# Case Study 1 - Explore

# Weiting Miao

### 2023-10-16

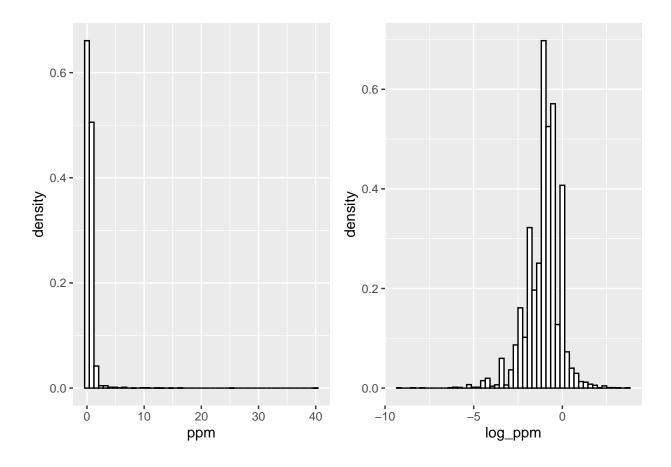
### Questions of Interest

To investigate factors related to the price per mg of your drug, accounting for potential clustering by location and exploring heterogeneity in pricing by location.

### **Data Cleaning**

### Variables:

- Outcome variable: ppm
- Purchasing time: year, month, day, quarter
- Location: country, state, city, USA\_region country: all US; city: many missing
- Source: source of information Unknown
- Formulation of the drug: factor no variation, drop it
- Dosage strength whether treat it as factor or numeric variable, or group them
- Bulk Purchase: dummy
- Primary reason: factor many missing values
- (1). Drop observations if the outcome variable is missing

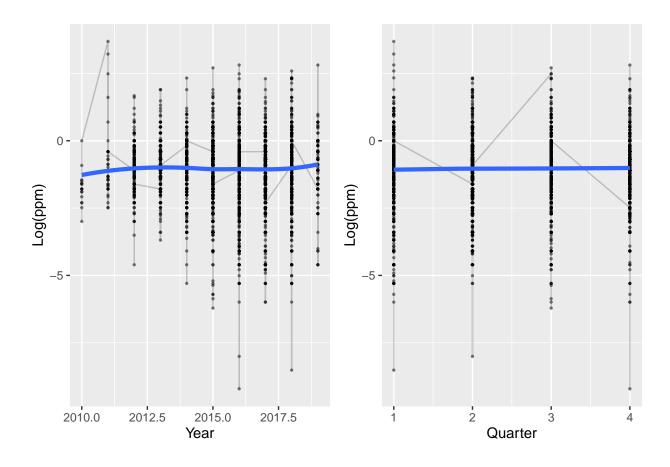


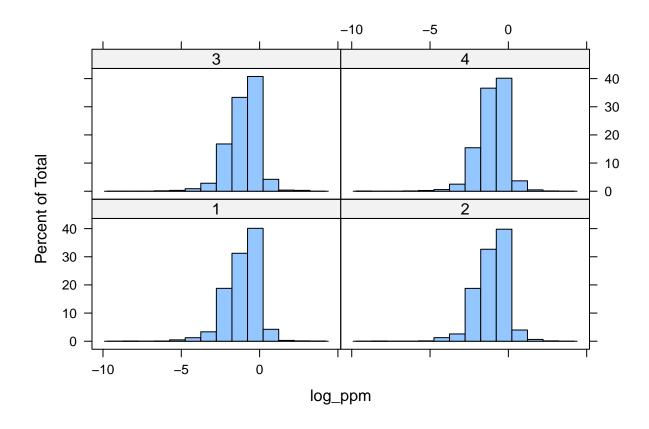
- (2). Drop variables without any variation country, formulation
- (3). Remove states with 1 observation, otherwise, we cannot estimate the within-group variance for these states. State has 1 missing values, and it has wrong category "USA". Since our goal is to understand the heterogeneity across locations, we remove observations with "USA" as the state name. City has a lot of missing values, so we will focus on the heterogeneity across states.

state	Count
California	1041
Florida	638
Texas	480
Michigan	439
Pennsylvania	377
Arizona	360
Ohio	313
New York	306
Washington	288
Tennessee	253
Georgia	236
Oklahoma	230
Indiana	225
Oregon	224
Illinois	214
Missouri	213
North Carolina	204
Colorado	199
Alabama	187
	171
Nevada	
Wisconsin	156
South Carolina	136
Virginia	136
Arkansas	135
New Jersey	133
Massachusetts	126
Maryland	119
Minnesota	110
Iowa	106
Kentucky	99
Louisiana	96
Kansas	89
Utah	75
Mississippi	62
Connecticut	60
Nebraska	54
USA	53
New Mexico	48
Hawaii	44
West Virginia	43
Idaho	39
Montana	35
Maine	30
Delaware	26
Rhode Island	20
Alaska	18
New Hampshire	17
North Dakota	13
Wyoming	12
Vermont	10
Washington, DC	10
	9
South Dakota	
Puerto Rico	2
A ma and C	
American Samoa	1
Guam	1
Midway Atoll	1

$USA\_region$	Count
South	3090
West	2554
Midwest	1941
Northeast	1079
Other/Unknown	55

(4). Create year and quarter variables. Very limited observations before year 2010. Given the nonlinear effects of year and quarter, we consider to treat year and quarter as factor variables.

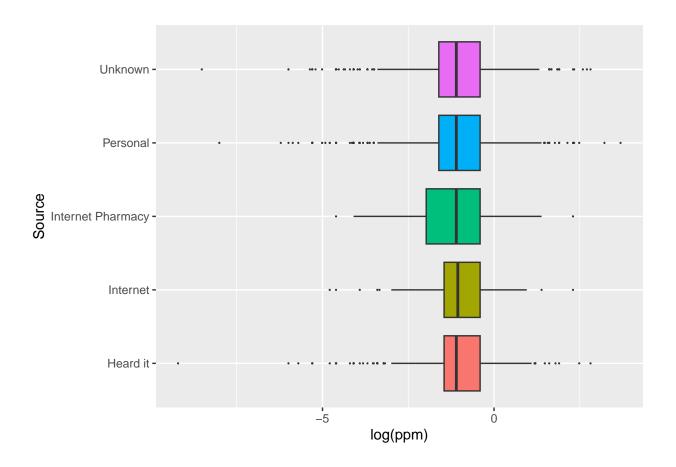




Quarter doesn't seem to be important.

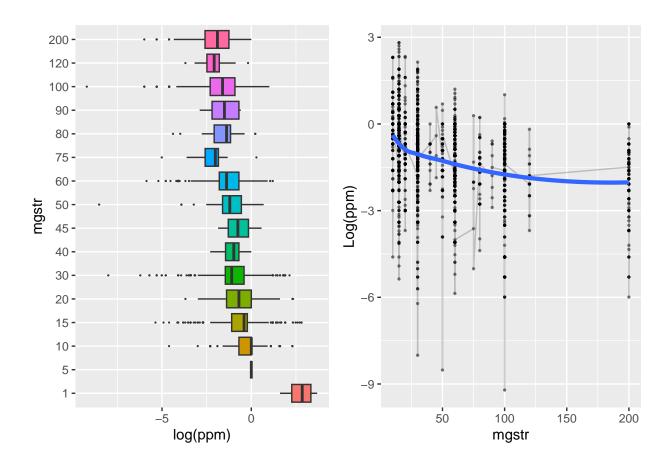
(5). Source: from the raw data, most can be coded as "Internet".

source	
D1	
Personal Hand it	
Heard it	
Internet	
Internet Pharmacy	_
http://forum.opiophile.org/showthread.php?37268-NationWide-OC-amp-Hydro-Morphone-Survey-Important-*Personal-latery//many blocking and only only only only only only only only	Π.
http://www.bluelight.ru/vb/showthread.php?t=480752&page=9	
http://silkroadvb5piz3r.onion/silkroad/category/240/50	_
http://silkroadvb5piz3r.onion/silkroad/category/51/200	_
http://silkroadvb5piz3r.onion/silkroad/category/51/25	
http://silkroadvb5piz3r.onion/silkroad/category/51	_
http://wiki.answers.com/Q/What_is_the_street_cost_of_morphine_sulfate_100mg_a_pill&dim1=UpdatedAns&dim	12
http://www.bluelight.ru/vb/showthread.php?t=480752&page=2	
http://silkroadvb5piz3r.onion/silkroad/category/51/150	
http://silkroadvb5piz3r.onion/silkroad/category/51/50	
http://www.bluelight.ru/vb/showthread.php?t=480752&page=3	
http://www.bluelight.ru/vb/showthread.php?t=480752&page=4	
Bluelight.com	
http://silkroadvb5piz3r.onion/silkroad/category/51/175	
https://www.drugs.com/price-guide/morphine	
Drug forum	
Drug forum.com	
Fuckoff.org	_
Google	
google.com	_
http://silkroadvb5piz3r.onion/index.php/silkroad/item/06ee6c0cfb	
http://silkroadvb5piz3r.onion/index.php/silkroad/item/268af26749	
http://silkroadvb5piz3r.onion/index.php/silkroad/item/2db123a294	
http://silkroadvb5piz3r.onion/index.php/silkroad/item/35e2f9fff0	
http://silkroadvb5piz3r.onion/index.php/silkroad/item/4603fc6c4c	
http://silkroadvb5piz3r.onion/index.php/silkroad/item/5442e57d37	
http://silkroadvb5piz3r.onion/index.php/silkroad/item/7259fa0fe6	
http://silkroadvb5piz3r.onion/index.php/silkroad/item/80acbc7f83	
http://silkroadvb5piz3r.onion/index.php/silkroad/item/8ba6726a41	
http://silkroadvb5piz3r.onion/index.php/silkroad/item/8e3b43f251	
http://silkroadvb5piz3r.onion/index.php/silkroad/item/9dba78d600	
http://silkroadvb5piz3r.onion/index.php/silkroad/item/a74ce13365	
http://silkroadvb5piz3r.onion/index.php/silkroad/item/a97c7d2ac8	
http://silkroadvb5piz3r.onion/index.php/silkroad/item/bcdebee234	
http://silkroadvb5piz3r.onion/index.php/silkroad/item/f5790bab0e	
http://silkroadvb5piz3r.onion/index.php/silkroad/item/f7774a3fca	
http://silkroadvb5piz3r.onion/silkroad/category/51/125	
http://silkroadvb5piz3r.onion/silkroad/category/51/225	
http://silkroadvb5piz3r.onion/silkroad/category/51/75	
http://silkroadvb5piz3r.onion/silkroad/item/03adfe43ed	
http://silkroadvb5piz3r.onion/silkroad/item/56fe5ee7bb	
http://silkroadvb5piz3r.onion/silkroad/item/c452141bb3	
http://silkroadvb5piz3r.onion/silkroad/item/cf888a9253	
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Reddit.com	_
USAsomething.com	



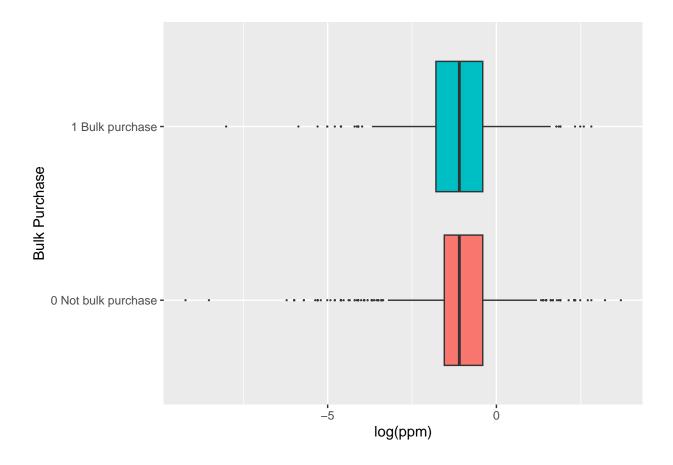
(6). Dosage strength: should we group them?

##																
##	1	5	10	15	20	30	40	45	50	60	75	80	90	100	120	200
##	4	1	286	2559	205	3399	16	4	78	1246	8	47	9	697	21	139



The effects are mostly monotone and linear except for when mgstr < 10 (5 obs).

## (7). Bulk Purchase



(8). Primary reason: 70% of the observations are NA or didn't answer the question. We decide not to use this variable.

Primary_Reason	Count
	4750
0 Reporter did not answer the question	1424
9 To self-treat my pain	1041
8 Prefer not to answer	805
6 Other reason	170
4 For enjoyment/to get high	148
7 Don't know	145
10 To treat a medical condition other than pain	77
5 To resell	76
3 To prevent or treat withdrawal	75
11 To come down	8

9)

##					
##	film	lollipop	lozenge/troche	multiple	N/A
##	0	0	0	0	0
##	nasal spray	oral spray	patch	pill/tablet	powder
##	0	0	0	8714	0
##	suppository	syrup/liquid			
##	5	0			

### Model Building & Model Selection

Predictors: year, quarter, mgstr, bulk purchase, source Random intercept: state Random slope:

(1) Random effect or fixed effect?

```
## [1] 23594.12
## [1] 23297.73
```

Random effect model has much smaller BIC

(2) Year as numeric variable or factor variable?

Treat it as numerical variable

(3) mgstr as numeric variable or factor variable?

```
## Data: df %>% filter(year > 2009 & state != "Unknown")
## Models:
## m2: log_ppm ~ year + quarter_factor + mgstr + bulk_purchase + source + (1 | state)
## m4: log_ppm ~ year + quarter_factor + mgstr_factor + bulk_purchase + source + (1 | state)
## npar AIC BIC logLik deviance Chisq Df Pr(>Chisq)
## m2 22 22947 23102 -11452 22903
## m4 36 22683 22937 -11305 22611 292.28 14 < 2.2e-16 ***
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1</pre>
```

Treat mgstr as factor variable

(4) Do we need quarter?

Quarter doesn't seem to be important. Drop quarter.

### (5) Do we need year?

Year doesn't seem to be important. Drop year.

### (6) Do we need source?

Adding source into the regression increases BIC, get rid of source

### (7) Any random slope

Having random slope of bulk purchase doesn't improve the performance

### (8) Any interaction term

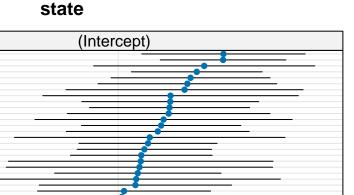
Not helpful to include the interaction term.

The final model is m7.

New Mashing Washing

Sout

Was Penns North



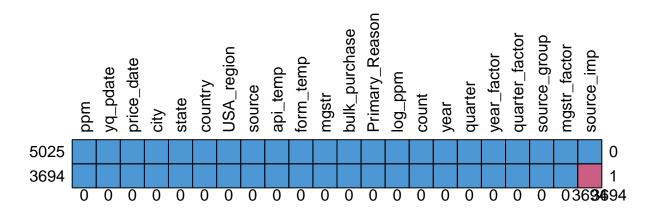
0.2

# Missing data imputation

Even though we choose to drop source variable, we decide to check if source useful after we impute missing data of source. We will use MICE to do missing data imputation. Let's first look into EDA of missing values. ### preprocess data

0.0

-0.2



##		ppm	yq_pda	ate p	rice_date	city	state	countr	y US	SA_region	sour	e ap	i_temp	
##	5025	1		1	1	1	1		1	1	L	1	1	
##	3694	1		1	1	1	1		1	1	_	1	1	
##		0		0	0	0	0		0	C	)	0	0	
##		form	_temp	mgst	r bulk_pu:	rchase	Prima	ary_Rea	son	log_ppm	count	year	quarte	er
##	5025		1		1	1	-		1	1	1	1		1
##	3694		1		1	1	-		1	1	1	1		1
##			0		0	C	)		0	0	0	0		0
##		year	_facto	or qu	arter_fac	tor so	urce_g	group m	gstr	_factor	source	e_imp		
##	5025			1		1		1		1		1	0	
##	3694			1		1		1		1		0	1	
##				0		0		0		0		3694	3694	

At the bottom: total number of missing values by variables. On the right: number of variables missing in each pattern. On the left: number of cases for each pattern.

Missing data: 1)State has 1 missing values, and it has wrong category "USA", so we also map to unknown 2)City has 3126 missing values and duplicate entries as well as abbreviations, MICE couldn't handle variable with over 50 categories, so we drop city. 3)source has 3695 missing values and messy website. 4)Primary\_Reason has 4754 missing values # drop it because of over 60% missing rate

source_imp
NA
Personal
Heard it
Internet
Internet Pharmacy
http://forum.opiophile.org/showthread.php? 37268-NationWide-OC-amp-Hydro-Morphone-Survey-Important-*Personal-Robert Properties and the properties of the p
http://www.bluelight.ru/vb/showthread.php?t=480752&page=9
http://silkroadvb5piz3r.onion/silkroad/category/240/50
http://silkroadvb5piz3r.onion/silkroad/category/51/200
http://silkroadvb5piz3r.onion/silkroad/category/51/25
http://silkroadvb5piz3r.onion/silkroad/category/51
$http://wiki.answers.com/Q/What\_is\_the\_street\_cost\_of\_morphine\_sulfate\_100mg\_a\_pill\&dim1=UpdatedAns\&dim2=UpdatedAns&dim2=UpdatedAns&dim2=UpdatedAns&dim2=UpdatedAns&dim2=UpdatedAns&dim2=UpdatedAns&dim2=Upda$
http://www.bluelight.ru/vb/showthread.php?t=480752&page=2
http://silkroadvb5piz3r.onion/silkroad/category/51/150
http://silkroadvb5piz3r.onion/silkroad/category/51/50
http://www.bluelight.ru/vb/showthread.php?t=480752&page=3
http://www.bluelight.ru/vb/showthread.php?t=480752&page=4
Bluelight.com
http://silkroadvb5piz3r.onion/silkroad/category/51/175
https://www.drugs.com/price-guide/morphine
Drug forum
Drug forum.com
Fuckoff.org
Google
google.com
http://silkroadvb5piz3r.onion/index.php/silkroad/item/06ee6c0cfb
http://silkroadvb5piz3r.onion/index.php/silkroad/item/268af26749
http://silkroadvb5piz3r.onion/index.php/silkroad/item/2db123a294
http://silkroadvb5piz3r.onion/index.php/silkroad/item/35e2f9fff0
http://silkroadvb5piz3r.onion/index.php/silkroad/item/4603fc6c4c
http://silkroadvb5piz3r.onion/index.php/silkroad/item/5442e57d37
http://silkroadvb5piz3r.onion/index.php/silkroad/item/7259fa0fe6
http://silkroadvb5piz3r.onion/index.php/silkroad/item/80acbc7f83
http://silkroadvb5piz3r.onion/index.php/silkroad/item/8ba6726a41
http://silkroadvb5piz3r.onion/index.php/silkroad/item/8e3b43f251
http://silkroadvb5piz3r.onion/index.php/silkroad/item/9dba78d600
http://silkroadvb5piz3r.onion/index.php/silkroad/item/a74ce13365
http://silkroadvb5piz3r.onion/index.php/silkroad/item/a97c7d2ac8
http://silkroadvb5piz3r.onion/index.php/silkroad/item/bcdebee234
http://silkroadvb5piz3r.onion/index.php/silkroad/item/f5790bab0e
http://silkroadvb5piz3r.onion/index.php/silkroad/item/f7774a3fca
http://silkroadvb5piz3r.onion/silkroad/category/51/125
http://silkroadvb5piz3r.onion/silkroad/category/51/225
http://silkroadvb5piz3r.onion/silkroad/category/51/75
http://silkroadvb5piz3r.onion/silkroad/item/03adfe43ed
http://silkroadvb5piz3r.onion/silkroad/item/56fe5ee7bb
http://silkroadvb5piz3r.onion/silkroad/item/c452141bb3
http://silkroadvb5piz3r.onion/silkroad/item/cf888a9253
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Reddit.com
USAsomething.com
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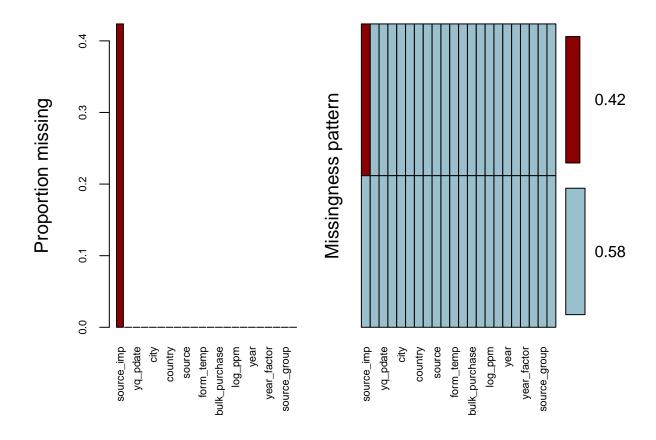
We need to group source\_imp.

source_imp	Count
NA	3694
Personal	2941
Heard it	1621
Internet	353
Internet Pharmacy	110

### Imputation

We assume that the data is MAR, the next step is to use MICE to impute missing data.

One problem: city has over 50 categories and is messed up with duplicate and abbreviation, so here we will drop city.



```
##
##
    Variables sorted by number of missings:
##
          Variable
                        Count
##
        source_imp 0.4236724
               ppm 0.0000000
##
##
          yq_pdate 0.0000000
##
        price_date 0.0000000
##
               city 0.0000000
             state 0.0000000
##
```

```
##
           country 0.0000000
##
        USA_region 0.0000000
##
            source 0.0000000
##
          api_temp 0.0000000
##
         form_temp 0.0000000
             mgstr 0.0000000
##
     bulk purchase 0.0000000
##
##
    Primary_Reason 0.0000000
##
           log_ppm 0.0000000
##
             count 0.0000000
##
              year 0.0000000
##
           quarter 0.0000000
##
       year_factor 0.0000000
    quarter_factor 0.0000000
##
##
      source_group 0.0000000
##
      mgstr_factor 0.0000000
```

The typical sequence of steps to perform a multiple imputation analysis is:

- 1) Impute the missing data by the mice() function, resulting in a multiple imputed data set (class mids);
- 2) Fit the model of interest (scientific model) on each imputed data set by the with() function, resulting an object of class mira;
- 3) Pool the estimates from each model into a single set of estimates and standard errors, resulting in an object of class mipo;
- 4) Optionally, compare pooled estimates from different scientific models by the D1() or D3() functions.

```
##
    iter imp variable
##
     1
             source_imp
##
     1
          2
             source_imp
##
     1
          3
             source_imp
##
     1
          4
             source_imp
##
     1
          5
             source_imp
##
     2
          1
             source_imp
##
     2
          2
             source imp
##
     2
          3
             source_imp
     2
##
          4
             source_imp
     2
##
          5
             source_imp
     3
##
          1
             source_imp
##
     3
          2
             source_imp
##
     3
          3
             source_imp
     3
##
          4
             source_imp
##
     3
          5
             source_imp
             source_imp
##
     4
##
     4
          2
             source_imp
##
     4
          3
             source_imp
     4
##
          4
             source_imp
##
     4
          5
             source_imp
##
     5
          1
             source_imp
##
     5
          2
             source_imp
     5
##
          3
             source_imp
##
     5
             source_imp
     5
##
             source_imp
```

##

#### model selection

The standard multiple imputation scheme consists of three phases:

- 1. Imputation of the missing data m = 5 times;
- 2. Analysis of the m = 5 imputed datasets;
- 3. Pooling of the parameters across m = 5 analyses.

The final model we have selected is m7 <- lmer(formula = log\_ppm ~ mgstr\_factor + bulk\_purchase + (1 | state), data=df %>% filter(year>2009 & state!="Unknown")) m7 BIC is 22815.

We compare m7 with models that include the source imputed by MICE.

```
## # A tibble: 10 x 10
##
      term
                  npar
                           AIC
                                  BIC
                                       logLik deviance statistic
                                                                       df
                                                                           p.value nobs
##
      <chr>
                 <dbl>
                        <dbl>
                               <dbl>
                                         <dbl>
                                                   <dbl>
                                                              <dbl> <dbl>
                                                                              <dbl> <int>
##
    1 lmer(log~
                    19 22681. 22815. -11322.
                                                 22643.
                                                               NA
                                                                       NA NA
                                                                                        0
    2 lmer(log~
                    22 22661. 22817. -11309.
                                                 22617.
                                                               25.7
                                                                        3
                                                                                        0
##
                                                                           1.11e-5
##
    3 lmer(log~
                    19 22681. 22815. -11322.
                                                 22643.
                                                               NA
                                                                       NA NA
                                                                                         0
                    22 22668. 22823. -11312.
##
    4 lmer(log~
                                                 22624.
                                                               19.3
                                                                        3
                                                                           2.34e-4
                                                                                        0
##
    5 lmer(log~
                    19 22681. 22815. -11322.
                                                 22643.
                                                               NA
                                                                       NA NA
                                                                                         0
    6 lmer(log~
                    22 22658. 22813. -11307.
                                                               29.2
                                                                        3
                                                                           2.08e-6
                                                                                         0
##
                                                 22614.
    7 lmer(log~
                    19 22681. 22815. -11322.
                                                 22643.
                                                                       NA NA
##
                                                               NA
                                                                                         0
##
    8 lmer(log~
                    22 22667. 22822. -11311.
                                                               20.5
                                                                        3
                                                                           1.32e-4
                                                                                         0
                                                 22623.
    9 lmer(log~
                    19 22681. 22815. -11322.
                                                                       NA NA
                                                                                         0
                                                 22643.
                                                               NA
                                                                           3.28e-8
## 10 lmer(log~
                    22 22649. 22805. -11303.
                                                 22605.
                                                               37.7
                                                                        3
                                                                                         0
```

## [1] 22815.36

## [1] 22816.08

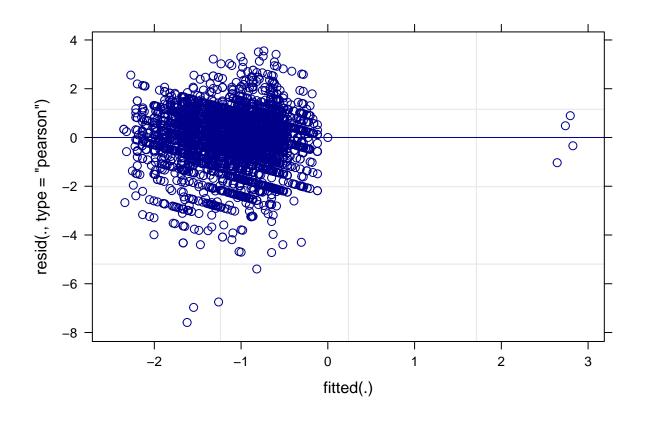
The average BIC on model:  $lmer(log\_ppm \sim mgstr\_factor + bulk\_purchase + source\_imp + (1 | state)$  is 22816>22815, so the model built with imputed source variable doesn't perform better. We conclude that using m7 model on original data performs better.

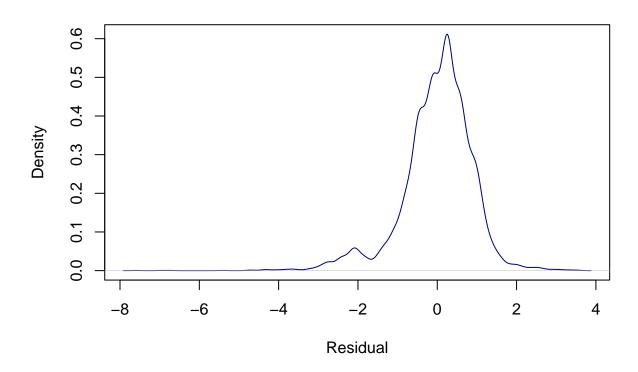
To do:

- 1. Missing data imputation + Adding source into the model and compare BIC(done)
- 2. Outliers or influential points
- 3. Model diagnostics
- 4. Model interpretation + Results visualization

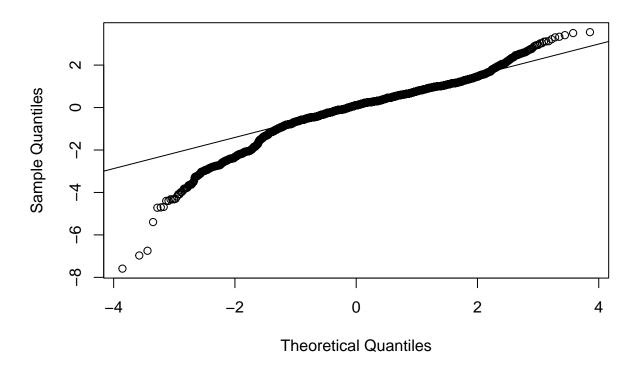
# Model Diagnostics

# Residual Analysis





## Normal Q-Q Plot



### Evaluation 3 plots

- 1. The residual distribution plot and residual vs. fitted values plot tell that the model follows constant variance assumption..
- 2. In Q-Q plot, we can see that the residuals tend to stray from the line quite a bit near the tails, which could indicate that they're not normally distributed. So the model violate the normality assumption

### ICC

Uncertainty quantification around effect estimates of interest

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
  Formula: log_ppm ~ mgstr_factor + bulk_purchase + (1 | state)
      Data: df %>% filter(year > 2009 & state != "Unknown")
##
##
## REML criterion at convergence: 22687.7
##
## Scaled residuals:
##
       Min
                1Q
                    Median
                                 3Q
                                        Max
##
  -8.4971 -0.4883
                    0.1267
                            0.6196
                                    3.9759
##
## Random effects:
    Groups
             Name
                         Variance Std.Dev.
```

```
state
             (Intercept) 0.0141
                                  0.1187
                         0.7976
                                  0.8931
##
  Residual
                                 state, 52
## Number of obs: 8654, groups:
##
## Fixed effects:
                                                              df t value Pr(>|t|)
##
                                  Estimate Std. Error
## (Intercept)
                                             0.05688 1953.48745 -5.033 5.26e-07
                                  -0.28631
## mgstr_factor15
                                  -0.34702
                                              0.05648 8630.18457
                                                                  -6.144 8.38e-10
## mgstr_factor20
                                  -0.47124
                                              0.08252 8625.37630 -5.710 1.16e-08
## mgstr_factor30
                                  -0.69897
                                              0.05579 8627.52523 -12.530
## mgstr_factor50
                                  -1.01511
                                              0.11528 8624.13244 -8.806
                                                                          < 2e-16
## mgstr_factor60
                                  -1.03761
                                              0.05939 8628.94224 -17.470
                                                                          < 2e-16
                                  -1.29660
## mgstr_factor80
                                              0.14113 8617.34133 -9.187
                                                                          < 2e-16
## mgstr_factor100
                                  -1.36658
                                              0.06365 8631.35129 -21.472
                                                                          < 2e-16
## mgstr_factor200
                                              0.09495 8631.64396 -17.709
                                  -1.68155
                                                                          < 2e-16
## mgstr_factor40
                                  -0.80751
                                              0.22990 8608.25147 -3.512 0.000446
## mgstr_factor75
                                  -1.83720
                                              0.32065 8606.74852 -5.730 1.04e-08
## mgstr factor90
                                  -1.22988
                                              0.30298 8611.77494 -4.059 4.97e-05
## mgstr_factor120
                                              0.20239 8611.07851 -8.032 1.08e-15
                                  -1.62570
## mgstr factor1
                                   2.94474
                                              0.45103 8634.01056
                                                                   6.529 7.00e-11
## mgstr_factor45
                                  -0.29653
                                              0.45055 8612.83501 -0.658 0.510457
## mgstr_factor5
                                              0.89545 8599.00139
                                                                   0.355 0.722478
                                   0.31803
## bulk_purchase1 Bulk purchase
                                              0.02559 8629.46162 -4.176 3.00e-05
                                  -0.10685
##
## (Intercept)
                                ***
## mgstr_factor15
                                ***
## mgstr_factor20
                                ***
## mgstr_factor30
                                ***
## mgstr_factor50
                                ***
## mgstr_factor60
                                ***
## mgstr_factor80
## mgstr_factor100
## mgstr_factor200
## mgstr_factor40
                                ***
## mgstr factor75
## mgstr_factor90
                                ***
## mgstr factor120
## mgstr_factor1
                                ***
## mgstr_factor45
## mgstr_factor5
## bulk purchase1 Bulk purchase ***
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
```

### **Evaluation**

- 1. The estimated standard error  $\sigma = 0.8931$  describes the within-state or remaining unexplained variation.
- 2. The estimated  $\tau = 0.1187$  describes the across-state variation attributed to the random intercept.
- 3. We can see that the variation between state is small compared to the variation within state.

$$\tau^2 = 0.01408, \sigma^2 = 0.79763$$

So,  $ICC=\frac{\tau^2}{\sigma^2+\tau^2}=\frac{0.01408}{0.79763+0.01408}=0.017$  The ICC is 0.017 so that we almost have no correlation between ppm in the same state.

### Confidence Interval

	lower bound	upper bound
(Intercept)	-0.3977734	-0.1750560
mgstr_factor15	-0.4576486	-0.2364473
mgstr_factor20	-0.6328723	-0.3096573
mgstr_factor30	-0.8082846	-0.5897797
mgstr_factor50	-1.2407912	-0.7892737
mgstr_factor60	-1.1539539	-0.9213306
mgstr_factor80	-1.5730649	-1.0203020
mgstr_factor100	-1.4912750	-1.2419943
mgstr_factor200	-1.8676987	-1.4957456
mgstr_factor40	-1.2576656	-0.3572172
mgstr_factor75	-2.4656391	-1.2096346
mgstr_factor90	-1.8231849	-0.6365000
mgstr_factor120	-2.0221433	-1.2294230
mgstr_factor1	2.0623634	3.8294341
mgstr_factor45	-1.1795426	0.5852616
mgstr_factor5	-1.4357166	2.0715248
bulk_purchase1 Bulk purchase	-0.1570025	-0.0567710

The confidence interval for fixed effect is listed above