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TAKING THE MEASURE OF A FATAL DRUG EPIDEMIC

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ABSTRACT

This analysis utilizes death certificate data from the Multiple Cause of Death (MCOD) files to better measure the specific drugs involved in drug poisoning fatalities. Statistical adjustment procedures are used to provide more accurate estimates, accounting for the understatement in death certificate reports resulting because no drug is specified in between one-fifth and one-quarter of cases. The adjustment procedures typically raise the estimates of specific types of drug involvement by 30% to 50% and emphasize the importance of the simultaneous use of multiple categories of drugs. Using these adjusted estimates, an analysis is next provided of drugs accounting for the rapid increase over time in fatal overdoses. The frequency of combination drug use introduces uncertainty into these estimates and so a distinction is made between any versus exclusive involvement of specific drug types. Many of the results are sensitive to the starting and ending years chosen for examination, with a key role of prescription opioids for analysis windows starting in 1999 but with other drugs, particularly heroin deaths, becoming more significant in more recent years and, again, with confirmatory evidence of the importance of simultaneous drug use.

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The poisoning death rate roughly tripled over the last three decades, with about 90% of these fatalities now caused by drugs (Warner et al., 2011). At least 80% of poisoning mortality was accidental in 2011 and this is now the leading cause of injury deaths (Chen et al., 2014). Increased rates of poisoning deaths are the most important reason for the striking result that the all-cause mortality rates of 45-54 year old non-Hispanic whites *increased* by around 0.5% per year between 1999 and 2013 (Case & Deaton, 2015). The involvement of prescription opioid analgesics, such as oxycodone, methadone and hydrocodone has received particular attention (Centers for Disease Control and Prevention, 2011, 2012; Volkow et al, 2014), including a White House Summit specifically addressing the problem in August 2014 (Hardesty, 2014). However, fatal drug poisonings are not limited to opioids. Sedatives and psychotropic drugs are frequently mentioned on death certificates and combination drug use is common (Jones et al., 2013; Paulozzi et al., 2014), with heroin-related overdoses recently emerging as a major killer (Jones et al., 2015; Rudd et al., 2016).

The rapid rise in fatal drug poisonings justifies the concerted efforts undertaken to reduce the negative consequences of the prescription drug epidemic such as: establishing prescription drug monitoring programs, restricting the ability of pain clinics and online pharmacies to dispense oxycodone and other controlled substances; and developing abuse-deterrent formulations of some prescription drugs (Centers for Disease Control and Prevention, 2013; Finklea, et al., 2013; Rannazzisi, 2013; Kirschner et al., 2014).

These endeavors have been partially successful. Drug poisoning deaths in Florida decreased 17% between 2010 and 2013, with a 52% decline in fatal oxycodone overdoses, following aggressive efforts to reverse the proliferation of pain clinics, prohibit the dispensing of schedule II or III drugs from physician offices, and other measures (Johnson, et al., 2014).

Deaths involving methadone peaked in 2007 and have since declined along with a fall in the amount of methadone distributed nationally (Centers for Disease Control and Prevention, 2012). However, the accomplishments are incomplete. After Florida's crackdown, some pain clinic owners moved out of the state or found ways to circumvent the laws, and there are questions whether prescription drug monitoring programs have reduced deadly overdoses (Paulozzi, et al., 2011; Gugelmann et al., 2011; Li et al., 2014). Most notably, some users may have substituted heroin for prescription opioids, with a more than tripling in the rate of heroin-related deaths between 2010 and 2014 (Rudd et al., 2016).

There are several barriers to formulating the most effective policies to deter dangerous use of prescription pharmaceuticals while avoiding the potential substitution to other harmful legal or illegal drugs. Importantly, we do not currently have reliable information on the specific drugs involved in poisoning fatalities because at least one of the drugs involved is unspecified on the death certificates of approximately half of fatal overdose deaths, and no specific drug is mentioned in between one-fifth and one-quarter of cases (depending on the year). This leads to an underestimate of the rates of involvement of specific legal and elicit drugs, as well as of the simultaneous use of drug combinations. Sedatives (particularly benzodiazepines) and psychotropic drugs are increasingly frequently mentioned on death certificates (Paulozzi, et al., 2014) and the use of these drugs alongside prescription opioids is likely to increase health risks beyond the separate consumption of either (Jones et al., 2012).

Economists have widely studied risky behaviors in general and substance abuse in particular (see Cawley & Ruhm, 2012 for a detailed summary of this literature), but there has been little investigation of the rapid rise in fatal overdoses, the role of specific drugs in contributing to it, or of policies designed to reverse or slow the increase. An important exception is Meinhofer's (2015) analysis showing that the supply-side intervention in Florida, starting in 2010 and briefly described above, increased oxycodone street prices, reduced their supply and decreased related consumption, hospitalizations and deaths, while leading to limited increases in heroin use. Others include Jena & Goldman's (2011) evidence that the growth in internet pharmacies between 2000 and 2007 may have contributed to rising rates of prescription drug abuse, Pacula et al.'s (2015) findings that the introduction of the Medicare Part D in 2006 may have similar had effects for the 65+ population, as well as for younger persons not directly affected by the program, Ruhm's (2015) demonstration that poisoning fatalities shifted over time from being procyclical to countercyclical during the period of rapid growing drug poisoning deaths, and Carpenter et al.'s (2016) indication of a procyclical variation in disorders related to the use of analgesics during the 2002-2013 period.

The analysis below uses death certificate data from the Multiple Cause of Death (MCOD) files for 1999-2014 to examine the specific drugs involved in fatal drug poisonings. The investigation is innovative in at least two ways. First, the statistical adjustment procedures applied here provide more accurate estimates of the drugs involved in these deaths, accounting for the understatement resulting from lack of specificity in death certificate reports.[1] These methods raise the prevalence estimates of specific categories of drug involvement by 30% to more than 50% and highlight the frequency of combination drug use. Second, using the adjusted estimates, I attempt to determine which drugs are responsible for the rapid rise in fatal overdoses. The frequency of multiple drug-taking introduces uncertainty into these estimates and so a distinction is made between *any* versus *exclusive* involvement of drug classes in the deaths. This investigation highlights the sensitivity of some findings to the choice of starting and ending years, a key role of prescription opioids for analysis windows starting early in the data period but

[1] An earlier exploration of these adjustment procedures is provided in Ruhm (2016).

with other drugs, particularly heroin, being more significant for the recent growth in drug poisoning deaths.

1. Data and Descriptive Patterns

The primary outcomes analyzed are counts of drug poisoning deaths using data from the 1999 through 2014 MCOD files. The MCOD data, available from the Centers for Disease Control and Prevention (Centers for Disease Control and Prevention, 2015), provide information from death certificates on: a single underlying cause of death, up to twenty additional causes, and limited demographic data. The cause-of-death information are categorized using four digit International Classification of Diseases, Tenth Revision (ICD-10) codes with details also provided on place of residence, age, race/ethnicity, gender, year, and weekday of death. The public use files lack geographic identifiers; however, information on the state and county of residence are available under restricted conditions and were obtained for use in this study.[2]

Poisoning and drug poisoning deaths are defined using ICD-10 underlying cause of death codes, where the where the underlying cause is the "disease or injury that initiated the chain of morbid events that led directly and inevitably to death" (Centers for Disease Control and Prevention, 2014).[3] In cases of drug poisoning, the death certificate lists one or more drugs involved as immediate or contributory causes of death. These are included separately as ICD-10 "T codes" and are referred to below as drug mentions or involvement. Specific drug categories to be examined include: narcotics, sedatives, psychotropics, other specified drugs and unspecified drugs. Important subcategories are also be analyzed. Narcotics are decomposed into (prescription) opioid analgesics, heroin, cocaine and other narcotics; opioid analgesics into

[2] The analysis is restricted to include of U.S. residents (i.e. foreign residents dying in the U.S. are excluded).
[3] Poisoning deaths include ICD-10 codes X40-X49, X60-X69, X85-X90 Y10-Y19, Y35.2, *U01(.6-.7); codes for drug poisoning deaths are X40-X44, X60-X64, X85, Y10-Y14, Y35.2, *U01.6, *U01..7 (World Health Organization, 2014).

methadone and other opioid analgesics. Benzodiazepines will sometimes be broken out as an important subclass of sedatives. Among psychotropics, antidepressants, antipsychotics and stimulants will be separately examined. “Other specified” drugs include a wide variety of medications including anesthetics, antiallergic and immunosuppressive drugs, histamine and anti-gastric secretion medications, cardiac drugs, antibiotics and many others. Poisoning by unspecified drugs, medicaments and biologicals (ICD-10 code, T50.9) is important because no specific drug is identified for approximately one-quarter of drug poisoning deaths and this code is mentioned in around half of cases. Combination drug use will be examined through a variable indicating mentions of two or more of the following drug categories: opioid analgesics, heroin, cocaine other narcotics, sedatives, psychotropics or other drugs. This classification somewhat understates the frequency of poly-drug use since it does not capture the use of multiple types of drugs within classes.[4]

The main analysis begins in 1999 because ICD-9 codes, used prior to that year, are not fully comparable to ICD-10 categories (Anderson et al., 2001). However, corresponding frequencies of the broad categories of poisoning and drug poisoning deaths (but not types of drugs involved) can be obtained using ICD-9 codes and so public-use MCOD files for years before 1999 are used to conduct a descriptive investigation examining broad trends in poisoning deaths from 1982 to 2014.

1.1 Trends in Poisoning Deaths

Poisoning fatalities rose 360% between 1982 and 2014, from 11,297 to 51,966 deaths, and drug poisoning mortality by an even larger 622%, from 6,518 to 47,055 (see the top panel of Figure 1). In 1982, there were four times more motor vehicle deaths than poisoning fatalities and

[4] Psychotropics may be most important in this regard, since this category includes heterogeneous types of drugs.

seven times more than deadly drug overdoses.[5] Conversely, in 2014, there were 33% more drug poisoning deaths than vehicle fatalities, with drug overdoses being responsible for 91% of all poisoning deaths. Importantly, most of this change occurred since 1999 (75% of the rise in fatal overdoses occurring between 1982 and 2014), so that the analysis period covers most of the secular increase. Although population growth accounts for a portion of the increase, the poisoning death rate rose by 234% between 1982 and 2014 (from 4.88 to 16.30 per 100,000) and the drug poisoning mortality rate by 425% (from 2.81 to 14.75 per 100,000).[6]

Figure 2 supplies information on the demographic distribution of drug poisoning deaths. Several patterns are worth noting. First, males have higher death rats from this source than females and the difference has become more pronounced over time (19% higher in 1982 versus 63% greater in 2014). Second, whites had higher fatal drug poisoning rates than blacks, but this pattern has only emerged since 2000; other races have consistently lower mortality rates.[7] Finally, drug poisoning deaths are almost nonexistent for persons under the age of 15 with 25-54 year olds now at highest risk, and with the fastest growth over time for 45-64 year olds.

Geographic variations in drug poisoning death rates at the end of the analysis period are displayed in Figure 3. The top figure shows state mortality rates for 2014, and the lower one three-year averages of county death rates for 2012-2014, for counties with populations averaging 5,000 persons or more.[8] At the state level, drug mortality is relatively low in the West North

[5] I often use the term "overdoses" to refer to drug poisoning deaths for convenience, while recognizing that some of these deaths are intentional.
[6] Population data (the denominator in the mortality rate calculations) come from the National Cancer Institute's *Surveillance Epidemiology and End Results (SEER)* program and are designed to supply more accurate population estimates for intercensal years than standard census projections. See http://www.seer.cancer.gov/data for additional details.
[7] Data on Hispanics, available since 1990, indicates that they generally have death rates below those of blacks but higher than non-Hispanics who are neither black nor white.
[8] Death rates are not displayed for counties with populations below 5,000 because the small sizes imply that such estimates will be variable and unreliable. The thresholds on the maps refer to population-weighted minimum, 25th, 50th, 75th and 90th percentiles, and maximum drug poisoning rates per 100,000.

Central region and much of the South, with the exceptions of Oklahoma and Louisiana, while being high in Alaska, most of the Mountain and Appalachian states (except Idaho), the rust belt and parts of New England. The picture is somewhat more nuanced when looking at counties, with continuing very high mortality risk in the South West, Appalachia and rust-belt but also with pockets of high mortality in otherwise relatively low drug death states such as California and Texas.

1.2 Death Certificate Reports in 2014

Table 1 shows death certificate reports of drug mentions and the manner of death (accidental, intentional, undetermined intent or homicide) for all drug poisonings occurring in 2014 (the last year of the analysis period), with corresponding ICD-10 codes (ChiroCode Institute, 2014) shown in parentheses. Numbers and percentages of deaths were calculated for all drug poisonings and by manner of death and type of drug (as well as alcohol mentions), with the shares referred to as prevalences below. I also show exclusive involvement of major class of drugs, defined as deaths where only a single specified class of drugs is mentioned on the death certificate (although unspecified drugs could also be reported), as well as cases where two or more major drug classes are identified.

More than four-fifths (82%) of drug poisonings in 2014 were classified as accidental, with fewer than one in eight categorized as intentional. Narcotics were mentioned in 65% of fatal overdoses, with reported prevalences of 40%, 23% and 12% for opioid analgesics, heroin and cocaine. However, involvement of other drugs is also common with sedatives and psychotropic drugs each listed in around one-fifth of fatal overdoses. Alcohol is mentioned in less than one-tenth of fatal drug poisonings. Most germane to this analysis, only unspecified drugs are listed in 20% of deaths. The percentage of fatal overdoses with at least one drug specified ranges across years from a low of 74.1% in 2008 to a high of 80.4% in 2014 (see Figure 4), with the smallest specification rates occurring during the great recession (2007-2009) and its aftermath, and rapid increases at the end of the sample period. For this reason, reported rates of drug involvement will understate the true prevalences for most drugs and may yield a misleading understanding of the nature of the fatal drug epidemic. A primary effort below is to assign reasonable attribution to specified drug types in as many of these deaths as possible.

Figure 5 displays the variation in county-level drug specification rates averaged over the 2012-2014 period for counties with at least 5,000 residents and a positive number of fatal drug overdoses. The figure shows some similarity with the corresponding map of drug poisoning rates (Figure 3b) raising the possibility that some geographic differences in drug poisoning mortality reflects differences in reporting patterns.

Also noteworthy is the frequency (34%) with which multiple drug classes are mentioned. One implication is that it may be hard to assign the responsibility of the death to any specific drug category.[9] For example, prescription opioid use was reported in 40% of drug poisoning deaths, but these were the only class of drugs mentioned in just 17%. Exclusive involvement of other drug types was reported only one-fifth to one-half as often as any use in most cases, except that sedatives were almost never the only drug class reported. In less than 1% of drug poisonings, no drug (even an unspecified one) was listed. While it would presumably be reasonable to add these to the exclusively unspecified category, this has not been done in the adjustment procedures below, possibly resulting in a slight continued understatement of the prevalences of specific drugs.[10]

[9] The prevalence of deaths involving multiple drugs rises to 38.7% when the combination drug use measure is expanded to include alcohol.

[10] There could also be some misclassification of underlying causes of death whereby fatalities not categorized as being due to drug poisonings actually involved them and vice versa. The solution to this problem is not obvious

2. Methods

A primary goal of this analysis is to calculate adjusted prevalences that account for drug poisoning deaths where the death certificates include unspecified drug classes. Towards this end, a dichotomous variable was constructed indicating if at least one specific drug was mentioned on the death certificate, rather than only the unspecified category. County-year averages of this variable were calculated and denoted as $SPECIFY$. For an initial descriptive analysis, counties were classified as "low diagnosis" if a specific drug was mentioned in fewer than 68.4% of drug poisoning deaths in 2014 and "high diagnosis" if this was done in more than 98.2% of cases. These thresholds reflect the 25th and 75th percentiles of $SPECIFY$ in 2014. Drug mention prevalences were then compared across high and low diagnosis counties to provide a first indication of how reported prevalences were affected by the frequent failure to identify the drugs involved in fatal overdoses.[11] Such comparisons are not fully informative, since high and low diagnosis states could differ along other dimensions.

To control for potential confounding factors, a series of probit models were separately estimated for each year. The basic model takes the form:

(1) $$Y_{ijt} = \alpha + \beta SPECIFY_{jt} + \gamma X_{ijt} + \mu_{ijt},$$

where Y_{ijt} is a binary dependent variable indicating if the death for individual i in county j and year t is reported to involve the specified drug. $SPECIFY$, the explanatory variable of primary interest, measures the county-year drug specification rate. The models also include supplementary covariates (X) for: gender, two race indicators (black and other nonwhite), currently married (versus never married, separated/divorced, widowed, or status not reported),

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(particularly since the information on drug involvement is less detailed for most deaths categorized not due to poisoning); however, it is possible to examine reported drug involvement in "non-drug" poisoning deaths. In 2014, there were 4,911 non-drug poisoning fatalities. A drug was mentioned on the death certificate in 236 (4.8%) cases, with most of these (118) being an unspecified drug and with a specific drug reported just 2.9% of the time (143 deaths), including opioid analgesic, sedative and psychotropic prevalences of 0.9%, 0.6% and 0.8% respectively.

[11] Average values of *SPECIFY* are 46.0% in low diagnosis and 99.4% in high diagnosis counties.

four educational categories (less than high school graduate, high school graduate, some college, college graduate), eight age categories (≤20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, >80, with missing age as the reference group), nine census regions (New England, Mid-Atlantic, East North Central, West North Central, South Atlantic, East South Central, West South Central, Mountain and Pacific), and seven day of the week indicators. A complicating issue is that education were sometimes reported in years rather than specific thresholds. In these cases, ≤11, 12, 13-15 and ≥16 years were classified as less than high school graduate, high school graduate, some college and college graduate. μ is the regression error term.

Predicted values of the dependent variable were calculated, for each drug poisoning death, and averaged over all observations to obtain estimated prevalences. Specifically, the average predicted prevalence, $\bar{P}_{jt}$, for drug type *j* at time *t*, is:

(2) $$\bar{P}_{jt} = \frac{1}{n}\sum_{i=1}^{n} \Phi\left(\hat{Y}_{ijt}\right) = \frac{1}{n}\sum_{i=1}^{n} \Phi\left(\hat{\alpha} + \hat{\beta}\, Specify_{jt} + \hat{\gamma}\, X_{ijt}\right),$$

where Φ(.) is the cumulative distribution function of the standard normal distribution. Since these predictions are based on actual values of the explanatory variables, the estimated prevalences are expected to be very close to the sample mean values. This was tested for and confirmed.

A second set of predicted values were next obtained after setting $SPECIFY$ to one for all observations. The average expected value, hereafter referred to as the “adjusted prevalence”, $\tilde{P}_{jt}$, was estimated as:

(3) $$\tilde{P}_{jt} = \frac{1}{n}\sum_{i=1}^{n} \Phi\left(\hat{\alpha} + \hat{\beta} + \hat{\gamma}\, X_{ijt}\right),$$

and indicates the predicted drug involvement rate if at least one drug had been specified on all drug overdose death certificates. Robust standard errors and the associated ninety-five percent confidence intervals (95% CI) were calculated with observations clustered by county. The predicted number of deaths involving the specified class of drugs, $\widetilde{D}_{jt}$, was calculated as the product of the adjusted prevalence and number of drug poisoning deaths in year t, D_t, or:

(4) $$\widetilde{D}_{jt} = \tilde{P}_{jt} \times D_t.$$

Corresponding prevalence estimates of exclusive drug mentions (e.g. opioid analgesic involvement without mention of heroin, cocaine, sedatives, psychotropics or other drugs) were also calculated. In addition, I test and report results controlling for alternative sets of covariates or estimating linear probability rather than probit specifications.

These represent "in-sample" estimates but two indications of the success of the adjustment procedures were examined. The first compared reported and adjusted prevalences of exclusive unspecified drug mentions (i.e. those where no drug is specified on the death certificate). As mentioned, the reported prevalence was approximately 25% in most years. Completely successful adjustment procedures would reduce this to zero, and the closer this is to being achieved, the greater the confidence in the adjustment procedure. The second test was the reverse of the first. Here, adjusted prevalences were calculated using the procedure above but assuming that drug types were never specified on the death certificates (i.e. by setting by predicting prevalence after setting $SPECIFY$ to zero).[12] Perfect adjustment implies that exclusive mentions of unspecified drugs would occur in 100% of fatal overdoses. Note that when using a probit model, predicted probabilities can never reach either zero or one, so that complete adjustment is not possible.

I also use the adjusted prevalences to indicate the contributions of specific drug types to the growth over time in fatal overdoses. Following the notation above, changes in prevalences between an earlier and a later period, denoted by $t = 0$ and $t = 1$, are:

[12] Thus, the estimated prevalence in this case is: $\tilde{P}_{jt} = \frac{1}{n}\sum_{i=1}^{n} \Phi\left(\hat{\alpha} + \hat{\gamma}\, X_{ijt}\right)$.

(5) $$\Delta\tilde{P}_j = \tilde{P}_{j1} - \tilde{P}_{j0},$$

and the change in deaths involving the drug is:

(6) $$\Delta\tilde{D}_j = \tilde{D}_{j1} - \tilde{D}_{j0} = \tilde{D}_{j1}\Delta\tilde{P}_j + \tilde{P}_{j0}\Delta D,$$

where $\Delta D = D_1 - D_0$. Notice that (6) depends on changes in both prevalences and the total number of drug deaths occurring between the two periods. Finally, the percentage of the change in drug deaths that involves drug type j is: $\{\Delta\tilde{D}_j/\Delta D\} \times 100\%$.

These calculations are conducted using prevalence estimates for both any and exclusive mentions. Previous investigations often focus on any mentions of a class of drugs and so correspond to the first set of estimates, except without adjusting the prevalences to account for cases where only unspecified drugs are mentioned on the death certificates. Such estimates almost certainly overstate the contribution of any specific drug class since combinations of drugs types are common and result in double-counting. The calculations based on exclusive prevalences address this but will conversely be understated since no attribution is made when multiple drugs contribute to the deaths.

Examining changes in drug poisoning deaths over the 1999-2014 period is dictated by the availability of comparable estimates of drug involvement using ICD-10 codes. Using the just described methods, two related strategies are implemented to determine whether the results are sensitive to the choice of starting of ending years. In the first, the starting year is always 1999 and the contributions to drug poisoning deaths are investigated for all possible ending years between 2003 and 2014.[13] The second strategy is the reverse of the first, with the always being 2014 and the initial analysis year ranges between 1999 and 2010.

3. Drug Poisoning Deaths in 2014

[13] Earlier ending periods are not examined since in short sample periods the estimates will be dominated by noise.

A first indication of the extent to which death certificates understate the prevalence of specific drug involvement in 2014 fatal drug poisonings was obtained by comparing the reported rates in low and high diagnosis counties, defined as those where $SPECIFY$ was ≤68.4% and ≥98.2% respectively (see Table 2). Differences in reported prevalences are dramatic. For example, opioid analgesics are mentioned 2.7 times as often in high versus low diagnosis counties (52.8% vs. 19.5%), with even larger relative differences for heroin, cocaine, and sedative mentions, and with the use of multiple drugs reported almost four times as frequently.[14] Particularly noteworthy is that *only* unspecified drugs are listed in 54% of fatal overdoses in low diagnosis areas compared to less than 1% of those in high diagnosis counties. Interestingly, combinations of specified and unspecified drug mentions are twice as common in the high diagnosis locations, which also have greater numbers of conditions listed on the death certificates. This comparison does not account for potential confounders, which could be important since deaths in low diagnosis counties are more likely to involve females, whites and married individuals (see Appendix Table A.1).

Table 3 displays reported and adjusted prevalences, with the latter obtained using the procedures described above. The adjusted prevalences are higher for all specific drug classes, implying that reported prevalences understate most types of drug involvement. For example, the adjusted opioid analgesic prevalence was 52.6% or 31% higher than the reported 40.2%. Adjusted prevalences of other major drug classes exceeded reported prevalences by 32% to 48%, and the involvement of multiple drug classes rose from 34.4% to 49.3%. The lower panel of the table shows corresponding results for exclusive drug mentions. The increases here are smaller and more varied, but still important, ranging from 10% for psychotropics to 24% for heroin.

[14] Alcohol is also mentioned much more frequently in the high diagnosis counties (11.7% vs. 4.2%).

The adjustment procedures work well, but not perfectly. Specifically, the prevalence of only unspecified drugs falls by more than four-fifths, from 19.6% to 3.5%, when using the adjustment procedures. Adjusted prevalences were calculated using the same procedure but under the assumption that drug types were *never* specified on the death certificates (by predicting probabilities with $SPECIFY = 0$). Here, perfect adjustment would imply predictions of exclusive mentions of unspecified drugs in 100% of fatal overdoses, versus an actual estimate of 96.3%. Thus, to the extent the adjustments remain incomplete, there is likely to be a small continuing understatement of specific drug mentions.

I tested the robustness of the adjustment procedures to a variety of alternative specifications including: 1) estimating linear probability rather than probit models; 2) excluding all covariates other than $SPECIFY$; 3) adding supplementary covariates for the manner of death (dummy variables for intentional and accidental deaths, with undetermined deaths and homicides as the reference group) and whether an autopsy was performed. The last specification could be problematic if the determination of manner of death or the use of autopsies is endogenous (e.g. if the latter are more commonly performed in high diagnosis counties).[15] However, Appendix Table A.2 shows that the adjusted prevalence estimates are insensitive to any of these alternatives. Particularly interesting is the similarity of the results of the specification without any supplementary covariates to those in the main model. This implies that almost all of the important variation captured is due to the cross-county variation in drug specification rates. The findings might change when controlling for other information (not included death certificates) but the similarity of results across specifications in the table makes this less likely.

[15] Kapusta et al. (2011) provide cross-national evidence suggesting that autopsy use and rates of intentional deaths (suicides) are positively related. A number of authors argue that drug poisoning deaths will frequently be classified as accidental or of undetermined intent when they are really intentional (Rockett et al., 2014a,b). Information on autopsies first became available on death certificates in 2003.

The adjustments to this point correct for cases where *no* drug is specified on the death certificate. However, prevalences could still be understated when using this procedure because it does not account for cases where the death certificate lists *both* specified and unspecified drugs. To investigate this possibility, I estimated the augmented model:

(7) $$Y_{ijt} = \alpha + \beta_1 SPECIFY_{jt} + \beta_2 SOME_{jt} + \gamma X_{ijt} + \mu_{ijt},$$

where $SOME$ is a dummy variable taking the value of one if the death certificate lists *both* specified and unspecified drugs and zero if *only* unspecified or specified drugs are reported. Adjusted prevalences assuming that all death certificates included only specified drugs ($SPECIFY = 1, SOME = 0$) were calculated as:

(8a) $$\tilde{P}_{jt} = \frac{1}{n}\sum_{i=1}^{n} \Phi\left(\hat{\alpha} + \hat{\beta}_1 + \hat{\gamma}\, X_{ijt}\right),$$

and those where all death certificates included mentions of *both* specified and unspecified drugs ($SPECIFY = 1, SOME = 1$) as:

(8b) $$\tilde{P}_{jt} = \frac{1}{n}\sum_{i=1}^{n} \Phi\left(\hat{\alpha} + \hat{\beta}_1 + \hat{\beta}_2 + \hat{\gamma}\, X_{ijt}\right).$$

The results of this exercise, displayed in Appendix Table A.3, yield almost uniformly *lower* estimated prevalences assuming that only specified drugs are included on the death certificates than when both specified and unspecified drugs are mentioned. The differences are particularly large for multiple drug use (42% vs. 61%), sedatives (23% vs. 39%) and psychotropic medications (23% vs. 34%), as well as for opioid analgesics (48% vs. 60%). The only exception is heroin, where the adjusted prevalences are higher (33% vs. 26%).

One explanation for this pattern is that combinations of specified and unspecified drug reports tend to occur when there are larger numbers of mentions on death certificates. Appendix Table A.4 shows the results of regressing the number of conditions listed against county values of $SPECIFY$ and $SOME$. As expected, the smallest number of drug mentions are predicted

(1.67) when only unspecified drugs are reported ($SPECIFY = 0, SOME = 0$). However, the predicted number of mentions is higher (4.26 vs. 3.40) when the death certificate includes both specified and unspecified drugs ($SPECIFY = 1, SOME = 1$) than when it only includes the former ($SPECIFY = 1, SOME = 0$). The gap between the two adjusted prevalences detailed in Appendix Table A.3 is substantially reduced, although not completely eliminated, in regressions (not shown) that additionally control for the number of conditions listed. This suggests that death certificates with combinations of specified and unspecified drugs are filled out in greater detail, with one result being that they have yield higher reported and adjusted prevalences of almost all types of drugs. Consistent with this possibility, death certificates may specify the type of drug involvement in one section, while reporting it as unspecified elsewhere.[16]

The aforementioned discussion leaves open the possibility that the primary adjustment procedures used in this analysis also yield downwards biased estimates because of incomplete reporting of drug involvement, even in cases where at least one drug class is specified. It is not obvious that this problem can be fully addressed but some indication of its severity was obtained by adding to the main model an additional control for the county average number of conditions listed on the death certificate, $NUMCTY$. More precisely, the regression equation was:

(9) $$Y_{ijt} = \alpha + \beta_1 SPECIFY_{jt} + \beta_2 NUMCTY_{jt} + \gamma X_{ijt} + \mu_{ijt},$$

and adjusted prevalences were calculated with $SPECIFY = 1$ and $NUMCTY = 4.264$:

(10) $$\tilde{P}_{jt} = \frac{1}{n}\sum_{i=1}^{n} \Phi\left(\hat{\alpha} + \hat{\beta}_1 + 4.286\, \hat{\beta}_2 + \hat{\gamma}\, X_{ijt}\right),$$

where 4.264 is the predicted number of conditions mentioned in counties with both specified and unspecified drug mentions. While not perfect, comparing these adjusted prevalences to those

[16] Robert Anderson, Chief of the Mortality Statistics Branch of the National Center for Health Statistics, notes that death certificates will often contain an unspecified listing such as "multi-drug toxicity" in the "cause-of-death" section and then mention of one or more specific drugs (e.g. heroin) in the "other significant conditions contributing to death" area (source: personal communications, October 2 and October 6, 2015).

from the model without controls for $NUMCTY$ provides some indication of the sensitivity of estimated prevalences to the completeness of reporting. Table 4 summarizes the findings. Model (1) shows estimates using the main adjustment procedure (from equation 3), with model (2) displaying corresponding results using equation (8) and the last column indicating percentage differences between the two.

Narcotics prevalences are relatively unaffected, whereas more complete listing of drug involvement increases sedative prevalences more than 15% and those of other specified drugs or combination drug use by 11% each, and psychotropic involvement by 8%. This implies is that that the main adjustment procedures probably provide a fairly accurate indication of prescription opioid, heroin and cocaine involvement but may understate the roles of other drug categories and multiple drug use.

Table 5 returns to the primary adjustment procedure and shows differences in reported and adjusted prevalences by manner of drug poisoning (accidental, intentional or undetermined intent).[17] The key differences are that, compared to intentional deaths, accidental drug poisonings are more likely to involve narcotics of all kinds with less common mentions of sedatives, psychotropics, other specified or unspecified drugs. Fatal drug poisonings of undetermined intent are usually intermediate between the two, although opioid analgesics are mentioned particularly frequently.

Table 6 compares county-level drug poisoning deaths rates (per 100,000) involving opioid analgesics or heroin, calculated using adjusted prevalences vs. those based on reported prevalences, for the 250 largest counties.[18] The table also shows the opioid analgesic and heroin-involved death rates, based on adjusted prevalences. The metric focused upon is the change in

[17] Since there were only 81 drug poisoning homicides in 2014, results for this manner of death are not shown.
[18] The 250 counties have a minimum population of 267,618 and their average population is 787,060.

the county ranking between death rates based on adjusted versus reported death rates, where a lower ranking indicates a worse outcome. For instance, Baltimore City Maryland had the highest reported rate of deaths involving opioid analgesics (26.8 per 100,000) and the second highest number based on adjusted prevalences. Thus, the ranking based on adjusted prevalences was one place better than based on reported prevalences (2 vs. 1). Large negative adjusted vs. reported rank differences therefore show worse performance based on adjusted rather than reported prevalences, with large positive rank differences indicated better performance. For instance, the largest deterioration in rankings for opioid-analgesic involved deaths was for Philadelphia, PA, which has the 226th (out of 250) highest death rate based on reported prevalences, but the 10th largest based on reported prevalences, a deterioration of 216 places. By contrast, Kent, MI has the largest improvement for opioid-involved death rates when comparing adjusted versus reported prevalences, ranking 117th out of 250 based on the latter versus 213th using the former.

Philadelphia country provides a striking example of the change from using adjusted, rather than reported, prevalences to calculate death rates. It has 226th highest opioid analgesic-involved rate of drug poisoning deaths (out of the 250 largest counties) based on death certificate reports, but the 10th highest rate when computed based on adjusted prevalences, the largest deterioration found. Similarly, it has the second highest deterioration (from 222nd to 4th) in heroin-involved overdose deaths. More generally, 9 (8) Pennsylvania counties are among the 20 with the worst deterioration in reported vs. adjusted rankings for opioid analgesic (heroin) involved fatal drug poisonings, with 3 (3) in New Jersey and 4 (2) in Florida. These reflect the relatively low diagnosis rates in these states, with the result that the number of deaths involving specified drugs rises relatively substantially when using adjusted rather than reported prevalences.[19] Interestingly, the patterns for counties with the largest improvement in rankings differ fairly sharply for opioid analgesic related deaths (3 counies each in New York and California) as compared to those involving heroin (led by 6 counties in North Carolina, 5 in Virginia).[20]

4. Fatal Drug Poisonings: 1999-2014

Using the methods discussed above, I next compare reported and adjusted prevalences for all sample years (1999 through 2014), as well as the corresponding numbers of deaths involving specified classes of drugs. Adjusted prevalences are calculated as $\tilde{P}_{jt}$, from equation (3), and the number of deaths as $\widetilde{D}_{jt}$ from equation (4). Prevalences are displayed in Figure 6 and corresponding numbers of deaths in Figure 7. In each case, the thin solid line shows results based on death certificate reports, the bold solid line indicates the adjusted estimates and the dotted line displays differences between the two. Adjusted prevalences and numbers of deaths exceed their reported counterparts for all years and drug types, except for the undefined category.

Several points are noteworthy. Psychotropic and multiple drug prevalences rise fairly steadily throughout the analysis period, as do sedative and opioid analgesic involvement through 2010 and 2011 (Figure 6). Cocaine prevalence decreases sharply until 2010, and then levels out, while heroin involvement declines through 2006 but increases thereafter, and dramatically so beginning in 2011. Since fatal overdoses rose rapidly over the sample period—from 16,849 in 1999 to 47,055 in 2014—deaths involving particular drugs could increase even with flat or declining prevalences. For instance, the number of drug deaths with cocaine mentions increased 40% between 1999 and 2014 (from 5,076 to 7,131), even while the prevalence fell from 30% to

[19] For example, county-level drug specification rates averaged 50.1%, 70.0% and 73.4% in Pennsylvania, New Jersey and Florida in 2014.
[20] Average county-level drug specification rates were 95.3%, 76.8%, 91.4% and 97.2% in New York, California, North Carolina and Virginia.

15% (see Figure 7).[21] On the other hand, rising prevalences reinforce this effect so that, for example, deaths involving psychotropic drugs more than tripled (from 3,577 to 12,837) while the prevalence rose “just” 28% (from 21.2% to 27.3%). The figures also highlight the recent explosion of fatal heroin overdoses: the estimated number of deaths involving heroin rose 18% (from 2,342 to 2,757) between 1999 and 2006, by an additional 53% (to 4,214) in 2010 and then by another 235% (to 14,103) in 2014. Finally, while their growth has not been particularly rapid, opioid analgesics remain the most common class of drugs involved in fatal drug poisonings, with mentions estimated to rise from 5,390 in 1999 to 24,271 in 2011 and 24,769 in 2014.

Figure 8 shows percentage differences in adjusted and reported prevalences or numbers of deaths across drug classes and over time. The upper panel shows the percentage differences in each year and the lower figure shows differentials normalized such that the 1999 value equals zero. Specifically, define the percentage difference between adjusted and reported prevalences for drug class j at time t as:

$$\Delta_{jt} = \{(\tilde{P}_{jt}/P_{jt}) - 1\} \times 100\%, \tag{11}$$

where P_{jt} and $\tilde{P}_{jt}$ are reported and adjusted prevalences, the normalized difference is calculated as:

$$\Delta_{jt}^{norm} = \{(\Delta_{jt}/\Delta_{j1999}) - 1\} \times 100\%.^{22} \tag{12}$$

The top panel of Figure 8 demonstrates that death certificate reports understate prevalences most severely for sedatives and combination drug use and, to a lesser extent, for psychotropic medications. Relative differences between adjusted and reported prevalences have grown most over time for heroin, other specified drugs and, to a smaller degree, for opioid analgesics while remaining roughly constant for most other drug classes (see the lower panel). An important consequence is that the rapid recent rise in heroin-related deaths has actually been

[21] The number of cocaine involved deaths was estimated to reach a maximum of 10,133 in 2006.
[22] Since the number of deaths involving the drug is the product of the prevalence and total number of deaths, percentage differences in prevalences and numbers of deaths are the same.

understated in death certificate reports. However, this may be less true for other drug types, since the difference between actual and adjusted prevalences generally declines after 2010. This reflects the higher rates of drug specification in recent years, an issue to which we return below.

Figure 9 shows absolute (rather than percentage) differences between adjusted and reported prevalences (top panel) or numbers of deaths (bottom panel). Since these depend on the absolute level of prevalences as well as relative (percentage) difference between adjusted and reported rates, it is not surprising that the largest disparities occur for opioid analgesic and multiple drug involvement (reaching 7,354 and 7,535 deaths respectively in 2011, before declining to 5,876 and 6,996 in 2014), although the gaps are also substantial for sedatives and psychotropic medications (5,351 and 3,528 deaths in 2011), as well as heroin in recent years (3,529 fatalities in 2014).

5. Drug Combinations

Table 7 provides further information on the role of multiple drug use by showing combinations of drugs involved in overdose deaths in 1999, 2006 and 2014 (the first, middle and last analysis periods). Drug combinations are calculated using adjusted prevalences.[23] The table shows percentages of cases where the drug listed in the first column is combined with the drug types listed in the column headings, except for the last column which indicates shares of exclusive drug use. For example, the first row shows that, in 1999, 13%, 18%, 18%, 21% and 5% of opioid analgesic-related deaths also involved the use of heroin, cocaine, sedatives, psychotropic medications and other specified drugs; with 43% involving no other specified drug category.[24]

[23] The exceptions are for combinations of heroin use with sedatives, psychotropics and other medications in 1999 and with other drugs in 2006, where the reported prevalences are too low (0.5%, 0.6%, 0.2% and 0.1%) to estimate adjusted prevalences.
[24] These total to more than 100% because more than two drug categories are involved in some deaths.

The table further emphasizes the role of drug "cocktails" in poisoning deaths. Exclusive drug use occurs less than half the time for all categories and years, and is particularly rare for sedatives in more recent years. However, the specific combinations of drugs involved varies considerably across drug types and years. For instance, opioid analgesics were more commonly combined with sedatives and psychotropics in 2014 than in 1999 or 2006, whereas simultaneous use of cocaine became less frequent.

Patterns for heroin differ somewhat from those for other drug categories. Deaths involving heroin have risen dramatically in recent years, as previously noted, with much of the growth involving exclusive use – increasing from 39% and 40% in 1999 and 2006 to 45% in 2014. Conversely, the share of heroin-related deaths involving the combined use of opioid analgesics fell from 30% in 1999 to 22% in 2006, and with a sharp recent reduction in the fraction that also involve cocaine (from 32% in 1999 and 38% in 2006 to 20% in 2014).[25] On the other hand, combinations of heroin with sedative or psychotropic medications have become much more frequent.

6. Errors Due to Changes Over Time in Drug Specification Rates

As mentioned, the fraction of overdose deaths with a specific drug identified varies over the analysis period between 74.1% and 80.4%. This introduces additional error in measures of changes in drug involvement when using death certificate reports. Table 8 illustrates this issue by calculating changes in specific drug involvement for overdose fatalities in 2012-2014 versus those in 2011, using information directly from death certificates and the more correct estimates obtained based on adjusted prevalences. This period is chosen because *SPECIFY* rose fairly sharply over this it – from 74.7% in 2011 to 80.4% in 2014.

[25] This reflects the very rapid rise in heroin-related deaths during a period where cocaine-involved fatalities were initially falling and then fairly stable. Note that the percentage of cocaine-involved deaths where heroin was also implicated rose from 15% in 1999 and 10% in 2006 to 41% in 2014.

While the higher specification rate is desirable in principle, it results in an overstatement of the increases (or an underestimate of decreases) in most types of drug involvement when using death certificate reports. For example, using data from death certificates, 1,976 additional drug poisoning deaths involved prescription opioids in 2014 than in 2011, a rise of nearly 12%. However, much of this was due to higher rates of drug identification in the later year, rather than an actual increase. Based on adjusted prevalence the growth was, at most, one-fourth as large (498 deaths or 2.1%). The overstatement is similarly dramatic for sedatives. By contrast, the increases are so dramatic for heroin that the error, while still large in absolute terms (141% vs. 129%) does not change the overall conclusions.

7. Drugs Responsible for the Increase in Fatal Overdoses

Considerable attention has been paid to the role of opioid analgesics as the contributor to fatal drug poisonings, with large fractions of both deaths at a point in time and of the increases in mortality over time involving mentions of these drugs. (e.g. Centers for Disease Control and Prevention, 2013). However, the role of specific drug classes is complicated by the frequent, and increasing prevalence in combination drug use. These issues are examined below by first decomposing the increase in drug poisoning deaths occurring between 1999 and 2014 into the fractions involving *any* or *exclusive* mentions of the various drug classes and second, by the sensitivity of the results to changes in the starting and ending analysis years.

Results of the first phase of the analysis are summarized in Table 9, with additional details in Appendix Table A.5. To illustrate the methods, there were 16,894 fatal drug poisonings in 1999 and 47,055 in 2014, a growth of 30,206. Opioid analgesics were mentioned in 4,030 of these deaths in 1999 and 18,893 in 2014, an increase of 14,863. Thus, based on death certificates, opioid analgesics were “responsible” for 49.2% (14,863/30,206) of the rise in fatal overdoses.

However, there are two reasons why such a conclusion may be incorrect. First, death certificates understate opioid analgesic prevalence, as highlighted above. Specifically, based on adjusted (rather than reported) prevalences, the point estimates indicate that prescription opioids were involved in 5,390 deaths in 1999 and 24,769 in 2014, an increase of 19,380, which corresponds to 64.2% (19,380/30,206) of the total growth in fatal overdoses.[26] Second, this method attributes to opioid analgesics all of the growth in deaths that involve them in some way. This is likely to be an overstatement because multiple drug classes are often implicated, implying that summing the contributions, measured in this way, across drug classes will total to more than 100%. The lower panels of Tables 9 and A.5 therefore focus on exclusive involvements. For example, based on adjusted prevalences, 2,300 drug poisoning deaths involved only opioid analgesics in 1999 and 9,099 in 2014, an increase of 6,800 or 22.5% (6,800/30,206) of the total. Thus, we can be reasonably confident that opioid analgesics were responsible for between 23% and 64% of the rise in fatal overdoses occurring between 1999 and 2014 but, without knowing how to assign responsibility in cases of multiple drug use, can say little more.[27]

Based on any mentions, opioid analgesics play the most important role in accounting for the rise in drug fatalities (64%). Even with the adjustment procedures, unspecified drugs explain 40% of the growth in deaths (reduced from 49% based on death certificate reports). Heroin, sedatives (mostly benzodiazepines) and psychotropic drugs (especially antidepressants and psychostimulants) each explain 31% to 39% of the trend, with less substantial roles for other specified drugs, cocaine and other narcotics.

[26] These estimates are based on adjusted prevalences of 32.0% in 1999 and 52.6% in 2014 (0.31989 x 16,849 = 5,390; 0.52639 x 47,055 = 24,769).

[27] Actually, the bounds are even wider. Taking the 95% confidence intervals into account, the range might be as large as 20% to 67%.

Corresponding calculations using exclusive mentions reveal much lower contributions but also some important differences in the patterns. Opioid analgesics continue to contribute the most (23%) but not that much more than heroin (18%). Conversely, use of sedatives explains almost none of the growth in fatal overdoses because these are almost never the only type of drug involved, but lone use of psychotropics plays a relatively important role – accounting for 7% of the increase –mostly due to psychostimulants.

A key result, reiterated in the last row of the tables, is that drug "cocktails" account for 55% of the rise in deaths, again emphasizing the importance of understanding the role of individual drug classes in these cases or of the higher risks implied by the use of multiple drugs. A possible exception is that exclusive deadly use appears to be relatively common for heroin. For instance, in 2014, 45% of fatal drug overdoses involving heroin (6,292 of 14,103) were characterized by exclusive use, compared to 37%, 7%, and 29% of opioid analgesic, sedative and psychotropic cases.[28]

Examination of the 1999-2014 period reflects the availability of comparable data rather than any theoretical justification. The remainder of this section considers the sensitivity of the results to the use of alternative analysis windows. Figure 10 summarizes estimated effects for periods that start in 1999 and end in the year specified on the X-axis. For instance, the left-most entry is for 1999-2003 while that farthest to the right covers the full 1999-2014 period (and so provides equivalent information to Table 9).[29]

Opioids analgesic mentions are most important for all sub-periods but have become somewhat less so for those that include the most recent years: *any* prescription opioid involvement "explains" 74% to 85% of the growth in deaths for periods ending between 2003

[28] Exclusive use also has fairly high proportions of total mentions for psychostimulants (44%), although the overall contributions are smaller for these because of their relatively low prevalences.
[29] Windows shorter than 4 years are dominated by noise and so are not shown here or on Figure 11.

and 2010, but the share rapidly declines for later ending years, to 63% for 1999-2013 and 64% for the full period. Conversely, role of *exclusive* opioid analgesic mentions falls virtually monotonically with the addition of later years, from 40% for 1999-2003 to 23% for 1999-2014. This occurs because the contribution of deaths involving combinations of drugs rises fairly steadily with the addition of recent years, from 42% for 1999-2003 to 56% for 1999-2014.

The other notable results in Figure 10 relate to the role of illicit opioids, with a declining role for cocaine initially and a rising contribution of heroin in later ending years. Specifically, cocaine involvement "explained" 21% to 29% of the rise in overdose deaths for periods starting in 1999 and ending between 2003 and 2007, with exclusive mentions accounting for 10% to 14%. However, cocaine-related deaths played almost no role in the overall change when the sample includes ending years of 2009 or later. By contrast, changes in heroin-related fatalities had little explanatory power for periods ending prior to 2007 – accounting for 0% to 3% of the total change – but became more consequential with the inclusion of subsequent years, particularly those after 2010. Specifically, *any* heroin mentions accounted for 9%, 15%, 24%, 32%, and 39% of the total change for analysis windows ending in 2010, 2011, 2012, 2013 and 2014, with exclusive mentions being responsible for 6%, 9%, 14%, 17%, and 18%. Results for the other drug classes are less sensitive to the choice of time periods, except for the continued rise in the explanatory power of sedative involvement when including recent years. However, as mentioned the sedatives are almost never exclusively responsible for drug poisoning deaths.

Figure 11 summarizes an alternative way of examining the data where the ending year is always 2014 but the starting year varies. Doing so yields remarkable changes. In particular, any mentions of opioid analgesics play a dominant role for analysis with early starting dates but account for less of the growth in overdose deaths than heroin when the first year analyzed is

2004 or later, and also for sedatives and psychotropics when it is after 2005 and 2006 respectively. Conversely, heroin-involved deaths make the largest contribution when the beginning year is subsequent to 2003 and exclusive heroin mentions explain more of the growth in fatal overdoses than corresponding involvement of opioid analgesics for all periods starting after 2001: any heroin involvement accounts for 60%, 97% and 113% percent of the rise in drug deaths for analysis windows starting in 2004, 2007 and 2010 with exclusive heroin involvement responsible for 26%, 43% and 47% of the increase.

This should not be taken to imply that multiple drug use play a less important role in recent periods. It accounted for 56% of the total change between 1999 and 2014 and 62%, 67% and 59% of the growth when starting the analysis in 2004, 2007 and 2010. The contribution of psychotropic medications also rises when restricting the analysis period to more recent years, from 31% for any mentions from 1999-2014 to 44% for 2006-2014, with 7% and 11% accounted for by exclusive mentions. The patterns are more variable for most other types of drugs, which usually also have less explanatory power.

Table 10 illustrates these differences in a fairly extreme way, showing the contributions towards the increases in drug deaths by splitting the sample equally across periods: 1999 to 2006 and 2007 to 2014. During the earlier timespan, increases in deaths involving any mentions of opioid analgesics account for 79% of the rise in drug deaths with exclusive mentions being responsible for 38%. By contrast, any mentions of these drugs are related to just 38% of the increase in deaths from 2007 to 2014, and exclusive use for none at all, largely because of the decline in methadone deaths. And heroin plays the dominant role in the increase between 2007 and 2014, with any mentions accounting for 97% of the change and exclusive mentions for 43%. Combination drug use also becomes more important in the later period (67% vs. 46%), as do psychotropics and other specified drugs, whereas cocaine mentions are considerably less so. Sedatives also play a great role in the second half of the period, but only because of the increasing prevalence of combination drug use – exclusive sedative prevalence declines slightly.

8. Discussion

Current death certificate data are problematic for understanding the drug poisoning epidemic, with a particular issue being the frequency that no specific drug is identified (Slavova et al., 2015). Additional training and standardization in states with low specification rates may be helpful, particularly since this is a bigger problem when death certificates are completed by coroners (instead of medical examiners) and in states without centralized oversight (Warner et al., 2013). Others have also recommended adding detail to death certificates on the drugs involved, toxicology levels, ICD categories, as well as more carefully distinguishing between cases where a given drug is the cause of mortality versus those where it was detected but not a major contributor (Webster & Dasgupta, 2011; Goldberger et al., 2013).

Until such information becomes available, predictive adjustment methods such as those developed here can provide more accurate prevalence estimates. The benefits are considerable since death certificates often understate the involvement of specific drug types by 30% to 60%, combination drug use by 50% or more, and exclusive use of drug classes by 20% to 30%. The adjustment procedures work well but not perfectly, for example reducing the prevalence of exclusive mentions of unspecified drugs from 20% to 4% in 2014. However, several issues remain. One is that death certificates may be incomplete, even when drugs are specified. A preliminary analysis suggests that more detailed reporting would considerably raise mentions of sedative, psychotropic, other specified and combination drug use but have smaller effects on opioid analgesic, heroin or cocaine involvement. A second is that the reporting itself may be inaccurate. For instance, heroin use may sometimes instead be attributed to morphine or codeine—because heroin metabolizes into morphine and codeine may be detected as an impurity in morphine or heroin (Mertz et al., 2014). Third, overdose deaths could also be misclassified as due to non-drug causes, and therefore excluded from the analysis, while non-drug causes could be primarily responsible for the death for some deaths that are included. Similarly, information on specific drug involvement is not provided for the small number of cases (727 in 2014) where the underlying cause of death is classified as a mental or behavioral disorder due to drug use (ICD-10 codes F11 through F16).

These caveats notwithstanding, the findings of this analysis have important implications. The number of U.S. residents dying from drug poisoning rose from 16,849 in 1999 to 47,055 in 2014. In all years analyzed, prescription opioids are the most common class of drugs involved, justifying the ongoing concerted actions to reduce the negative consequences associated with their use. At least partially due to these efforts, the number of fatal overdoses involving opioid analgesics declined more than 7% between 2011 and 2013 (from 24,271 to 22,501), before rising again in 2014 (to 24,769); however, the total number of drug poisoning deaths has continued to rise (from 41,340 to 47,505). Indeed, deadly overdoses have increased in *every* year since 1990, even as the involvement of specific drugs has changed. For example, deaths involving cocaine fell 30% (from 10,133 to 7,131) between 2006 and 2014 whereas those where heroin was implicated skyrocketed 498% (from 2,360 to 14,103) from 2004 to 2014, with most of this growth since 2010.[30]

A key finding is that a majority of overdose fatalities involve multiple classes of drugs, making it difficult or impossible to attribute the secular increase to specific drugs. Combination

[30] All of the fatality numbers in this paragraph, other than the total number of deaths, are estimated based on adjusted prevalences and so are measured with error.

drug use itself is likely to be a risk factor. For example, benzodiazepines were estimated to be involved in 11,843 deaths in 2014 versus just 1,847 in 1999 but were virtually never the *only* drug playing a role. However, the health risks of using opioids and benzodiazepines together are almost certainly greater than of either in isolation (Jones, et al., 2012; Park, et al., 2015) and interactions between types of drugs are poorly understood. Most significantly, the modest decline since 2011 in opioid analgesic-related mortality has been accompanied by an enormous increase in deaths involving heroin, but with mixed evidence on whether the two types of drugs are substitutes (Cicero et al. 2012; Markon & Crites, 2014) or complements (Rudd et al., 2014).

Finally, attribution of the secular increase in fatal overdoses to specific drug categories turns out to be sensitive to the time periods analyzed. Because deaths involving opioid analgesics rose extremely rapidly at the start of the 21st century (e.g. from 5,275 in 1999 to 22,015 in 2009), they appear to be "responsible" for a large percentage of growth in drug poisoning deaths for any period that begins at or near 1999 (regardless of the ending year). Conversely, heroin plays the most important role for periods starting in 2004 or later, and beginning as early as 2001 when basing the calculations on exclusive drug involvement. This reflects the very rapid growth in heroin-related fatalities since the mid-2000s. By contrast, the role of combination drug use is large and robust to the choice of starting and ending years – almost always explaining 40% to 60% of the growth in deaths – further highlighting its importance for the design of effective policies to reduce fatal drug poisonings.

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Table 1: Manner and Types of Reported Drug Involvement in 2014 Drug Poisoning Deaths

	#	%
All Drug Poisoning Deaths (X40-44, X60-64, X85, Y10-14, Y35.2, *U01.6, *U01.7)	47,055	100.0%
Manner of Death		
Accidental (X40-44)	38,718	82.3%
Intentional (X60-64)	5,433	11.5%
Undetermined Intent (Y10-Y14)	2,823	6.0%
Homicide (X85)	81	0.2%
Reported Mentions (T-Codes)		
Narcotics (40.0-40.9)	30,731	65.3%
Opioid Analgesics (40.2-40.4)	18,893	40.2%
Methadone (40.3)	*3,400*	*7.2%*
Other Opioid Analgesics (40.2, 40.4)	*16,371*	*34.8%*
Heroin (40.1)	10,574	22.5%
Cocaine (40.5)	5,415	11.5%
Other Narcotics (40.0, 40.6-40.9)	2,822	6.0%
Sedatives (42.0-42.8)	9,308	19.8%
Benzodiazepines (42.4)	*7,945*	*16.9%*
Other Sedatives (42.0-42.3, 42.5-42.8)	*2,450*	*5.2%*
Psychotropics (43.0-43.9)	9,614	20.4%
Antidepressants (43.0-43.2)	*4,768*	*10.1%*
Antipsychotics (43.3-43.5)	*1,588*	*3.4%*
Psychostimulants (43.6)	*4,298*	*9.1%*
Other Specified (36.0-38.9, 41.0, 41.9, 44.0-48.7, 49.0-50.8)	3,573	7.6%
Unspecified (50.9)	23,347	49.6%
Alcohol (51.0-51.4)	4,089	8.7%
Exclusive Mentions		
Opioid Analgesics	7,769	16.5%
Heroin	5,067	10.8%
Cocaine	1,747	3.7%
Sedatives	814	1.7%
Psychotropics	3,390	7.2%
Other Specified	1,476	3.1%
Unspecified	9,201	19.6%
>1 Major Drug Class	16,187	34.4%
No Drug Mentioned	406	0.9%

Note: Data from the Multiple Cause of Death files. Entries in parentheses refer to ICD-10 X and Y codes for the underlying causes of death and T codes for drug mentions. >1 Major drug class refers to drug mentions of two or more of the following drug types: opioid analgesics, heroin, cocaine, other narcotics, sedatives, psychotropics, or other specified drugs. Exclusive drug mentions indicates deaths where only the specified class of drugs is mentioned (but unspecified drugs could also be listed on the death certificate).

Table 2: Reported Drug Involvement in Drug Poisoning Deaths in Low and High Diagnosis Counties, 2014

Drug Mentions	Low Diagnosis Counties	High Diagnosis Counties
Narcotics	34.3%	83.7%
Opioid Analgesics	19.5%	52.8%
Methadone	*3.8%*	*9.5%*
Other Opioid Analgesics	*16.4%*	*46.0%*
Heroin	10.8%	29.5%
Cocaine	5.0%	15.1%
Sedatives	7.2%	26.5%
Psychotropics	10.8%	24.6%
Other Specified	3.8%	10.1%
>1 Major Drug Class	12.0%	47.6%
Unspecified & Specified	17.2%	34.3%
Unspecified Only	54.0%	0.6%
# of Conditions Listed	2.57	3.72

Note: See note on Table 1. Low diagnosis counties are those with at least one drug specified for fewer than 68.4% of drug poisoning deaths in 2014. High diagnosis counties are those with at least one drug specified in more than 98.2% of drug poisoning deaths in 2014. The number of conditions listed refers to record-axis conditions shown on the Multiple Cause of Death files.

Table 3: Reported and Adjusted Drug Prevalences in Drug Poisoning Deaths, 2014

Drug Mentions	Reported Prevalence	Adjusted Prevalence Estimate	Adjusted Prevalence Standard Error	Difference
Any Mention				
Opioid Analgesics	40.2%	52.6%	1.0%	31.1%
Heroin	22.5%	30.0%	1.0%	33.4%
Cocaine	11.5%	15.2%	0.7%	31.7%
Sedatives	19.8%	29.2%	0.9%	47.6%
Psychotropics	20.4%	27.3%	0.9%	33.5%
Other Specified	7.6%	10.3%	0.3%	35.5%
Unspecified	49.6%	38.4%	1.6%	-22.6%
>1 Major Drug Class	34.4%	49.3%	0.9%	43.2%
Exclusive Mention				
Opioid Analgesics	16.5%	19.3%	0.6%	17.1%
Heroin	10.8%	13.4%	0.7%	24.2%
Cocaine	3.7%	4.3%	0.3%	16.1%
Sedatives	1.7%	2.1%	0.1%	22.4%
Psychotropics	7.2%	7.9%	0.4%	10.2%
Other Specified	16.5%	19.3%	0.6%	17.1%
Unspecified	19.6%	3.5%	0.1%	-82.2%

Note: See note on Table 1. Reported prevalences are from death certificates and indicate the percentage of drug poisonings where the specified type of drug is mentioned. Adjusted prevalences are average predicted values from probit models, where at least one specific drug is mentioned for all poisoning deaths in the county (SPECIFY =1). Models also control for: sex, race (black, other), Hispanic, currently married, education (high school dropout, high school graduate, some college, college graduate), age (≤20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, >80), day of the week of death, and census region. Robust standard errors are calculated with clustering at the county level. Difference refers to the percentage difference between the adjusted and reported prevalences. These are calculated using more significant digits than are shown in the table, so some differences may appear due to rounding error. Lower panel indicates exclusive mentions of specified drug type (but possibly also with unspecified drugs mentioned).

Table 4: Reported and Adjusted Drug Prevalences at Specified Numbers of Conditions Mentioned, 2014

	SPECIFY = 1		SPECIFY = 1 & NUMCTY = 4.264		
Drug Mentions	Adjusted Prevalence	Standard Error	Adjusted Prevalence	Standard Error	% Δ
	(1a)	(1b)	(2a)	(2b)	(3)
Opioid Analgesics	52.6%	1.0%	54.2%	0.9%	2.9%
Heroin	30.0%	1.0%	29.2%	1.1%	-2.6%
Cocaine	15.2%	0.7%	15.7%	0.8%	3.6%
Sedatives	29.2%	0.9%	33.7%	0.8%	15.6%
Psychotropics	27.3%	0.9%	29.6%	0.8%	8.5%
Other Specified	10.3%	0.3%	11.5%	0.3%	11.4%
Unspecified	38.4%	1.6%	41.6%	1.8%	8.4%
>1 Major Drug Class	49.3%	0.9%	54.8%	0.8%	11.1%

Note: See note on Table 1 and 3. Adjusted prevalences in (1a) are average predicted values from probit models, where at least one specific drug is mentioned for all poisoning deaths in the county (SPECIFY =1). Models also control for: sex, race (black, other), Hispanic, currently married, education (high school dropout, high school graduate, some college, college graduate), age (≤20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, >80), day of the week of death, and census region. Column (2a) shows corresponding adjusted prevalences for models that also control for the county average number of conditions mentioned on the death certificates (NUMCTY), and interpreted where this value is set to 4.263754. Column (3) shows the percentage difference between columns (2a) and (1a). Robust standard errors in (1b) and (2b) are calculated with clustering at the county level.

Table 5: Reported and Adjusted 2014 Prevalence by Manner of Drug Poisoning Death

	Accidental			Intentional			Undetermined Intent		
Drug Mentions	Reported Prevalence	Adjusted Prevalence	% Δ	Reported Prevalence	Adjusted Prevalence	% Δ	Reported Prevalence	Adjusted Prevalence	% Δ
Opioid Analgesics	41.1%	53.8%	41.1%	31.0%	41.3%	33.4%	45.1%	58.8%	30.5%
Heroin	25.9%	34.2%	25.9%	1.7%	2.7%	59.7%	16.0%	20.6%	28.2%
Cocaine	13.3%	17.6%	13.3%	1.5%	2.5%	64.7%	6.0%	7.5%	25.5%
Sedatives	19.0%	28.4%	19.0%	26.9%	38.1%	41.5%	16.9%	27.4%	61.6%
Psychotropics	19.0%	25.3%	19.0%	31.1%	42.6%	37.0%	19.1%	26.4%	38.4%
Other Specified	5.6%	7.7%	5.6%	22.2%	28.7%	29.2%	7.2%	10.3%	43.2%
Unspecified	48.4%	37.0%	48.4%	62.9%	55.1%	-12.5%	41.8%	29.2%	-30.2%
>1 Major Drug	35.2%	50.4%	35.2%	30.8%	44.3%	44.0%	30.9%	44.8%	45.0%
Only Unspecified	19.0%	3.2%	19.0%	22.7%	5.8%	-74.5%	21.5%	4.0%	-81.4%

Note: See note on Table 3. Reported prevalences are from death certificates and indicate the percentage of drug poisonings where the specified type of drug is mentioned. Adjusted prevalences are average predicted values from probit models, where at least one specific drug is mentioned for all poisoning deaths in the county (SPECIFY =1). Models also control for: sex, race/ethnicity, currently married, education, age, day of the week of death, and census region. Robust standard errors are calculated with clustering at the county level. The manner of death (accidental, intentional or of undetermined intent, is based on the death certificate ICD-10 code. The analytic sample contains 38,718, 5,433 and 2,823 drug poisoning deaths classified as accidental, intentional and of undetermined intent. Standard errors on the adjusted prevalences range from 0.3% to 1.8% for accidental deaths, 0.3% to 1.7% for intentional deaths and 0.7% to 3.1% for deaths of undetermined intent.

Table 6: County-Level Differences in Opioid Analgesic & Heroin Involvement: Adjusted vs. Reported Prevalences, 2014

Opioid Analgesics				Heroin			
County	Ranking		Death Rate	County	Ranking		Death Rate
	Adj.	Rep.			Adj.	Rep	
20 Counties with Largest Deterioration in Rankings							
PHILADELPHIA, PA	10	226	15.27	CAMDEN, NJ	15	236	11.18
WESTMORELAND, PA	15	230	14.61	PHILADELPHIA, PA	4	222	14.02
CAMDEN, NJ	34	244	12.31	DAUPHIN, PA	42	219	7.33
ORLEANS, LA	43	249	11.75	GLOUCESTER, NJ	20	186	10.20
GLOUCESTER, NJ	50	236	11.12	ALLEN, IN	71	231	5.84
BUCKS, PA	41	227	11.85	BURLINGTON, NJ	53	212	6.59
LUZERNE, PA	63	246	10.28	LUZERNE, PA	36	195	8.09
DELAWARE, PA	19	187	13.85	WESTMORELAND, PA	21	161	10.18
MARION, IN	32	182	12.48	PASCO, FL	04	234	4.42
ST. LUCIE, FL	73	210	9.55	CHESTER, PA	74	201	5.79
LEHIGH, PA	102	235	8.63	KNOX, TN	54	180	6.57
BREVARD, FL	30	152	12.62	BUCKS, PA	25	150	9.37
WINNEBAGO, IL	23	144	13.47	BRISTOL, MA	18	141	10.58
PALM BEACH, FL	64	183	10.25	LANCASTER, PA	89	207	5.01
ERIE, PA	57	173	10.57	HAMILTON, TN	17	229	4.05
OCEAN, NJ	47	156	11.64	OKLAHOMA, OK	13	214	4.12
JEFFERSON, KY	14	121	14.62	PINELLAS, FL	18	217	4.01
POLK, FL	93	192	8.95	SEDGWICK, KS	22	213	3.94
YORK, PA	18	115	13.91	MARION, IN	9	96	12.09
CHESTER, PA	145	241	7.01	LEHIGH, PA	33	120	8.25
20 Counties with Largest Improvement in Rankings							
KENT, MI	213	117	4.37	HENRICO, VA	204	84	2.49
MONROE, NY	138	57	7.39	DURHAM, NC	216	105	2.11
MORRIS, NJ	189	111	5.15	GUILFORD, NC	185	75	2.82
CLEVELAND, OK	132	54	7.58	VIRGINIA BEACH, VA	192	94	2.70
SAN JOAQUIN, CA	124	47	7.94	THE DISTRICT, DC	161	64	3.25
LEON, FL	227	151	3.97	KING, WA	145	49	3.50
PINAL, AZ	208	134	4.53	FAIRFAX, VA	234	138	1.69
FRESNO, CA	159	85	6.29	WAKE, NC	223	129	1.96
JOHNSON, KS	196	123	4.84	FORSYTH, NC	153	61	3.39
ORANGE, CA	177	104	5.53	PRINCE GEORGES, MD	231	139	1.77
CUMBERLAND, ME	106	35	8.43	MECKLENBURG, NC	203	116	2.49
NASSAU, NY	161	90	6.24	PRINCE WILLIAM, VA	214	131	2.13
ERIE, NY	118	48	8.02	E. BATON ROUGE, LA	173	92	3.04
DANE, WI	135	67	7.46	TARRANT, TX	215	136	2.12
RICHLAND, SC	139	71	7.39	MULTNOMAH, OR	128	52	3.82
HILLSBOROUGH, FL	128	60	7.73	SHELBY, TN	111	36	4.15
ANOKA, MN	222	154	4.10	DALLAS, TX	164	90	3.20
HOWARD, MD	225	159	4.00	DE KALB, GA	225	151	1.93
DOUGLAS, NE	206	140	4.59	HENRICO, VA	204	84	2.49
JACKSON, MO	126	62	7.81	DURHAM, NC	216	105	2.11

Note: Table refers to 250 largest counties and shows the 20 with the largest deterioration and improvements in rankings when comparing death rates involving opioid analgesics and heroin based on adjusted (Adj.) versus reported (Rep.) prevalences. Lower numerical rankings indicate smaller death rates. Death rates displayed are based on adjusted prevalences and are per 100,000 population.

Table 7: Drug Combinations in Drug Poisoning Deaths: 1999, 2006 and 2014

Drug Category	Frequency of Combination With: Opioid Analg.	Heroin	Cocaine	Seda-tives	Psycho-tropics	Other	Exclu-sive Use
				1999			
Opioid Analg.		13.1%	18.1%	18.1%	21.0%	5.0%	42.7%
Heroin	30.1%		31.7%	3.9%	4.5%	1.1%	38.6%
Cocaine	19.2%	14.6%		7.7%	7.9%	2.8%	39.1%
Sedatives	38.0%	3.6%	15.3%		32.2%	10.0%	24.5%
Psychotropics	31.6%	2.9%	11.3%	23.1%		10.9%	43.5%
Other	17.2%	1.7%	8.9%	16.3%	24.8%		60.6%
				2006			
Opioid Analg.		3.2%	17.5%	26.3%	18.7%	6.0%	46.9%
Heroin	22.2%		38.0%	7.4%	7.4%	1.1%	40.3%
Cocaine	33.3%	10.3%		10.6%	9.7%	2.9%	44.1%
Sedatives	70.8%	2.8%	15.0%		29.7%	10.8%	12.4%
Psychotropics	49.0%	2.8%	13.4%	28.9%		12.7%	31.8%
Other	40.2%	1.0%	10.1%	26.7%	32.2%		40.3%
				2014			
Opioid Analg.		13.7%	15.6%	38.1%	24.8%	8.8%	36.7%
Heroin	24.1%		20.6%	18.0%	14.1%	3.2%	44.6%
Cocaine	33.0%	40.8%		17.7%	13.4%	4.0%	28.4%
Sedatives	68.7%	18.5%	9.2%		36.6%	13.6%	7.3%
Psychotropics	47.9%	15.4%	7.5%	39.1%		14.7%	29.1%
Other	44.9%	9.2%	5.8%	38.7%	39.0%		34.2%

Note: Table shows percentage of drug poisoning deaths involving the drug category listed in the first column that also involve other major drug categories. Percentages are based on adjusted prevalences, except for deaths involving combinations of heroin use with sedative, psychotropic or other drug use in 1999 and heroin and other drug use in 2006, where reported prevalences are shown.

Table 8: Change in Number of Deaths Involving Specified Drugs: 2012-2014 Versus 2011

Drug Category	# of Deaths in 2011	Δ in # Deaths Since 2011			% Δ in Deaths Since 2011		
		2012	2013	2014	2012	2013	2014
Based on Death Certificate Reports							
Opioid Analg.	16,917	-910	-682	1,976	-5.4%	-4.0%	11.7%
Heroin	4,397	1,528	3,860	6,177	34.8%	87.8%	140.5%
Cocaine	4,681	-277	263	734	-5.9%	5.6%	15.7%
Sedatives	8,089	-335	90	1,219	-4.1%	1.1%	15.1%
Psychotropics	6,990	477	1,652	2,624	6.8%	23.6%	37.5%
>1 Drug	12,341	69	1,304	3,846	0.6%	10.6%	31.2%
Based on Adjusted Prevalences							
Opioid Analg.	24,271	-1,737	-1,770	498	-7.2%	-7.3%	2.1%
	(477)	(260)	(294)	(322)	(1.1%)	(1.2%)	(1.3%)
Heroin	6,165	2,124	4,959	7,938	34.5%	80.4%	128.8%
	(394)	(259)	(413)	(471)	(4.8%)	(9.8%)	(13.3%)
Cocaine	6,756	-591	-137	376	-8.7%	-2.0%	5.6%
	(324)	(163)	(210)	(226)	(2.3%)	(3.1%)	(3.5%)
Sedatives	13,440	-983	-864	297	-7.3%	-6.4%	2.2%
	(466)	(276)	(290)	(315)	(2.0%)	(2.0%)	(2.4%)
Psychotropics	10,518	281	1,522	2,320	2.7%	14.5%	22.1%
	(362)	(225)	(249)	(299)	(2.2%)	(2.5%)	(3.1%)
>1 Drug	19,876	-378	577	3,308	-1.9%	2.9%	16.6%
	(407)	(252)	(289)	(311)	(1.3%)	(1.5%)	(1.7%)

Note: Table shows 2011 deaths involving the specified drug category, and levels and percentage changes in deaths, versus the 2011, in 2012-2014. Upper panel shows results based on death certificate reports. Lower panel shows findings based on adjusted prevalences. Robust standard errors, with clustering at the county level, are shown in parentheses.

Table 9: Estimated Changes of Drug Involvement in Drug Poisoning Deaths, 1999 to 2014

Drug Category	Δ in # Deaths		% of Total Δ Explained	
	Estimate	St. Error	Estimate	St. Error
Any Mention				
Opioid Analgesics	19380	470	64.2%	1.6%
Methadone	3253	164	10.8%	0.5%
Other Opioid Analg.	17294	462	57.3%	1.5%
Heroin	11760	558	38.9%	1.8%
Cocaine	2055	313	6.8%	1.0%
Other Narcotic	-967	542	-3.2%	1.8%
Sedatives	11173	368	37.0%	1.2%
Bezodiazepines	9996	335	33.1%	1.1%
Other Sedative	2702	176	8.9%	0.6%
Psychotropics	9260	373	30.7%	1.2%
Antidepressants	4321	224	14.3%	0.7%
Antipsychotics	1915	127	6.3%	0.4%
Psychostimulants	4440	266	14.7%	0.9%
Other Specified	3271	172	10.8%	0.6%
Unspecified	12209	721	40.4%	2.4%
Exclusive Mention				
Opioid Analgesics	6800	312	22.5%	1.0%
Methadone	940	83	3.1%	0.3%
Other Opioid Analg.	5501	267	18.2%	0.9%
Heroin	5388	375	17.8%	1.2%
Cocaine	42	129	0.1%	0.4%
Sedatives	367	65	1.2%	0.2%
Psychotropics	2181	199	7.2%	0.7%
Antidepressants	-13	82	0.0%	0.3%
Antipsychotics	114	*29*	0.4%	*0.1%*
Psychostimulants	1937	161	6.4%	0.5%
Other Specified	707	96	2.3%	0.3%
Unspecified	1004	53	3.3%	0.2%
>1 Major Drug	16778	441	55.5%	1.5%

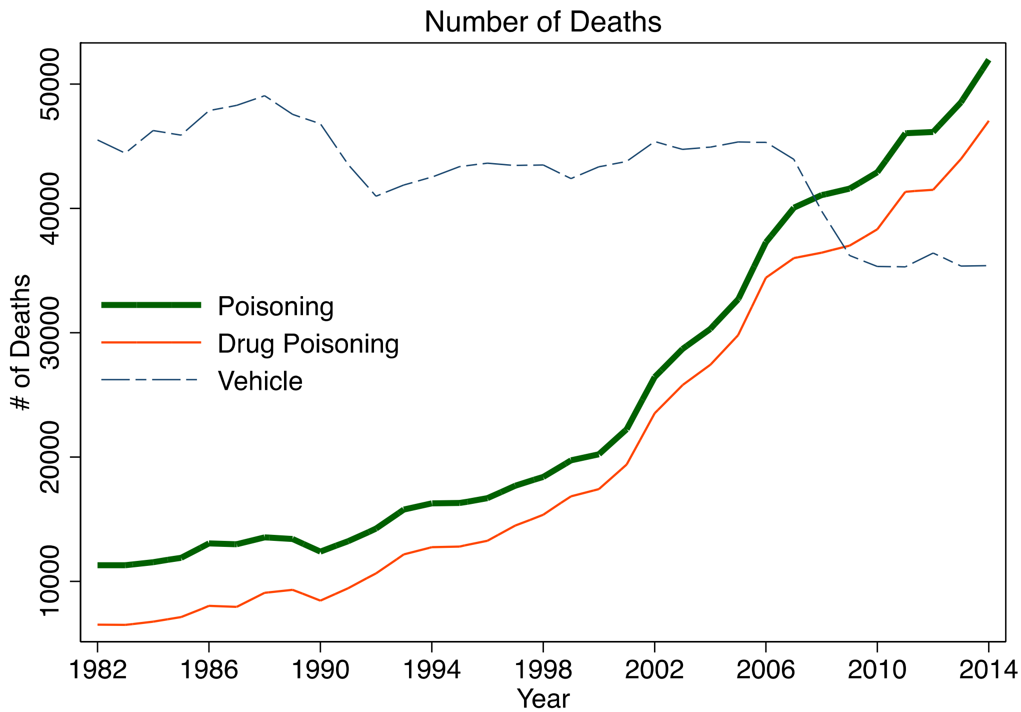
Note: See notes on Tables 1 and 3. Estimates are based on adjusted prevalences. Δ in # Deaths is the difference between 2014 and 1999 deaths involving the specified drug. % of Total Δ Explained is Δ in # Deaths divided by 30,206 (the increase in drug poisoning deaths occurring between 2014 and 1999). Robust standard errors are calculated with clustering at the county level.

Table 10: Percent of Change in Drug Poisoning Deaths Explained, 1999 to 2006 and 2007 to 2014

Drug Category	2006 vs. 1999		2014 vs. 2007	
	Estimate	St. Error	Estimate	St. Error
<u>Any Mention</u>				
Opioid Analgesics	78.7%	2.2%	37.9%	3.2%
Methadone	*37.3%*	*1.8%*	*-32.4%*	*2.3%*
Other Opioid Analg.	*50.2%*	*2.3%*	*65.7%*	*3.5%*
Heroin	2.4%	1.5%	97.2%	4.4%
Cocaine	28.8%	1.4%	-17.8%	2.5%
Other Narcotic	1.3%	1.9%	-6.5%	4.1%
Sedatives	26.0%	1.8%	44.1%	3.5%
Bezodiazepines	*22.9%*	*1.6%*	*41.2%*	*3.3%*
Other Sedative	*6.0%*	*0.8%*	*8.4%*	*2.1%*
Psychotropics	21.4%	1.3%	41.0%	3.3%
Antidepressants	*11.8%*	*1.1%*	*13.2%*	*2.3%*
Antipsychotics	*5.9%*	*0.6%*	*5.1%*	*1.3%*
Psychostimulants	*6.0%*	*0.7%*	*30.5%*	*1.9%*
Other Specified	7.5%	0.9%	14.6%	1.5%
Unspecified	32.8%	2.4%	48.5%	5.1%
<u>Exclusive Mention</u>				
Opioid Analgesics	38.2%	1.7%	-3.0%	2.7%
Methadone	*15.8%*	*0.9%*	*-18.3%*	*1.5%*
Other Opioid Analg.	*19.8%*	*1.3%*	*16.3%*	*2.3%*
Heroin	1.2%	0.6%	42.6%	3.3%
Cocaine	14.1%	0.9%	-17.0%	1.4%
Sedatives	1.5%	0.3%	0.6%	0.6%
Psychotropics	4.4%	0.7%	12.6%	1.5%
Antidepressants	*0.3%*	*0.5%*	*-0.4%*	*0.7%*
Antipsychotics	*0.9%*	*0.2%*	*-0.4%*	*0.3%*
Psychostimulants	*2.7%*	*0.5%*	*13.1%*	*1.1%*
Other Specified	1.2%	0.4%	3.9%	0.8%
Unspecified	3.7%	0.3%	2.2%	0.5%
>1 Major Drug	46.3%	1.9%	67.4%	3.6%

Note: See notes on Tables 1, 3 and 6. Estimates are based on adjusted prevalences and show the % of Total Δ Explained. The total number of drug poisoning deaths were 16,849, 34,425, 36,010 and 47,055 in 1999, 2006, 2007 and 2014.

Figure 1: Poisoning and Motor Vehicle Deaths and Death Rates



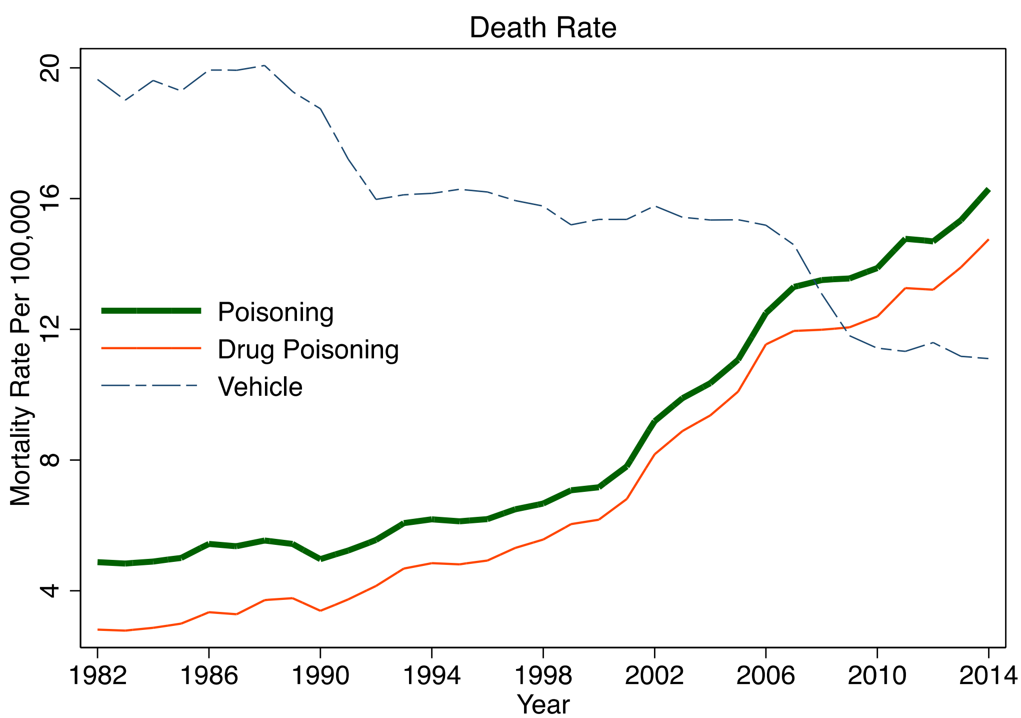
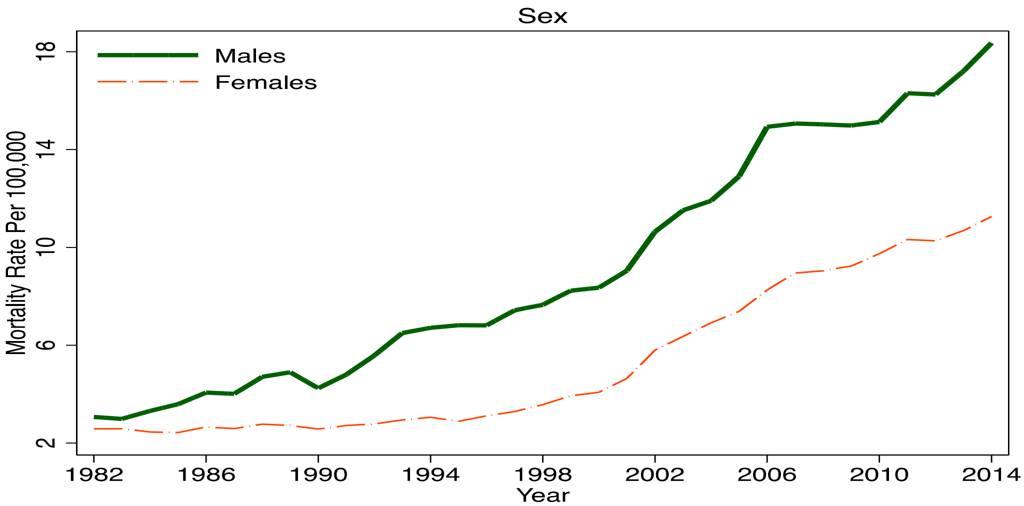
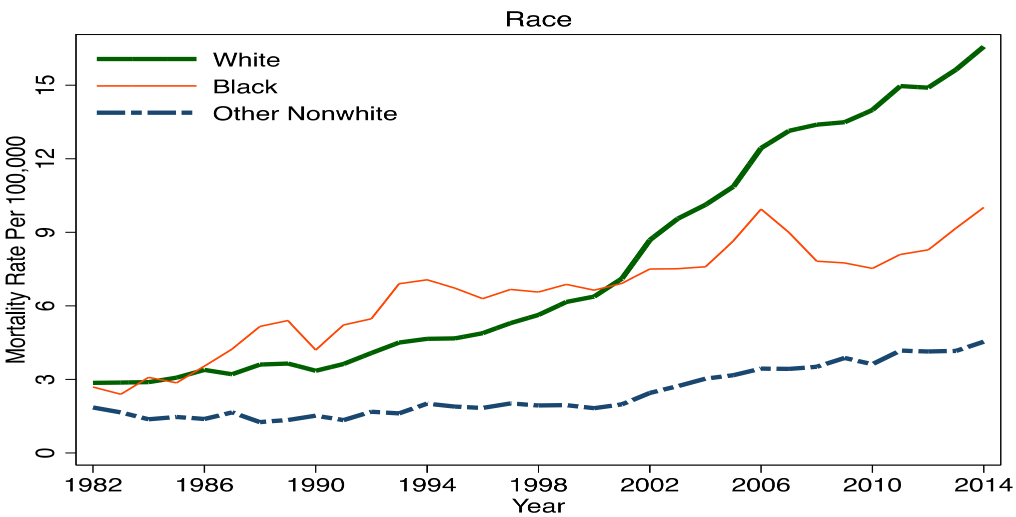


Figure 2: Group-Specific Drug Poisoning Rates





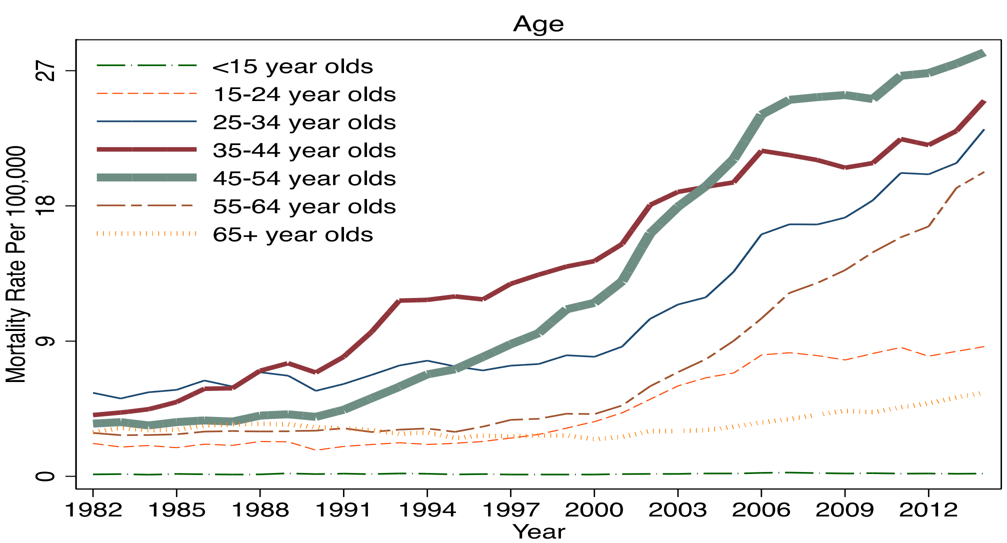


Figure 3: County and State Drug Poisoning Death Rates

Fig. 3a: State Rates, 2014

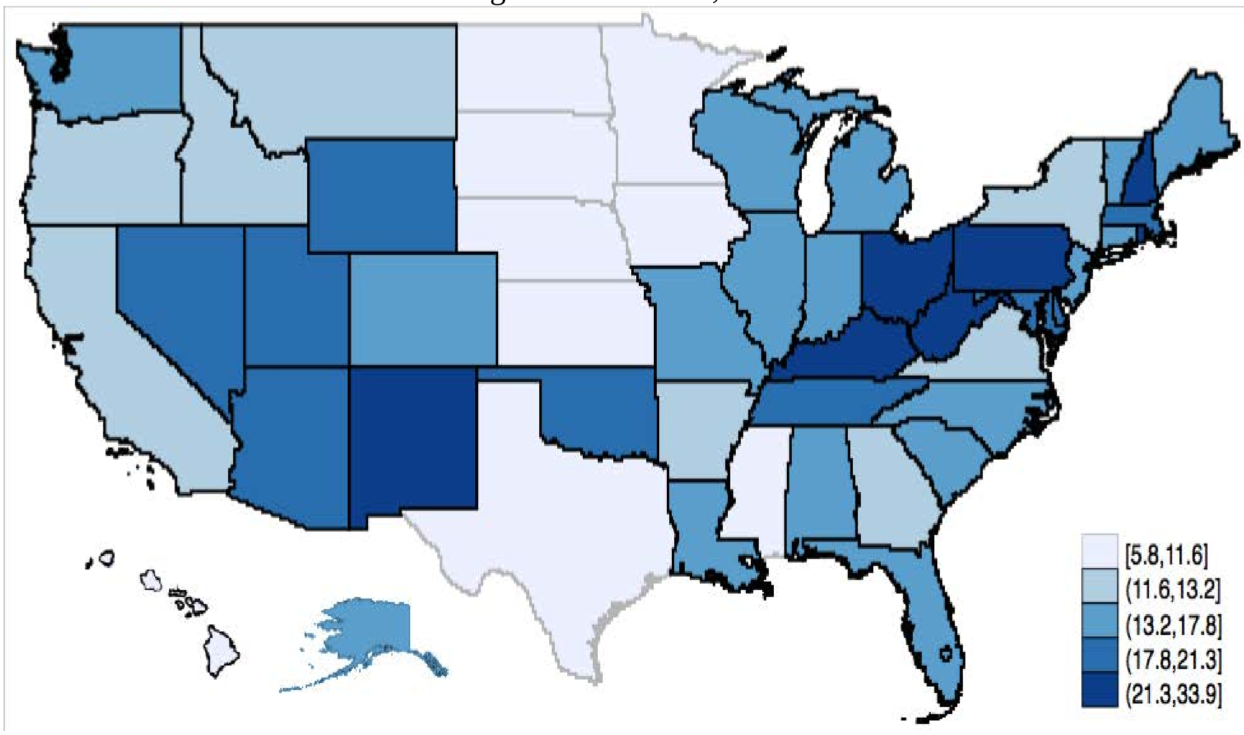
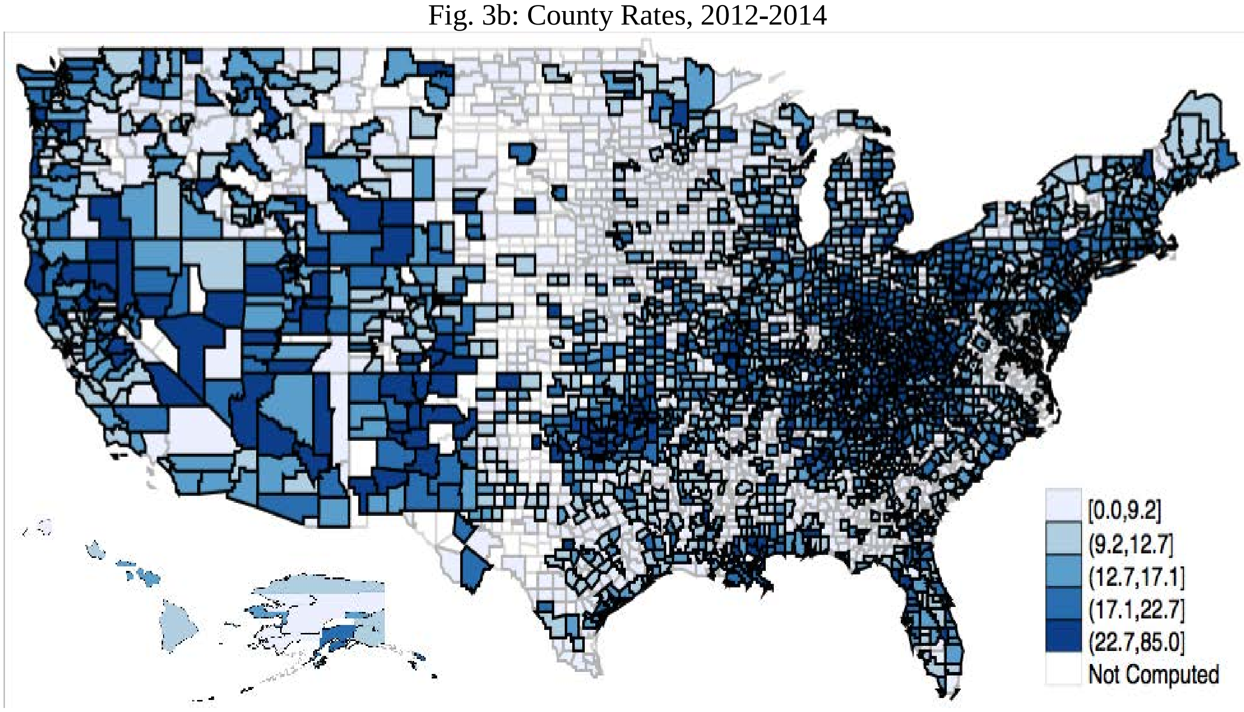


Fig. 3b: County Rates, 2012-2014



Note: Drug poisoning death rates are per 100,000 population. State death rates refer to 2014; county rates are averages for 2012-2014, for counties with populations of 5,000 or more.

Figure 4: Share of Drug Poisoning Deaths with ≥1 Specific Drug Mentioned

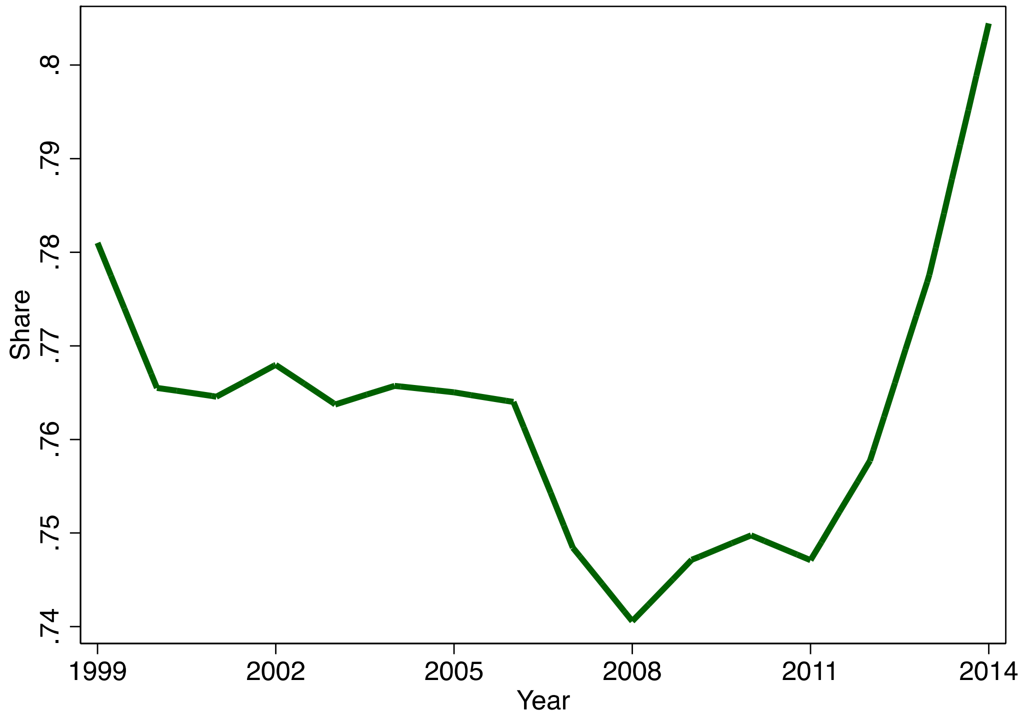
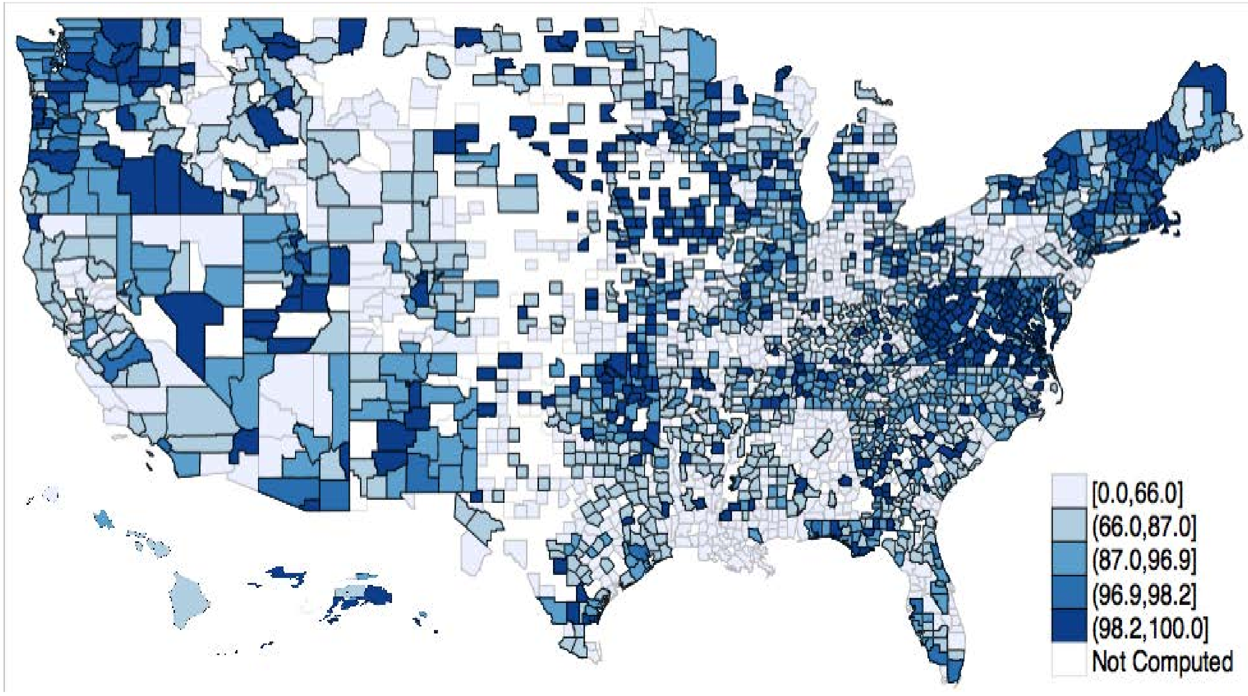


Figure 5: County Drug Average Specification Rates, 2012-2014



Note: Map shows percentage of drug poisoning deaths in the county where at least one specific drug is mentioned. Data are average for 2012-2014, for counties with populations of 5,000 or more and where positive numbers of drug poisoning deaths are reported.

Figure 6: Reported and Adjusted Prevalences by Type of Drug

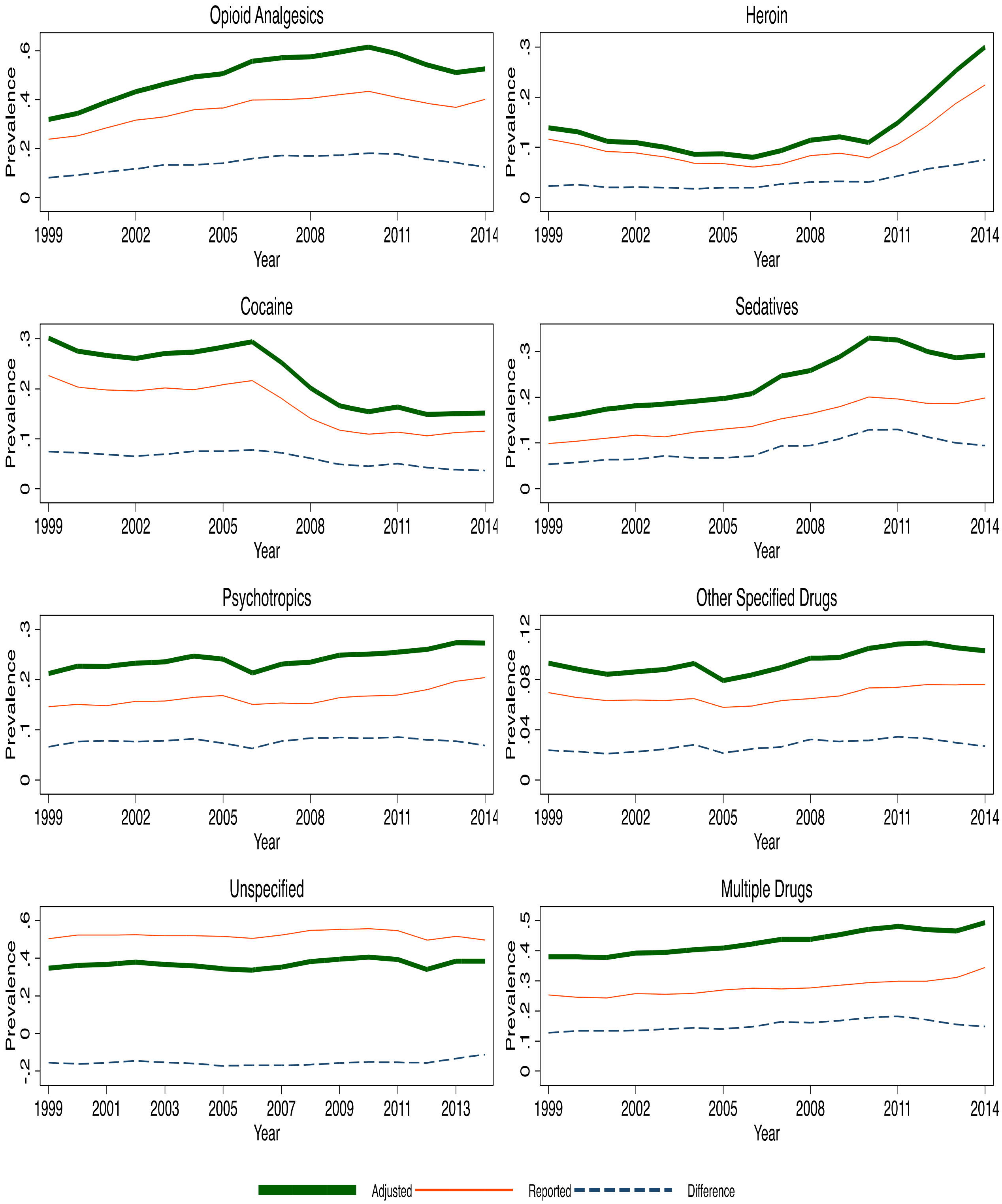


Figure 7: Reported and Adjusted Number of Deaths by Type of Drug

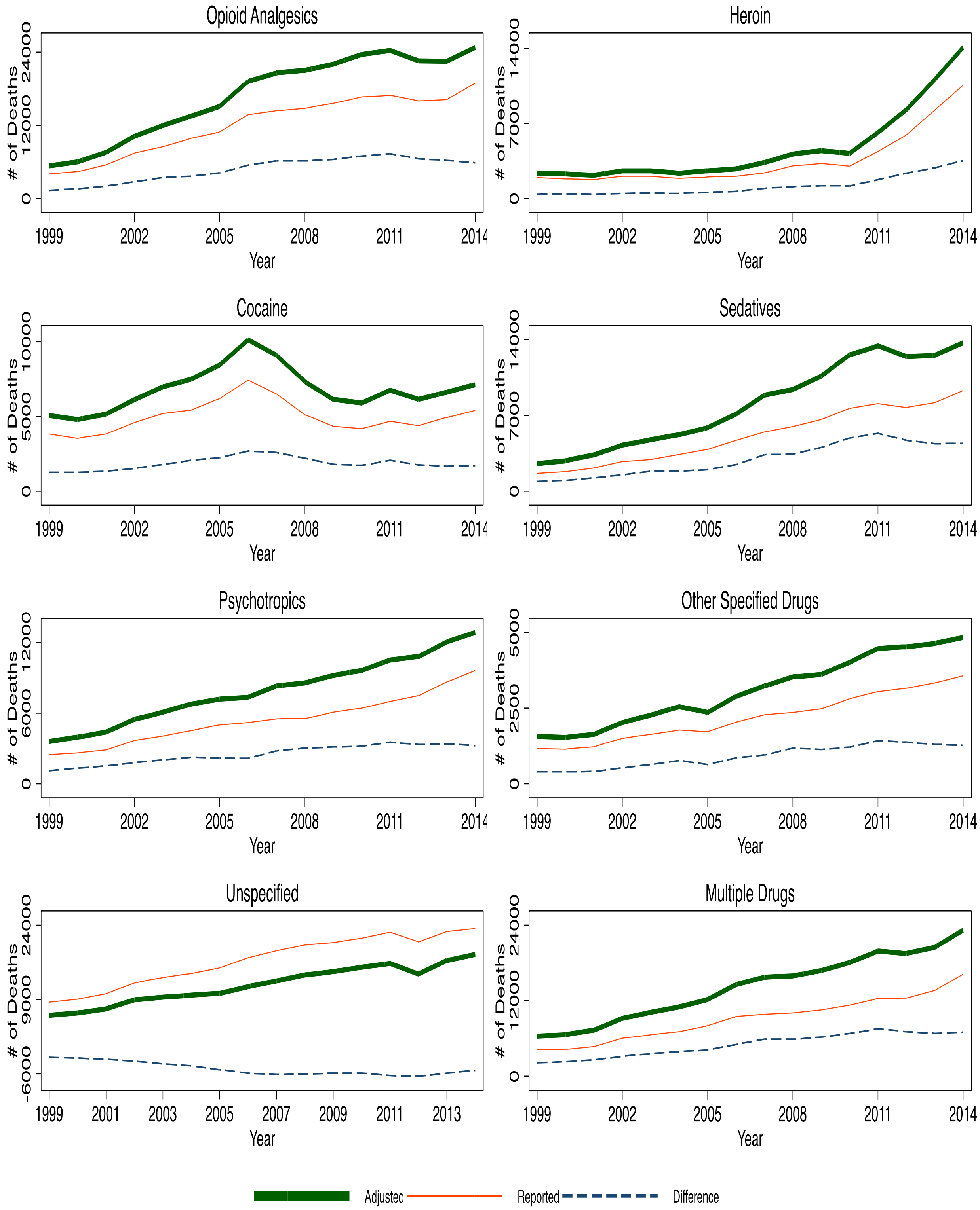
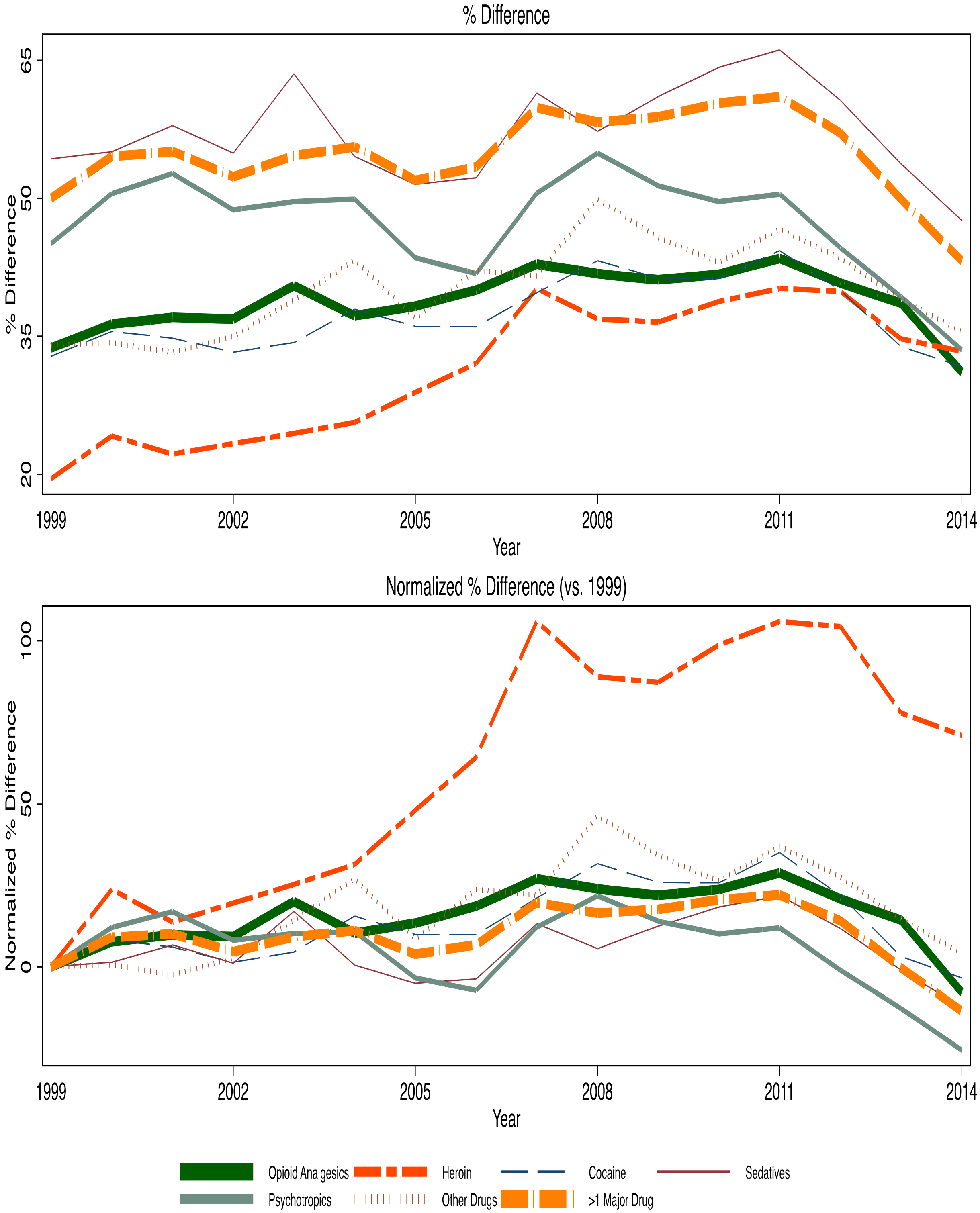


Figure 8: Percent Difference Between Adjusted and Reported Prevalence or Number of Deaths



Note: Lower figure shows percentage differences normalized such that 1999 equals zero.

Figure 9: Difference Between Adjusted and Reported Prevalence or # Deaths

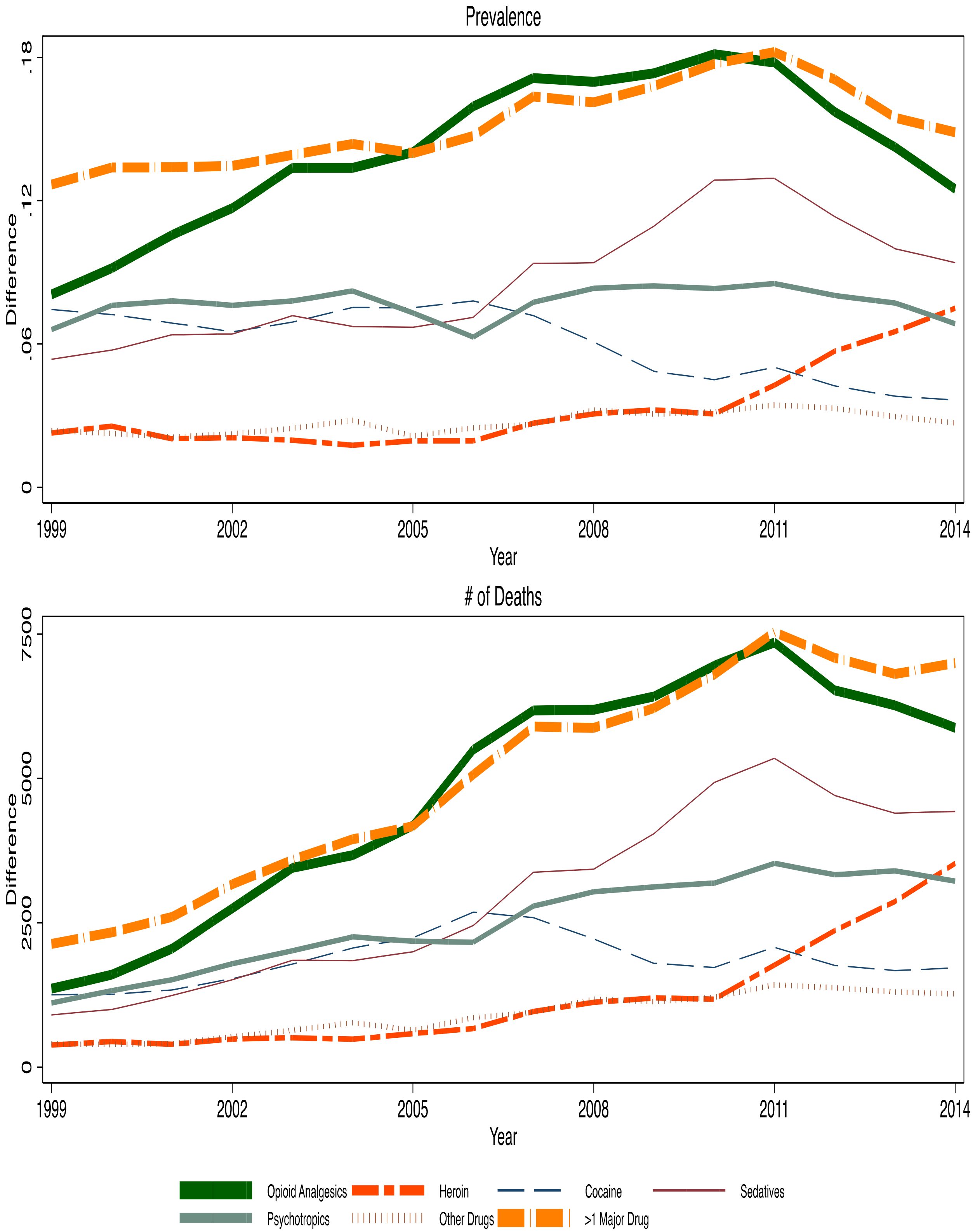


Figure 10: Change in Overdose Deaths Accounted For: 1999 through Stated Year

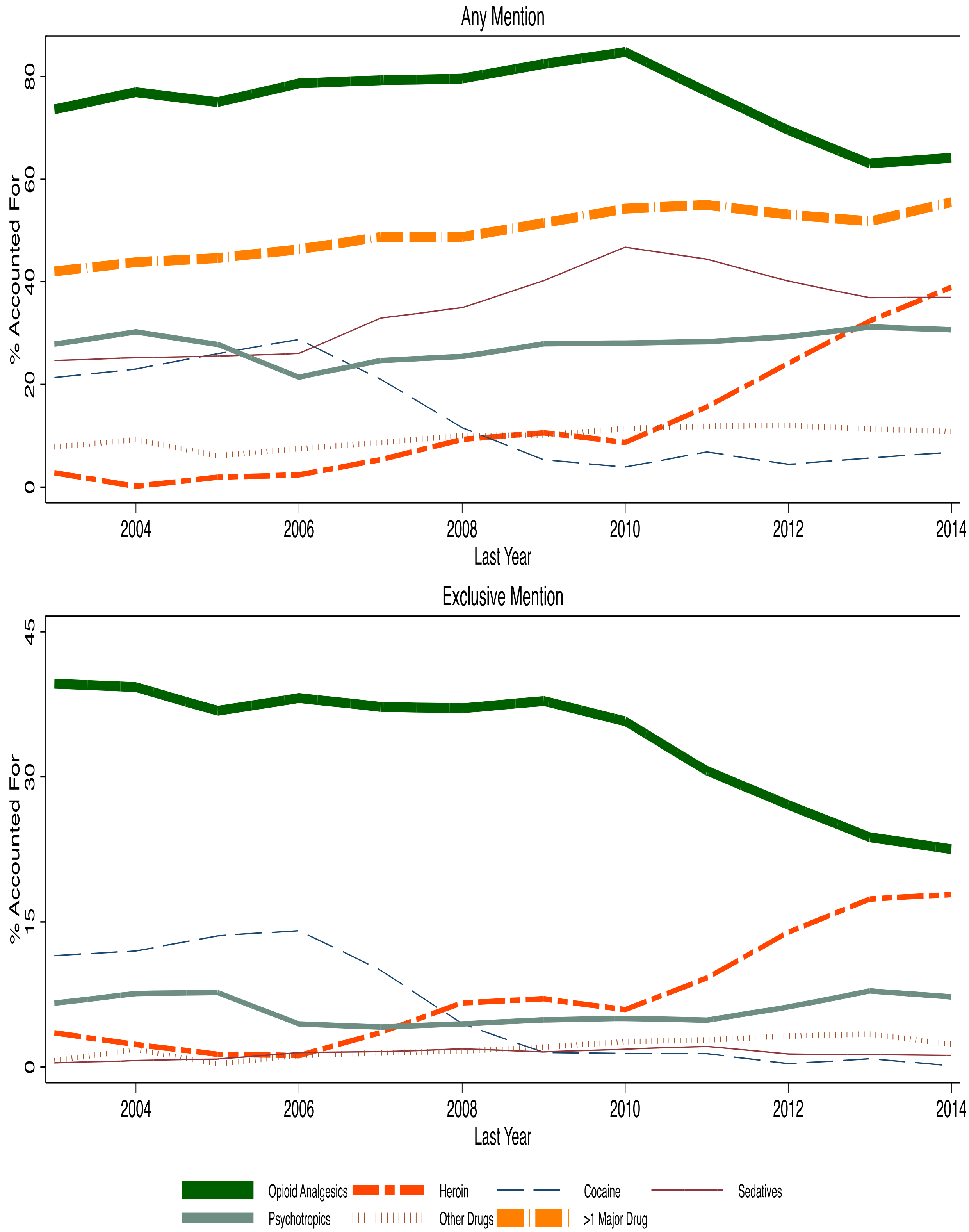
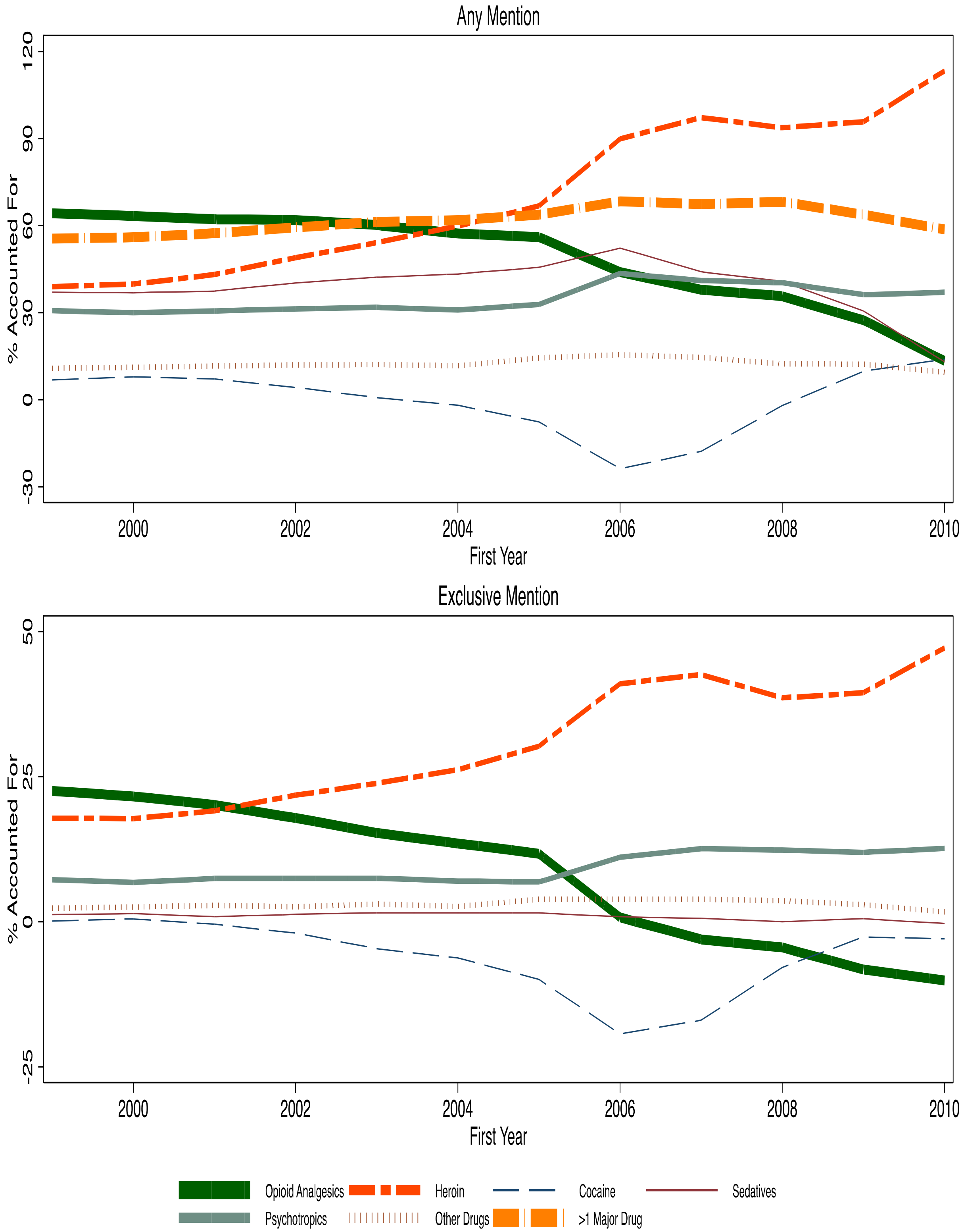


Figure 11: Change in Overdose Deaths Accounted For: Stated Year through 2014



Appendix

Table A.1. Characteristics of Low and High Diagnosis Counties, 2014

Characteristic	Low Diagnosis Counties	High Diagnosis Counties
Female	40.8%	37.0%
Black	8.3%	11.4%
Other Nonwhite	1.7%	2.5%
Hispanic	6.0%	6.7%
Married	25.3%	23.7%
< High School Grad	19.5%	18.5%
High School Grad	45.5%	45.1%
Some College	24.2%	22.6%
College Grad	8.8%	9.1%
Age: <20	2.4%	2.4%
Age: 21-30	17.3%	17.4%
Age: 31-40	22.0%	22.1%
Age: 41-50	23.7%	24.6%
Age: 51-60	24.2%	24.0%
Age: 61-70	7.8%	6.9%
Age:71-80	1.6%	1.6%
Age:≥80	0.9%	1.0%
Type of Death		
Accidental	82.0%	81.7%
Intentional	11.2%	10.9%
Undetermined	6.6%	7.1%
Homicide	0.2%	0.2%
Autopsy Performed	71.6%	80.8%

Note: See note on Table 2.

Table A.2: 2014 Adjusted Prevalences Using Alternative Specifications

	Method of Adjusting Prevalence			
Drug Mentions	Basic	Linear Probability Model	No Covariates	Supple-mentary Covariates
	(1)	(2)	(3)	(4)
Opioid Analgesics	52.6%	51.4%	53.0%	52.4%
Heroin	30.0%	29.2%	30.2%	29.8%
Cocaine	15.2%	14.7%	15.5%	15.1%
Sedatives	29.2%	27.5%	28.4%	29.1%
Psychotropics	27.3%	26.0%	26.8%	27.1%
Other Specified	10.3%	9.8%	10.2%	10.3%
Unspecified	38.4%	39.0%	36.4%	38.4%
>1 Major Drug Class	49.3%	47.0%	49.2%	49.1%

Note: See note on Tables 1 and 3. Adjusted prevalences are average predicted values, where at least one specific drug is mentioned for all poisoning deaths in the county (SPECIFY =1). Probit models are estimated, except in (2) which shows linear probability model estimates. Columns (1), (2) and (4) also control for: sex, race/ethnicity, marital status, education, age, day of the week of death, and census region. Model (4) adds supplementary covariates for whether the death was intentional or accidental (versus undetermined or homicide) and whether an autopsy was performed.

Table A.3: Estimates of Adjusted Prevalences With and Without *Any* Unspecified Drug Mentions Conditional on At Least One Report of a Specified Drug

Drug Mentions	Unspecified Drugs Not Mentioned		Unspecified Drugs Mentioned	
	Adjusted Prevalence	Standard Error	Adjusted Prevalence	Standard Error
	(1a)	(1b)	(2a)	(2b)
Opioid Analgesics	48.2%	1.4%	59.6%	1.8%
Heroin	32.6%	1.6%	25.9%	2.4%
Cocaine	14.9%	1.0%	15.6%	1.5%
Sedatives	23.2%	1.3%	39.3%	1.9%
Psychotropics	23.0%	1.2%	34.2%	1.5%
Other Specified	9.1%	0.5%	12.4%	0.8%
Unspecified	6.3%	0.2%	93.9%	0.2%
>1 Major Drug Class	41.9%	1.4%	60.8%	1.9%

Note: See notes on Tables 1 and 3. Adjusted prevalences are average predicted values from probit models, where at least one specific drug is mentioned for all poisoning deaths in the county (SPECIFY =1). In model (1) the calculations assume that there are *no* mentions of unspecified drugs (SOME=0); model (2) assumes that ≥1 unspecified drugs are also mentioned (SOME=1). Models also control for: sex, race/ethnicity, marital status, education, age, day of the week of death, and census region. Robust standard errors are calculated with clustering at the county level.

Table A.4: Predicted Number of Conditions Listed, 2014 Drug Poisoning Deaths

	Estimate	Standard Error
SOME Not Controlled For		
SPECIFY = actual value	3.318	0.043
SPECIFY= 0	1.613	0.096
SPECIFY=1	3.732	0.050
SOME Controlled For		
SPECIFY & SOME = actual value	3.318	0.043
SPECIFY = 0, SOME = actual value	1.926	0.105
SPECIFY = 1, SOME = actual value	3.656	0.050
SPECIFY = 0, SOME =0	1.665	0.096
SPECIFY = 1, SOME =0	3.395	0.068
SPECIFY = 1, SOME =1	4.264	0.094

Note: Table shows predicted number of conditions listed on 2014 drug poisoning death certificates obtained by regressing the number of conditions on the county share of deaths where at least one drug is specified (SPECIFY) and, in the bottom panel, on the county share of deaths where there are both specified and unspecified drugs mentions (SOME). Predicted values are displayed at the listed values of SPECIFY and (in the bottom panel) SOME. All models also control for: sex, race/ethnicity, marital status, education, age, day of the week of death, and census region. Robust standard errors are calculated with clustering at the county level.

Table A.5: Estimates of Drug Involvement in Drug Poisoning Deaths, 1999 and 2014

	Based on Reported # of Deaths				Based on Adjusted # of Deaths			
Drug Mentions	1999	2014	Δ	% Total Δ	1999	2014	Δ	% Total Δ
All Deaths	16,849	47,055	30,206	100.0%	16,849	47,055	30,206	100.0%
<u>Any Mention</u>								
Opioid Analgesic	4,030	18,893	14,863	49.2%	5,390	24,769	19,380	64.2%
Methadone	*784*	*3,400*	2,616	8.7%	*1,266*	*4,520*	3,253	*10.8%*
Other Opioid Anal	*3,360*	*16,371*	13,011	43.1%	*4,375*	*21,669*	17,294	*57.3%*
Heroin	1,960	10,574	8,614	28.5%	2,342	14,103	11,760	38.9%
Cocaine	3,822	5,415	1,593	5.3%	5,076	7,131	2,055	6.8%
Other Narcotic	2,931	2,822	-109	-0.4%	4,487	3,519	-967	-3.2%
Sedatives	1,662	9,308	7,646	25.3%	2,564	13,737	11,173	37.0%
Bezodiazepines	*1,135*	7,945	6,810	22.5%	*1,847*	*11,843*	9,996	*33.1%*
Psychotropics	2,466	*9,614*	7,148	23.7%	3,577	12,838	9,260	30.7%
Antidepressants	*1,749*	4,768	3,019	10.0%	*2,669*	*6,989*	*4,321*	*14.3%*
Antipsychotics	*321*	*1,588*	1,267	4.2%	*529*	*2,444*	*1,915*	*6.3%*
Psychostimulants	*547*	*4,298*	3,751	12.4%	*718*	*5,158*	*4,440*	*14.7%*
Other Specified	1,171	*3,573*	2,402	8.0%	1,570	4,841	3,271	10.8%
Unspecified	8,477	23,347	14,870	49.2%	5,860	18,069	12,209	40.4%
<u>Exclusive Mention</u>								
Opioid Analgesic	1876	7,769	5,893	19.5%	2,300	9,099	6,800	22.5%
Methadone	*309*	*1251*	*942*	*3.1%*	*457*	*1,397*	*940*	*3.1%*
Other Opioid Anal	*1528*	*6217*	*4,689*	*15.5%*	*1,817*	*7,317*	*5,501*	*18.2%*
Heroin	799	5067	4,268	14.1%	904	6,292	5,388	17.8%
Cocaine	1695	1747	52	0.2%	1,986	2,028	42	0.1%

Sedatives	504	814	310	1.0%	629	996	367	1.2%
Psychotropics	1212	3390	2,178	7.2%	1,556	3,737	2,181	7.2%
Antidepressants	*820*	*887*	*67*	*0.2%*	*1,080*	*1,068*	*-13*	*0.0%*
Antipsychotics	*68*	*167*	*99*	*0.3%*	*100*	*213*	*114*	*0.4%*
Psychostimulants	276	2188	1,912	6.3%	*329*	*2,267*	*1,937*	*6.4%*
Other Specified	791	1476	685	2.3%	951	1,658	707	2.3%
Unspecified	3690	9201	5,511	18.2%	629	1,634	1,004	3.3%
>1 Major Drug	4,270	16187	11,917	39.5%	6,406	23,184	16,778	55.5%

Note: Adjusted number of deaths is calculated as the product of the adjusted prevalence and the number of deaths in the specified year. Δ in # Deaths is the difference between 2014 and 1999 deaths involving the specified drug.