Influence of Prescription Drug Monitoring Programs on Acetaminophen-related Liver Toxicity

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Introduction

Drug Diversion

Within the last two decades, prescription drug abuse and diversion have become major threats to the public health. According to the Office of National Drug Control Policy, prescription pain killers are the second most abused drugs (second only to marijuana).[1] These drugs are not inherently illegal or unsafe. They are intended for use by a patient, under the supervision of a doctor, for a legitimate medical need. Drug diversion occurs when a prescription drug is taken by someone other than the individual for whom the prescription was written.[2] Selling of controlled substances to individuals that abuse them is highly profitable. Until the advent of prescription drug monitoring programs (PDMPs), it was relatively easy for individuals to visit multiple doctors to gain multiple prescriptions for the same condition. The individual would then present the prescriptions at different pharmacies so that the pharmacist could not know that multiple prescriptions were obtained. This was possible because there was little to no communication between healthcare professions.

Prescription Drug Monitoring Programs

While the federal government (Drug Enforcement Administration and Food and Drug Administration) is a resource in the "war on drugs," it is left up to each state to utilize its policing power to control the diversion of Scheduled drugs. Scheduled or controlled drugs are medications that have a potential to cause physiological or psychological dependency in individuals taking them (see Table 1). The states required a way to monitor prescriptions for

drugs with a high potential for abuse so that doctors, pharmacists and law enforcement could prevent doctor shopping (using multiple doctors to receive controlled prescriptions). Prescription drug monitoring programs collect the names of the patient, prescribing physician and pharmacy involved in the dispensing of the controlled drugs. This information is sent from the pharmacy to a database. The PDMP database is maintained and monitored by team members under a state government organization.

The federal government recognized the value of PDMPs and, since 2003, has provided financial assistance through the Harold Rogers Grant program to states wanting to implement a PDMP in their state. A major criticism of this grant is that it permits states to establish their own requirements with regard to controlled substance Schedules monitored, information sharing and accessibility to the program data. Beyond having the desire to implement a PDMP, a state does not have to meet any criteria or guidelines. As a result, the state monitoring programs often differ greatly. Some monitor Schedules II though IV and some track only the drugs with the most abuse potential (Schedule II). Some are administered by a health departments and some by a Board of Pharmacy.[3] Regardless of differing characteristics, federal assistance and the success of early PDMPs have encouraged most states to establish their own program. As of September 2011, 36 states have implemented a PDMP.[4]

Prescription drug monitoring programs were created to reduce prescription misuse and abuse, but were not intended to intimidate prescribers to change their prescribing patterns. This seems to be an unfortunate side effect of the implementation of PDMPs. Widely referred to as the "chilling effect," a number of studies have shown that prescribers tend to shy away from prescribing Schedule II analgesics in favor of lower Scheduled or over-the-counter drugs for pain management.[5,6] This may be due to the fear of regulatory oversight, a belief that a lower

Scheduled drug is safer, or simply convenience for the practitioner.[7] This raises the question of whether or not patients are receiving adequate treatment for their pain. When prescribers choose a Schedule III analgesic or an OTC analgesic, is the chosen drug as effective as a Schedule II opioid? Is the prescribing of Schedule III pain medications truly safer than Schedule II analgesics?

Table 1: Scheduled Drugs

Schedule	**Characteristics**	**Example**
Schedule I	No legitimate medical use	Heroin
Schedule II	High potential for physical and psychological dependency	Oxycodone (Oxycotin)
Schedule III	High potential for psychological dependency, lower potential for physical dependency	Hydrocodone (Lortab)
Schedule IV	Comparatively low potentials for physical and psychological dependency	Diazepam (Valium)
Schedule V	Low potentials for physical and psychological dependency	Codeine syrup (Robitussin Ac)

Acetaminophen Toxicity

PDMPs have been shown to cause a substitution effect, with prescribers shifting from prescriptions for Schedule II drugs to Schedule III drugs. In a study looking at analgesic related overdoses, the results showed that the prescribing rates of hydrocodone (the most prescribed Schedule III analgesic) were significantly higher in states with PDMPs than in non-PDMP states. The results also showed that other opioids were prescribed less frequently in states with a PDMP.[5] In another study, multiple copy prescription programs (MCPPs; an early version of PDMPs), were studied to determine program impact on prescribing patterns. The results from this study revealed that when all other factors were held constant, the presence of a MCPP in a

state has a negative effect on the probability that a Schedule II analgesic will be prescribed and a positive influence on the probability that a Schedule III analgesic will be prescribed.[6] This is more evidence of the substitution effect; a switching from Schedule II to Schedule III drugs.

Most Schedule III pain medications are opioid and acetaminophen combinations. Acetaminophen is a common pain reliever and fever reducer. It is the active ingredient in over-the-counter Tylenol. It is widely accepted that acetaminophen is toxic to the liver and a dangerous intoxicant when used in excess of 4 grams per day. Acetaminophen related liver toxicity is a serious concern of the FDA. In June of 2009, an advisory committee voted that acetaminophen/opioid combination products should be removed from the market. Their decision was based on numerous studies showing acetaminophen to be the leading cause of acute liver failure (ALF) in the United States. One study showed that among the ALF patients, 63% of unintentional overdoses were associated with the use of acetaminophen/opioid combinations.[9] For many decades, the maximum daily limit for ingestion of acetaminophen was 4 grams. In June 2011, McNeil Consumer Healthcare, the primary manufacturer of acetaminophen, announced that in response to FDA concerns, they were lowering the maximum daily dose to 3 grams a day.[8]

Opioid and acetaminophen combination products are very commonly prescribed for pain management. Many experts believe that the popularity of these drugs is due in part to the substitution effect. In fact, the most prescribed drugs in the United States are hydrocodone/acetaminophen combination products. The Institute for Healthcare Informatics (IHS) reports that the number one prescribed drug in 2010 was hydrocodone with acetaminophen.[10] The fear of investigation, litigation, or censure may cause many physicians to "play it safe," by avoiding highly regulated Schedule II opioids. Another manifestation of the

chilling effect is the use of over-the-counter acetaminophen or other analgesics in the place of controlled substances. In a large survey of 979 physicians, 74 percent stated that they refrained from prescribing controlled analgesics during the past 12 months due to a concern that a patient might become addicted.[11] This creates a very real potential for under treatment of pain. PDMPs are implemented to keep physicians and patients honest, but not intimidate physicians from prescribing Schedule II narcotics to patients that need them. One common mechanism for acetaminophen overdose arises from a patient attempting to manage their pain with the "lesser" drug (acetaminophen or acetaminophen/opioid product instead of a pure opioid). The patient unwittingly overdoses when pain relief is not forthcoming. Another common mechanism of overdose arises from tolerance or misuse of an acetaminophen/opioid combination product to get opiate effects. [12]

This study seeks to determine whether an unintended consequence of PDMPs has been an increase in the number of cases of acetaminophen overdose or hepatotoxicity. The hypothesis is that states with PDMPs will have an increased number of acetaminophen related hepatotoxicity cases as documented by emergency department visits and hospitalizations when compared to states that do not have PDMPs. The secondary hypothesis is that states with PDMPs that monitor only Schedule II drugs will have an increased number of cases of acetaminophen-related hepatotoxicity when compared to states that have PDMPs that monitor all Schedules of controlled substance prescriptions

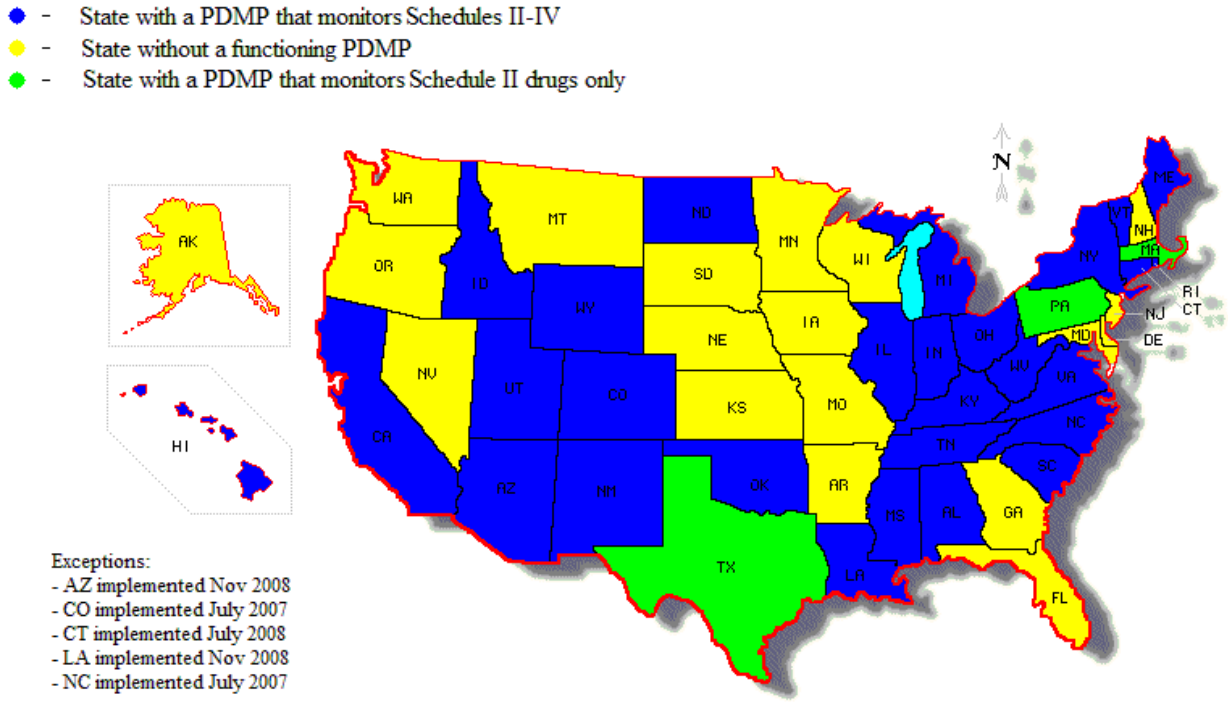
Methods

This study seeks to determine whether prescription drug monitoring program implementation may cause an increase in the number of cases of acetaminophen overdose or

hepatotoxicity. Data for the analysis were pulled from a large commercially insured employed population of approximately 15 million individuals across the United States. The data contain de-identified health records including enrollment spans, medical claims, prescription claims, and lab results from January 1, 2007 to December 31, 2009. Cases of acetaminophen overdose and hepatotoxicity were identified through the use of ICD-9 codes 965.4 for acetaminophen overdose and 570 for acute hepatic injury. Since the number of participants in each state varied greatly, the number of cases in each state was normalized by dividing by the number of covered lives for the state. Appendices B, C and D provide the raw data for acetaminophen overdose, acute liver toxicity, and both, expressed in rate per thousand covered lives.

States were separated into three categories: states with a PDMP that monitors schedules II-V, states with a PDMP that monitors schedule II drugs only, and states without a functioning PDMP. Figure A shows the PDMP status by state for the 2007-2009 periods. Appendix A shows the PDMP type for each state and year, reduced to a dummy variable. Regression analysis was used to evaluate the impact of a state PDMP on acute liver toxicity and acetaminophen overdose. SAS 9.3 was used to develop models and analyze the data. This research has been approved by the University of Kentucky Institutional Review Board.

Figure A: Status of State Prescription Drug Monitoring Programs for 2007-2009



Results

One-way Pool Data Analysis

A one-way pooled data analysis model for PDMP effects was used to examine how intercepts vary across different PDMP types. To run a Least Squares Dummy Variable Regression (LSDV) for this model, three dummy variables were used to represent the three levels of PDMP: no PDMP (PDMP 0), a PDMP that monitors Schedules II-V (PDMP 1) and a PDMP that monitors Schedule II only (PDMP 2). The dummy variable representing no functioning PDMP (PDMP 0) was used as a reference. According to this model, the null hypothesis is that all dummy variables are 0, indicating there is no PDMP effect on the number of acetaminophen overdoses within a state. With small F-value=0.03 (p-value=0.9687), the null hypothesis is not rejected. Since the t-test analysis shows no statistical significance from the

reference variable (PDMP 0), there is no significant fixed PDMP effect. An R^2 value so low (0.0004) is an indication that the model with pooled analysis one-way group effect (PDMP) is a weak fit.

Table 2: One-way Pooled Data Analysis Model for PDMP Effects on Acetaminophen Overdose (0965)

Parameter Estimates

Variable	Parameter Estimate	Standard Error	t Value	Pr>|t|
PDMP 0	0.44309	0.03437	12.89	<0.0001
PDMP 1	0.00389	0.04728	0.08	0.9345
PDMP 2	-0.01974	0.09476	-0.21	0.8353

Analysis of Variance

F value	0.03
P value	0.9687
R-squared	0.0004

A one-way time effects model was used to determine if the incidence of acetaminophen toxicity varied across the three years studied. Three dummy variables were used to represent the three years of data: Year 2007, Year 2008, and Year 2009. The dummy variable representing Year 2007 was used as a reference. According to this model, the null hypothesis is that all dummy variables are 0, indicating there is no time effect. It is not possible to reject the null hypothesis and there seems to be no significant fixed time effect. The R^2 value is very low for this model as well (0.0179). The pooled analysis one-way group effect for time is a weak fit.

Table 3: One-way Pooled Analysis Model for Time Effects on Acetaminophen Overdose (0965)

Parameter Estimates

Variable	Parameter Estimate	Standard Error	t Value	Pr>|t|
Intercept	0.42928	0.03915	10.97	<0.0001
Year 2008	0.06516	0.05536	1.18	0.2411
Year 2009	-0.02191	0.05539	-0.4	0.6929

Analysis of Variance

F value	1.34
P value	0.2654
R-squared	0.0179

Two-way Pooled Analysis

The two-way pooled analysis model was used to examine the PDMP and time effects together. For this model, six dummy variables were used to represent the three levels of PDMP and the three years studied: no PDMP (PDMP 0), a PDMP that monitors Schedules II-V (PDMP 1), a PDMP that monitors Schedule II only (PDMP 2), Year 2007, Year 2008, and Year 2009. The dummy variables PDMP 0 and Year 2007 were used as reference variables. The null hypothesis is that all dummy variables are 0, indicating there is no combined PDMP and time effect. Once again, the null hypothesis cannot be rejected and there is no statistically significant difference between the variables. The R^2 value is slightly higher than the one-way models(0.0183), but is still a poor fit.

Table 4: Two-way Pooled Analysis Model for PDMP and Time Effects on Acetaminophen Overdose (0965)

Parameter Estimates

Variable	Parameter Estimate	Standard Error	t Value	Pr>|t|
Intercept	0.42944	0.03915	10.97	<0.0001
Year 2008	0.06448	0.05536	1.18	0.2411
Year 2009	-0.02266	0.05539	-0.4	0.6929
PDMP 1	0.00316	0.04741	0.07	0.947
PDMP 2	-0.01863	0.09457	-0.2	0.8441

Analysis of Variance

F value	0.67
P value	0.6111
R-squared	0.0183

Group Effects with Repeated States

A group effects model with repeated states was created for PDMP effects to determine if a statistically significant relationship can be found using a repeated states model instead of pooled data. The repeated state model utilized the same PDMP dummy variables that were used for the pooled data analysis models. This model allowed for a comparison of the least square means of the variables. This model was created for both the PDMP effects on acetaminophen

toxicity (0965) and on acute liver toxicity (0570). Unfortunately, none of the relationships were statistically significant in either case. According to the repeated states models, PDMP status has no significant effect of the frequency of acetaminophen overdose or acute liver toxicity.

Table 5: Group Effects Model with Repeated States for PDMP Effects on Acetaminophen Overdose (0965)

Differences of Least Squares Means

Variable Comparison	Parameter Estimate	Standard Error	t Value	Pr>|t|
PDMP2 to PDMP1	-0.04078	0.1698	-0.24	0.8110
PDMP2 to PDMP0	0.07214	0.1708	0.42	0.6743
PDMP1 to PDMP0	0.1129	0.0863	1.31	0.1954

Table 6: Group Effects Model with Repeated States for PDMP Effects on Acute Liver Toxicity (0570)

Differences of Least Squares Means

Variable Comparison	Parameter Estimate	Standard Error	t Value	Pr>|t|
PDMP2 to PDMP1	-0.00142	0.1113	-0.01	0.9899
PDMP2 to PDMP0	0.01072	0.1125	0.10	0.9244
PDMP1 to PDMP0	0.01214	0.0553	0.22	0.8268

Time Effects with Repeated States

A time effects model with repeated states was created in case a repeated states model is a better fit for the data than a pooled data model. The same time related dummy variables utilized for the pooled data analysis were used for the repeated state model. Models were created to determine the effects of time on acetaminophen toxicity (0965) and on acute liver toxicity (0570). As before, none of the relationships were statistically significant for either model.

Table 7: Time Effects Model with Repeated States for PDMP Effects on Acetaminophen Overdose (0965)

Differences of Least Squares Means

Variable Comparison	Parameter Estimate	Standard Error	t Value	Pr>|t|
Year 2009 to 2008	0.2507	0.1308	1.92	0.0611
Year 2009 to 2007	0.1776	0.1303	1.36	0.1791
Year 2008 to 2007	-0.0732	0.0736	-0.99	0.3254

Table 8: Time Effects Model with Repeated States for PDMP Effects on Acute Liver Toxicity (0570)

Differences of Least Squares Means

Variable Comparison	Parameter Estimate	Standard Error	t Value	Pr>|t|
Year 2009 to 2008	-0.08707	0.0465	-1.87	0.0671
Year 2009 to 2007	-0.02191	0.0458	-0.48	0.6342
Year 2008 to 2007	0.06516	0.0532	1.23	0.2262

Discussion

Limitations

There are a number of limitations to the design of study. Data were obtained using an administrative database with only 3 years of claims data available. With more years, it might also be possible to look at states before and after implementation of a PDMP to see the program impact on acetaminophen toxicity. Another problem with the database was that the number of covered lives in each state varied greatly. This was accounted for by calculating the rate per thousand covered lives. Some states had few participants. It may not be reasonable to compare these states to other states with large numbers of participants in the study. An additional limitation is that acetaminophen overdose seems to be a relatively rare event with the incidence averaging at approximately 5 patients overdosed per 10,000. In five states (Arizona, Colorado,

Connecticut, Louisiana, and North Carolina), the PDMP was implemented in the middle of year. For the purpose of analysis, these states were treated as though the PDMP started collecting data at the beginning of the year. It was necessary to do so to keep the year and PDMP status categorical, but this was another limitation. In retrospect, it would have made more sense to treat the state data as though the PDMP was implemented at the beginning of the next year. The implementation process, the acceptance by users, and the PDMP effects all take time.

This study looked at an entire population of participants without the use of any exclusion criteria to correct for any sociodemographic or medical variables. There are a number of confounders that were not accounted for. External causes of acetaminophen overdose could have been identified by searching for ICD-9 E codes; then, cases of attempted suicide (E950.0) or assault (E962.2) involving acetaminophen could have been excluded (though these events are uncommon). In cases where hepatotoxicity was identified, any chronic liver disease such as alcoholic cirrhosis should have been excluded (identified by code 571). This study did not look at the demographics of the study population. The data may not be representative of the US population. That being said, the data set was large enough to reflect the sociodemographic characteristics of individuals with prescription drug insurance.

The reliance on administrative data was a limitation of the study. The validity of the hospital and ER data should be considered. The data were submitted and coded independently at each local hospital. Some of the diagnoses may be based on information obtained from patients concerning drug use and illnesses. If this information is used by physicians to assist them with their diagnoses, poor patient recall can contribute to inaccurate diagnoses. ICD-9 codes are based on the discharge diagnosis, which are assigned by the attending physician. It possible that the physicians will assign an incorrect diagnosis or that errors could occur in coding or

documentation. The reliance on a third party database requires the assumption the correct diagnosis and documentation were given in each case.

Next Steps

A next step that can be taken is using the current database to look at the substitution effect in the context of prescription volumes. Looking at a state, before and after the implementation of a PDMP, it may be possible to note a marked increase in Schedule III prescriptions and a decrease in Schedule II prescriptions. Even if prescription volumes for both are steadily increasing (with the national trend), a change in the rate after PDMP implementation may indicate a substitution effect. Another step would be to use a database with more years of data collection. It would be interesting to look at change in the number of acetaminophen overdoses before and after each individual state implement PDMPs. With enough years of data before and after PDMP implementation, it may be possible to look at the PDMP impact individually as well as categorically as states with and without PDMPs. Also, with a larger data set, it may be possible to correct for sociodemographic and medical variables. The analysis done is this study involved broad strokes. It may be important to control for intentional overdoses or alcohol consumption. Further analysis is needed.

Conclusions

While the statistical modeling was unable to uncover a significant relationship, it seems plausible that the substitution effect is a factor when a PDMP is first implemented. A couple of studies have shown a shift from Schedule II to Schedule III drugs when PDMPs are implemented.[5,6] These studies looked at changes in prescription volumes corresponding to

Schedule II and Schedule III analgesics in a particular state, before and after the implementation of a PDMP. This study sought evidence for the presence of a substitution effect through an increase in acetaminophen toxicity and acute liver toxicity. There seems to be too many confounding factors to determine any meaningful relationships from the data. Despite this fact, it is important to address any prescriber fear or intimidation stemming from the implementation of a PDMP.

Although prescribers understand the intent of prescription monitoring programs, some may believe that the prescribing of controlled substances to patients may bring unwanted attention from authorities. This may prevent patients from receiving adequate pain control and result in negative health outcomes. Most PDMP data is accessed by other prescribers, not by law enforcement. Kentucky's PDMP, Kentucky All Schedule Prescription Electronic Reporting (KASPER), is accessed primarily by other prescribers. KASPER administrators report that only 3.5% of all KASPER reports are accessed by law enforcement.[2] Prescribers need to understand that PDMP data are intended to be used to prevent patient drug diversion, not to keep tabs on their prescribing patterns. It is a tool to keep prescribers informed of a patient's other controlled prescriptions. Physicians and patients should also understand that there is nothing inherently wrong with Schedule II drugs. These drugs, despite having addictive properties, have a legitimate place in medication therapy.

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Appendix A: PDMP Status 2007-2009, Expressed in Dummy Variables

State	PDMP 2007	PDMP 2008	PDMP 2009
AK	0	0	0
AL	1	1	1
AR	0	0	0
AZ	0	1	1
CA	1	1	1
CO	1	1	1
CT	0	1	1
DE	0	0	0
FL	0	0	0
GA	0	0	0
HI	1	1	1
IA	0	0	0
ID	1	1	1
IL	2	1	1
IN	1	1	1
KS	0	0	0
KY	1	1	1
LA	0	1	1
MA	2	2	2
MD	0	0	0
ME	1	1	1
MI	1	1	1
MN	0	0	0
MO	0	0	0
MS	0	0	0

State	PDMP 2007	PDMP 2008	PDMP 2009
MT	0	0	0
NC	1	1	1
ND	1	1	1
NE	0	0	0
NH	0	0	0
NJ	0	0	0
NM	1	1	1
NV	0	0	0
NY	1	1	1
OH	1	1	1
OK	1	1	1
OR	0	0	0
PA	2	2	2
RI	1	1	1
SC	0	1	1
SD	0	0	0
TN	1	1	1
TX	2	2	2
UT	1	1	1
VA	1	1	1
VT	0	0	1
WA	0	0	0
WI	0	0	0
WV	1	1	1
WY	1	1	1

Note: PDMP 0 = no functioning PDMP
PDMP 1 = functioning PDMP that monitors Schedules II-V
PDMP 2 = functioning PDMP that monitors Schedule II drugs only

Appendix B: Raw Data for States for Acetaminophen Overdose in Rate per Thousand Covered Lives, 2007-2009

State	965 2007	965 2008	965 2009
AK	0.00	0.88	0.00
AL	0.26	0.21	0.34
AR	0.60	0.12	0.30
AZ	0.45	0.68	1.13
CA	0.37	0.45	0.36
CO	0.39	0.46	0.47
CT	0.19	0.42	0.04
DE	0.51	0.60	0.13
FL	0.56	0.41	0.42
GA	0.20	0.34	0.29
HI	1.04	0.00	0.13
IA	0.49	0.68	0.32
ID	0.79	0.98	0.94
IL	0.73	0.57	0.52
IN	0.54	0.68	0.39
KS	0.11	0.33	0.78
KY	0.12	0.52	0.68
LA	0.29	0.30	0.25
MA	0.25	0.31	0.21
MD	0.29	0.35	0.32
ME	0.18	0.00	0.00
MI	0.61	0.29	0.35
MN	0.71	0.69	0.78
MO	0.66	0.60	0.37
MS	0.46	0.32	0.27

State	965 2007	965 2008	965 2009
MT	0.00	0.36	0.33
NC	0.58	0.48	0.59
ND	0.00	0.94	0.20
NE	0.24	0.37	0.63
NH	0.82	0.77	1.26
NJ	0.39	0.49	0.40
NM	0.39	0.30	0.44
NV	0.74	0.44	0.38
NY	0.37	0.36	0.48
OH	0.30	0.40	0.32
OK	0.08	0.64	0.15
OR	0.11	0.63	0.26
PA	0.33	0.82	0.35
RI	1.12	0.62	1.14
SC	1.00	0.73	0.31
SD	0.80	0.55	0.00
TN	0.34	0.47	0.13
TX	0.49	0.36	0.39
UT	0.78	0.63	0.31
VA	0.33	0.34	0.60
VT	0.00	0.00	0.00
WA	0.60	0.48	0.60
WI	0.77	0.35	0.65
WV	0.10	1.01	0.66
WY	0.00	0.98	0.00

Appendix C: Raw Data for States for Acute Liver Toxicity in Rate per Thousand Covered Lives, 2007-2009

State	570 2007	570 2008	570 2009
AK	0.92	0.00	5.55
AL	0.93	0.92	1.17
AR	0.61	0.22	0.32
AZ	0.82	1.82	1.53
CA	0.99	0.89	1.11
CO	0.79	0.68	0.83
CT	0.52	0.71	0.93
DE	0.51	0.00	1.03
FL	1.12	0.86	1.09
GA	0.79	1.03	1.05
HI	2.07	1.76	1.82
IA	0.65	0.98	0.68
ID	1.22	0.75	0.35
IL	1.16	0.53	0.96
IN	0.54	0.47	0.85
KS	0.37	0.33	0.50
KY	0.94	0.84	0.88
LA	1.00	0.77	0.66
MA	0.46	0.78	0.69
MD	0.81	1.00	1.05
ME	0.00	0.71	3.43
MI	1.18	0.91	1.11
MN	1.12	0.77	0.89
MO	0.60	0.69	0.61
MS	0.79	0.63	0.49

State	570 2007	570 2008	570 2009
MT	1.04	0.90	1.67
NC	1.57	0.95	0.92
ND	1.57	0.00	0.30
NE	0.60	0.27	0.69
NH	0.73	0.21	0.35
NJ	0.71	0.94	0.79
NM	0.47	0.65	1.18
NV	0.48	1.12	1.37
NY	0.81	1.07	1.04
OH	0.87	0.79	1.22
OK	0.34	0.27	0.66
OR	0.43	0.87	0.42
PA	0.63	0.65	0.65
RI	1.01	0.65	1.30
SC	0.59	0.47	0.48
SD	1.83	0.44	1.19
TN	0.92	0.60	0.79
TX	1.00	0.90	1.16
UT	0.43	0.30	0.44
VA	0.79	1.03	1.00
VT	0.00	1.36	1.05
WA	0.54	0.48	0.53
WI	0.74	1.48	0.73
WV	0.48	1.01	0.07
WY	1.41	0.79	0.19

Appendix D: Raw Data for States for Acetaminophen Overdose or Acute Liver Toxicity in Rate per Thousand Covered Lives, 2007-2009

State	Both 2007	Both 2008	Both 2009
AK	0.92	0.88	5.55
AL	1.19	1.14	1.51
AR	1.21	0.34	0.61
AZ	1.27	2.50	2.66
CA	1.35	1.34	1.47
CO	1.19	1.14	1.31
CT	0.71	1.12	0.97
DE	1.03	0.60	1.16
FL	1.68	1.27	1.51
GA	0.99	1.37	1.34
HI	3.11	1.76	1.95
IA	1.15	1.66	1.00
ID	2.02	1.73	1.29
IL	1.89	1.10	1.49
IN	1.07	1.15	1.24
KS	0.48	0.66	1.28
KY	1.06	1.36	1.57
LA	1.29	1.07	0.91
MA	0.72	1.09	0.90
MD	1.10	1.35	1.37
ME	0.18	0.71	3.43
MI	1.80	1.20	1.47
MN	1.83	1.46	1.67
MO	1.26	1.29	0.99
MS	1.25	0.95	0.76

State	Both 2007	Both 2008	Both 2009
MT	1.04	1.26	2.00
NC	2.15	1.42	1.51
ND	1.57	0.94	0.51
NE	0.84	0.64	1.32
NH	1.55	0.98	1.61
NJ	1.10	1.43	1.19
NM	0.85	0.95	1.62
NV	1.23	1.57	1.75
NY	1.18	1.43	1.52
OH	1.16	1.19	1.53
OK	0.42	0.91	0.81
OR	0.54	1.50	0.68
PA	0.96	1.48	1.00
RI	2.13	1.27	2.43
SC	1.59	1.20	0.79
SD	2.63	0.99	1.19
TN	1.26	1.07	0.92
TX	1.48	1.26	1.55
UT	1.21	0.93	0.75
VA	1.11	1.37	1.60
VT	0.00	1.36	1.05
WA	1.14	0.96	1.13
WI	1.51	1.83	1.38
WV	0.58	2.02	0.73
WY	1.41	1.77	0.19