IMPACT OF PRESCRIPTION OPIOID ACCESS RESTRICTIONS
ON ALCOHOL-INDUCED MORTALITY IN KENTUCKY

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Executive Summary

Prescription drug monitoring programs (PDMPs) are state policy tools to combat risky opioid prescribing. Since 2012, several states began to mandate PDMP use. As mandating use laws have settled down, evaluating potential adverse events becomes possible.

In this study, I focus on alcohol-induced mortality as a potential unintended consequence via substituting alcohol for prescription opioids, since alcohol and opioids are often concurrently misused as a part of pain self-management. Therefore, the aim of this study is to analyze the unintended consequences of prescription opioid access restrictions on alcohol-induced mortality.

I compare the alcohol-induced mortality among adults during pre- and post-revision of the Kentucky PDMP from 2007 to 2017 by using a difference-in-differences design. The county-level alcohol-induced death data was extracted from Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research. Missouri was chosen as a comparison state because state-level PDMP have not been existed.

The finding indicated that mandating PDMP use in Kentucky did not enhance alcohol-induced mortality. In conclusion, prescription opioid access restrictions do not appear to result in unintended consequences on alcohol-induced mortality for adults. Therefore, I recommend retaining the mandatory features of Kentucky’s PDMP. This study is the first assessment of alcohol-related adverse events resulting from PDMPs. Further studies should be conducted to evaluate the finding.
Introduction

Opioid Crisis: Pain Management Failure

During the 1990s, the healthcare system experienced a renewed focus on pain management. The American Pain Society and the United States Department of Veterans Affairs promoted pain as the ‘fifth vital sign’, along with body temperature, blood pressure, pulse, and respiratory rate. Then in 2001, the Joint Commission on Accreditation of Healthcare Organizations also adopted pain as the ‘fifth vital sign’ and certified hospitals only when pain assessments were conducted for all patients. These institutional policies led medical providers to making pain treatment a priority for patients (Christie, et al., 2017). This, coupled with several publications by healthcare providers who claimed little to no addictive tendencies in their patients after prescribing opioids—specifically a letter titled "Addiction Rare in Patients Treated with Narcotics (Jick, 1980)" published in the New England Journal of Medicine – led medical professionals toward opioids as a solution for the pain treatment. All the while, manufacturers of prescription opioids, including Percocet, Vicodin, and OxyContin advertised the concept that their medicines are safe, resulting in their prevalent use (Moghe, 2016). This frequent prescribing of opioids for pain management continued nationally for years and contributed as a major cause of the current opioid epidemic in the United States (U.S. Department of Health and Human Services, 2019).

As the increased trend in opioid prescribing continued, so did deaths associated with prescription opioids. Nearly 218,000 deaths were caused by prescription opioids from 1999 to 2017. The number of yearly deaths during this period rose rapidly, as the mortality rate in 2017 was five times as great as in 1999. In 2017, 46 people died each day due to prescription opioids. Accordingly, among total deaths related to opioid overdose, more than 35 percent of deaths
involved prescription opioids. Methadone, oxycodone, and hydrocodone were the major culprit drugs contributing to prescription opioid overdose deaths. The highest prescription opioid induced deaths were in West Virginia, Maryland, Kentucky, and Utah (Centers for Disease Control and Prevention, 2018). The misuse of prescribed opioids is prevalent as well. About nine out of ten people using opioid analgesics nonmedically got the drugs from their friend/relative or from prescriptions for themselves (Substance Abuse and Mental Health Services Administration, 2014). In 2017, 11.4 million people misused prescription opioids, including 2 million first-time misusers (U.S. Department of Health and Human Services, 2019). Although President Trump signed a package of bills including the Support for Patients and Communities Act to combat the opioid crisis in October 2018 (Lopez, 2018), most states had implemented a policy solution, namely, prescription drug monitoring programs, decades earlier to alleviate the financial, physical, and emotional strain that was resulting from the opioid crisis.

**Prescription Drug Monitoring Programs**

Prescription drug monitoring programs, or PDMPs, are state-operated programs that track the prescribing and dispensing of medications classified as federally controlled substances, including opioids (Drug Enforcement Administration, 2018). A central system collects the electronic prescription data, allowing only authorized users—healthcare providers, and occasionally law enforcement—to access it. The purpose of these programs is to support the detection and prevention of controlled substance misuse, abuse, and diversion. The program mitigates the information asymmetry issue among healthcare providers, patients, and law enforcement by allowing the authorized users access to patient prescription records. This monitoring is expected to reduce the prevalence of ‘doctor shopping’, a phenomenon whereby
patients obtain multiple prescriptions for controlled substances intentionally by visiting numerous clinics (Blumenschein, et al., 2010; Goodin, 2015). In California, doctor shopping occurs more often for prescription opioids than for any other controlled substances (Campbell, et al., 2018).

PDMPs have been implemented throughout the United States, as early as 1939 in California and as late as February 1st, 2019 in four jurisdictions of Missouri. Currently, 49 states, the District of Columbia, Puerto Rico, Guam, and 72 jurisdictions in Missouri are operating their own PDMPs (Brandeis University, 2018a; Saint Louis County Public Health, 2019). While most PDMPs resemble the electronic database mentioned previously, operational details vary between the states (Blumenschein, et al., 2010). Most early PDMPs did not legally mandate prescribers to use the program. Consequently, the role of PDMPs in controlling prescription opioids and opioid-associated overdose was not as effective as their intention (Haffajee, et al., 2018; Shev, et al., 2018; Strickler, et al., 2019; Wen, Schackman, Aden, & Bao, 2017). As a result, over 40 states amended or enacted their PDMPs by adding mandatory features from 2012 to January 2019 (The Pew Charitable Trusts, 2018; Legal Science, 2016; Brandeis University, 2019). However, the comprehensiveness of required usage by prescribers, and sometimes dispensers as well, varies between the state programs.

Several studies described comprehensive mandatory use laws as mandates for: prescriber enrollment, querying previous prescription opioid use history (Strickler, et al., 2019; Haffajee, et al., 2018; Sun, et al., 2018; Brandeis University, 2019), and comprehensive use with specific objective criteria (Haffajee, et al., 2018). Other important features of PDMPs include delegate access (Haffajee, Jena, & Weiner, 2015; The Pew Charitable Trusts, 2018), monitoring drugs in Schedules II to IV, more frequent data collections at regular intervals (Legal Science, 2016), and
sharing data with other states (Brandeis University, 2018b). Among these features, the use mandate was the most important factor improving PDMPs effectiveness on reducing mean morphine-equivalent dosage, risky opioid prescribing, Schedule II prescriptions, and expenditures for opioids. These studies commonly selected Kentucky, Tennessee, and New York as states operating robust PDMPs among the early enactors of mandatory laws (Haffajee, Jena, & Weiner, 2015; Haffajee, et al., 2018; Strickler, et al., 2019; Wen, Schackman, Aden, & Bao, 2017).

Implementation of mandatory PDMP use aroused concerns about unintended consequences (Haffajee, Jena, & Weiner, 2015). One possible unintended consequence from reduced access to prescription opioids is that individuals may seek alternative therapies to substitute for the opioids that they are no longer able to obtain from their physician. In some cases, that means the individual will seek opioids on the illicit black-market, including heroin or synthetic opioids. In other cases, the individual may look for psychoactive substances that are available legally (Islam & McRae, 2014; Columbia University, 2018). Alcohol is a legal psychoactive substance that may be an attractive alternative for an individual who no longer has access to prescription opioids. Attempts to self-medicate pain can result in unhealthy alcohol consumption (Atkinson R. M., 1990a; Atkinson, Tolson, & Turner, 1990b). Alcohol is often used with opioids concurrently to induce early onset of psychoactive (euphoric) effects (Maldonado, 2018; Gudin, Mogali, Jones, & Comer, 2013). Several studies argued that drinking alcohol leads to endogenous opioid release in humans and rodents (Mitchell, Marks, Jagust, & Fields, 2012; Gianoulakis, 2001), which implies opioid abusers could rely on more alcohol consumption to simulate opioid use when they cannot access opioids. Therefore, the aim of this study is to
evaluate the substitution effect, or unintended consequences, of the PDMP use mandate implementation on alcohol-induced mortality.

**Literature Review**

Several studies have evaluated the early PDMPs. The opioid supply decreased in PDMP-implemented states compared to non-implemented states from 1997 to 2003 according to Drug Enforcement Administration (DEA) data. On the other hand, PDMP implementation had no association with lowering opioid consumption and overdose mortality rates during 1999 to 2005 in other DEA analyses (Paulozzi, Kilbourne, & Desai, 2011). In 2002, the U.S. Government Accountability Office also reported that implementing PDMPs reduced the number of investigation days that law enforcement officials required to detect doctor shopping in Kentucky, which was 156 days on average before implementation and 16 days on average after implementation (U.S. General Accounting Office, 2002).

Previous studies examining PDMPs show varying impacts. Several studies have been conducted comparing states with PDMPs versus those without, specifically for Medicare Part D participants. Between 2007 and 2012, states with PDMPs showed a decrease in opioid use (Moyo, et al., 2017), while another examination between 2010 and 2013 revealed modest effects on oxycodone use and smaller effects on opioid use (Yarbrough, 2018). PDMP and pill mill law implementation in Florida also led to a reduction of prescription opioid utilization in high-risk patients compared to Georgia, which had less robust policies limiting opioid access (Chang, Murimi, Faul, Rutkow, & Alexander, 2018).
However, some studies suggest that PDMP implementation results in a substitution effect within the Drug Scheduling system – for example, a decrease in prescriptions for Schedule II opioids leading to an increase in prescriptions for alternative painkillers or Schedule III drugs, so that the overall number of prescriptions does not change significantly (Goodin, 2015; Paulozzi, Kilbourne, & Desai, 2011; Bao, et al., 2016). In addition, recent publications found that mandating PDMP use is related to reducing high-risk opioid prescriptions, and risk of prescription opioid-related poisoning (Bao, et al., 2018; Pauly, Slavova, Delcher, Freeman, & Talbert, 2018). By 2013, six states—Kentucky, New Mexico, Tennessee, New York, Vermont, and West Virginia—strengthened their PDMPs by mandating prescribers to register with the PDMP, and mandating comprehensive use of the program (Haffajee, et al., 2018).

A number of studies have investigated outcomes associated with PDMPs, and as described above, findings are mixed. Surprisingly, no robust evaluation of the unintended consequences of PDMPs currently exists. While PDMPs could be a policy solution for the current prescription opioid problem, it is important to gauge the potentially harmful outcomes that may result from their implementation.

Objective and Hypothesis

The goal of this project is to evaluate the potential adverse effect on alcohol-induced mortality of prescription opioid restriction policy executed by mandating the use of PDMPs. In this analysis, the outcome measure is specified as the change of alcohol-induced mortality among Kentucky counties. Therefore, I hypothesized that the PDMP use mandate introduced in mid-2012 increased alcohol-induced mortality in Kentucky counties after the implementation.
Research Design

The aim of this study is to compare the alcohol-induced death rate between pre- and post-2012 revision of the Kentucky PDMP from 2007 to 2017 by using a difference-in-differences design compared with a neighboring state, Missouri, where a state-wide PDMP did not exist. The difference-in-differences design evaluates the causal effect of a policy change on the outcome of interest by comparing a policy-implementation group with a non-implementation group. This analysis observed aggregated county-level data for the time period before and after implementation. Data are annual.

State Selection

As mentioned above, Kentucky has operated an early, robust PDMP. Thus, Kentucky was selected as a treatment state in this study. According to the Kentucky House Bill 1 (KyHB1), prescribers and dispensers were mandated to register with the state’s PDMP and prescribers must query the PDMP before prescribing opioids as of July 20, 2012 (Kentucky Revised Statutes 218A, 172). The policy change was immediately adopted by practitioners. In 2012, the compliance rate of prescriber registration among DEA (Drug Enforcement Administration) registered practitioners went up from approximately 35% to 93% after the implementation. Moreover, the total number of queries increased more than four times after the implementation in the same year (Freeman, Goodin, Troske, & Talbert, 2015).

I selected Missouri as a neighboring comparison state because it did not operate a state-level PDMP during the time period. In addition, alcohol sales policy in Missouri has been consistent throughout all counties, which will be discussed further below.
Population and Data Source

The targeted population was 18 years or older between the time period from 2007 to 2017.

The county-level mortality data was obtained from the Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research (CDC WONDER), which is a publicly available database. In this analysis, I used detailed mortality data, which could specify underlying cause of death.

Measure

I used alcohol-induced mortality by place of residence in Kentucky and Missouri counties among people age 18 or more during 2007 to 2017. CDC WONDER uses the definition of ‘alcohol-induced causes’ from the National Center for Health Statistics to identify alcohol-induced mortality (Centers for Disease Control and Prevention, 2018). The definitions for ‘alcohol-induced causes’ are made using the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10) codes, which is used to categorize cause of death by the World Health Organization. Detailed ICD-10 codes involved in this study are presented in Table 1.

The death rate was calculated as the number of deaths per 100,000 people and was transformed into logarithms so that estimated effects are approximately percentage changes.
### Table 1. ICD-10 codes for alcohol-induced causes

<table>
<thead>
<tr>
<th>Underlying Cause of death</th>
<th>ICD-10 code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol-induced pseudo-Cushing syndrome</td>
<td>E24.4</td>
</tr>
<tr>
<td>Mental and behavioural disorders due to use of alcohol, acute intoxication</td>
<td>F10.0</td>
</tr>
<tr>
<td>Mental and behavioural disorders due to use of alcohol, harmful use</td>
<td>F10.1</td>
</tr>
<tr>
<td>Mental and behavioural disorders due to use of alcohol, dependence syndrome</td>
<td>F10.2</td>
</tr>
<tr>
<td>Mental and behavioural disorders due to use of alcohol, withdrawal state</td>
<td>F10.3</td>
</tr>
<tr>
<td>Mental and behavioural disorders due to use of alcohol, withdrawal state with delirium</td>
<td>F10.4</td>
</tr>
<tr>
<td>Mental and behavioural disorders due to use of alcohol, psychotic disorder</td>
<td>F10.5</td>
</tr>
<tr>
<td>Mental and behavioural disorders due to use of alcohol, amnesic syndrome</td>
<td>F10.6</td>
</tr>
<tr>
<td>Mental and behavioural disorders due to use of alcohol, residual and late-onset psychotic disorder</td>
<td>F10.7</td>
</tr>
<tr>
<td>Mental and behavioural disorders due to use of alcohol, other mental and behavioural disorders</td>
<td>F10.8</td>
</tr>
<tr>
<td>Mental and behavioural disorders due to use of alcohol, unspecified mental and behavioural disorder</td>
<td>F10.9</td>
</tr>
<tr>
<td>Degeneration of nervous system due to alcohol</td>
<td>G31.2</td>
</tr>
<tr>
<td>Alcoholic polyneuropathy</td>
<td>G62.1</td>
</tr>
<tr>
<td>Alcoholic myopathy</td>
<td>G72.1</td>
</tr>
<tr>
<td>Alcoholic cardiomyopathy</td>
<td>I42.6</td>
</tr>
<tr>
<td>Alcoholic gastritis</td>
<td>K29.2</td>
</tr>
<tr>
<td>Alcoholic fatty liver</td>
<td>K70.0</td>
</tr>
<tr>
<td>Alcoholic hepatitis</td>
<td>K70.1</td>
</tr>
<tr>
<td>Alcoholic fibrosis and sclerosis of liver</td>
<td>K70.2</td>
</tr>
<tr>
<td>Alcoholic cirrhosis of liver</td>
<td>K70.3</td>
</tr>
<tr>
<td>Alcoholic hepatic failure</td>
<td>K70.4</td>
</tr>
<tr>
<td>Alcoholic liver disease, unspecified</td>
<td>K70.9</td>
</tr>
<tr>
<td>Alcohol-induced acute pancreatitis</td>
<td>K85.2</td>
</tr>
<tr>
<td>Alcohol-induced chronic pancreatitis</td>
<td>K86.0</td>
</tr>
<tr>
<td>Finding of alcohol in blood</td>
<td>R78.0</td>
</tr>
<tr>
<td>Accidental poisoning by and exposure to alcohol</td>
<td>X45</td>
</tr>
<tr>
<td>Intentional self-poisoning by and exposure to alcohol</td>
<td>X65</td>
</tr>
<tr>
<td>Poisoning by and exposure to alcohol, undetermined intent</td>
<td>Y15</td>
</tr>
</tbody>
</table>
**Covariates**

The policy was implemented in the middle of 2012, therefore, the years after 2012 (*Post*) were coded as “1”, otherwise years are coded as “0”. I considered the latter part of 2012 as a lag-phase of the policy effect and coded it as “0”. The treatment state (*TS*) was coded as “1”, otherwise “0”. The variable indicating the policy implementation in Kentucky was expressed as an interaction (*TS* × *Post*) and was coded as “1” after 2012, otherwise “0”, i.e. the difference-in-differences. Population by county (*Pop*) was included in the analysis. The population was expressed per 100,000 people. In CDC WONDER data, if the death count is less than 20, those crude death rates, which are automatically calculated, are shown as ‘unreliable’ (Centers for Disease Control and Prevention, 2018). Since the death rate was re-calculated with the raw number, unreliable variable (*Unrel*) were coded as “1” with all other observations coded as “0” to control potential reporting bias or other biases due to small observations.

Alcohol sales regulation policy that could be potentially interacting with PDMP was considered in this analysis. Some states have different alcohol sales regulations among counties. Kentucky operates by county-level, or even smaller jurisdictions such as towns or cities, based on votes and categorized dry, wet, and moist. Dry counties do not allow the sale of alcohol at all, whereas wet counties permit alcohol sales with minimal restrictions uniformly. Besides dry or wet policies, all the other counties are classified as ‘moist’, which allow the sale of alcohol in certain designated locations and/or situations (NABCA Research, 2016). This restricted accessibility to alcohol in dry or moist counties could lower the substitution effect and limit the alcohol use. Therefore, since the variation of alcohol regulations could affect the outcomes of interest, alcohol sales policy is included as one of covariates in this research design. Kentucky Alcoholic Beverage Control kindly provided the voting results of alcohol sales regulations from
each jurisdiction between 2007 and 2015 and also posted the legal status of each jurisdiction on their website from 2016 to 2017 (Estep, 2016; Kentucky Alcoholic Beverage Control, 2017). Unfortunately, because of the limitation of data from CDC WONDER, counties with dry alcohol policies in Kentucky were not included (i.e., there were too few alcohol-induced deaths in these Kentucky counties to permit public reporting. This will be discussed below). The alcohol sales regulations in Missouri counties were uniformly wet policy since 1934 (Missouri Department of Public Safety, 2019). Uniform alcohol sales policy combined with a lack of state-level PDMP makes Missouri an excellent candidate to use as a control state. Thus, given the limitations of the mortality data, moist counties (Alc) were coded as “1”, and wet counties were coded as “0

**Statistical Analysis**

The regression model of the difference-in-differences design is shown below:

\[ Y_{ijt} = \alpha_0 + \alpha_1 TS_i + \alpha_2 Post_t + \alpha_3 (TS \times Post)_{it} + \alpha_4 Alc_{jt} + \alpha_5 Pop_{jt} + \alpha_6 Unrel_{jt} + e_{ijt} \]

The dependent variable \( Y_{ijt} \), is the measure of alcohol-induced mortality for county \( j \) in state \( i \) at year \( t \); \( \alpha_0 \) is a constant term of this model, representing the expected mean value of \( Y_{ijt} \). The covariates mentioned above were all included as independent variables in the model. \( TS \) indicates treatment state \( i \), and \( Post \) specifies a post-policy period at year \( t \); \( \alpha_3 \) represents the difference-in-differences estimator, which captures the overall secular trend of alcohol-induced mortality for state \( i \). \( Alc, Pop, \) and \( Unrel \) are indicators for the alcohol sales policy, population per 100,000 people, and unreliable crude death rate, respectively, in county \( j \) at year \( t \). The random unobserved error term is \( e_{ijt} \), including all that is omitted or unobserved. The statistical analysis was executed using Stata v13.1. All the coefficients were estimated through a linear regression analysis and the estimation is heteroscedasticity-consistent.
**Results**

The robust PDMP in Kentucky did not increase alcohol-induced mortality significantly. The alcohol-induced death rates are higher in Kentucky than in Missouri and are increasing in both Kentucky and Missouri after the policy change. Nonetheless, there is no evidence to reject the null hypothesis that the robust PDMP does not increase the alcohol-induced death rates in Kentucky.

**Sample Characteristics**

Total 146 counties were observed regarding alcohol-induced mortality in the difference-in-differences analysis of the adult population residing in Kentucky and Missouri from 2007 to 2017 (Table 2). In detail, Kentucky observations accounted for 40% (n=58), which is 13 counties among total 120 counties (11%; Table 3). Counties that were observed each year during the whole time period were Fayette, Jefferson, and Kenton. These counties include or are located around big cities, which are Lexington, Louisville, and Cincinnati. Meanwhile, Missouri amounted to the rest of the observations (60%; n=88), which contained 15 counties out of 114 counties (13%). The most frequently observed counties for 11-year timeframe were Clay, Greene, Jackson, St. Louis City, and St. Louis, where they are, or they possess, or they are near big cities such as Kansas City or Springfield. Among these observations, approximately 42% of the counties (n=61) exhibited unreliable crude death rates. Four Kentucky counties – Hardin (n=5), Madison (n=1), Pulaski (n=1), and Warren (n=1) – had moist alcohol sales laws for at least one year in the time period. All the counties that had less than 100,000 residents in both states had less than 20 alcohol-induced deaths. Some time-points in five counties – Kenton
(Kentucky), Boone (Missouri, MO), Clay (MO), Jefferson (MO), and St. Charles (MO) – showed unreliable crude mortalities.

Table 2. The number of counties collected to measure alcohol-induced mortality from 2007 to 2017

<table>
<thead>
<tr>
<th>Year</th>
<th>Kentucky</th>
<th>Missouri</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>3</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>2008</td>
<td>4</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>2009</td>
<td>7</td>
<td>6</td>
<td>13</td>
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<tr>
<td>2010</td>
<td>4</td>
<td>5</td>
<td>9</td>
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<tr>
<td>2011</td>
<td>5</td>
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<td>2012</td>
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<td>2013</td>
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<td>2014</td>
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<td>2016</td>
<td>7</td>
<td>10</td>
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</tr>
<tr>
<td>2017</td>
<td>8</td>
<td>10</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>58</td>
<td>88</td>
<td>146</td>
</tr>
</tbody>
</table>
Table 3. List of counties involved in the outcome of alcohol-induced mortality from 2007 to 2017

<table>
<thead>
<tr>
<th>Kentucky Counties</th>
<th>Frequency</th>
<th>Missouri Counties</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boone County</td>
<td>3</td>
<td>Boone County</td>
<td>4</td>
</tr>
<tr>
<td>Bullitt County</td>
<td>2</td>
<td>Buchanan County</td>
<td>4</td>
</tr>
<tr>
<td>Campbell County</td>
<td>4</td>
<td>Butler County</td>
<td>2</td>
</tr>
<tr>
<td>Clark County</td>
<td>1</td>
<td>Camden County</td>
<td>1</td>
</tr>
<tr>
<td>Daviess County</td>
<td>6</td>
<td>Cass County</td>
<td>1</td>
</tr>
<tr>
<td>Fayette County</td>
<td>11</td>
<td>Clay County</td>
<td>11</td>
</tr>
<tr>
<td>Hardin County</td>
<td>5</td>
<td>Franklin County</td>
<td>1</td>
</tr>
<tr>
<td>Jefferson County</td>
<td>11</td>
<td>Greene County</td>
<td>11</td>
</tr>
<tr>
<td>Kenton County</td>
<td>11</td>
<td>Jackson County</td>
<td>11</td>
</tr>
<tr>
<td>Madison County</td>
<td>1</td>
<td>Jasper County</td>
<td>1</td>
</tr>
<tr>
<td>Meade County</td>
<td>1</td>
<td>Jefferson County</td>
<td>8</td>
</tr>
<tr>
<td>Pulaski County</td>
<td>1</td>
<td>Platte County</td>
<td>2</td>
</tr>
<tr>
<td>Warren County</td>
<td>1</td>
<td>St. Charles County</td>
<td>9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>58</strong></td>
<td><strong>St. Louis city</strong></td>
<td><strong>11</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>St. Louis County</strong></td>
<td><strong>11</strong></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td><strong>88</strong></td>
</tr>
</tbody>
</table>
Effect of robust PDMPs on alcohol-induced mortality

In the difference-in-differences model (Table 3; F=22.09; p<0.001), the shift of alcohol-induced mortality after restricting prescription opioid use through mandating PDMP use was not statistically significant (p>0.05) among adults residing in Kentucky compared to Missouri.

Table 4. Alcohol-induced mortality outcomes of robust PDMP implementation among adults living in Kentucky (treatment state) compare to Missouri (control state).

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Alcohol-Induced Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimates</td>
</tr>
<tr>
<td>Difference-in-differences</td>
<td>14.49</td>
</tr>
<tr>
<td>Treatment State (vs. Control State)</td>
<td>17.32</td>
</tr>
<tr>
<td>Post-Policy (vs. Pre-Policy)</td>
<td>16.19</td>
</tr>
<tr>
<td>Moist Counties (vs. Wet Counties)</td>
<td>-5.55</td>
</tr>
<tr>
<td>Population (Per 100,000)</td>
<td>-11.85</td>
</tr>
<tr>
<td>Counties with Unreliable Mortality</td>
<td>-34.19</td>
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</tbody>
</table>

*p<0.05, **p<0.001

Change in alcohol-induced mortality from 2007 to 2017

The average mortality in Kentucky was significantly 17.3% higher than Missouri during the entire time period when other things remain equal (Table 4; p<0.05). As shown in Figure 1, the average mortality in Kentucky was always higher than Missouri, except the year 2008. The overall mortality trend was positively associated with time in each state, Kentucky (correlation coefficient, ρ=0.40) and Missouri (ρ=0.25). When comparing the mortality in both states before and after the policy change in 2012, the post-policy period had 16.2% higher death rate than the pre-policy period while everything else stays equal (p<0.05). The counties with moist alcohol
sales policy did not show any significant results on the mortality change compare to those with the wet policy. When population in a county increased by 100,000 people, the alcohol-induced death rate decreased by 11.8% on average while holding other conditions equal (p<0.001). The counties that had less than 20 count of deaths showed 34.2% lower death rate on average than the other counties (p<0.001).

Figure 1. Trend in average alcohol-induced mortality among adults living in Kentucky (treatment state) and Missouri (control state) between 2007 and 2017.

*Kentucky House Bill 1 was implemented in 2012 (red line).
Discussion

I evaluated the alteration of alcohol-induced mortality after implementing PDMP use mandate in Kentucky. The finding suggested that the causal effect of comprehensive PDMP in Kentucky was not statistically significant in changing alcohol-induced deaths among the adult population. The alcohol-induced mortality in Kentucky was mostly greater than that in Missouri. Each state had an increase trend in alcohol-induced mortality over time period, therefore, the mortality in the post-policy period for both states was greater than that in the pre-policy period. This increase trend of crude mortality corresponds with the national increasing trend since 2010 (Xu, Murphy, Kochanek, Bastian, & Arias, 2018). Regardless of these trends, the trajectory of outcomes from Kentucky did not diverge significantly from Missouri.

It could be possible that the policy change had an effect on maintaining the status quo of alcohol-induced mortality. Instead of depending on alcohol use, people could substitute illicit opioids or other alternative substances. The heterogeneous response toward the policy change could also generate non-significant result. For example, appropriate pain management guidance from practitioners using Kentucky PDMP could mute the increase tendency of drug misusers substituting alcohol for prescription opioids. In addition, migration effect is neglected. Kentuckians could migrate to Missouri or other neighboring states without robust PDMPs to obtain prescription opioids without relying on alcohol use. Likewise, moist county residents could easily migrate to neighboring counties and generate non-significant results versus wet county residents. The last possible cause is that in both Kentucky and Missouri, deaths by alcohol have been increasing, and any effects of PDMPs may be difficult to detect within the increasing trends in both states.
The control state has several concerns in serving as a counterfactual. One concern is that Kentucky did operate a PDMP prior to 2012, while Missouri has never had a state-wide PDMP. It could be better to find another comparison state that had a PDMP similar to Kentucky’s before 2012 and has not implemented robust features. However, without a use mandate, people can easily find prescribers who do not use the PDMP in order to receive inappropriate prescription opioids, as was the case prior to KyHB1 adoption when most prescribers did not utilized the PDMP (Freeman, Goodin, Troske, & Talbert, 2015). Hence, I assumed both Kentucky and Missouri had non-treated status before 2012. Another concern is about satisfying the common trend assumption in difference-in-differences design. Apparently in Figure 1, similar trends are observed between 2009 to 2012, sharing similar upward slopes. Therefore, the common trend assumption is not violated in this study. One last concern is that PDMP implementation in Missouri started in 2017 in 43 counties (approximately a third of counties). This started on April 25th among 14 jurisdictions and expanded gradually via those counties (Saint Louis County, 2019). These PDMPs could be negligible since they do not uniformly cover the state, so people could easily travel to avoid the effect of PDMPs.

Larger population in a county was related to a lower percentage of mortality. This finding could imply potential urban-rural disparity on alcohol-induced mortality. However, Dixon and Chartier (2016) reviewed that urban residents tend to use more alcohol than rural residents and the alcohol use disorder incident trend was similar across the regions. Furthermore, adults older than 50 living in urban Kentucky presented higher rates of hospitalization caused by concurrent alcohol and medication use between 2002 and 2012 compare to those in rural area (Zanjani, et al., 2016).
Limitations

This study has several limitations. Firstly, the research design might not capture the true causal effect of policy change. Unobserved or unconsidered variables could be the cause. Drug abusers could prepare for the policy change, and this is not reflected in this analysis. For example, they could receive excessive prescription opioids beforehand and use them instead of substituting alcohol. Accordingly, latency of policy adoption could be longer than the research design in this study, although the policy compliance rate among practitioners was quite fast. Another possible cause of the error is that the predicted outcome is too narrow to observe the hypothesis. For instance, substance misusers might be healthy enough to survive after increasing alcohol consumption. Also, age-adjusted mortality might be an appropriate outcome measure instead of the crude rate because age distribution might vary between the counties. Thus, the crude death rate may not represent the effect of PDMP on alcohol-induced mortality caused by substituting alcohol for prescription opioid use.

Secondly, the obtained data has several defects. As mentioned above, CDC WONDER does not rely on the death count less than 20. They considered it as statistically unreliable based on a relative standard error of 23 percent or more. However, this study was designed by county with a specific underlying reason, so quite a few counties are likely to have small numbers of deaths. If a county has low population, the number of deaths less than 20 could be meaningful. Thus, I re-calculated the mortality with raw data and included those counties labeled unreliable. Moreover, because of confidentiality constraints, they suppressed the data when the count is less than 10 (Centers for Disease Control and Prevention, 2018). Consequently, the amount of data obtained was less than the actual state overall counts. The state-level death counts were much
greater than what I actually extracted. Therefore, a selection bias threat exists because higher population counties are more likely to be posted.

Thirdly, this study did not account for some policies that could affect the result. KyHB1 included a pain management facility regulation in addition to the use mandate. The PDMP could encompass abusive prescription behaviors from those clinics, but it is difficult to account on the sole effect of PDMP. Also, alcohol-related tax policies are not included, which are another factor causing behavior change in alcohol use.

Finally, this analysis cannot be generalized to other states, nation-wide level, individual-level, or population under age 18. Also, it does not present long-term effect of the policy change.
Conclusion and Policy Recommendation

In conclusion, prescription opioid access restriction did not have a statistically significant substitution effect of alcohol-induced mortality among adults. This is one of the first studies assessing adverse events of PDMPs, especially about unintended consequences of alcohol-induced death. In addition, this analysis did not find alcohol sales policy to be a significant variable in evaluating the relationship between the program and alcohol-induced mortality.

For these reasons, I recommend retaining the mandate use feature in Kentucky PDMP and evaluating the findings with further studies as follow:

- Evaluate using other outcomes such as age-adjusted mortality, morbidity, and drunken driving caused deaths/crashes.
- Analyze using individual-level deidentified death report data.
- Expand the range of population (adolescent) and region (other states with mandatory use laws).
- Assess long-term effects of PDMPs on alcohol-related outcomes.
- Investigate potential urban-rural disparities on alcohol-related outcomes after adopting the revised PDMP in Kentucky.
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References


