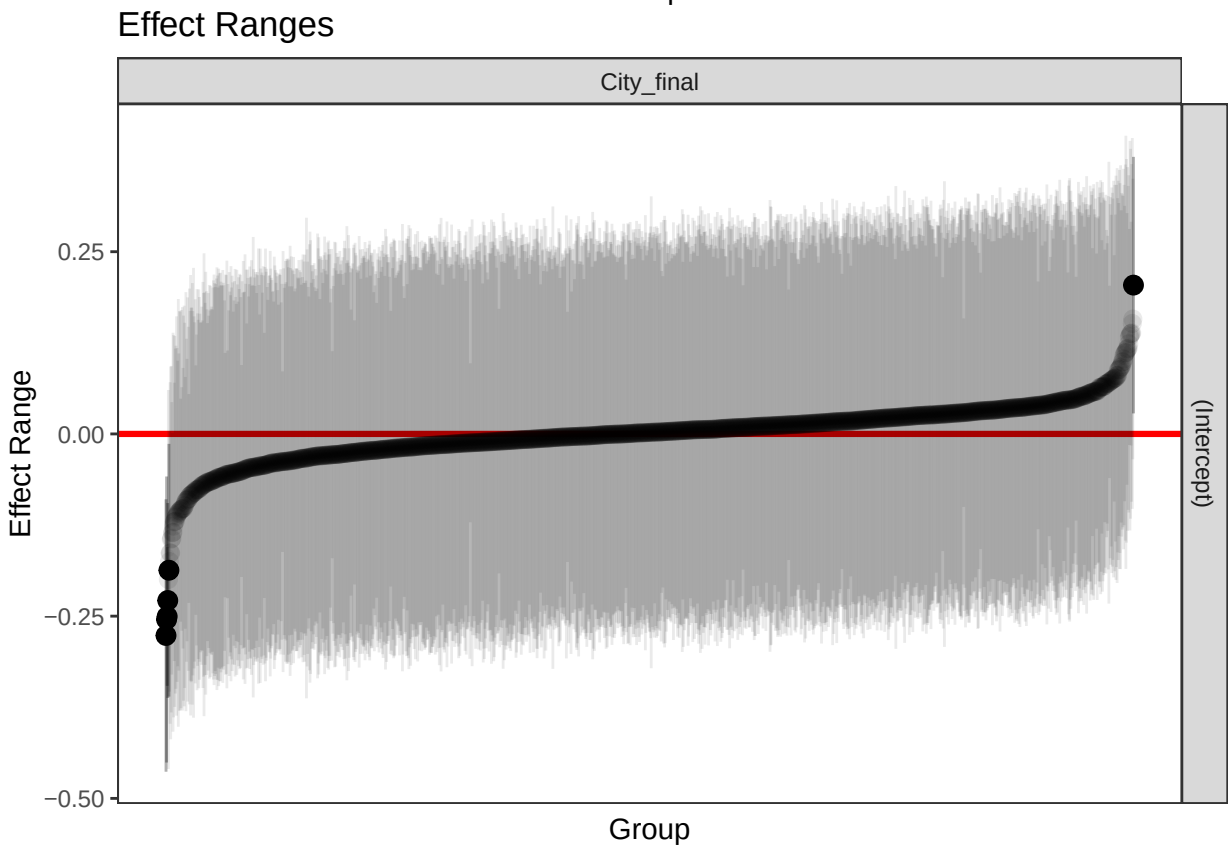
Limitation

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. Second, we did not exhaust all possible interactions, either. In the modeling process, we chose interactions based on logical reasoning and physical significance of such interactions. However, there might be other interactions or variable transformations that can improve the performance of the model but physically meaningless. 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. We were also worried about the potential overfit when involving more terms in the model, which was another reason that we did not try to exhaust all possible interactions from the data set.

Appendix


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


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

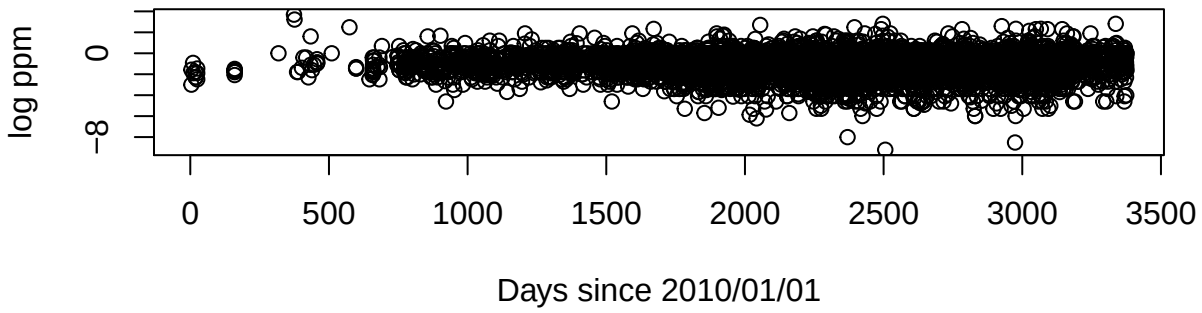


Figure 7: Relationship between log ppm and Days Elasped

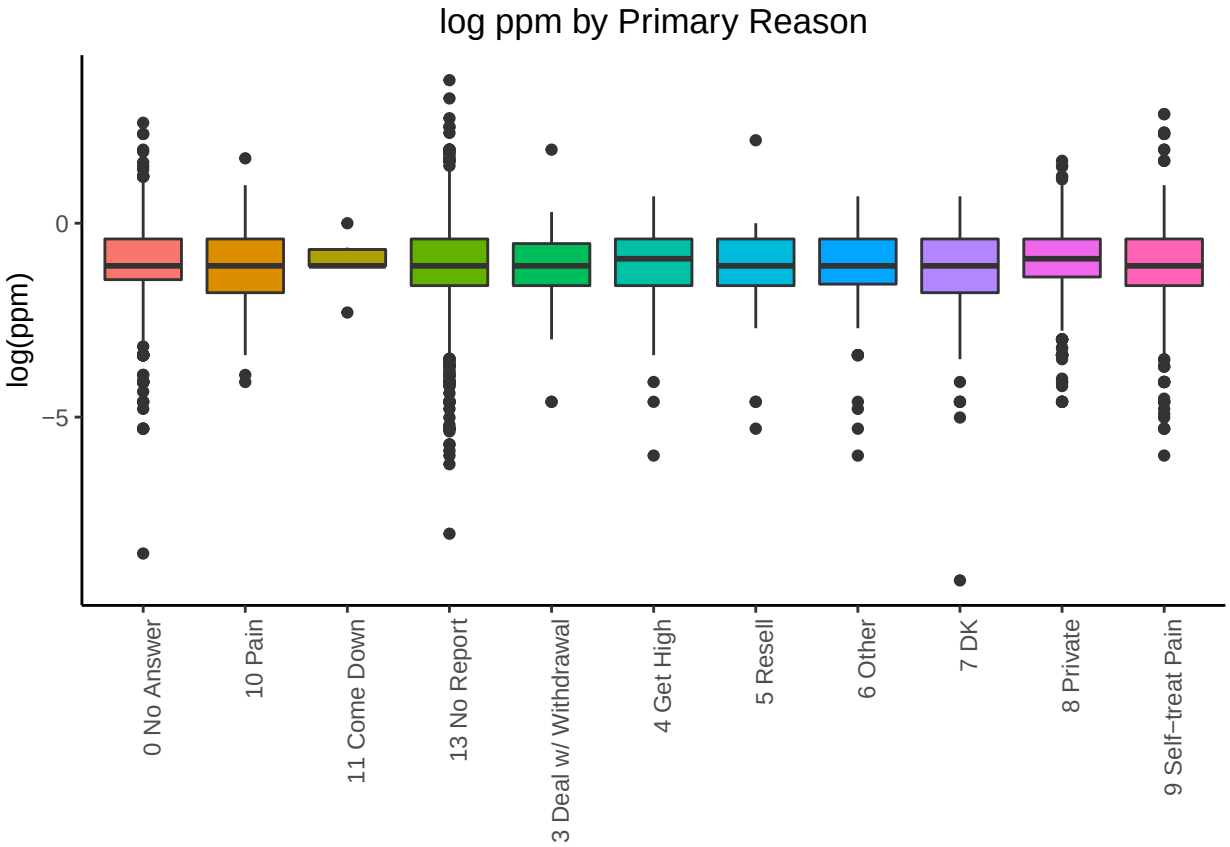


Figure 8: Relationship between log ppm and Primary Reasons

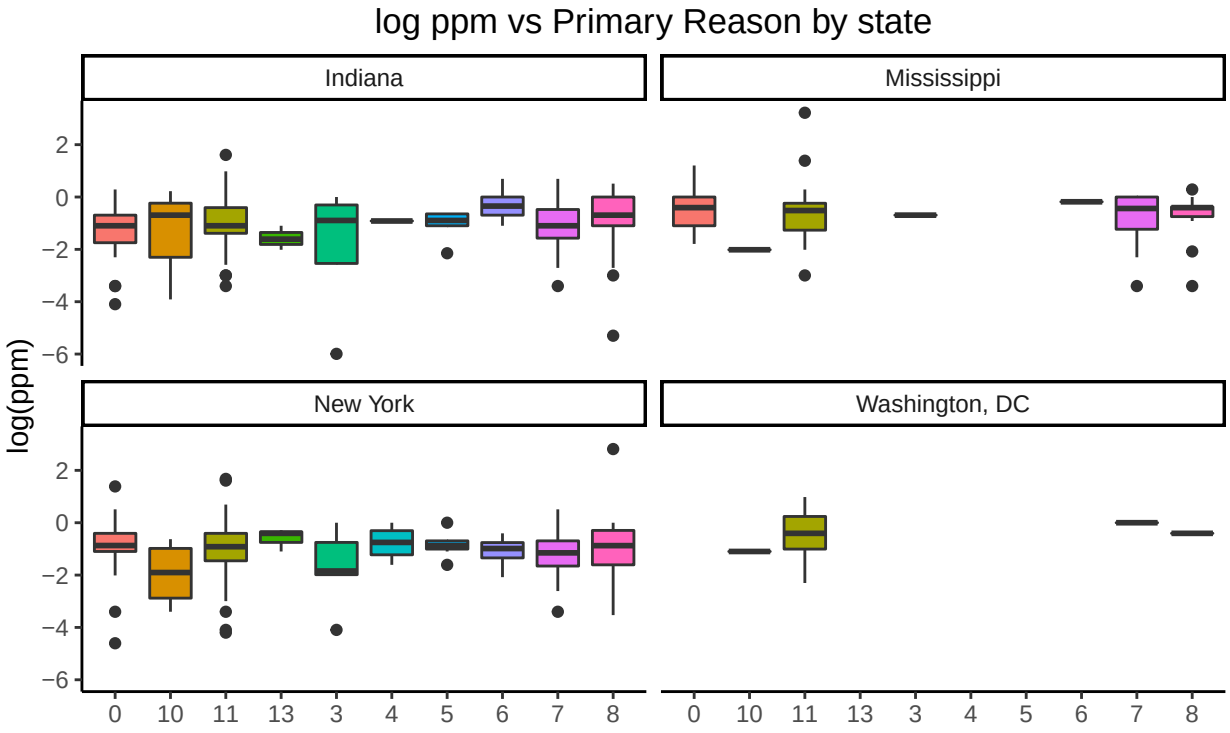


Figure 9: Analysis: random slopes of Primary Reasons by State

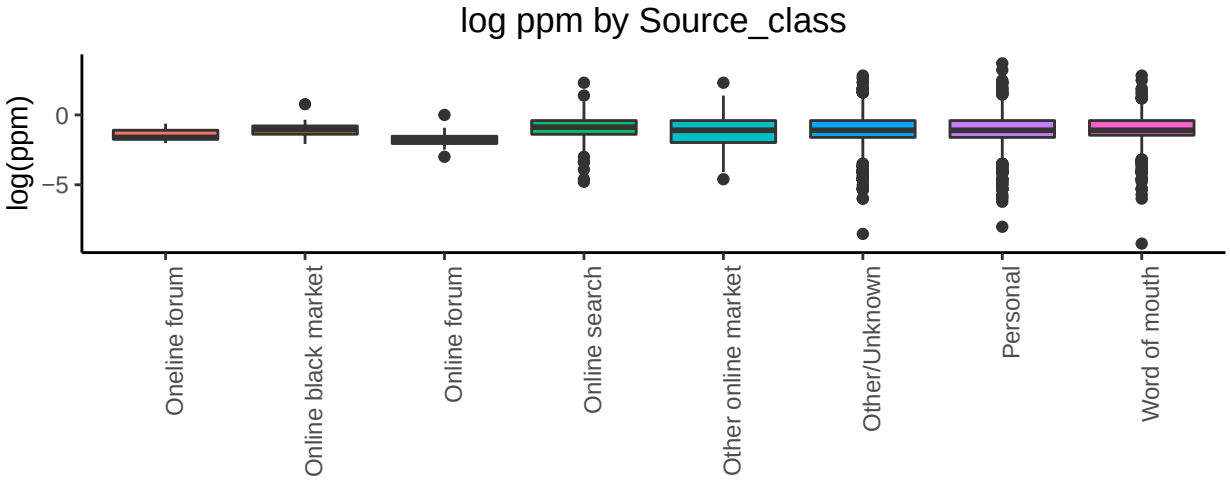


Figure 10: Relationship between log ppm and Source Class

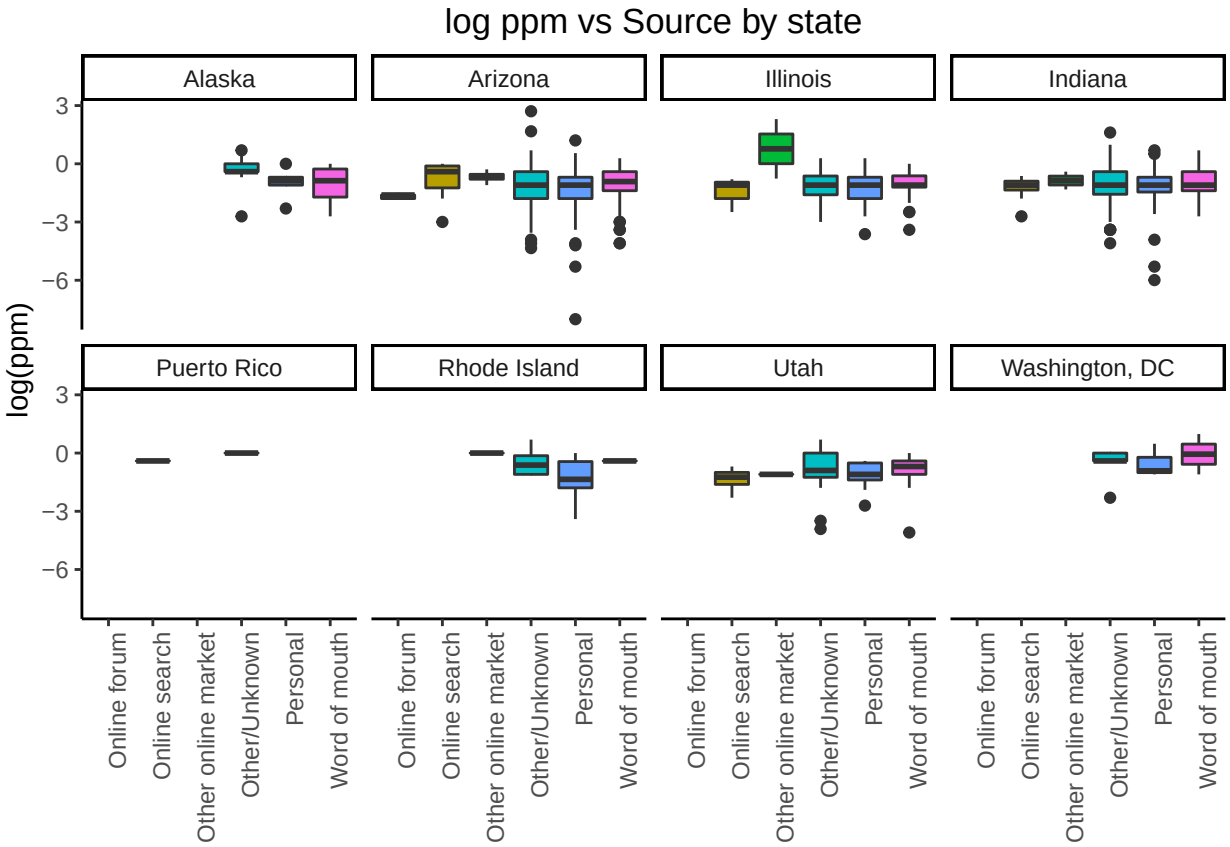


Figure 11: Analysis: random slopes of Source class by State

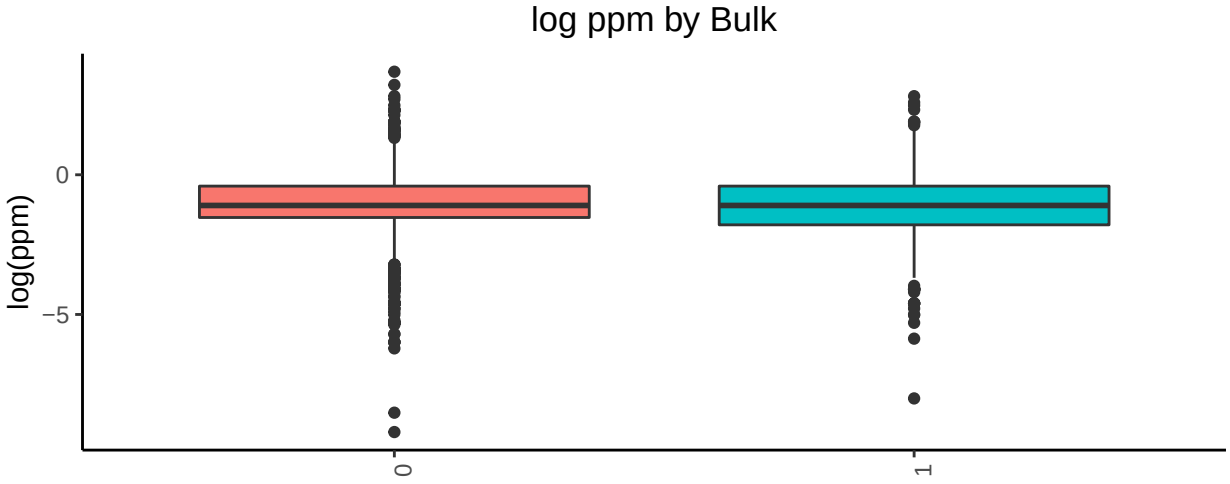


Figure 12: Relationship between log ppm and Bulk

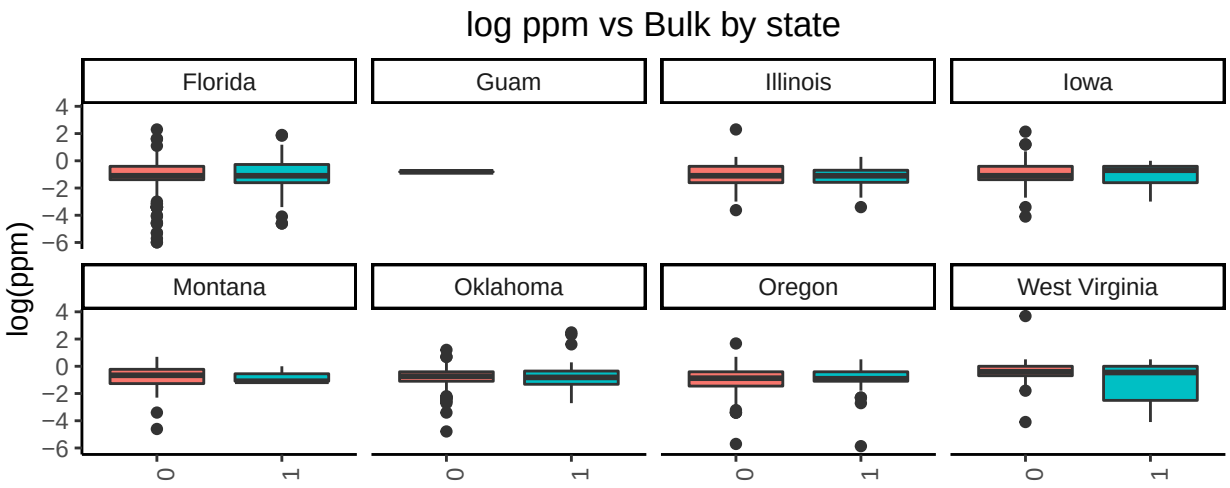


Figure 13: Analysis: random slopes of Bulk by State

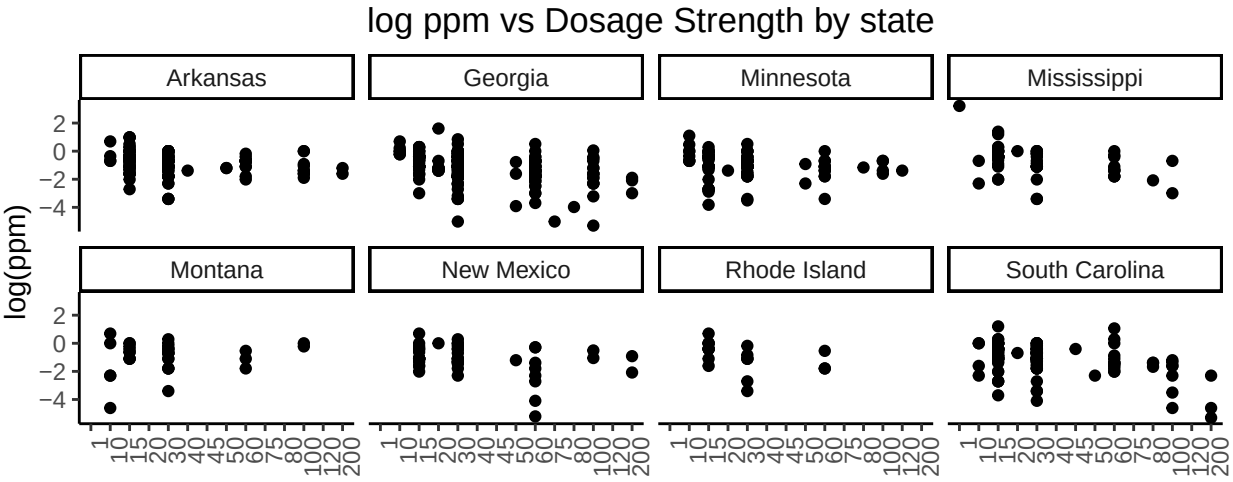


Figure 14: Analysis: random slopes of Dosage Strength by State