IMPERFECT SUBSTITUTES:
EXAMINING WHETHER AND TO WHAT EXTENT OFFERING OPIOID SUBSTITUTION THERAPY (OST) MAY BE INCREASING REGIONAL POLYDRUG USE

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Devin Charles Ringger, B.A.

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ABSTRACT

Opioid Substitution Therapy (OST) attempts to curb opioid addiction by substituting a treatment opioid (i.e. methadone, buprenorphine, naltrexone, etc.) for an addict’s primary drug of abuse (i.e. heroin, oxycodone, etc.). However, insofar as patients continue abusing their preferred drug during treatment, OST programs may be increasing the absolute number of drugs patients are abusing. To the extent that some OST patients “divert” their treatment drugs into illicit markets, OST programs may also be increasing the absolute number of opioids abused by the surrounding population, as well. If corroborated, these trends would indicate a connection between OST treatments and the phenomenon most correlated with drug overdoses—“polydrug use,” or the concurrent use multiple drugs by one person.

To ascertain whether and to what extent OST treatment provisioning may be affecting regional polydrug use, this study models the annual number polydrug treatment episodes reported in a state as a function of that state’s OST patient population. The study relies primarily on two administrative datasets—the National Survey of Substance Abuse Treatment Services (N-
SSATS) and the Treatment Episode Data Set-Admissions (TEDS-A)—collected between 2002 and 2006.¹

Using a two-way fixed-effects model that controlled for both state and annual fixed-effects, as well as for state populations and population densities, this study discovered a statistically significant positive correlation (p<.002) between a state’s OST patient population and the number of polydrug treatment episodes reported in the state. The model predicts that a doubling of a state’s OST patient population will be correlated with a 6.16-percent increase in polydrug episodes. These results suggest that OST treatment may be producing a dangerous side effect. At the very least, they suggest that, when considering potential expansions to OST programs, circumspect policymakers should also consider simultaneous expansions to services that address the predicted increase in polydrug use.

¹ Unfortunately, because the N-SSATS data from 2007 to 2012 are currently undergoing additional disclosure review, this study only analyzed data from the years 2002 to 2006. However, once the N-SSATS data from 2007 to 2012 become available in mid-2016, the analysis could be extended to include all years from 2002 to 2012.
DEDICATION

This study is dedicated my grandfather, Robert Doris Charles, Jr., who will always be my best friend and my hero, and who taught me that everyone deserves respect, compassion, a smile, and a helping hand. Not to mention a joke. You will always be with me, Big Dad.

And to all those throughout the world suffering from addiction, in its many and terrible forms. To the mothers, fathers, sons, and daughters; to the friends and strangers; and to ourselves (if we dare to be honest). May we all see ourselves in the eyes of others, and realize that to extend a hand to another is to lift ourselves up.

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-Devin Charles Ringger
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INTRODUCTION

Opioids are a family of narcotic painkillers derived from the poppy plant, including opium, morphine, heroin, hydrocodone, oxycodone, and fentanyl. (Amato et al. 2005). Opioid addiction is associated with immense costs—both fiscal and human—borne by both those who are addicted, as well as the nation as a whole (Stein 2015). For example, the United Nations has estimated that the total social and economic costs in developed nations averages 0.4 percent of GDP for heroin addiction alone. (Amato et al. 2005; UNIDCP 2001). The total costs of opioid addiction are much higher. (Amato et al. 2005). From 1992 to 2012, the number of Americans addicted to prescription opioids increased from 4.9 million to 12.5 million. (McHugh et al. 2015). In the last two decades alone, the number of Americans seeking treatment for opioid (narcotic painkiller) addiction has increased by more than 500 percent and the number of Americans who die each year from accidental prescription opioid overdoses increased nearly 400 percent. (SAMHSA & Center for Behavioral Health Statistics and Quality, 2014). Of particular concern is the fact that the rates of drug abuse and overdoses closely “parallel” similar increases in the rate at which Americans receive prescriptions for opioids. (McHugh et al. 2015). A significant portion of these prescriptions are written to individuals as part of addiction treatments. (McHugh et al. 2015).

Opioid Substitution Therapy (OST), the most widely supported and the most widely deployed treatment for opioid addiction, proposes to substitute a prescribed opioid that boasts more manageable addictive properties (the “opioid substitution drug” or OSD) for the addict’s opioids of abuse and then leverage those more manageable properties to wean opioid addicts off
of opioids entirely (Amato et al 2005). While the research literature generally supports the efficacy of OST, the same studies have noted several alarming trends: 1) that OST patients often persist in using their primary opioids of abuse during treatment (Teter, Christian 2006; Petrushevska, Tatjana 2015); 2) that many OST patients “divert” their OSDs into regional drug markets to finance purchases of their primary opioids of abuse (Bretteville-Jensen, Anne 2015; Teter, Christian 2006; McCabe, S. E. 2014); and 3) that at least some OST patients who have never used heroin prior to entering OST end up abusing heroin by the end of treatment (Oser, Carrie B. 2015; Potter, Jennifer Sharpe 2015; McHugh, R. Kathryn 2015; Dasgupta, Nabarun 2014). Furthermore, a recent study found that polydrug use (i.e. the concurrent use of multiple drugs simultaneously) is the strongest predictor of both lethal and non-lethal overdoses (Petrushevska, Tatjana 2015).

Taken together, these findings suggest that while OST services may be helping to raise a substantial portion of patients out of addiction, they may also be increasing polydrug use—and thereby overdoses—in the surrounding communities. This study seeks to either corroborate or dispel some of these suggestions by evaluating the relationship between the magnitude of OST services in a geographic region (i.e. higher per capita OST patient counts) and the annual number of polydrug episodes reported.

**LITERATURE REVIEW**

I) **Substantive Literature Review**

In the past 20 years, prescription drug abuse in the United States has increased by over 250 percent (SAMHSA, 2013). From 2000 to 2010 alone, the number of Americans seeking

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2 Opioid Substitution Therapy (OST) is the only Opioid Treatment Program (OTP) approved in the United States; thus, as used in this paper and with respect to data collected in the United States, the acronyms OST and OTP are synonymous.
addiction treatment for prescription opioids (painkillers) increased by more than 500 percent (SAMHSA; Center for Behavioral Health Statistics and Quality, 2014). Opioid-addicts are now the second largest group of addiction treatment-seekers in the United States, behind alcohol addicts (SAMHSA, 2013), and more American high school students admit to having abused opioids than any other medications. (Monitoring the Future, 2013; McCabe, West, Teter, & Boyd, 2012).

Opioid drug addiction is correlated with a host of negative outcomes, both for individual addicts and for the countries in which they reside. With respect to the addicts themselves: opioid users (especially heroin users) live shorter lifespans than non-opioid users (Davoli et al., 1997). Between 2000 and 2010, accidental overdoses on prescription opioids—including but not limited to oxycodone, hydrocodone, and fentanyl—increased almost 400 percent (Calcaterra, Glanz, & Binswanger, 2013).

Fortunately, several addiction treatment methods have arisen in the wake of this prescription opioid addiction crisis, (Veilleux, Jennifer C. 2010), and preliminary studies suggest that some such treatment methods are effective at treating addiction to prescription opioids (Stein, Michael D. 2015; Hilario, E. Yvette 2015; Cochran, Bryan N. 2014; Gryczynski, Jan 2014; Dakwar, Elias 2015; Martin, Caitlin E. 2015; Potter, Jennifer Sharpe 2015; Oser, Carrie B. 2015; Hadland, Scott E. 2014). Such treatments fall into two general categories.

The first category—abstinence, or “cessation” treatment—is fairly straightforward; such programs simply require participants to completely terminate their drug. The second category—maintenance treatment (MT)—seeks to gradually wean addicts off of opioids entirely by tapering their drug use using successively lower doses. Understandably, this category of addiction treatment is more nuanced than its abstinence counterpart, at least insofar as the same
shared goal can be achieved using several different techniques, each of which may be applied separately, or in combination with one another. (Veilleux et al. 2010; Amato et al. 2005; Sees et al. 2000). In the United States, two forms of maintenance treatment have become generally available: 1) Opioid Substitution Treatments (OSTs) that seek to wean opioid addicts off of opioids using “opioid substitution drugs”\(^3\) (OSDs) instead of addicts’ primary substances of abuse, and 2) opioid antagonist treatments that seek to attenuate the negative effects of opioid withdrawal using medications such as naloxone and suboxone (Hilario, E.Yvette 2015). A third category of maintenance treatment specifically designed to treat the most virulent forms of heroin addiction—Heroin Maintenance Treatment (HMT)—applies the same logic as OST but without the substitution of OSDs for the primary substance of abuse. (Ferri, Davoli, & Perucci 2003). However, HMT is not currently available in the United States because heroin’s status as a Schedule I controlled substance under the United States Controlled Substances Act prohibits doctors from prescribing heroin to patients. (21 U.S.C. §801 et seq.).

Of all the maintenance treatments, Opioid Substitution Treatment (OST) is by far the most widely studied, as well as the most widely deployed (Veilleux et al. 2010; Amato et al. 2005; Sees et al. 2000). The use of OST treatment is supported by a large body of empirical literature attesting to its strengths. (Amato et al. 2005; Sees et al. 2000). Medications currently prescribed for OST treatments include methadone (Amato, Laura 2005), LAAM (Clark et al. 2003), and buprenorphine (Mattick 2009).

\(^3\) Opioid Substitution Drugs (OSDs) are also frequently referred to as opioid “agonists,” a term that refers to their general tendency to be processed by the body in the same manner as other opioids and to produce similar effects. The opposite of an “agonist” is an “antagonist,” a chemical that blocks the physical reaction created by the “agonist.”
Unfortunately, several recent studies have revealed that OST treatments are not without unintended consequences. For example, it has become apparent that some prescription drug users who had never tried heroin before seeking OST maintenance treatments end up transitioning to heroin use by the end of treatment. (Oser, Carrie B. 2015; Potter, Jennifer Sharpe 2015; McHugh, R. Kathryn 2015; Dasgupta, Nabarun 2014). Furthermore, prescription drug users who use heroin have been found to have higher incidences of other substance abuse disorders (Wu, Woody, Yang, & Blazer, 2011) and poorer outcomes in addiction treatments (Weiss et al., 2011). Worse yet, the research community is coalescing around the consensus that OST is demonstrably less effective at treating heroin addiction than it is at treating prescription opioid addiction. (Charles J. Robertson 2015; Delcher, Chris 2015; Al-Tayyib, Alia A. 2014; Nielsen, Suzanne 2015; Arreola, Sonya 2014; Cochran, Bryan N. 2014; Dasgupta, Nabarun 2014; McHugh, R. Kathryn 2015; Darke, Shane 2014). This suggests that, while the aforementioned OST maintenance treatments may help pull one subset of addicts out of their opioid addiction, the very same treatments may also be pushing another subset deeper into the morass.

This suggestion is especially troubling in light of recent research suggesting that the strongest predictor of fatal drug overdose is polydrug use, or the use of more than one drug at the same time (Petrushevska, Tatjana 2015). Underscoring this danger, several studies have demonstrated that many opioid addicts in OST maintenance treatments persist in using their primary opioid of choice during treatment (Teter, Christian 2006; Petrushevska, Tatjana 2015). In this light, it is plausible that participation in OST maintenance treatments may actually increase an individual’s risk of overdose. Furthermore, given that other studies have demonstrated that many addicts in maintenance treatments “divert” their substitute medications into the illegal market in order to buy their drug of choice (Bretteville-Jensen, Anne 2015; Teter,
Christian 2006; McCabe, Sean Esteban 2014), it is even plausible that the use of OST maintenance treatments might be increasing the entire surrounding community’s overall risk of overdose. For these reasons and more, some scholars have suggested that certain subcategories of individuals at high risk of transitioning into heroin addiction might benefit from other, more tailored forms of intervention (Jamison et al, 2010).

II) GAPS IN THE SUBSTANTIVE LITERATURE

Unfortunately, many of the questions posed above remain unanswered in the research literature. For instance, while several studies have surveyed OST patients to glean the extent to which individual patients divert their OSDs into local markets (Bretteville-Jensen, Anne 2015) and while demographic surveys have revealed the extent to which the drug using population at large has gained access to drugs that were originally prescribed to third-parties (SAMHSA), to the author’s knowledge no studies have attempted to parse out exactly what impact OST services themselves may be contributing to community drug markets and drug use patterns. In part, this gap is the result of insufficient data. As an illustration, while the most direct means of studying the impact of OSD diversion on local drug use would be to examine the number of prescriptions for OSDs written by zip code (such as the data collected various Prescription Drug Monitoring Programs), such data are understandably sensitive and thus unavailable for analysis except by a very limited subset of researchers. (Brady, JE 2014). Furthermore, the administrative data on OTP facility and patient counts that this study proposes using to surmount this problem (N-SSATS) have only recently been collected in a standardized format for enough consecutive years
to perform the requisite analysis. Prior to the current period of standardized collection, no set of consecutive years existed for more than a four year span.  

Similarly, much of the data currently available on potentially negative consequences of OST services have been produced in studies using samples that are unrepresentative of the United States. (Hondebrink, Laura 2015; 2014; Onyeka, Ifeoma N. 2015; Ekholm, Ola 2014). This significantly limits the ability to apply the conclusions reached in such studies to the United States (i.e. they have limited external validity).

Likewise, many of the studies revealing the weaknesses of OST services cannot currently be replicated in the United States because the original studies were produced by comparing OST against treatments that cannot be practiced legally in the United States. (Blanken, P. 2012). For instance, while the most prominent alternative to OST maintenance treatment for heroin addicts in Europe is heroin maintenance treatment (HMT), and while the only therapeutic difference between receiving HMT and receiving OST is that HMT participants are actually prescribed their drug of abuse—heroin—rather than a substitute, the United States Controlled Substances Act completely prohibits the scientific study of any Schedule I controlled substance, including heroin. (23 U.S.C. §801 et seq.). Furthermore, America’s widespread influence over the world of international diplomacy has resulted in the widespread adoption of similar prohibitions on heroin research. Notwithstanding the general prohibition against HMT globally, several studies have undertaken to examine the efficacy of HMT, and their preliminary results are promising (Minozzi, S. 2014; Uchtenhagen, Ambros A. 2011; Ferri, M. 2011; Blanken, Peter 2010; Eiroa-Orosa, Francisco José 2010; Karow, A. 2010; Oviedo-Joekes, Eugenia 2010; Strang, John 2010).

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III) Empirical Literature Review

a) Data Collection

Most studies on individual drug user characteristics have relied on author-conducted surveys of specific groups of individuals identified (or inferred) *ex ante* to be drug users. (Bretteville-Jensen, Anne 2015; 2014). Some of the more successful studies have leveraged specific conditions (i.e. proximity to a treatment center, local laws requiring treatment seekers to fill out intake forms, etc.) to create panel (cross-sectional, time series) datasets whose analysis can reveal prevalence and frequency data within the surveyed population. (Bretteville-Jensen, Anne Line 2015, 2014; Kecojevic et al. 2012). Unfortunately, one consequence of choosing a specific population in advance is the fact that the results are often limited to similar populations (i.e. the studies have limited external validity).

Other studies have utilized “natural experiments” by exploiting unique, exogenous changes in variables of interest, including changes in the rate of prescribing pharmaceutical opioids (Darke and Farrell 2014), supply-shocks in the heroin market (Hempstead & Yildrim 2014), and legislative changes that created a *per se* drugged driving blood toxicity level (Vindenes et al. 2014).

Still other studies have relied upon administrative data, including nationwide surveys (Robinson, Charles J. 2015), morbidity and mortality data (Calcaterra, Glanz, and Binswanger 2013), and data from prescription monitoring services (Ringwalt et al. 2014). The benefits of using administrative data are compelling. Such datasets usually contain expansive demographic and socioeconomic variables for each observation; they are often collected at regular intervals; and they often boast immense sample sizes. Several researchers have taken advantage of these and other characteristics of administrative data to produce longitudinal cross-section panel
datasets to analyze, amongst other topics, the price elasticity of heroin (Olmstead et al. 2014), the rate at which other opioids substitute for heroin in the illicit marketplace (Hempstead and Yildrim 2014), and the longitudinal effect of supervised injection services (Potier et al. 2014).

b) Methods of Analysis

Regardless of the means by which the underlying data are collected, many of the aforementioned surveys used similar methods of data analysis to arrive at their conclusions. For example, many researchers have relied on binary logistic\(^5\) and multinomial logistic regressions\(^6\) to study the impact of various determinants of drug use outcomes (e.g. environmental factors, sub-population densities/proportions, prior drug use histories, etc.) (Bretteville-Jenson et al. 2015; Hadland et al. 2014; Bali et al. 2013; Fiellin et al. 2013; Højsted, Jette 2013), as well as to reveal the odds-mean ratios for various subsets of respondents. (Bretteville-Jensen et al. 2015).

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\(^5\) A binary logistic regression is a regression that models the probability of a categorical dependent variable that is dichotomous (i.e. a dependent variable with only two discrete outcomes) as a function of the model’s independent variables. One example would be a model of the probability that an overdose took place in the previous calendar year (where 1=overdose and 0=no overdose) as a function of the respondent’s characteristics.

\(^6\) A multinomial logistic regression models the probability of a categorical dependent variable that can take more than two discrete values as a function of the model’s independent variables. For example, multinomial logistic regression has been used to model the probability of having either zero overdoses (category=0), one overdose (category=1), and more than one overdose (category=2) during the previous year as a function of the treatment-seeker’s characteristics (i.e. the treatment-seeker’s age, drug history, gender, etc.) (Bretteville-Jenson et al. 2015). Significantly, even though the values of these variables appear to be numerically ordered from least to most overdoses, the values are not ordinal and thus are not directly comparable (i.e. a value of “2” indicating more than one overdose does not indicate that the variable is twice the magnitude of the “1” values). Instead, the variables are categorical in nature, and the numbers used denote categories of discrete outcomes.
Likewise, several studies have used two-step hurdle models\(^7\) (Cameron & Trivedi, 2005) to generate both independent and dependent variables. (Bretteville-Jensen et al. 2015; 2014).

More generally, the construction of cross-sectional panel datasets from consecutively administered annual surveys is a widely accepted statistical practice, as is the use of time-series and instrumental variable models to analyze such datasets. (Baltagi et al. 2013). These practices are also widely used by social scientists engaged in analyzing drug using populations. (Petrushevska, Tatjana 2015; McCabe et al. 2014; Bali et al. 2013; Kecojevic et al. 2012; Bohnert et al. 2011; McCabe et al. 2008a; 2008b; 2007).

**HYPOTHESIS**

All else being equal, higher magnitudes of Opioid Substitution Therapy services in a geographic region (i.e. higher per capita OST patient counts) will be positively correlated with the number of substance abuse related treatment episodes involving polydrug use.

**STUDY DESIGN**

I) **Preliminary Design Choices**

An important initial decision in designing this study involved deciding on what unit of measure would be best for analyzing the data. At first glance, it seemed appropriate to use

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\(^7\) A two-step hurdle model is a “count” model in which two separate processes are used to generate the counts: one process is used to produce the zeros, and another is used to produce the values other than zero. In general, an initial binary probability model is used to determine whether an outcome will be zero or non-zero. Then, a second model (which is not required to be the same model as the binary probability model used in the first step) is used to generate the “counts” for the values already determined to be non-zero. Using the same example as above, a researcher might first model the probability of a treatment-seeker having experienced any number of overdoses in the previous year (1=at least one overdose, 0=no overdoses), and then use a separate model to estimate the number of overdoses for each non-zero value produced in the first step.
individual treatment episodes (i.e. asking whether and to what extent the number of substances of abuse reported in an individual treatment episode may be correlated with the state-level treatment provisioning characteristics of the state-year in which the observation occurred). Doing so would have allowed the model to control for the influences of any additional treatment-seeker characteristics that may be relevant to the number of substances of abuse reported (i.e. gender, age, number of previous treatment episodes, etc.). Additionally, the sheer number of observations available in the TEDS-A dataset (over 1 million each year) would have ensured that such a study could have measured any observed effects with a high degree of statistical significance.

Nonetheless, other considerations weighed against using episode-level data. Most importantly, by limiting itself exclusively to a universe of treatment-seekers, an episode-level model would suffer from substantial selection bias and thus yield results with significantly limited external validity. Such a model could not, for instance, consider how state-level OST provisioning might be affecting individuals who were not represented in the treatment-episode dataset (i.e. those who did not use substances of abuse in a given year, either because they had never abused them, stopped abusing them, or had yet to abuse them). In other words, an episode model would only be able to ascertain any effects that arose within the population of continuing substance abusers; this study would thus remain blind to the most significant changes substance abuse—those that indicate vast improvement and those that indicate vast deterioration. In addition, such a study would also fail to account for many of the externalities of opioid maintenance treatment that have already been observed in the research literature. For example, an episode-level study would be incapable of accounting for the impact that treatment
provisioning may have on the larger community’s drug use, such as the price and substitution effects created by the black-market diversion of treatment drugs.

Fortunately, an appropriately coded state-level model can surmount these problems and introduce several other benefits as well. First, by controlling for state population, a state-level analysis can recapture the previously unobserved non-substance abusers and take account for improvements and deteriorations in state-level substance abuse (as opposed to merely observing changes within the universe of patients involved in treatment-episodes). Second, by looking at the entire state population and the entire state’s polydrug use, a state-level study can take full account of any intermediary forces (i.e. black-market diversions, price effects, increases in illicit use of maintenance drugs by third-parties, etc.) that could be obscured otherwise by looking too granularly at the data. Third, by looking at consistent geographic regions, a state-level model can use fixed-effects to control for any other unobserved differences between states; thus, such a model should boast a higher explanatory power (i.e. higher R²) than merely an episode-level study examining unlinked patient data. Fourth, using state-level data will enable this study to be replicated more easily at a later time, and thus ensure its results are more conducive to subsequent verification or refutation.

Finally—as a practical matter in designing a public policy study—while an episode-level study might provide useful information to healthcare professionals by describing the effects of certain treatment-seeker profiles, policy-makers—not healthcare professionals—are in the best position to effect changes in the independent variable (opioid maintenance treatment provisioning). Instead, those most capable of making policy decisions on the basis of any of this study’s observed results are those who control the funding of substance abuse treatments and the legality of the most conspicuous alternatives (treatments, such as HMT, that use the actual
substances of abuse), decisions that predominantly take place at the state and federal levels. This is particularly noteworthy with respect to the proposed Medicaid expansion instrument, which represents a state-level decision that influences treatment provisioning indirectly with a funding mechanism.

II) Data Sources

Two principle data sources were used in constructing the study’s dataset. Each source was selected for its ability to capture an annual state-level measurement of an essential element of the proposed hypothesis using data collected from sources with sufficiently high response rates (i.e. greater than 95-percent) to be considered representative of the underlying state population.

a) The National Survey of Substance Abuse Treatment Services (N-SSATS), 2002-2006

The first source—the National Survey of Substance Abuse Treatment Services (N-SSATS)—is an annually conducted point-prevalence (i.e. “snapshot”) survey survey survey survey survey survey survey of all substance abuse treatment facilities in the United States that receive federal funding. It is administered by the Substance Abuse and Mental Health Services Administration (SAMHSA) in conjunction with the Drug and Alcohol Services Information System (DASIS), and is designed to collect data on the availability, character, and utilization of substance abuse treatment facilities (both public and private) throughout all 50 States and the the U.S. Territories. N-SSATS collects data on both drug and alcohol treatment services, as well as detailed client counts (using the last weekday in March as a reference date). While participation is not mandatory, only those treatment facilities that have provided responses are included in SAMHSA’s Substance Abuse Treatment Facility Locator. Like the TEDS-A dataset, the facility response rates are consistently above 95-percent.

8 http://findtreatment.samhsa.gov
Currently, comprehensive N-SSATS data are available for the years 2000 to 2006, but additional data from 2007 to 2014 are expected to be released during 2016.

In order to comply with the N-SSATS survey, each substance abuse treatment facility is required to submit a summary of the substance abuse treatments it currently offers, including a count of its patients who receive various opioid treatment programs (OTP). While several changes in the format of the N-SSATS questionnaire has led to different measures of such clients being reported each year, the total number of patients receiving OTP opioid addiction treatments can still be calculated by summing each facility’s client count from each category. Likewise, these individual facility sums can be collapsed at the state level for each year to reveal the total number of patients in the state receiving opioid maintenance therapy at the time. This state-level opioid maintenance patient count is used as the independent variable for this study—otppatient.

b) The Treatment Episode Data Set – Admissions (TEDS-A), 2002-2006

The second source—the Treatment Episode Data Set – Admissions (TEDS-A)—is a national data system that collects patient-level data from all publicly funded health facilities in the United States, including data on individual admissions to substance abuse treatment facilities. It provides annual data on the number and characteristics of individuals utilizing substance abuse services that have received public funding, including detailed data on the treatment-seeker’s prior drug use and substance abuse treatment history, as well as demographic and socio-economic characteristics. With over 95-percent of all health facilities in the United States

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9 For example, in 2002, the N-SSATS collected data on total clients who received methadone and/or LAAM (levo-alpha acetyl methadol), another opioid treatment drug. By 2006, however, the use of LAAM had fallen into disfavor in the United States, and the N-SSATS questionnaire only inquired as to total methadone clients. Likewise, by 2013, similar changes in the relative use of various opioid maintenance drugs had led to the questionnaire inquiring about any patients using methadone, buprenorphine, or vivitrol.
reporting TEDS-A data, the dataset is highly reflective of the total number of treatment episodes that occur in the United States each year. TEDS-A data are available for all years from 1992 to 2012.

Significantly, rather than looking at individual treatment-seekers themselves, the primary unit of analysis in TEDS-A data is a “treatment episode”—any individual incident in which a patient is required to submit to a substance abuse screening at treatment admission. Thus individuals who seek treatment multiple times in a single year appear as multiple observations in the dataset. For this reason, the dataset should not be used as a measure of the drug using population, but rather as measure of the overall incidence of particular kinds of substance abuse treatment episodes.

The data collected are particularly useful for this study because each patient involved in a treatment episode is required to divulge the number of substances currently being abused (up to three substances). The resulting variable—numsubs—is thus capable of being used to create a new binary dummy variable—polydrug—to indicate each treatment episode in which a patient reported abusing more than a single substance (i.e. when numsubs>1). When this variable is summed at the state level for each year, the resulting count represents the total number of treatment episodes in the state in which the patient reported being a polydrug user. This state-level polydrug count is used as the dependent variable in this study.

c) Wolfram|Alpha Knowledgebase, 2015

Additional control variables were added using Wolfram|Alpha Knowledgebase, 2015, a computational search engine that cross-references publically available datasets to provide precise answers to statistical inquiries inputted as regular expressions (e.g. “Arkansas population, 2006

\(^{10}\) http://www.wolframalpha.com/
to 2012”)

This study leveraged Wolfram|Alpha’s ability to output tabular data in order to code demographic data (e.g. population and population density data) at the state level by year. In producing these demographic data, Wolfram|Alpha relied upon U.S. Census Bureau data, including: American FactFinder’s “2005-2007 American Community Survey 3-Year Estimates,” The National Data Book’s “The 2009 Statistical Abstract,” and the National Center for Education Statistics’s “Digest of Education Statistics.”

d) The Advisory Board Company’s “Where the states stand on Medicaid expansion”

Finally, because the anticipated high correlation between OTP treatment provisioning and state polydrug use was expected to introduce substantial simultaneity problems in the proposed regression, this study attempted to create an instrumental variable using the Advisory Board Company’s Daily Briefing “Where the states stand on Medicaid expansion,” a continuously updated map indicating which States have thus far accepted the Affordable Care Act’s Medicaid Expansion provision. Produced in conjunction with American Health Line, the Daily Briefing represents a collective effort to track each state’s posture by evaluating the comments and actions of state-level legislators and public officials. As of this writing, the most recent update occurred on January 13, 2016. In anticipation of using a state-level instrumental variable that would capture any exogenous change in opioid maintenance treatment provisioning, the Advisory Board Company’s briefing was used to add two additional variables to the dataset.

The first variable—medicaid_expansion—was added as an instrumental variable whose value equals “1” for every year in which the state had accepted the additional federal funding available under the Affordable Care Act’s Medicaid expansion, and “0” for every other

---


12 https://www.advisory.com/daily-briefing/resources/primers/medicaidmap
observation. This variable is considered to be a valid instrument for opioid maintenance provisioning because 1) at least some of the funding would provide payment for substance abuse treatments by Medicaid recipients who were previously unable to qualify for treatment, and 2) the motivations and considerations behind accepting or refusing to accept the Medicaid expansion include far more factors (including political ones) than simply the state’s level of polydrug use. In theory, this instrument should satisfy the inclusive and exclusive conditions required to create a valid instrumental variable. The second variable—republican_governor—is a binary indicator variable used to indicate that a state’s governor is a member of the Republican party. The variable was added to purge any omitted variable bias that would have been introduced by simply including a politically-influenced instrumental variable.

Nonetheless, despite the potential validity of this instrumental design, the study was ultimately unable to perform its proposed instrumental variable analysis because too little time has passed since most states have accepted or rejected the Medicaid expansion (less than one year in nearly all cases). In particular, because the TEDS-A and N-SSATS surveys generally take additional time to collect and process, the relevant data are simply unavailable at this time.\textsuperscript{13} Thus, the two newly created variables—medicaid_expansion and republican_governor—were removed from the dataset.

\textsuperscript{13} The most recent TEDS-A data available is the 2012 survey. In addition, the available N-SSATS public use data contains a gap for the years 2006 to 2012.
### III) Variables

*Table 1: Description of variables of interest, predicted relationships, and basis in literature for consideration*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
<th>Predicted Relationship</th>
<th>Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dependent Variables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>polydrug</em></td>
<td>Number of substance abuse treatment episodes where treatment-seeker reported being a polydrug user; summed at the state level, by year</td>
<td>+</td>
<td>Petrushevskaya, Tatjana 2015; Teter, Christian 2006</td>
</tr>
<tr>
<td>n:</td>
<td>247</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range:</td>
<td>{926; 207,580}</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean:</td>
<td>20,979</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD:</td>
<td>31,800</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>ln_polydrug</em></td>
<td>Natural log of <em>polydrug</em> variable.</td>
<td>+</td>
<td>Petrushevskaya, Tatjana 2015; Teter, Christian 2006</td>
</tr>
<tr>
<td>n:</td>
<td>247</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range:</td>
<td>{6.830874; 12.24327}</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean:</td>
<td>9.357384</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD:</td>
<td>1.056978</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Independent Variables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Time Characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>year</em></td>
<td>Year of survey/treatment episode/summary statistic.</td>
<td></td>
<td>Baltagi, <em>Econometric Analysis of Panel Data</em></td>
</tr>
<tr>
<td>Range:</td>
<td>2002-2006</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>State Characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>State Geographic Characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>stfips</em></td>
<td>State FIPS code</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>State Population Characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>population</em></td>
<td>State population (in millions)</td>
<td>+</td>
<td>Baltagi, <em>Econometric Analysis of Panel Data</em></td>
</tr>
<tr>
<td>n:</td>
<td>247</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range:</td>
<td>{497,100; 35,980,000}</td>
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<td></td>
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<tr>
<td>Mean:</td>
<td>5,899,813</td>
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<td></td>
</tr>
<tr>
<td>SD:</td>
<td>6,459,431</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>ln_population</em></td>
<td>State population (in millions)</td>
<td>+</td>
<td>Baltagi, <em>Econometric Analysis of Panel Data</em></td>
</tr>
<tr>
<td>n:</td>
<td>247</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range:</td>
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</tr>
<tr>
<td>Mean:</td>
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<td></td>
</tr>
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<td>SD:</td>
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<tr>
<th>Independent Variables</th>
<th>State Characteristics</th>
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<td><strong>State Population Characteristics</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>popdens</strong></td>
<td>State population density</td>
</tr>
<tr>
<td>n: 247</td>
<td>Range: 0.000004404 ; 0.0036657</td>
</tr>
<tr>
<td></td>
<td><strong>+</strong></td>
</tr>
<tr>
<td></td>
<td><strong>ln_popdens</strong></td>
</tr>
<tr>
<td>n: 247</td>
<td>Range: -14.64825 ; -5.608737</td>
</tr>
<tr>
<td></td>
<td><strong>+</strong></td>
</tr>
<tr>
<td></td>
<td><strong>State Treatment Characteristics</strong></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>otppatient</strong></td>
<td>Raw Count of patients receiving Opiate Treatment Programs (OTP); summed at state level, by year</td>
</tr>
<tr>
<td>n: 247</td>
<td>Range: 0 ; 45,237</td>
</tr>
<tr>
<td></td>
<td><strong>+</strong></td>
</tr>
<tr>
<td></td>
<td><strong>ln_otppatient</strong></td>
</tr>
<tr>
<td>n: 232</td>
<td>Range: 0 ; 10.71967</td>
</tr>
<tr>
<td></td>
<td><strong>+</strong></td>
</tr>
</tbody>
</table>

### IV) Figures and Tables

The panel dataset aggregates state-level characteristics for all fifty (50) States in the United States and the District of Columbia for the years 2002 to 2006. Of the 255 possible observations in this panel dataset, only 232 observations are included in the regression. This reduction occurred for two separate reasons. First, seven (7) observations are missing because
several states failed to submit N-SSATS data for various years during the 5-year window.\textsuperscript{14} Second, model specification chosen for this regression uses logarithmic variables whose values are undefined when the underlying variables equal zero. Thus, any observation in which a state reported either zero OTP patients or zero polydrug episodes (not applicable) were necessarily excluded.\textsuperscript{15} This resulted in a further reduction of the sample space by fifteen (15) observations. The final sample size is thus 232 observations.

Several features of the data are worth noting prior to describing the regression analysis. First, Figure 1a illustrates that, in any given year, the independent variable—*otppatient*—varies widely across the states, from 0 to over 45,000. Of particular interest are those states without any patients in opioid maintenance treatment, as any observed value of *polydrug* in a given year will not be attributable to the *otppatient* variable. Neither would any observed variation in the *polydrug* dependent variable in these states be attributable to the *otppatient* variable across periods in which the *otppatient* variable does not vary.

\textsuperscript{14} The following States failed to submit N-SSATS data for the years indicated in parentheses: Alaska (2004, 2005, and 2006); Arkansas (2004); the District of Columbia (2004, 2005, and 2006); and West Virginia (2002).

Figure 1a: Total OTP patients in state, during 2006 (ranked from low to high, without controlling for state population)

Figure 1b depicts the number of polydrug episodes across the same time-period.

Notwithstanding the unexplained variation that appears in Figure 1b, a comparison of the two figures appears to reveal a visual consistency: States with high numbers of OTP patients also tend to have high numbers of polydrug episodes.
Figure 1b: Total count of polydrug treatment episodes in state, during 2006 (ranked from low to high by state OTP patient count, without controlling for state population)

However, raw patient count signifies very little about the relative levels of state provisioning without first controlling for state population, which varies widely as well (from less than 1 million to over 39 million). Figure 2a and 2b show the new relative measures of state OTP patients and state polydrug episodes after controlling for state population. The most apparent change is that, after controlling for state population, the high degree of state variation observed above becomes attenuated and the graph becomes smoother. State rankings also change noticeably. This is due, in part, to the fact that states with low aggregate numbers of otppatient, such as Rhode Island, nonetheless have high relative proportions of their small state populations in treatment.
Figure 2a: Proportion of state population in OTP treatment, during 2006 (ranked from low to high)

In particular, looking at Figure 2b, controlling for state population also reveals that many of the states with the lowest aggregate count of polydrug episodes (i.e. South Dakota), actually have polydrug incidence ratios that far exceed other states.
Combining Figure 2a and 2b, Figure 2c was expected to visually display the proposed relationship of this study: that increases in \textit{otppatient} might be correlated with increases in \textit{polydrug} episodes. However, the anticipated relationship is not at all visually apparent in the resulting figure. Instead, high levels of \textit{polydrug} episodes appears to occur at both low and high levels of \textit{otppatient}. 

\textit{Figure 2b: Ratio of total polydrug episodes in state to state population (ranked from low to high by proportion of state population in OTP treatment)}
Figure 2c: Combined figure representing the ratios of OTP patients and polydrug episodes to state population, during 2006 (ranked from low to high by proportion of state population in OTP treatment)

Figure 2c thus reveals that otppatient cannot be considered the sole factor correlated with polydrug episodes, otherwise states with relative otppatient values close to zero—such as South Dakota, Wyoming, Idaho, and Nebraska—would be expected to have relative polydrug episode values close to zero as well. The contrary results that appear in Figure 2c support the notion that factors other than state OTP patients are influencing the number of polydrug episodes, a conclusion that is supported by the existing research literature. Looking at the states with low otppatient and high polydrug values, several plausible explanations might be offered to connect them. One such factor may be a low state population itself, which could overstate the severity of a problem by inflating the relative values; if so, a direct comparison of paired cities of
comparable size in different states would be a possible vehicle for surmounting the possible inflation created by using state-level populations. Another plausible factor that has not been considered in the research literature may be geographic isolation, or the relative ruralness of a state. Finally, there may be a more complex relationship between _otppatient_ population and _polydrug_ episode count such that very low and very high levels of _otppatient_ (i.e. those states that under- and over-provide treatment) are those more likely to experience high _polydrug_ episode measures. These, however, and other considerations are beyond the scope of this study.

Notwithstanding the fact that other factors may independently explain some portion of the high relative values of state _polydrug_ episode ratios, there does seem to be an accumulation of the highest polydrug levels at high _otppatient_ levels (to the right of the graph). Figure 2d illustrates this observation by highlighting the ten highest state polydrug episode ratios with the color yellow and an icon (UIImageView).
This high concentration of large polydrug measures on the right side of Figure 2d supports the possibility that a high number of polydrug episodes may be correlated with high values of otppatient (notwithstanding other possible relationships that might explain additional high values of polydrug at low values of otppatient). This study seeks to quantify the underlying relationship between otppatient and polydrug that forms the basis of this trend.

**REGRESSION MODEL AND METHOD OF ANALYSIS**

I) **REGRESSION MODEL**

To ascertain whether and to what extent providing opioid substitution treatments (OST) for opioid addiction may be increasing the number of state polydrug episodes, this study models...
the number of polydrug episodes as a function of the number of patients within the state receiving OTP treatment. To analyze the panel data, this study deployed a two-way fixed effects model to control for state-level unit effects and annual fixed effects. It also used control variables to control for state population and population density. Finally, to facilitate the interpretation of coefficients across all variables, all variables were transformed into their natural logarithms, which will facilitate expressing the effect of changing the underlying variable values by discrete percentages. The complete regression equation is depicted in Equation 1, below.

\[
\ln(\text{polydrug})_{it} = \beta_0 + \beta_1 \ln(\text{otppatient})_{it} + \beta_2 \ln(\text{population})_{it} + \beta_2 \ln(\text{popdens})_{it} + \alpha_i + u_t + \varepsilon_{it}
\]

II) MODEL DIAGNOSTICS

Prior to running this regression equation, several diagnostic tests were performed to ascertain whether and to what extent the model would suffer from several commonly-occurring obstacles to statistical validity (see Appendix B for detailed diagnostic results).

First, the Chow Test confirmed that panel data was poolable.\(^{16}\)

Next, a test for pairwise correlations between independent variables revealed a high degree of multicollinearity.\(^{17}\) While the high pairwise correlations of 0.7391 between the natural logs of population and OTP patient population was expected (to the extent that larger populations are generally expected to have larger sub-populations of all varieties, including treatment populations), it will nonetheless increase the observed standard errors and reduce the precision of the observed coefficients.\(^{18}\) However, it will not reduce the accuracy of any observed coefficient.

---

\(^{16}\) The F-statistic for the null hypothesis that all unit fixed effects were equal to zero was calculated to be \(F=49.56\) (Prob >\(F = 0.0000\)).

\(^{17}\) See Appendix B for full results.

\(^{18}\) The variance inflation factor (VIF) test likewise produce results indicating moderate to high multicollinearity (mean VIF=2.53). See Appendix B for full results.
Next, various tests for heteroskedasticity were performed. First, a plot of the standardized residuals revealed no overt heteroskedasticity problems. This remained true when the standardized residuals from a regression computed with “robust” errors were plotted. It is also worth noting that, while the regression coefficient on ln_ottpatient remained the same (0.863) regardless of whether regular or robust standard errors were used, the model run with regular standard errors produced a substantially larger t-statistic (t=2.066) than the model run with robust standard errors (t=3.135). This observation ran contrary to expectations, as heteroskedasticity generally tends to increase the measured standard errors, and thus reduce the statistical significance of the measured coefficient. In an effort to avoid introducing confounding manipulations such as this—and in the absence of any observable heteroskedasticity problems\textsuperscript{19}—the final model was run using regular standard errors.

Several diagnostics were also run to test for model specification errors. A link test revealed no apparent model specification errors.\textsuperscript{20} Likewise, the Ramsey reset test revealed no omitted variables.\textsuperscript{21} Finally, a confirmatory F-test calculated using STATA’s two-way fixed-effect regression “xtreg” command rejected the null hypothesis that unit and year fixed effects were insignificant, and thus verified that the inclusion of unit and year fixed effects was statistically justified.\textsuperscript{22}

\textsuperscript{19} The White test also failed to reveal any apparent heteroskedasticity problems. See Appendix B for full results.
\textsuperscript{20} The link test indicated a highly significant (t=7.96) variable of prediction, and a highly insignificant (t=-0.24) squared variable of prediction. See Appendix B for full results.
\textsuperscript{21} See Appendix B for full results.
\textsuperscript{22} The F test for the null hypothesis that all unit coefficients were equal to zero 0 revealed an F-statistics of 51.24 (Prob > F = 0.0000), a result that is consistent with the F-statistics calculated previously in the Chow test. See Appendix B for full results.
III) Regression Results

Table 2 depicts excerpted results from the multivariate panel regression. See Appendix A for complete regression results.

Table 2: Excerpted regression results, multivariable two-way fixed effects regression, all variables expressed as their natural logarithms (t-statistics in parentheses)

<table>
<thead>
<tr>
<th>VARIABLES</th>
<th>ln_polydrug</th>
</tr>
</thead>
<tbody>
<tr>
<td>ln_otppatient</td>
<td>0.0863***</td>
</tr>
<tr>
<td></td>
<td>(3.135)</td>
</tr>
<tr>
<td>ln_population</td>
<td>1.860</td>
</tr>
<tr>
<td></td>
<td>(0.470)</td>
</tr>
<tr>
<td>ln_popdens</td>
<td>-1.071</td>
</tr>
<tr>
<td></td>
<td>(-0.350)</td>
</tr>
<tr>
<td>IOWA</td>
<td>0.877***</td>
</tr>
<tr>
<td></td>
<td>(6.020)</td>
</tr>
<tr>
<td>OHIO</td>
<td>0.680***</td>
</tr>
<tr>
<td></td>
<td>(2.970)</td>
</tr>
<tr>
<td>TENNESSEE</td>
<td>-0.768*</td>
</tr>
<tr>
<td></td>
<td>(-1.870)</td>
</tr>
<tr>
<td>VIRGINIA</td>
<td>0.668*</td>
</tr>
<tr>
<td></td>
<td>(1.934)</td>
</tr>
<tr>
<td>Year = 2003</td>
<td>-0.0246</td>
</tr>
<tr>
<td></td>
<td>(-0.692)</td>
</tr>
<tr>
<td>Year = 2004</td>
<td>-0.00654</td>
</tr>
<tr>
<td></td>
<td>(-0.168)</td>
</tr>
<tr>
<td>Year = 2005</td>
<td>0.0594</td>
</tr>
<tr>
<td></td>
<td>(1.391)</td>
</tr>
<tr>
<td>Year = 2006</td>
<td>0.0669</td>
</tr>
<tr>
<td></td>
<td>(1.365)</td>
</tr>
<tr>
<td>Constant</td>
<td>-30.94</td>
</tr>
<tr>
<td></td>
<td>(-0.336)</td>
</tr>
</tbody>
</table>

Observations 232
R-squared 0.981
F-test 162.5
Prob > F 0

t-statistics in parentheses - *** p<0.01, ** p<0.05, * p<0.1

Analysis

I) Findings

The regression results in Table 2 indicate that—after controlling for state population, population density, and both state and year fixed effects—the number of polydrug episodes that
occur in a state (polydrug) are strongly correlated with the number of state citizens receiving OTP treatment. This correlation is statistically significant at the 99% level (p=.002). The interpretation of the 0.0863 coefficient, however, is not as straightforward.

First, when interpreting coefficients in a log-log elasticity model (such as the model deployed here), a 1-percent increase in the independent variable is correlated with a $((1.01^{\beta_1} - 1)\times100)-100$ percent change in the dependent variable. Thus, using the value of $\beta_1$ from this study’s model, changes in $otp$ are predicted to correlate to changes in polydrug episodes as depicted in Chart 1.

Table 3: Percent changes in polydrug episodes predicted to be correlated with percent changes in OTP patients, after controlling for state population, population density, and both state and year fixed effects

<table>
<thead>
<tr>
<th>Percent Change in OTP Patients in State</th>
<th>Percent Change in State Polydrug Episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.086</td>
</tr>
<tr>
<td>10</td>
<td>0.826</td>
</tr>
<tr>
<td>25</td>
<td>1.945</td>
</tr>
<tr>
<td>50</td>
<td>3.562</td>
</tr>
<tr>
<td>100</td>
<td>6.166</td>
</tr>
<tr>
<td>200</td>
<td>9.947</td>
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<tr>
<td>300</td>
<td>12.712</td>
</tr>
<tr>
<td>400</td>
<td>14.904</td>
</tr>
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</table>

While this method of modelling might seem counter intuitive at first, its usefulness becomes apparent when one notes that a 100-percent increase in OTP patients is equivalent to doubling the current OTP patient population, just as a 200-percent increase is equivalent to tripling it, and so on. Thus, the model is capable of expressing—in general terms—the predicted outcome of various levels of policy adjustment at the state level. For example, according to this

23 More generally, a $Z$-percent change in $X$ is correlated with a $((1+(Z/100))^{\beta_1}\times100)-100$ percent change in $Y$. 
model, if a state were to double its OTP patient population while holding all other variables constant, it should expect to find a correlated 6.2 percent increase in the number of polydrug episodes. The substantive significance of these results becomes more clear when these predicted outcomes are juxtaposed with recent studies indicating that polydrug use is the primary correlate to lethal and non-lethal overdose and that OTP treatment is especially poor at helping polydrug users quit their addictions.

II) CONCLUSIONS

One the one hand, these results appear to assuage (but not extinguish) the concerns expressed by this study’s hypothesis—namely, that the provisioning of OTP treatment may be increasing the incidence of a dangerous behavior. While the predicted relationship is positive, and statistically significant, its magnitude is small and is predicted to grow at smaller and smaller rates across larger and larger increases in the OTP patient population (i.e. the predicted increase in polydrug episodes is larger from 1 to 100 percent increases in oppatient than it is from 100 to 200 percent increases). This would seem to dampen the alarm bell that OTP critics would like to sound.

However, it is unclear as to what extent the observed plateauing slope may simply be a product of the selected model. Natural logarithm models are designed to have decreasing slopes over time, and often this phenomenon is assumed from the beginning. Such an assumption may make sense when the effect of the variable under analysis (i.e. population, market penetration, etc.) is thought to vary with density, but perhaps the use of a logarithmic model specification in this study inadvertently imposed what it now purports to reveal—a declining correlation over the range of the independent variable. This is not to say that the observed coefficient is invalid, but instead, ripe for further inquiry.
III) AVENUES FOR FURTHER STUDY

Unfortunately, without the ability to perform an instrumental variable analysis using an exogenous instrument such as Medicaid expansion, this study’s conclusions are limited to expressing correlations, rather than making more causal claims. As such, any observed correlation between the independent and dependent variables may reflect any of the following possible relationships: 1) a causal relationship in which a change in the independent variable effects the observed change in the dependent variable, 2) a causal relationship in which the dependent variable, in fact, is exerting a causal change in the independent variable (i.e. that the increase in polydrug episodes is driving the provisioning of OTP treatment--the reverse of this study’s hypothesis, but nonetheless a plausible relationship), or 3) no causal relationship at all between the independent and the dependent variables, which are instead both influenced by other unobserved variables.

Future studies should attempt to leverage an instrumental variable model to try to surmount the causation hurdle. As of now, so little time has passed since most states that have accepted the Medicaid Expansion have chosen to do so, the underlying datasets that this study relies upon have not yet been released for the relevant time periods. Nonetheless, to the extent that this study has revealed a correlative relationship between OTP provisioning and polydrug use, it should provide a statistically valid justification for future study. Furthermore, the instrument proposed herein provides a statistically valid analytical framework for future researcher that may one day be able to pierce through the correlation observed here to make causal claims about the relationship between OTP treatment and polydrug use.

In addition, a portion of these results beg additional explanation and further analysis, as well. For example, the state fixed-effects for a few states reveal statistically significant coefficients. To
the extent that these fixed-effects may reflect underlying patterns/commonalities that could have been expressed as variables in this dataset, this study may still suffer from omitted variable bias, even after controlling for population, population density, and unit/year fixed effects. The relevant question now becomes: What do Iowa (0.877), Ohio (0.680), and Virginia (0.668) have in common that leads their incidence of polydrug episodes to be so much higher than other states? Or, more optimistically: What is different about Tennessee that makes its polydrug incidence so much lower (-0.768)? Taken together, these questions highlight the fact that, despite this study’s high $R^2$ value, which measures the portion of variation explained by the model, the study was unable to capture all of the contributors to polydrug episodes and include them as control variables. Case in point: the fact that South Dakota was completely excluded from this regression because it has never reported an OTP patient, and yet it has one of the highest polydrug episode to population ratios in the country (See Fig. 2c, supra).

These concerns demonstrate the lingering possibility that polydrug use and the number of state OTP patients may both be correlated to other factors that were not included (i.e. poverty, unemployment, education levels, relative facility availability/density). Such correlations might even counteract or interact with one another at the state level. Unfortunately, this study was unable to include these control variables because—while such data is now routinely collected by the U.S. Census Bureau as part of its annual American Community Survey (ACS)—such data is unavailable in a consistent form for years earlier than 2005 (the first year the ACS began being systematically administered).\textsuperscript{24} Fortunately, as with the instrumental variable proposed earlier,

\textsuperscript{24} Additional information about the U.S. Census Bureau’s American Community Survey can be found at \url{https://www.census.gov/programs-surveys/acs/}.
subsequent studies using these control variables will become possible when enough N-SSATS
data from years after 2005 become avaialbe for public study later this year.

IV) POLICY RELEVANCE AND RECOMMENDATIONS

Several aspects of contemporary drug policy are implicated by this study. First, on the
most basic level, this study’s results corroborate the suggestions from previous studies that OTP
services may be positively—and even possibly, causally (not addressed)—correlated with
community polydrug use. It thus reveals a potentially significant and as-yet-unconsidered
negative externality of providing OST treatment in its current form. In particular, the suggestion
that OTP treatments may be increasing state polydrug use is particularly alarming given the
growing body of research literature supporting the conclusions that polydrug use is the primary
correlate to drug overdose, that polydrug users are the most difficult to treat with OTP addiction
treatments, and that polydrug use is associated with a host of negative mental, physical, and
social outcomes for the user, as well as for society.

Similarly, if the results of this study withstand further scrutiny (ideally by repeating its
methodology with more control variables, once a larger dataset becomes available), this study
holds the potential to substantially change the cost-benefit analyses undertaken in future debates
over the form and manner that OST treatments should take (i.e. in highly-monitored in-patient
settings such as “supervised injection sites) vs. in residential out-patient settings where diversion
may reasonably be suspected to take place more frequently). Already, some studies have
indicated support for more controlled treatment administrations. (Hadland, Scott E. 2014). While
this study did not determine what proportion of any changes in polydrug use are attributable to
the subset of OST services that take a particular form, it does conclude that OST contributes to
polydrug use and should hopefully precipitate additional studies with a more fine-toothed comb.
Third, the study results are part of the important dialogue between physicians, legislators, law enforcement personnel, and the world community at large about the best ways to treat problematic and addictive drug use without losing sight of any treatment’s negative side-effects. For example, notwithstanding the general support for OST in the literature, even though the study does not demonstrate a causal connection between the provisioning of OST services and community polydrug use, it may inspire future studies on the efficacy of other maintenance treatments besides OST that might be less prone to this polydrug use effect (i.e. HMT treatment).

Further, the study’s support of its hypothesis provides at least some evidence that the very concept of substitution treatments as a whole may be flawed from inception. At the very least, the results call into question the core principle underlying the use of OST treatment—the belief that a treatment substituting one drug for another will produce better outcomes than an alternative treatment using the illicit drug itself. This study suggests that such a presumption be subject to greater scrutiny instead, at least to the extent that an alternative non-substitution treatment may not be correlated with the increase in polydrug use observed here.

Unfortunately, in the United States and throughout most of the world, the current legal framework that criminalizes many of the world’s most abused drugs (heroin, most conspicuously) also criminalizes the very statistical and scientific studies on non-substitution addiction treatments that could help provide answers to the most difficult questions about drug addiction. This study hopes to stem this tide of ignorance by revealing one of the consequences of stumbling in the dark.

As part of a larger body of work that is beginning to reveal some of the negative consequences of deploying OST services, this study may even help lead to the legislative changes required for Americans to study other non-substitution maintenance treatments (and
HMT in particular) that have shown promise in other settings. (Ferri 2011; Ferri 2006; Amato, Laura 2005). This study is thus part of the ongoing dialogue about the competency and rationality of drug laws that prohibit specific scientific study. From this perspective, this study’s highest aspiration may simply be to beg the question that is most often overlooked when discussing how to treat addiction: Why use substitutes at all?
APPENDIX A: COMPLETE REGRESSION RESULTS
Table 4: Complete regression results, multivariable two-way fixed effects regression, all variables expressed as their natural logarithms (t-statistics in parentheses)

<table>
<thead>
<tr>
<th>VARIABLES</th>
<th>ln_polydrug</th>
<th>NEBRASKA</th>
<th>-0.281</th>
</tr>
</thead>
<tbody>
<tr>
<td>ln Otppatient</td>
<td>0.0863***</td>
<td>(-0.670)</td>
<td></td>
</tr>
<tr>
<td>ln_population</td>
<td>1.860</td>
<td>-0.981</td>
<td></td>
</tr>
<tr>
<td>ln_popdens</td>
<td>-1.071</td>
<td>-1.646</td>
<td></td>
</tr>
<tr>
<td>ALASKA</td>
<td>-2.461</td>
<td>-1.494</td>
<td></td>
</tr>
<tr>
<td>ARIZONA</td>
<td>-1.543</td>
<td>-0.682</td>
<td></td>
</tr>
<tr>
<td>ARKANSAS</td>
<td>0.313</td>
<td>-0.327</td>
<td></td>
</tr>
<tr>
<td>CALIFORNIA</td>
<td>-0.645</td>
<td>-0.381</td>
<td></td>
</tr>
<tr>
<td>COLORADO</td>
<td>-0.273</td>
<td>-0.161</td>
<td></td>
</tr>
<tr>
<td>CONNECTICUT</td>
<td>3.581</td>
<td>0.373</td>
<td></td>
</tr>
<tr>
<td>DELAWARE</td>
<td>4.157</td>
<td>0.479</td>
<td></td>
</tr>
<tr>
<td>DIST OF COLUMBIA</td>
<td>7.469</td>
<td>4.739</td>
<td></td>
</tr>
<tr>
<td>FLORIDA</td>
<td>-0.298</td>
<td>-0.229</td>
<td></td>
</tr>
<tr>
<td>GEORGIA</td>
<td>-0.279</td>
<td>-1.870</td>
<td></td>
</tr>
<tr>
<td>HAWAII</td>
<td>2.395</td>
<td>-2.380</td>
<td></td>
</tr>
<tr>
<td>IDAHO</td>
<td>-0.0953</td>
<td>-0.369</td>
<td></td>
</tr>
<tr>
<td>ILLINOIS</td>
<td>0.414</td>
<td>-0.432</td>
<td></td>
</tr>
<tr>
<td>INDIANA</td>
<td>0.798</td>
<td>2.738</td>
<td></td>
</tr>
<tr>
<td>IOWA</td>
<td>0.877***</td>
<td>1.394</td>
<td></td>
</tr>
<tr>
<td>KANSAS</td>
<td>-0.0166</td>
<td>0.239</td>
<td></td>
</tr>
<tr>
<td>KENTUCKY</td>
<td>0.525</td>
<td>-0.0158</td>
<td></td>
</tr>
<tr>
<td>LOUISIANA</td>
<td>0.645</td>
<td>-0.105</td>
<td></td>
</tr>
<tr>
<td>MAINE</td>
<td>1.174</td>
<td>-0.0246</td>
<td></td>
</tr>
<tr>
<td>MARYLAND</td>
<td>2.871</td>
<td>-0.692</td>
<td></td>
</tr>
<tr>
<td>MASSACHUSETTS</td>
<td>2.889</td>
<td>-0.00654</td>
<td></td>
</tr>
<tr>
<td>MICHIGAN</td>
<td>0.335</td>
<td>0.0594</td>
<td></td>
</tr>
<tr>
<td>MINNESOTA</td>
<td>0.334</td>
<td>0.365</td>
<td></td>
</tr>
<tr>
<td>MISSISSIPPI</td>
<td>-0.0901</td>
<td>0.0669</td>
<td></td>
</tr>
<tr>
<td>MISSOURI</td>
<td>0.250</td>
<td>-30.94</td>
<td></td>
</tr>
<tr>
<td>MONTANA</td>
<td>-0.221</td>
<td>-0.336</td>
<td></td>
</tr>
</tbody>
</table>

Robust t-statistics in parentheses - *** p<0.01, ** p<0.05, * p<0.1
**Table 5: Two-way fixed effects regression results, testing against a null hypothesis that all unit effects equal zero, all variables expressed as their natural logarithms**

| ln_poly       | Coef.  | Std. Err. | t     | P>|t| | [95% Conf. Interval] |
|---------------|--------|-----------|-------|-----|----------------------|
| ln_otppatient | .0863  | .0275     | 3.13  | 0.002 | .0319772 - .1406636  |
| ln_population | .7888  | .8960     | 0.88  | 0.380 | -.9795779 - 2.55717  |
| ln_popdens    | 0      |           |       |      |                      |
| year          |        |           |       |      |                      |
| 2003          | -.0246 | .0356     | -0.69 | 0.490 | -.0949878 - .0456891 |
| 2004          | -.0065 | .0388     | -0.17 | 0.867 | -.0832597 - .0701743 |
| 2005          | .0593  | .0427     | 1.39  | 0.166 | -.0248977 - .143657  |
| 2006          | .0669  | .0490     | 1.36  | 0.174 | -.0298519 - .1636286 |
| _cons         | -3.22  | 13.62     | -0.24 | 0.813 | -30.10126 - 23.65728 |

\[
F(6, 176) = 6.07  \quad \text{Prob} > F = 0.0000
\]

Fixed-effects (within) regression

<table>
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<tr>
<th></th>
<th>Number of obs = 232</th>
<th>Number of groups = 50</th>
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<tbody>
<tr>
<td>R-sq:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>within</td>
<td>0.1714</td>
<td></td>
</tr>
<tr>
<td>between</td>
<td>0.7480</td>
<td></td>
</tr>
<tr>
<td>overall</td>
<td>0.7027</td>
<td></td>
</tr>
<tr>
<td>Obs per group:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>min</td>
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<td></td>
</tr>
<tr>
<td>avg</td>
<td>4.6</td>
<td></td>
</tr>
<tr>
<td>max</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>corr(u_i, Xb)</td>
<td>-0.0424</td>
<td></td>
</tr>
<tr>
<td>F(6, 176) = 6.07</td>
<td></td>
<td>0.0000</td>
</tr>
</tbody>
</table>

F test that all u_i=0: F(49, 176) = 51.24  \quad \text{Prob} > F = 0.0000
APPENDIX B: MODEL DIAGNOSTICS

I) MULTICOLLINEARITY DIAGNOSTICS

a) Pairwise correlations among all variables

<table>
<thead>
<tr>
<th></th>
<th>ln_oppatient</th>
<th>ln_population</th>
<th>ln_popdens</th>
</tr>
</thead>
<tbody>
<tr>
<td>ln_oppatient</td>
<td>1.0000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ln_population</td>
<td>0.7391</td>
<td>1.0000</td>
<td></td>
</tr>
<tr>
<td>ln_popdens</td>
<td>0.6618</td>
<td>0.4794</td>
<td>1.0000</td>
</tr>
</tbody>
</table>

b) “Variable Inflation Factor” or “VIF” test

<table>
<thead>
<tr>
<th>Variable</th>
<th>VIF</th>
<th>1/VIF</th>
</tr>
</thead>
<tbody>
<tr>
<td>ln_oppatient</td>
<td>3.45</td>
<td>0.289959</td>
</tr>
<tr>
<td>ln_population</td>
<td>2.29</td>
<td>0.436825</td>
</tr>
<tr>
<td>ln_popdens</td>
<td>1.85</td>
<td>0.541056</td>
</tr>
<tr>
<td>Mean VIF</td>
<td>2.53</td>
<td></td>
</tr>
</tbody>
</table>

II) HETEROSKEDASTICITY DIAGNOSTICS

a) Plotted Standardized Regression Residuals

i) Before using robust error calculation during regression

Figure 3a: Plotted standardized regression residuals, derived without using "robust" error calculation during regression
ii) After using robust error calculation during regression

![Figure 3b: Plotted standardized regression residuals, derived using "robust" error calculation during regression](image)

b) The White Test

<table>
<thead>
<tr>
<th>Source</th>
<th>SS</th>
<th>df</th>
<th>MS</th>
<th>Number of obs = 232</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td>177.931061</td>
<td>3</td>
<td>59.3103537</td>
<td>F(3, 228) = 193.29</td>
</tr>
<tr>
<td>Residual</td>
<td>69.9613891</td>
<td>228</td>
<td>.306848198</td>
<td>Prob &gt; F = 0.0000</td>
</tr>
<tr>
<td>Total</td>
<td>247.89245</td>
<td>231</td>
<td>1.07312749</td>
<td>R-squared = 0.7178</td>
</tr>
</tbody>
</table>

Adj R-squared = 0.7141

Root MSE = .55394

| ln_poly      | Coef. | Std. Err. | t     | P>|t|  | [95% Conf. Interval] |
|--------------|-------|-----------|-------|------|----------------------|
| ln_ottpatient| .0473415 | .037211 | 1.27  | 0.205| -.0259798 - .1206628 |
| ln_population| .7458981 | .0565439| 13.18 | 0.000| .6336827 - .8565135  |
| ln_popdens   | .1263178 | .0373936| 3.38  | 0.001| .0526366 - .199999   |
| _cons        | -.9685329 | .7922081| -1.22 | 0.223| -2.529518 - .5924523 |
III) MODEL SPECIFICATION DIAGNOSTICS

a) The Link Test

Table 9: The "Link" test

<table>
<thead>
<tr>
<th>Source</th>
<th>SS</th>
<th>df</th>
<th>MS</th>
<th>Number of obs = 232</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td>243.107624</td>
<td>2</td>
<td>121.553812</td>
<td>F(2, 229) = 5817.52</td>
</tr>
<tr>
<td>Residual</td>
<td>4.78482596</td>
<td>229</td>
<td>.020894437</td>
<td>R-squared = 0.9807</td>
</tr>
<tr>
<td>Total</td>
<td>247.89245</td>
<td>231</td>
<td>1.07312749</td>
<td>Root MSE = .14455</td>
</tr>
</tbody>
</table>

| ln_poly   | Coef.   | Std. Err. | t     | P>|t|  | [95% Conf. Interval] |
|-----------|---------|-----------|-------|------|----------------------|
| _hat      | 1.030916 | .1295685  | 7.96  | 0.000 | .7756169 1.286215   |
| hatsq     | -.0016168| .0067587  | -0.24 | 0.811| -.0149339 .0117003 |
| _cons     | -.1460691| .6169159  | -0.24 | 0.813| -1.361626 1.069488 |

b) The Ramsey Reset Test

Table 10: The "Ramsey Reset" test

Ramsey RESET test using powers of the fitted values of ln_poly
Ho: model has no omitted variables
F(3, 173) = 6.60
Prob > F = 0.0003
BIBLIOGRAPHY


Cameron, A. C., & Trivedi, P. K. (2009). Microeconometrics using stata. College Station, Tex: Stata Press.


Results from the 2012 national survey on drug use and health: Detailed tables(2013). Substance Abuse and Mental Health Services Administration (SAMHSA).


