Taking the Measure of a Fatal Drug Epidemic

EXTREMELY PRELIMINARY: DO NOT QUOTE OR CITE

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Abstract

This analysis uses 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 approximately 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. The investigation reveals the sensitivity of many results to the starting and ending years chosen for examination, with a key role of prescription opioids for analysis windows that starting in 1999 but with other drugs, particularly heroin deaths, being more significant in more recent years and, again, with confirmatory evidence of the importance of simultaneous drug use.

The poisoning death rate has 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). 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).

The rapid rise in deaths involving prescription drugs 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 drugs (Centers for Disease Control and Prevention, 2013; Finklea, et al., 2013; Rannazzisi, 2013; Kirschner et al., 2014).

These endeavors have had some success. 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 then 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 overdose deaths (Paulozzi, et al., 2011; Gugelmann et al., 2011; Li et al., 2014). Most notably, some users may have substituted heroin for prescription opioids, with near doubling of the rate of heroin overdose deaths between 2011 and 2013 (Jones et al., 2015).

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 identified in almost one-quarter of cases. This leads to an underestimate of the rates of involvement of specific legal and elicit drugs, as well as of the simultaneous use of combinations of drugs. Sedatives (particularly benzodiazepines) and psychotropic drugs are increasingly frequently mentioned on death certificates (Paulozzi, et al., 2014) and the combined use of these drugs with prescription opioids is likely to increase health risks beyond the separate use of either (Jones et al., 2012).

Although economists have widely studied risky behaviors in general and substance abuse in particular (see Cawley & Ruhm, 2012 for a detailed summary of this literature), there has been almost no investigation of the rapid rise in overdose fatalities, the role of specific drugs in contributing to it, or the policies that might reduce its severity. Exceptions include Jena & Goldman (2011), who present evidence that the growth in internet pharmacies between 2000 and 2007 may have contributed to rising rates of prescription drug abuse, and Pacula et al. (2015)

who show 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.

The primary analysis below uses death certificate data from the Multiple Cause of Death (MCOD) files for 1999-2013 to examine the specific drugs involved in fatal drug poisonings. The investigation is innovative in at least two ways. First, statistical adjustment procedures are used to provide more accurate estimates of the drugs involved in these deaths, accounting for the understatement resulting from lack of specificity in death certificate reports. These adjustment methods raise the prevalence estimates of specific categories of drug involvement by 30% to more than 50% and highlight the frequency of drugs involvement. Second, using the adjustment estimates, I examine drug classes, or combinations therefore, are responsible for the rapid rise in fatal overdoses. The frequency of multiple drug use introduces uncertainty into these estimates and so a distinction is made between *any* versus *exclusive* involvement of drug classes in deadly poisonings. The investigation reveals the sensitivity of some of the findings to the starting and ending years chosen for investigation, with the key role of prescription opioids for analysis windows starting early in the data period but with other drugs, particularly heroin, being more significant for the growth in drug poisoning deaths occurring more recently.

1. Data and Descriptive Patterns

The primary outcomes to analyzed below are counts (and sometimes rates) of drug poisoning deaths using data from the 1999 through 2013 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. Each certificate contains a single underlying cause of death, up to twenty additional causes, and limited demographic data. Information will be utilized on cause of death, using four digit International Classification of

Diseases, Tenth Revision (ICD-10) codes, 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 I obtained permission to use these data for the 1999-2013 period. The analysis samples include deaths to U.S. residents (i.e. foreign residents dying in the U.S. are excluded).

Poisoning and drug poisoning deaths are defined using ICD-10 underlying cause of death (UCD) codes, where the UCD 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).[1] 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 in the MCOD files as ICD-10 "T codes" and are referred to below as drug mentions. 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 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 at least one drug is unspecified in around half of such cases. Combination drug use will be examined through a

[1] Poisoning deaths include ICD-10 codes X40-X49, X60-X69, X85-X90 Y10-Y19; codes for drug poisoning deaths are X40-X44, X60-X64, X85, Y10-Y14 (World Health Organization, 2014).

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.[2]

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 deaths from drug and other poisonings from 1982-2013.

1.1 Trends in Poisoning Deaths

Poisoning fatalities rose 330% between 1982 and 2013, from 11,297 to 48,545 deaths, and drug poisoning mortality by an even larger 575% over the same period, from 6,518 to 41,340 fatal overdoses (see the top panel of Figure 1).[3] In 1982, the risk of a motor vehicle death was four times that from poisoning and seven times that from a drug overdose. Conversely, in 2013, the drug poisoning fatality rate was 24% higher than that from vehicle accidents and fatal overdoses accounted for 91% of all poisoning deaths. Importantly, most of this change occurred since 1999 (70% of the rise in overdose deaths occurring between 1982 and 2013), so that the analysis period covers most of the secular increase. Population growth accounts for only a portion of the increase: the poisoning death rate rose by 215% between 1982 and 2013 (from

[2] Psychotropics may be most important in this regard, since this category includes heterogeneous types of drugs.
[3] I will use the term "overdoses" to refer to drug poisoning deaths for convenience, while recognizing that in some cases the death may be intentional.

4.88 to 15.36 per 100,000) and the drug poisoning mortality rate by 394% (from 2.81 to 13.91 per 100,000).[4]

Although not the focus of this analysis, Figure 2 supplies information on the demographic distribution of drug poisoning deaths. Several patterns are worth noting. First, the males more likely to die from fatal overdose than females and this effect has become more pronounced over time (e.g. they had a 19% higher drug poisoning death rate in 1982 versus a 61% higher probability in 2013. Second, whites had higher fatal drug poisoning rates than blacks, but this pattern has only emerged since 2000; other races are consistently less likely to die due to poisoning.[5] Finally, drug poisoning deaths are almost nonexistent for persons under the age of 15 with 25-54 year olds now being at highest risk, and with the fastest growth over time occurring for 45-64 year olds.

1.2 Drug Poisoning Deaths in 2013

Table 1 shows the reported manner of death (accidental, intention, undetermined intent or homicide) for all drug poisonings occurring in 2013, the last year of the analysis period, as well are drug mentions reported on the death certificates. ICD-10 codes for each category of drug mentions (ChiroCode Institute, 2014) are shown in parentheses. Numbers and percentages of deaths were calculated for all drug poisonings and by manner of death and type of drug, with the shares referred to as prevalences below. I also show exclusive mentions of major class of drugs, where these are defined as deaths where only a single drug class is mentioned on the death certificate, as well as cases where two or more major drug classes are mentioned.

[4] Population data (the denominator in the mortality rate calculations) come from the National Cancer Institute's *Surveillance Epidemiology and End Results (SEER)* program. The *SEER* data are designed to supply more accurate population estimates for intercensal years than standard census projections, and to adjust for population shifts in 2005, resulting from Hurricanes Katrina and Rita. See http://www.seer.cancer.gov/data for additional details.
[5] 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.

The large majority of drug poisoning (over 80%) in 2013 were classified as being accidental with only around one in eight categorized as intentional. Narcotics were mentioned in over 60% of fatal overdoses, with reported opioid analgesic prevalence of 37% and heroin and cocaine mentioned in 19% and 11% of these deaths. However, involvement of other drugs is also common with sedatives and psychotropic drugs each listed in around one-fifth of fatal overdoses. Most germane to this analysis is that unspecified drugs are listed in over half (52%) of deaths and they are the *only* listing in 22%. 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 78.1% in 1999 (see Figure 3). For this reason, reported rates of drug involvement will understated the true prevalences for most types of drugs and may give a misleading understanding of the fatal drug epidemic. The primary effort below is to assign reasonable attribution to specified drug types in as many of these cases as possible.

Also noteworthy is the frequency (31%) with which multiple drug classes are mentioned. One implication of this is that it may be hard to assign the responsibility of the death to any given drug. For example, while prescription opioid use was reported in 37% of drug poisoning deaths, these were the only class of drugs mentioned in just 10%. Similarly, exclusive use of other class of drugs were mentioned only one-fifth to one-half as often as any use in most cases, with the exception being that sedatives are almost never the only reported on the death certificates. In less than 1% of drug poisonings, no drug 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 continued slight understatement of the prevalences of specific drugs.[6]

[6] Another potential issue is that there could be some misclassification of underlying causes of death whereby not categorized as due to drug poisonings actually should be classified as occurring for this reason, and vice versa.

2. Methods

Rates of drug involvement reported on death certificates are not accurate because no drug is specified for around one-quarter of cases and at least one drug is unspecified in approximately one-half of overdose deaths. The primary goal of this analysis is to calculate adjusted prevalences that account for this. 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 drug category being listed. County-year averages of this variable were calculated, denoted as SPECIFY. For an initial descriptive analysis, counties were classified as "low diagnosis" if a specific drug was mentioned in fewer than 63.3% of drug poisoning deaths in 2013 and as "high diagnosis" if this was done on more than 97.8% of cases. These thresholds reflected the 25th and 75th percentiles of drug specification rates in 2013. Drug mention prevalence rates were then compared across high and low diagnosis counties in 2013 to provide a first indication of how reported prevalence rates were affected by the frequent failure to identify the drugs involved in fatal overdoses. 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 are separately estimated for each year. The basic model takes the form:

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

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

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Although it a solution to this problem is not obvious (particularly since less information on drug involvement is obtained for most deaths not categorized as due to poisoning), it is possible to examine drug involvement in "non-drug" poisoning deaths. In 2013, there were 4,563 non-drug poisoning fatalities, with some type of drug mentioned in 4.4% of these cases. However, these were frequently unspecified drugs, with specific classes identified just 2.4% of the time, including opioid analgesic, sedative and psychotropic prevalences of 1.0%, 0.7% and 0.7% respectively.

supplementary covariates (X) including dichotomous controls for: gender, two race indicators (black and other nonwhite), currently married (versus never married, separated/divorced, widowed, or status not reported), 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 is sometimes reported on death certificates in years rather than specific thresholds. In these cases, ≤11, 12, 13-15 and ≥16 years will 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 are next calculated, for each drug poisoning death, and then averaged over all observations to obtain estimated prevalences. Specifically, the average predicted prevalence for drug type *j* at time *t*, $\bar{P}_{jt}$ 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 the reported and estimated values were virtually identical.

A second set of predicted values are then be obtained, after setting $SPECIFY$, equal to one for all observations. The average predicted 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 drug involvement rate predicted to have occurred 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) are calculated with observations clustered by county. The predicted number of deaths involving specific drugs, $\widetilde{D}_{jt}$, is calculated as the product of the adjusted prevalence and the number of drug poisoning deaths in that year, D_t, or:

$$\widetilde{D}_{jt} = \tilde{P}_{jt} \times D_t, \tag{4}$$

The associated lower (upper) threshold of the 95% CI is the product of the number of overdose fatalities times the lower (upper) value of the adjusted prevalence rate 95% CI. Corresponding prevalence estimates of exclusive drug mentions (e.g. opioid analgesic involvement without mention of heroin, cocaine, sedatives, psychotropics or other drugs) are also be calculated. I also test and report on the results obtained when changing the set of covariates controlled for and estimating a linear probability rather than probit specification.

Although these represent "in-sample" estimates, two indications of the success of the adjustment procedures will be examined. The first will involve comparing the 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 is approximately 25% in most years. Completely successful adjustment procedures would reduce the estimated prevalence rate to zero, and the closer this is to being achieved, the greater the confidence in the adjustment procedure. The second test is the reverse of the first. Here, adjusted prevalence rates will be calculated using the procedure described above but under the assumption that drug types were never specified on the death certificates (by predicting prevalence after setting SPECIFY to zero).[7] In this situation, perfect adjustment implies that exclusive mentions of unspecified drugs

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

would occur in 100% of fatal overdoses. Deviations of the adjusted prevalence rates from 100% suggest the extent to which the procedure fails to achieve this goal, while noting that with a probit specification, predicted probabilities can never reach either zero or one, so that complete adjustment is not possible.

I also use the reported and adjusted prevalences to indicate the contributions of specific drug types to the rise, from 1999-2013, in drug poisoning mortality by calculating the change in the number of fatalities involving the specified drug divided by the total change in the number of drug poisoning fatalities. These calculations are conducted using prevalence estimates for both any mention and exclusive mentions of the drug types. Previous investigations often focus on any mentions of a class of drugs and so correspond to the first set of estimates here, except that those that use adjusted prevalence rates that account for cases where drug types are not specified on the death certificates. These almost certainly overstate the contribution of any specific drug class since combination drug use is common and, in such cases, there will be double-counting. The estimates based on exclusive prevalences address this, but will conversely undercount since no attribution will be made when multiple drug classes are involved in the deaths. For these estimates, the upper (lower) threshold of the 95% CI's will be calculated by subtracting the lower (upper) threshold of the confidence interval for 2013 from the corresponding upper (lower) threshold of the 1999 CI. These are likely to overstate the true 95% CI's to the extent that any errors in the estimates are positively correlated across years.

Examining changes in drug poisoning deaths over the 1999-2013 period is dictated by the availability of comparable estimates of drug involvement using ICD-10 codes. Using the methods just described, two related strategies are employed 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 2013. Earlier ending periods are not examined since the sample period would be so short that the estimates would be dominated by noise. The second strategy is the reverse of the first. In this case, the ending year is always 2013 and the initial analysis year ranges between 1999 and 2009.

3. Drug Poisoning Deaths in 2013

A first indication of the extent to which death certificates understate the prevalence of specific drug involvement in 2013 fatal drug poisonings was obtained by comparing the reported rates in low and high diagnosis, defined as those where fewer than 63.3% and more than 97.8% of overdose deaths had at least one specific drug mentioned. As might be expected, the differences in reported prevalences are dramatic. For example, opioid analgesics were mentioned three times as often in the high diagnosis areas (49.5% vs. 16.5%), with even larger relative differences for heroin, cocaine, sedative and psychotropic drug mentions. Particularly noteworthy is that *only* unspecified drugs are listed in almost 60% of these deaths in low diagnosis counties compared to less than 1% for areas with high diagnosis rates. On the other hand, a combination of specified and unspecified drug mentions was more common in the latter area and these counties also had a greater number of conditions listed on the death certificates. This comparison does not account for potential confounders, which could be important since a greater proportion of the deaths in low diagnosis counties involve females, whites and married individuals although the age and education distributions are fairly similar (see Appendix Table A.1).

Table 3 displays reported and adjusted prevalence rates. The adjustment procedures significantly raised the predicted frequency of all specific drug mentions, implying that death

certificates understated most types of drug involvement. For example, the adjusted prevalence for opioid analgesic mentions was 51.2% or 39% higher than the reported 36.9%. Adjusted prevalences other major drug classes exceeded reported prevalences by 35% to 54%, and the involvement of multiple drug class rose from 31% to 47%.

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 a low of 12% for psychotropics to a high of 30% for heroin. The findings for unspecified drugs indicate that the adjustment procedures work well, but not perfectly. Specifically, the prevalences of only unspecified drugs fall by five-sixths, from 22.2% to 3.7%, whereas these would be completely eliminated if the methods were completely successful. As mentioned, adjusted prevalences were also calculated using the same procedure but under the assumption that drug types were *never* specified on the death certificates (by predicting probabilities after setting $SPECIFY$ to zero). In this situation, perfect adjustment would imply predictions of exclusive mentions of unspecified drugs in 100% of fatal overdoses. The actual estimated prevalence rates were 96.1%. Thus, to the extent the adjustments remain incomplete, there is likely to be a small continuing understatement of specific drug mentions.

Next, 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 (by including 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 potential problematic since determination of the manner of death and the use of autopsies could be endogenous (e.g. the latter are more commonly performed in high diagnosis counties) and

information on autopsies first became available on death certificates in 2003.[8] 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 in these models is due to the cross-county variation in drug specification rates. While it is possible that the findings could change with the inclusion of characteristics for which data are not available on the death certificates, the similarity of results across specifications in the table makes this less likely.

The adjustments to this point correct for cases where *no* drug is specified on the death certificate. My original hypothesis was that prevalences would still be understated when using this procedure because it does not account for cases where the death certificate listed mentioned both specified and unspecified drugs, since no assignment of the latter would have been made. To investigate this possibility, I estimated the augmented model:

$$Y_{ijt} = \alpha + \beta_1 SPECIFY_{jt} + \beta_2 SOME_{jt} + \gamma X_{ijt} + \mu_{ijt}, \quad (5)$$

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 mentioned. Adjusted prevalences assuming that all death certificates included only specified drugs ($SPECIFY = 1, SOME = 0$) were calculated as:

$$\tilde{P}_{jt} = \frac{1}{n}\sum_{i=1}^{n} \Phi\left(\hat{\alpha} + \hat{\beta}_1 + \hat{\gamma}\, X_{ijt}\right), \quad (6a)$$

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

$$\tilde{P}_{jt} = \frac{1}{n}\sum_{i=1}^{n} \Phi\left(\hat{\alpha} + \hat{\beta}_1 + \hat{\beta}_2 + \hat{\gamma}\, X_{ijt}\right). \quad (6b)$$

[8] Kapusta et al. (2011) provide cross-national evidence suggesting that autopsy and measured rates of intentional deaths (suicides) are positively related. A number of authors argue that the manner of drug poisoning mortality will frequently be misclassified, with intentional deaths understated and those that are accidental or of undetermined intent being overestimated (Rockett et al., 2014a,b).

The results of this exercise are displayed in Table 4. Contrary to my initial expectation, the estimated prevalences are almost uniformly *lower* when assuming that all drugs are specified on the death certificates than when there are both specified and unspecified drug mentions. The differences are particularly large for multiple drug use (39% vs. 59%), sedatives (24% vs. 33%) and psychotropic medications (24% vs. 33%), as well as for opioid analgesics (47% vs. 58%). The only exception is heroin where adjusted prevalences are higher by statistically insignificant amounts (26% vs. 24%).

Further investigation revealed likely reasons for this pattern. First, combinations of specified and unspecified drug use tend to occur in cases when there are a larger number of mentions on death certificates. For example, Appendix Table A.3 shows the results of regressing the number of conditions listed on the death certificate against county values of $SPECIFY$ and $SOME$. As would be expected, the smallest number of mentions are predicted (1.77) when only unspecified drugs are listed ($SPECIFY = 0, SOME = 0$). However, particularly relevant here is that the number of mentions is higher (4.28 vs. 3.21) when the death certificate includes both specified and unspecified drugs ($SPECIFY = 1, SOME = 1$) than when it only includes the former ($SPECIFY = 1, SOME = 0$). Consistent with this, the gap between the two adjusted prevalences is substantially reduced(although not completely eliminated) in regressions (not shown) that additionally control for the number of conditions listed. What this suggests is 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. Supporting this possibility, 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" section (personal communications, October 2 and October 6, 2015).

Although the evidence just presented indicates that adjusted prevalences estimated under the assumption that only specified drugs are listed on the death certificate are likely to understate the true prevalences, they leave open the possibility that the primary adjustment procedures used also yield downwards biased estimates because some they rely on potentially incomplete reporting, even in cases where at least one drug is specified. Although it is not obvious that this problem can be fully addressed, I attempted to provide some indication of its severity by adding to the main model an additional control for the county average number of conditions listed on the death certificate, $NUMCTY$:

$$Y_{ijt} = \alpha + \beta_1 SPECIFY_{jt} + \beta_2 NUMCTY_{jt} + \gamma X_{ijt} + \mu_{ijt}, \tag{7}$$

and then calculating average prevalences with $SPECIFY = 1$ and this $NUMCTY = 4.284$:

$$\tilde{P}_{jt} = \frac{1}{n}\sum_{i=1}^{n} \Phi\left(\hat{\alpha} + \hat{\beta}_1 + 4.286\,\hat{\beta}_2 + \hat{\gamma}\, X_{ijt}\right), \tag{8}$$

which is the predicted number of conditions mentioned in counties with both specified and unspecified drug mentions. While not a perfect solution, since the true difference in numbers of drugs involved in the fatal overdoses may differ between counties in ways not fully accounted for, it is likely to provide some indication of the sensitivity of estimated prevalence rates to the completeness of reporting.

Table 5 summarizes the findings. Model (1) shows estimates using the main adjustment procedure (i.e. from equation 3) with model (2) displaying corresponding estimates from equation (8). The last column shows percentage differences between the two. The primary result is that narcotics prevalences are relatively unchanged, whereas more complete listing of drug involvement increases sedative prevalences by more than 20% and those of other drug types or

multiple drug use by 10% to 15%. What this implies is that that the main adjustment procedures presented so far, and exclusively focused upon below, probably provide a fairly accurate indication of opioid, heroin and cocaine involvement but may understate the importance of other types of drugs and combinations of use.

Finally, Table 6 returns to the primary adjustment procedure and shows differences in reported and adjusted prevalences by manner of drug poisoning (accidental, intentional or undetermined intent).[9] The key differences are that, compared to intentional deaths, accidental drug poisonings are more likely to involve narcotics of all kinds and less often sedatives, psychotropics, other specified or unspecified drugs. Poisoning fatalities of undetermined intent are usually intermediate between the two, although opioid analgesics are mentioned particularly frequently. Since reports of drug involvement may play a role in classifying the manner of death, the remaining analysis combines all manners of drug poisoning.

4. Overdose Fatalities Across Years

Using the methods discussed above, and detailed for 2013 in the previous section, I next compare reported and adjusted prevalences for all sample years (1999 through 2013), as well as the corresponding numbers of deaths involving the 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). Adjusted and reported prevalences are displayed in Figure 4 and the corresponding numbers of deaths in Figure 5. In each case, the thin solid line shows results based on death certificate reports, the bold solid line the adjusted estimates and the dotted line indicates 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, which the adjustment procedures are designed to reduce.

[9] Since there were only 86 drug poisoning homicides in 2013, results for this manner of death are not shown.

Several points are worth noting. Prevalences of psychotropic, other specified and multiple drug mentions rise fairly steadily throughout the analysis period, as does corresponding sedative opioid analgesic involvement up through 2010 and 2011 respectively (Figure 4). Conversely, cocaine prevalences over time as do heroin mentions through 2006, after which point they begin to increase and do so dramatically after 2010. The proportion of death certificates remains fairly constant across sample years. However, since the number of fatal overdoses also rose rapidly over the sample period—from 16,849 in 1999 to 43,892 in 2013—the number of deaths involving particular drugs could easily increase even while prevalences were flat or declining. For instance, the number of overdose fatalities where cocaine was implicated increased by 26% between 1999 and 2013 (from 5,237 to 6,619), even while the prevalence fell from 31% to 15% (see Figure 5).[10] On the other hand rising prevalence rates reinforce this effect so that, for example, the number of deaths involving psychotropic drugs more than triples (from 3,568 to 12,039) while the prevalence rises by "just" 29% (from 21.2% to 27.4%). The figures also highlight the recent re-emergence of heroin overdose in fueling the fatal drug epidemic. The estimated number of such deaths involving heroin rose by a relatively modest 16% (from 2,370 to 2,757) between 1999 and 2006, increased by an additional 53% (to 4,214) in 2010 and then exploded, growing by an additional 164% (to 11,123) in 2013. Finally, although the growth has not been particularly rapid, opioid analgesics continue to be the most common class of drugs to be involved in overdose deaths, with mentions estimated to rise from 5,275 in 1999 to 24,271 in 2011, before declining by 7% (to 22,501) in 2013.

Figure 6 provides information on percentage differences in adjusted and reported estimates of prevalences or numbers of deaths across drug classes and over time. The upper panel shows the percentage differences between the two in each year and the lower figure shows

[10] However, the number of cocaine involved deaths was estimated to reach a maximum of 10,133 in 2006.

these differences normalized such that the 1999 value equals zero. Specifically, define the percentage difference between adjusted and reported prevalence rates for drug class j at time t as:

$$\Delta_{jt} = \{(\tilde{P}_{jt}/P_{jt}) - 1\} \times 100\%, \quad (9)$$

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

$$\Delta_{jt}^{norm} = \{(\Delta_{jt}/\Delta_{j1999}) - 1\} \times 100\%.^{11} \quad (10)$$

The top panel of Figure 6 demonstrates that death certificate reports understate prevalences most severely for sedatives and multiple drug use as well as, to a lesser extent, for psychotropic medications. However, the lower panel of the figure shows that the relative understatement differences have grown has grown over time by the highest amount for heroin, other drugs and, to a smaller degree, for opioid analgesics while remaining roughly constant for most other types of drugs. One important consequence is that the rapid recent rise in deaths involving heroin has actually been understated when relying on mentions on death certificates.

Figure 7 shows absolute (rather than percentage) differences between adjusted and reported prevalences (top panel) or numbers of deaths (bottom panel). Since these depend on overall prevalences as well as relative (percentage) differences between adjusted and reported rates, it is no surprise that the largest disparities are shown for opioid analgesic and multiple drug involvement (reaching 7,354 and 7,535 deaths respectively in 2011, before declining to 6,266 and 6,807 in 2013), 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 (2,866 fatalities in 2013).

[11] Notice that since the number of deaths involving the drug is the product of the prevalence and total number of deaths involving the drug, percentage differences in prevalence rates and numbers of deaths are the same.

5. Drugs Responsible for the Increase in Fatal Overdoses

As mentioned, a great deal of attention has been paid to the role of opioid analgesics in contributing to fatal drug poisonings. Typically, it is noted that a large fraction of both deaths at a point in time and of the increases in mortality involves mentions of these drugs. (e.g. Centers for Disease Control and Prevention, 2013). While certainly true, such discussions are overly simplified because of the frequent, and increasing prevalence in combination drug use that has been noted above. This section provides a more in-depth analysis of these issues by separately considering "any" versus "exclusive" mentions of specific types of drugs in overdose fatalities. The first step involves decomposing the increase in drug poisoning deaths occurring between 1999 and 2013 into the fractions with any or exclusive mentions of various drug classes. For illustrative purposes, I also show how the results vary when based on reported versus adjusted prevalences. Second, I display corresponding results, based on adjusted prevalences, obtained when 1999 is the base year and increases are considered for all final years ranging between 2003 and 2013.[12]

Results of the first phase of the analysis are summarized in Table 7, with full details provided in Appendix Table A.4. To flesh out the methods, consider mentions of opioid analgesics. There were 16,894 drug poisoning fatalities in 1999 and 43,982 in 2013, an increase of 27,133. The death certificates included mention of opioid analgesics in 4,030 of these deaths in 1999 and 16,235, an increase of 12,205. Thus, based on these reports, opioid analgesics were "responsible" for 45.0% (12,205/27,133) of the increase in deaths.

However, there are two reasons why such a conclusion may be incorrect. First, opioid analgesic prevalence will be understated since these drugs will sometimes be involved in the

[12] Results where 2000 through 2002 are not shown because the increase since 1999 is relatively modest and these are likely to be dominated by noise in the estimates.

death in cases where death certificates report only unspecified drug use. The results based on adjusted prevalence rates take this into account. Specifically, the point estimates based on adjusted prevalence rates indicate that opioid analgesics were involved in 5,275 deaths in 1999 and 22,501 in 2013. The 17,276 increase corresponds to 63.5% (17,276/27,133) of the total growth in fatal overdoses.[13] Second, this method attributes to opioid analgesics any higher number of deaths that mention them. This is likely to be an overstatement because other drugs are often involved in the deaths as well (and adding the contributions measured in this way across drugs will certainly sum to more than 100%). The first row of the lower panels of Tables 7 and A.4 therefore focus on exclusive opioid analgesic mentions. For example, the adjusted estimates indicate that 1,271 drug poisoning deaths involved only opioid analgesics in 1999 and 5,468 did so in 2013, an increase of just 4,197 or 15.5% (4,197/27,133) of the total. Thus, we may feel reasonably confident in stating that opioid analgesics are responsible for somewhere between 15% and 64% of the rise in fatal overdoses but, without knowing how to assign responsibility in cases of multiple drug use, can say little more than this.[14]

Based on any mentions, opioid analgesics play the most important role in accounting for the rise in drug fatalities (64%), with methadone being involved in around one-fifth of the time and other prescription opioids in 85% (which adds to more than the total since both can be use simultaneously). Interestingly, even with the adjustment procedures, increased mentions of unspecified drugs explain over 40% of the growth in deaths (reduced from 53% based on death certificate reports). Approximately equal contributions, of between 31% and 37% each, are made by heroin, sedatives (mostly benzodiazepines) and psychotropic drugs (especially antidepressants

[13] These estimates are based on adjusted prevalences of 31.3% in 1999 and 51.2% in 2013 ($0.31308 \times 16{,}849 = 5{,}275; 0.51159 \times 43{,}982 = 22{,}501$). These estimates are measured with error. Therefore, Table A.4 also shows 95 percent confidence intervals.

[14] Actually, the bounds are even wider than this. Taking the 95% confidence intervals into account, we might conclude that the range can be as large as 12.6% to 69.9%.

and psychostimulants), with less substantial roles for other specified drugs, cocaine and other narcotics.

Corresponding calculations using exclusive mentions reveal much lower contributions, by definition, but also some important differences in the patterns. Opioid analgesics continue to be most important (15.5%) but only slightly more so than deaths exclusively involving heroin (13.7%). It is also noteworthy that exclusive use of sedatives explains almost none of the growth, the reason being that these are virtually never the only ones mentioned on death certificates. Conversely, lone use psychotropic medications play a relatively important role – accounting for over 5% of the rise in deaths – with almost all of this being due to psychostimulants. However, a key result, detailed in the last row of the tables, is that combinations of major classes of drugs account are estimated to account for over half of the rise in drug poisoning mortality, making it crucial to either recognize the importance of the use of multiple drugs in contributing to the fatalities, or to make efforts to better identify the role of individual drug types when there is such combination use. A possible exception to this conclusion is for heroin, where deadly exclusive use appears to be relatively common. For instance, in 2013, the adjusted estimates imply that 39% (4,369 of 11,123) of fatal drug overdoses involving heroin included exclusive mentions of this drug. The corresponding rates of exclusive use were 24%, 4%, and 18% and 32% for opioid analgesics, sedatives and psychotropics.[15]

The decision to examine 1999 to 2013 when examining sources of the growth in drug poisoning fatalities is somewhat arbitrary, so the remainder of this section uses the same methods to consider the sensitivity of the results to the use of alternative time periods. Figure 8 summarizes point estimates of the effects for periods that start in 1999 and end in the year

[15] Exclusive use also has fairly high proportions of total mentions for psychostimulants (34%) and other specified drugs (32%), although the overall contributions are smaller for these because of their relatively low prevalence rates.

specified on the X-axis. For instance, the left-most entries are for the 1999 to 2003 timespan while those furthest to the right cover the full 1999-2013 period (and so provide equivalent information to that in Table 7).[16]

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" between 75% and 85% of the growth in deaths for periods starting in 1999 and ending anytime between 2003 and 2010, but for those concluding subsequently, the share accounted for rapidly declines, to 63% from 1999-2013. Interestingly, the share of the growth accounted for by exclusive mentions of opioid analgesics falls virtually monotonically as later years are added to the analysis window, falling from 27% for 1999-2003 to 15% from 1999-2013. This occurs because the share of increase in deaths with multiple drug use rises fairly steadily with the addition of more recent years, from 38% for 1999-2003 to 54% from 1999-2011, before falling modestly to 50% for the full 1999-2013 time span.

The other notable results in Figure 8 relate to the role of illicit opioids, with a declining role for cocaine and rising contribution of heroin in recent year. Thus, cocaine involvement "explained" between 20% and 28% of the rise in overdose deaths for periods starting in 1999 and ending between 2003 and 2007, with exclusive mentions of this drug accounting for 10% to 12% of the increase. However, cocaine involved deaths fell rapidly in more recent years and have played almost no role in the overall change when the analysis window 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 2% of the total change in such periods – but became more consequential when subsequent years, particularly end years after 2010 were added to the calculations. The rise for periods that include the last four years in the data set is

[16] Windows shorter than 4 years will be dominated by noise and so are not shown on this or the next figure.

remarkable: any mentions accounted for 9%, 15%, 24% and 32% of the total change for analysis windows beginning in 1999 and ending in 2010 through 2013 respectively, with exclusive mentions being responsible for 5%, 7%, 12% and 14% of the change.

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 more recent years are incorporated. However, as mentioned this is difficult to evaluate because deaths involving sedatives almost always also involve mentions of other drugs. The results for other types of drugs are either insensitive to the choice of analysis periods (e.g. psychotropics) or are of sufficiently limited importance that it does not much matter (e.g. other specified drugs).

An alternative way of examining the data is to always end the investigation in 2013 but to vary the first year of the period. This is done in Figure 9. The differences when doing so are fairly remarkable. In particular, where any mentions of opioid analgesics play a dominant role for analysis beginning near the start of the available data, they account for less of the growth in overdose deaths than a number of other sources (sedatives, psychotropics and particularly heroin) when the starting year is 2006 or later. Conversely, heroin-involved deaths play make the largest contribution when the first year is 2005 or later and exclusive mentions of heroin explain more of the growth in fatal overdoses than corresponding figures for opioid analgesics for all periods beginning in 2001 or later. For example, any mentions or heroin account for 60%, 97% and 95% percent of the increase in deaths for analysis windows starting in 2005, 2007 and 2009 (and ending in 2013) with exclusive heroin involvement being responsible for 25%, 38% and 36% of the increase.

This should not be taken to imply that multiple drug use has played a less important role in recent periods: it accounted for 50% of the total change between 1999 and 2013 and 58%,

59% and 53% of the growth in fatal overdose deaths when the beginning year is 2005, 2007 and 2009. The contribution of psychotropic medications also rises when restricting the analysis period to more recent years, from 31% for any mentions from 1999-2013 to 49% for 2006-2013 and with a corresponding 5% and 9% accounted for by exclusive mentions. The patterns are more variable for most other types of drugs, and these are in most cases have less explanatory power.

5. Discussion

Current death certificate data are problematic for understanding the drug poisoning epidemic, with a particular issue being the frequency with which 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). Recommendations include 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 be used to provide more accurate prevalence estimates. The benefits are considerable since death certificates often understate the involvement of specific types of drugs by 30% to 60%, combination drug use by 50% or more, and exclusive use of specific drugs by 20% to 30%. The adjustment procedures work well but not perfectly reducing, for example, the prevalence of exclusive mentions of unspecified drugs from 22% to 4% in 2013. However, several issues remain. One is that death certificates may be incomplete, even when one or more

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, there is reason to believe that heroin use is sometimes instead 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). Some overdose deaths could also be misclassified as due to non-drug causes, and therefore excluded from the analysis, while for other that are included, non-drug causes could be primarily responsible for the death.

Notwithstanding the just mentioned caveats, the findings of this analysis have a number of important implications. The number of U.S. residents dying from drug poisoning rose from 16,849 in 1999 to 43,982 in 2013. In all years analyzed, prescription opioids are the most common class of drugs involved in the fatalities, justifying the previously discussed concerted actions to reduce the negative consequences associated with their use. Probably, due in large part 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). However, the overall picture is less sanguine, with the total number of drug poisoning deaths continuing to rise by over 6% (41,340 to 43,982) since the role of opioid analgesics peaked. Indeed, deadly overdoses have increased in *every* year since 1990, even as the role of specific drugs changed considerably. For example, deaths involving cocaine fell 35% (from 10,133 to 6,619) between 2006 and 2013 and, most

distressingly, those where heroin played a role rose 371% (from 2,360 to 11,123) from 2004 to 2013, with most of this growth since 2010.[17]

A key finding is that a majority of overdose fatalities involve the use of multiple classes of drugs, making it difficult or impossible to specify the role of specific categories in accounting for the secular increase. Combination drug use itself is likely to be a risk factor. For example, benzodiazepines were estimated to be involved in 10,855 deaths in 2013 versus just 1,925 in 1999 but were virtually never the *only* drug mentioned. However, the health risks of using opioids and benzodiazepines together are almost certainly greater than that of either in isolation (Jones, et al., 2012; Park, et al., 2015). Interactions between types of drugs are also poorly understood. Most significantly, the modest decline since 2011 in overdose mortality involving opioid analgesics has been accompanied by an enormous increase in heroin-related deaths, but the evidence is conflicting on whether use of the latter is substituting for the former (Cicero et al. 2012; Markon & Crites, 2014), or whether the two drug types are complements (Rudd et al., 2014).

Finally, attribution of the secular increase in fatal overdoses to specific drug categories turns out to be quite sensitive to the choice of periods analyzed. Because deaths involving opioid analgesics grew extremely rapidly at the twenty-first 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 deaths for any period that begins at or near 1999 (regardless of the ending year). However, in sharp contrast, similar calculations indicate that heroin plays the most important role for periods starting in 2004 or later (and for those beginning as early as 2001 when basing the calculations on exclusive drug involvement). This reflects the very rapid growth in heroin-involved fatalities since the mid-

[17] 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. Appendix Table A.4 shows the 95% confidence intervals on these estimates for 1999 and 2013.

2000s. By contrast, the role of combination drug use in accounting for the secular increase in deaths is large and much more robust to the choice of starting and ending years – almost always ranging between 40% and 60% -- further highlighting its importance for the design of effective policies to reduce fatal drug poisonings.

References

Anderson RN, Miniño AM, Hoyert DL, Rosenberg HM. Comparability of Cause of Death Between ICD-9 and ICD-10: Preliminary Estimates. Natl Vital Stat Rep. 2001; 49(2): 1-32.

Cawley J, Ruhm CJ. The Economics of Risky Behaviors. in Pauly MV, McGuire TG, Barros PP (eds). Handbook of Health Economics, Volume 2. New York: Elsevier, 2012, 95-199.

Centers for Disease Control and Prevention. Vital Signs: Overdoses of Prescription Opioid Pain Relievers - United States, 1999-2008. MMWR. Morb Mortal Wkly Rep. 2011 Nov 4;60(43):1487-92.

Centers for Disease Control and Prevention. Vital Signs: Risk for Overdose from Methadone Used for Pain Relief – United States, 1999-2010. MMWR. Morb Mortal Wkly Rep. 2012 July 6;61(26):493-497.

Centers for Disease Control and Prevention. Opioids Drive Continued Increase in Drug Overdose Deaths. 2013 February 20. http://www.cdc.gov/media/releases/2013/p0220_drug_overdose_deaths.html.

Centers for Disease Control and Prevention, National Center for Health Statistics. Instructions for Completing the Cause-of-Death Section of the Death Certificate. http://www.cdc.gov/nchs/data/dvs/blue_form.pdf. Accessed August 22, 2014.

Centers for Disease Control and Prevention Wonder. Multiple Cause of Death 1999-2013. http://wonder.cdc.gov/help/html, 2015.

Chen LH, Hedegaard H, Warner M. Drug-Poisoning deaths involving opioid analgesics: United States, 1999-2011. NCHS data brief, no 166. Hyattsville, MD: National Center for Health Statistics. 2014.

ChiroCode Institute. ICD-10-CM (ICD10) Diagnosis Codes – T Codes. http://www.chirocode.com/medical-codes/icd-10-cm/icd-10-cm-diagnosis-T-codes.html. 2014.

Cicero TJ, Ellis MS, Surratt HL. Effect of Abuse-Deterrent Formulation of OxyContin. N Engl J Med. 2012 Jul 12;367(2):187-9.

Finklea KM, Bagalman E, Sacco LN. Prescription drug monitoring programs. Washington, DC: Library of Congress, Congressional Research Service. 2013.

Hardesty C. White House Summit on the Opioid Epidemic. Washington DC: Office of National Drug Policy. 2014 June 19. http://www.whitehouse.gov/blog/2014/06/19/white-house-summit-opioid-epidemic.

Goldberger BA, Maxwell JC, Campbell A, Wilford BB. Uniform Standards and Case Definitions for Classifying Opioid-Related Deaths: Recommendations by a Samhsa Consensus Panel. Journal of Addictive Diseases. 2013;32(3):231-243.

Gugelmann HM, Perrone J. Can prescription drug monitoring programs help limit opioid abuse? JAMA. 2011 Nov 23;306(20):2258-9.

Jena AB, Goldman DP. Growing internet use may help explain the rise in prescription drug abuse in the United States. Health Aff. 2011 June;30(6): 1192-1199.

Johnson H, Paulozzi L, Poruncznik C, Mack K, Herter B, Hal Jonson Consulting, Division of Disease Control and Health Promotion, Florida Department of Health. Decline in drug overdose deaths after state policy changes – Florida, 2010-2012. Morb Mortal Wkly Rep. 2014 July 4;63(26):569-74.

Jones CM, Logan J, Gladden RM, Bohm MK. Demographic and substance use trends among heroin users – United States, 2002-2013. Morb Mortal Wkly Rep. 2015 July 10;64(26):719-725.

Jones CM, Mack KA, Paulozzi LJ. Pharmaceutical overdose deaths, United States, 2010. JAMA. 2013 February 20;309(7):657-659.

Jones JD, Mogali S, Comer SD. Polydrug abuse: a review of opioid and benzodiazepine combination use. Drug Alcohol Depend. 2012 Sep 1;125(1-2):8-18

Kapusta ND, Tran US, Rockett IH, et al. Declining Autopsy Rates and Suicide Misclassification: A Cross-national Analysis of 35 Countries. Arch Gen Psychiatry. 2011;68(10):1050-1057.

Kirschner N, Ginsburg J, Sulmasy LS; Health and Public Policy Committee of the American College of Physicians.Prescription drug abuse: executive summary of a policy position paper from the American College of Physicians. Ann Intern Med. 2014 Feb 4;160(3):198-200.

Li G, Brady JE, Lang BH, Giglio J, Wunsch H, DiMaggio C. Prescription drug monitoring and drug overdose mortality. Inj Epidemiol. 2014; 9.

Markon J, Crites A. Experts: Officials Missed Signs of Prescription Drug Crackdown's Effects on Heroin Use. Washington Post. 2014, Mar 6.

Meara E. Why is Health Related to Socioeconomic Status? The Case of Smoking and Low Birthweight. National Bureau of Economic Research Working Paper 8231. 2001.

Mertz KJ, Janssen JK, Williams KE. Underrepresentation of heroin involvement in unintentional drug overdose deaths in Allegheny County, PA. J Forensic Sciences. 2014;59(6): 1583-1585.

Pacula RL, Powell D, Taylor A. Does Prescription Drug Coverage Increase Opioid Substance Abuse? Evidence from Medicare Part D. National Bureau of Economic Research Working Paper 21072. 2015

Park TW, Saitz R, Ganoczy D, Ilgen M, Bohnert AS. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study. BMJ 2015;350:h2698.

Paulozzi LJ, Kilbourne EM, Desai HA. Prescription drug monitoring programs and death rates from drug overdose. Pain Med. 2011 May;12(5):747-54.

Paulozzi LJ, Mack KA, Hockenberry JM. Vital Signs: Variation Among States in Prescribing of Opioid Pain Relievers and Benzodiazepines – United States, 2012. MMWR Morb Mortal Wkly Rep. 2014 Jul 4;63(26):563-8.

Rannazzisi JT. Testimony for "Curbing Prescription Drug Abuse in Medicare". Hearing before the Committee on Homeland Security and Governmental Affairs, United States Senate, 113th Congress, June 24, 2013, retrieved from: http://www.gpo.gov/fdsys/pkg/CHRG-113shrg82571/pdf/CHRG-113shrg82571.pdf.

Rockett IR, Kapusta,ND, Coben, JH. Beyond suicide: action needed to improve self-injury mortality accounting. JAMA psychiatry. 2014 March; 71(3): 231-232. (2014a)

Rockett, IR, Smith GS, Caine ED, Kapusta ND, Hanzlic RL, Larkin GL, Naylor CPE, Nolte KB, Miller TR, Putnum SL, De Leo D, Kleinig J, Stack S, Todd KH, Fraser DW. Confronting death from self-intoxication (DDSI): prevention through a better definition. AJPH. 2014, December; 104(12): e49-e55. (2014b)

Rudd RA, Paulozzi LJ, Bauer MJ, Burleson RW, Carlson RE, Dao D, et al. Increase in Heroin Overdose Deaths – 28 States, 2010 to 2012. MMWR. Morb Mortal Wkly Rep. 2014 Oct 3;63(39):849-854.

Slavova S, O'Brien DB, Creppage K, Dao D, Fondario A, Haile E, Hume B, Largo TW, Nguyen C, Sabel JC, Wright D; Members of the Council of State and Territorial Epidemiologists Overdose Subcommittee. Drug overdose deaths: let's get specific. Public Health Rep. 2015 Jul-Aug;130(4):339-42.

Volkow ND, Frieden TR, Hyde PS, Cha SS. Medication-Assisted Therapies – Tackling the Opioid Overdose Epidemic. N Engl J Med. 2014 May 29;370(22):2063-6.

Warner M, Chen LH, Makuc DM, Anderson RN, Miniño AM. Drug poisoning deaths in the United States, 1980–2008. NCHS data brief, no 81. Hyattsville, MD: National Center for Health Statistics. 2011.

Warner M, Paulozzi LJ, Nolte KB, Davis GG, Nelson LS. State variation in certifying manner of death and drugs involved in drug intoxication deaths. Acad Forensic Pathol. 2013 June; 3(2): 231-237.

Webster LR, Dasgupta N. Obtaining adequate data to determine causes of opioid-related overdose deaths. Pain Med. 2011 Jun;12 Suppl 2:S86-92.

World Health Organization. International Classification of Diseases (ICD). http://www.who.int/classifications/icd/en/. 2014.

Table 1: Manner and Types of Drug Involvement in 2013 Drug Poisoning Deaths

	#	%
All Drug Poisoning Deaths (X40-44, X60-64, X85, Y10-14, Y35.2, *U01.6, *U01.7)	43,982	100.0%
Manner of Death		
Accidental (X40-44)	35,663	81.1%
Intentional (X60-64)	5,432	12.4%
Undetermined Intent (Y10-Y14)	2,801	6.4%
Homicide (X85)	86	0.2%
Reported Drug Mentions (T-Codes)		
Narcotics (40.0-40.9)	27,232	61.9%
Opioid Analgesics (40.2-40.4)	16,235	36.9%
Methadone (40.3)	*3,591*	*8.2%*
Other Opioid Analgesics (40.2, 40.4)	*13,547*	*30.8%*
Heroin (40.1)	8,257	18.8%
Cocaine (40.5)	4,944	11.2%
Other Narcotics (40.0, 40.6-40.9)	2,971	6.8%
Sedatives (42.0-42.8)	8,179	18.6%
Benzodiazepines (42.4)	*6,973*	*15.9%*
Other Sedatives (42.0-42.3, 42.5-42.8)	*2,157*	*4.9%*
Psychotropics (43.0-43.9)	8,642	19.6%
Antidepressants (43.0-43.2)	*4,458*	*10.1%*
Antipsychotics (43.3-43.5)	*1,474*	*3.4%*
Psychostimulants (43.6)	*3,627*	*8.2%*
Other Specified (36.0-38.9, 41.0, 41.9, 44.0-48.7, 49.0-50.8)	3,336	7.6%
Unspecified (50.9)	22,726	51.7%
Exclusive Drug Mentions		
Opioid Analgesics	4,475	10.2%
Heroin	3,353	7.6%
Cocaine	1,493	3.4%
Sedatives	428	1.0%
Psychotropics	1,999	4.5%
Other Specified	1,301	3.0%
Unspecified	9,782	22.2%
>1 Major Drug Class	13,645	31.0%
No Drug Mentioned	419	1.0%

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.

Table 2: Drug Involvement in Drug Poisoning Deaths in Low and High Diagnosis Counties, 2013

Drug Mentions	Low Diagnosis Counties	High Diagnosis Counties
Narcotics	29.8%	82.1%
Opioid Analgesics	16.5%	49.5%
Methadone	*3.7%*	*11.0%*
Other Opioid Analgesics	*13.3%*	*41.6%*
Heroin	8.8%	24.1%
Cocaine	4.9%	15.9%
Sedatives	6.4%	28.2%
Psychotropics	8.7%	25.5%
Other Specified	3.5%	10.6%
>1 Major Drug Class	9.7%	46.2%
Unspecified & Specified	14.5%	34.7%
Unspecified Only	59.9%	0.8%
# of Conditions Listed	2.51	3.70

Note: See note on Table 1. Low counties are defined as those with at least one drug specified for fewer than 63.3% of drug poisoning deaths in 2013. High diagnosis counties are those with more than 97.8% of drug poisoning deaths in 2013. The number of conditions listed refers to the number of record-axis conditions shown on the Multiple Cause of Death files.

Table 3: Reported and Adjusted Drug Mention Prevalences, 2013

Drug Mentions	Reported Prevalence	Adjusted Prevalence		Difference
		Estimate	Standard Error	
Any Drug Mention				
Opioid Analgesics	36.9%	51.2%	1.0%	38.6%
Heroin	18.8%	25.3%	1.0%	34.7%
Cocaine	11.2%	15.0%	0.7%	33.9%
Sedatives	18.6%	28.6%	0.9%	53.7%
Psychotropics	19.6%	27.4%	0.9%	39.3%
Other Specified	7.6%	10.5%	0.4%	39.0%
Unspecified	51.7%	38.4%	1.6%	-25.7%
>1 Major Drug Class	31.0%	46.5%	0.9%	49.9%
Exclusive Drug Mention				
Opioid Analgesics	10.2%	12.4%	0.5%	22.2%
Heroin	7.6%	9.9%	0.6%	30.3%
Cocaine	3.4%	4.1%	0.4%	20.7%
Sedatives	1.0%	1.2%	0.1%	21.9%
Psychotropics	4.5%	5.1%	0.3%	11.7%
Other Specified	3.0%	3.4%	0.1%	14.3%
Unspecified	22.2%	3.7%	0.1%	-83.5%

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.

Table 4: Estimates of Adjusted Prevalences With and Without *Any* Unspecified Drug Mentions

Drug Mentions	Unspecified Drugs Mentioned		Unspecified Drugs Not Mentioned	
	Adjusted Prevalence (1a)	Standard Error (1b)	Adjusted Prevalence (2a)	Standard Error (2b)
Opioid Analgesics	47.0%	1.3%	57.7%	2.0%
Heroin	26.2%	1.5%	23.8%	2.4%
Cocaine	14.7%	1.0%	15.7%	1.4%
Sedatives	22.2%	1.3%	39.5%	2.0%
Psychotropics	23.9%	1.2%	32.9%	1.6%
Other Specified	10.0%	0.5%	11.4%	0.8%
Unspecified	6.3%	0.2%	94.0%	0.2%
>1 Major Drug Class	38.6%	1.4%	58.8%	1.8%

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), while 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 5: Reported and Adjusted Drug Mention Prevalences at Specified Numbers of Conditions Mentioned, 2013

Drug Mentions	SPECIFY = 1		SPECIFY = 1 & NUMCTY = 4.286		
	Adjusted Prevalence	Standard Error	Adjusted Prevalence	Standard Error	% Δ
	(1a)	(1b)	(2a)	(2b)	(3)
Opioid Analgesics	51.2%	1.0%	53.1%	1.0%	3.9%
Heroin	25.3%	1.0%	24.3%	1.1%	-4.1%
Cocaine	15.0%	0.7%	15.8%	0.8%	4.9%
Sedatives	28.6%	0.9%	34.6%	0.8%	20.9%
Psychotropics	27.4%	0.9%	30.2%	0.8%	10.4%
Other Specified	10.5%	0.4%	12.0%	0.3%	13.9%
Unspecified	38.4%	1.6%	43.0%	1.8%	11.9%
>1 Major Drug Class	46.5%	0.9%	53.6%	0.8%	15.2%

Note: See note on Table 1. 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. Robust standard errors are calculated with clustering at the county level. Columns (2a) and (2b) show 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 4.286177. Column (3) shows the percentage difference between columns (2a) and (1a).

Table 6: Reported and Adjusted 2013 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	37.8%	52.4%	38.6%	28.4%	40.1%	41.3%	42.3%	59.7%	40.9%
Heroin	22.0%	29.3%	33.5%	1.2%	2.0%	63.9%	12.0%	15.4%	28.2%
Cocaine	13.3%	17.8%	34.5%	1.2%	1.8%	46.6%	5.2%	6.7%	28.0%
Sedatives	17.8%	27.8%	56.5%	25.5%	36.6%	43.7%	16.1%	25.7%	59.5%
Psychotropics	18.1%	25.2%	39.0%	29.4%	41.4%	40.6%	19.8%	30.1%	52.2%
Other Specified	5.4%	7.8%	44.7%	22.7%	29.1%	28.1%	6.3%	9.8%	56.4%
Unspecified	50.1%	36.3%	-27.5%	64.0%	55.7%	-13.0%	47.9%	33.9%	-29.3%
>1 Major Drug	31.6%	47.3%	49.5%	28.2%	43.1%	52.9%	29.2%	44.4%	51.9%
Only Unspecified	21.6%	3.2%	-85.1%	24.0%	6.1%	-74.6%	26.6%	5.5%	-79.3%

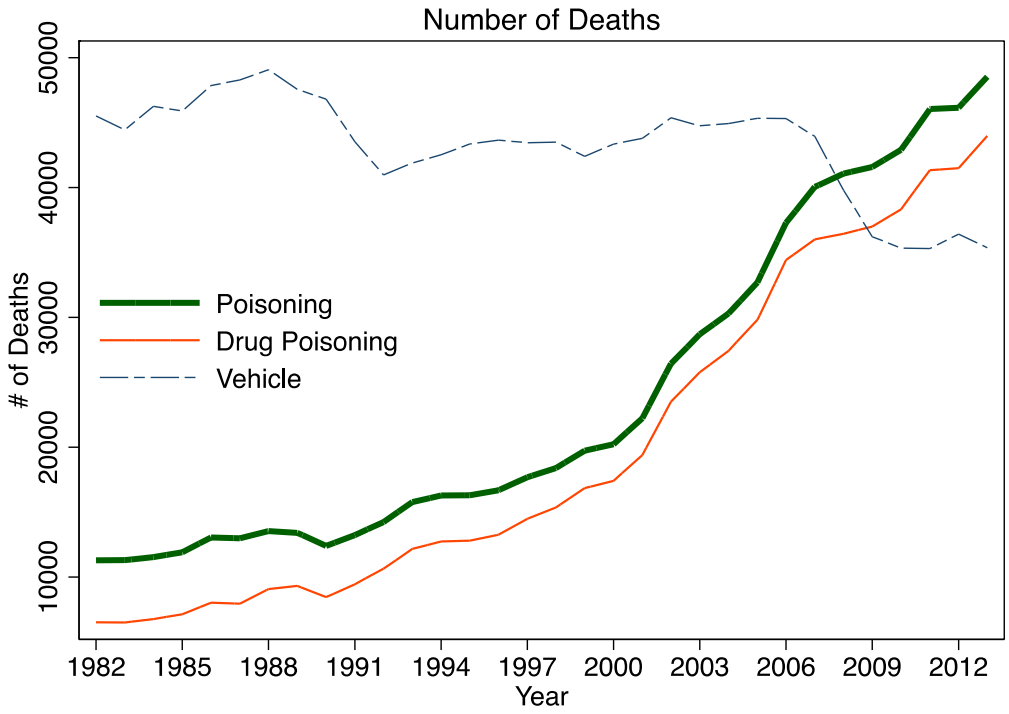
Note: See note on Table 3. Reported prevalences are from death certificates and indicate the percentage of drug poisonings where the specified type of drug is mentioned. Adjusted prevalences are average predicted values from probit models, where at least one specific drug is mentioned for all poisoning 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 35,663, 5,432 and 2,801 drug poisoning deaths classified as accidental, intentional and of undetermined intent. Standard errors range from 0.4% to 1.8% for accidental deaths, 0.3% to 1.6% for intentional deaths and 0.7% to 3.2% for deaths of undetermined intent.

Table 7: Estimates of Changes of Drug Involvement in Drug Poisoning Deaths, 1999 and 2013

Drug Mentions	Reported Drug Involvement		Adjusted Drug Involvement	
	Δ in # Deaths	% of Total Δ Explained	Δ in # Deaths	% of Total Δ Explained
All Deaths	27,133	100.0%	27,133	100.0%
Any Mention				
Opioid Analgesics	12,205	45.0%	17,276	63.5%
Methadone	*2,907*	*10.3%*	*3,730*	*13.7%*
Other Opioid Analg.	*10,187*	*37.5%*	*14,802*	*54.6%*
Heroin	6,297	23.2%	8,753	32.3%
Cocaine	1,122	4.1%	1,381	5.1%
Other Narcotic	40	0.1%	-917	-3.4%
Sedatives	6,517	24.0%	9,942	36.6%
Bezodiazepines	*5,838*	*21.5%*	*8,931*	*32.9%*
Psychotropics	6,176	22.8%	8,472	31.2%
Antidepressants	*2,709*	*10.0%*	*4,175*	*15.4%*
Antipsychotics	*1,153*	*4.2%*	*1,788*	*6.6%*
Psychostimulants	*3,080*	*11.4%*	*3,815*	*14.1%*
Other Specified	2,165	8.0%	3,156	11.6%
Unspecified	14,249	52.5%	10,920	40.2%
Exclusive Mention				
Opioid Analgesics	3,410	12.6%	4,197	15.5%
Methadone	*748*	*2.8%*	*828*	*3.1%*
Other Opioid Analg.	*2,520*	*9.3%*	*3,150*	*11.6%*
Heroin	2,761	10.2%	3,721	13.7%
Cocaine	253	0.9%	306	1.1%
Sedatives	160	0.6%	205	0.8%
Psychotropics	1,316	4.9%	1,456	5.4%
Antidepressants	*1*	*0.0%*	*6*	*0.0%*
Psychostimulants	*1,228*	*4.5%*	*1,333*	*4.9%*
Other Specified	713	2.6%	875	3.2%
Unspecified	6,092	22.5%	889	3.3%
>1 Major Drug	9,375	34.6%	13,698	50.5%

Note: See note on Table 7. Total Δ Explained is Δ in # Deaths number divided by 27,133 (the increase in drug poisoning deaths occurring between 2013 and 1999). 95 percent confidence intervals (CI) are shown in the lower (upper) threshold calculated calculated by subtracting the lower (upper) threshold of the 2013 CI from the upper (lower) threshold of the 1999 CI. Adjusted prevalence could not be calculated for exclusive mentions of antipsychotics due to the small numbers of exclusive mentions from this source (41 in 1999 and 101 in 2013).

Figure 1: Poisoning and Motor Vehicle Deaths and Death Rates



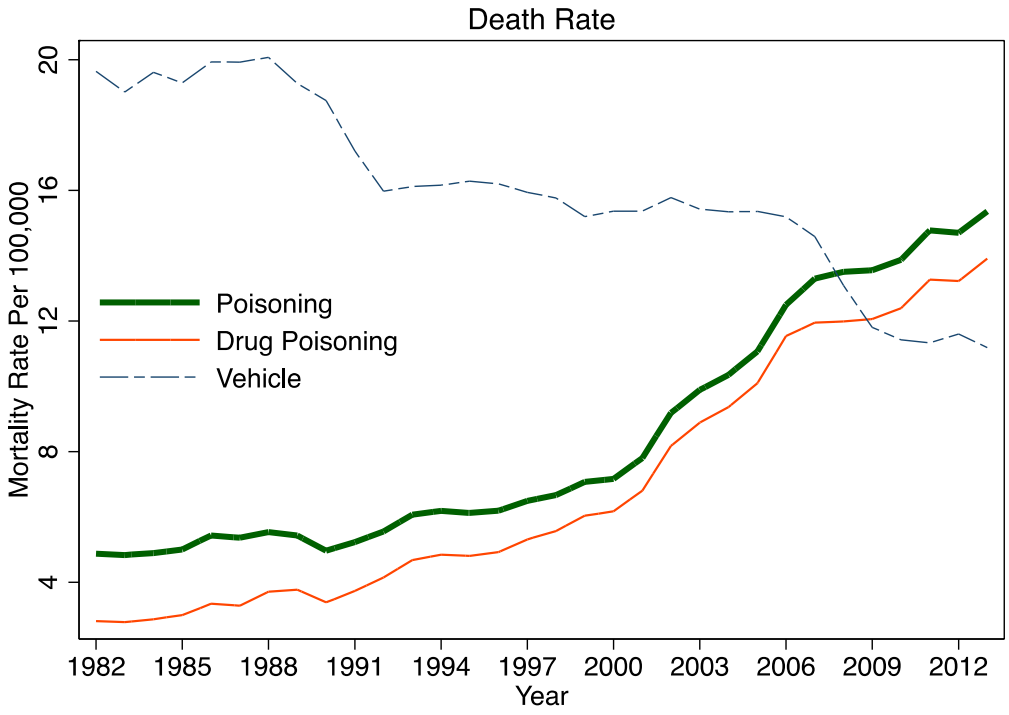


Figure 2: Group-Specific Drug Poisoning Rates

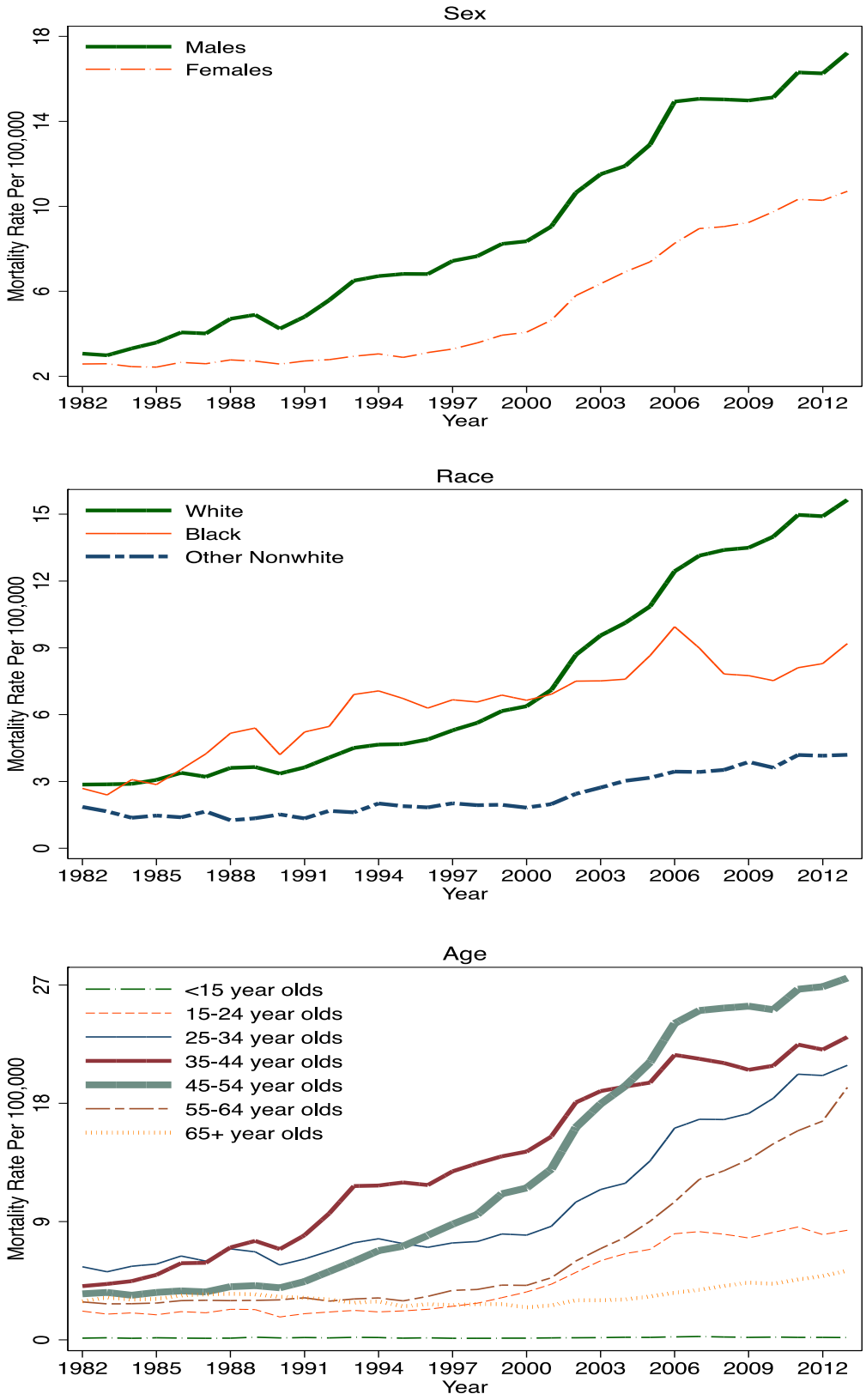


Figure 3: Share of Drug Poisoning Deaths with ≥1 Specific Drug Mentioned

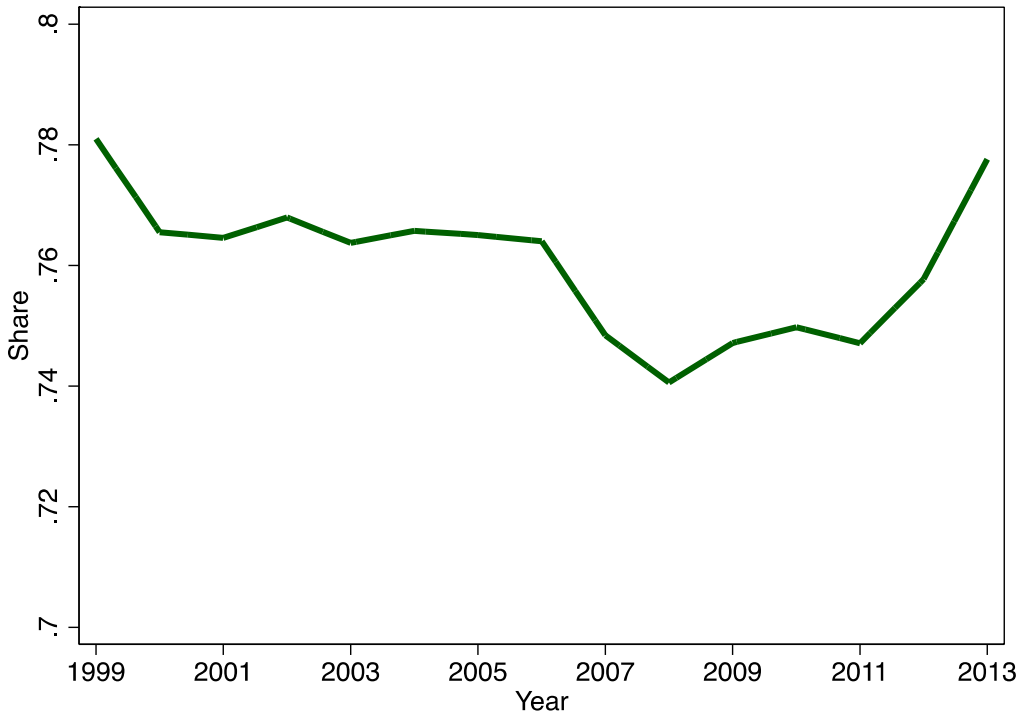


Figure 4: Reported and Adjusted Prevalences by Type of Drug

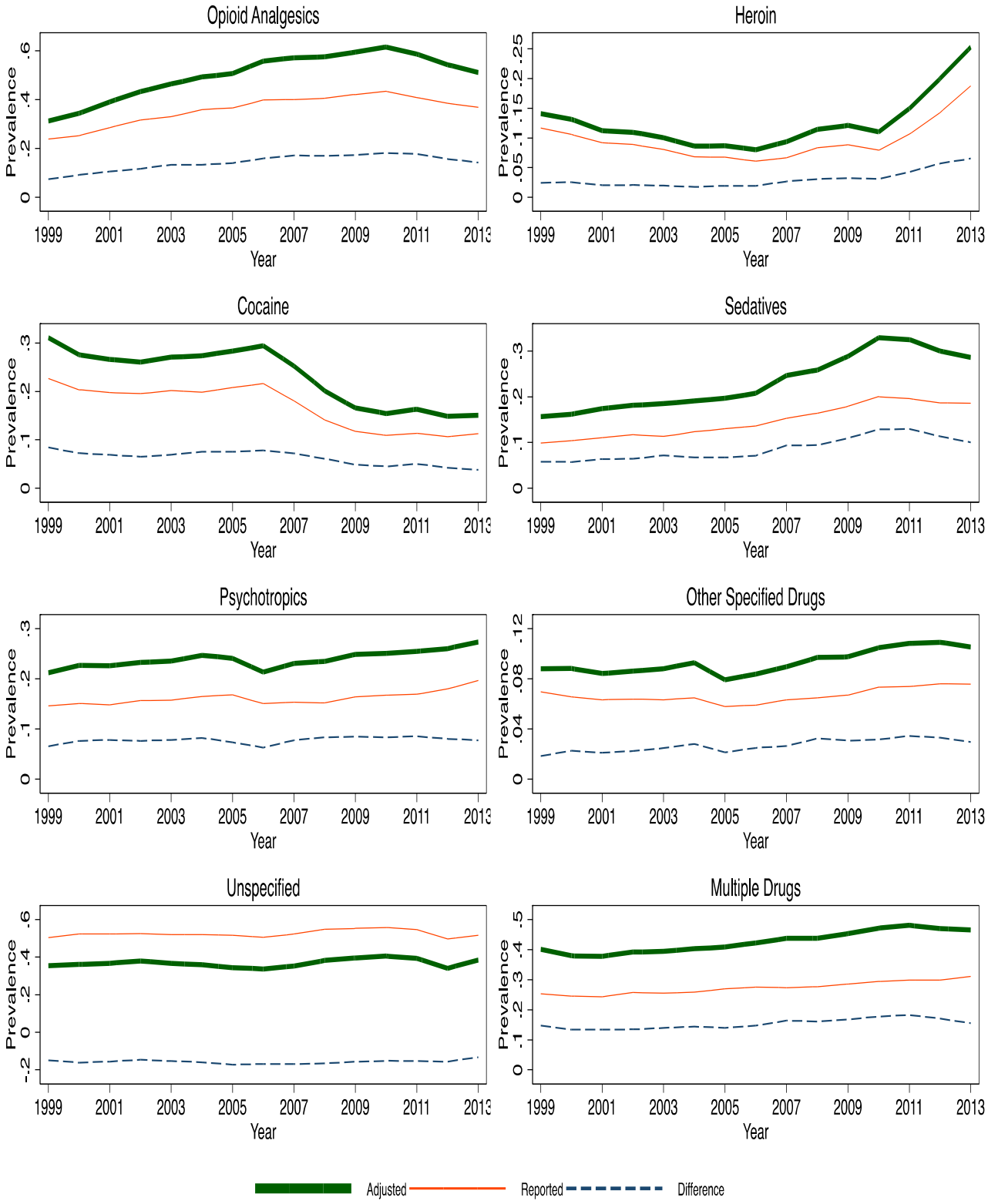


Figure 5: Reported and Adjusted Number of Deaths by Type of Drug

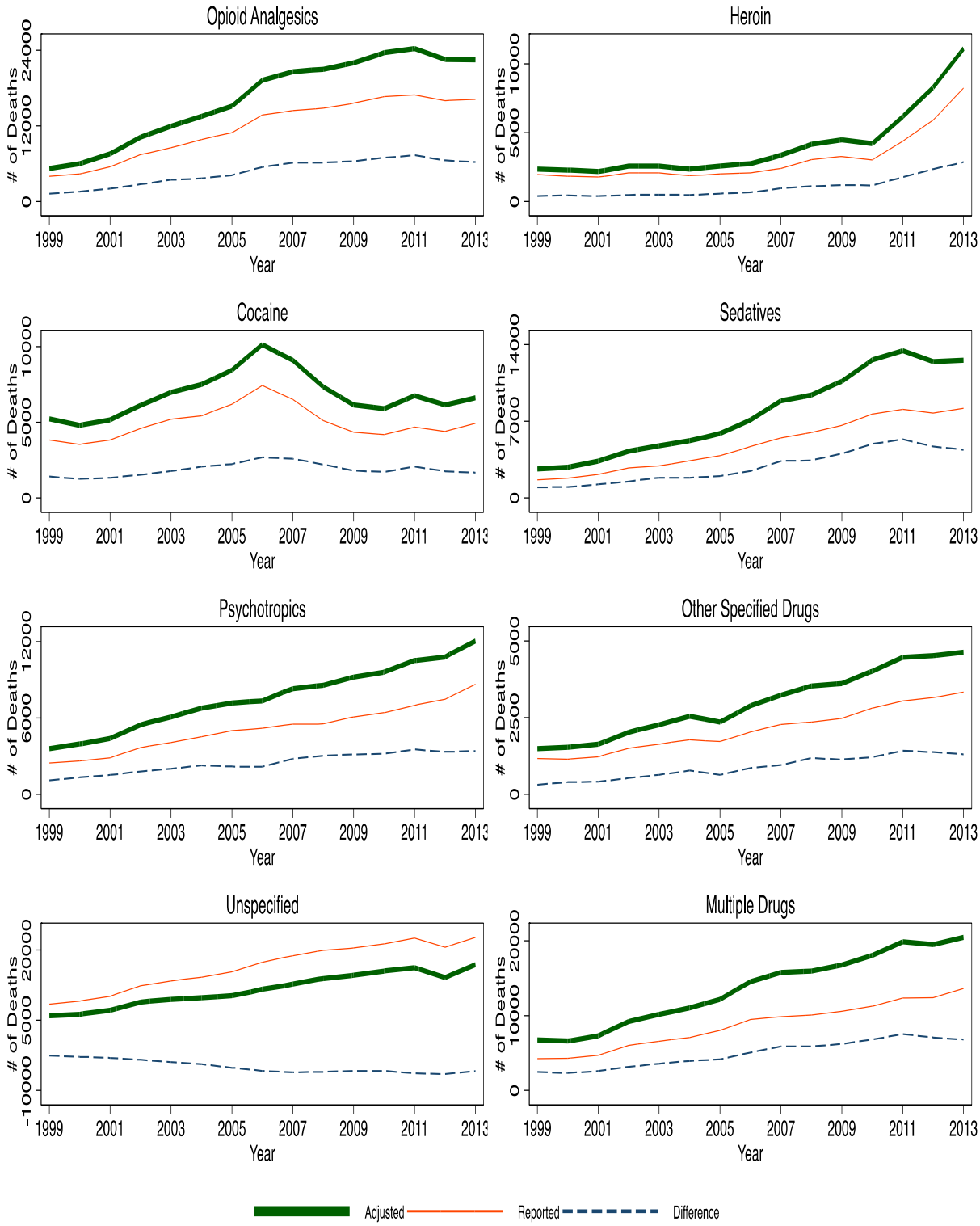
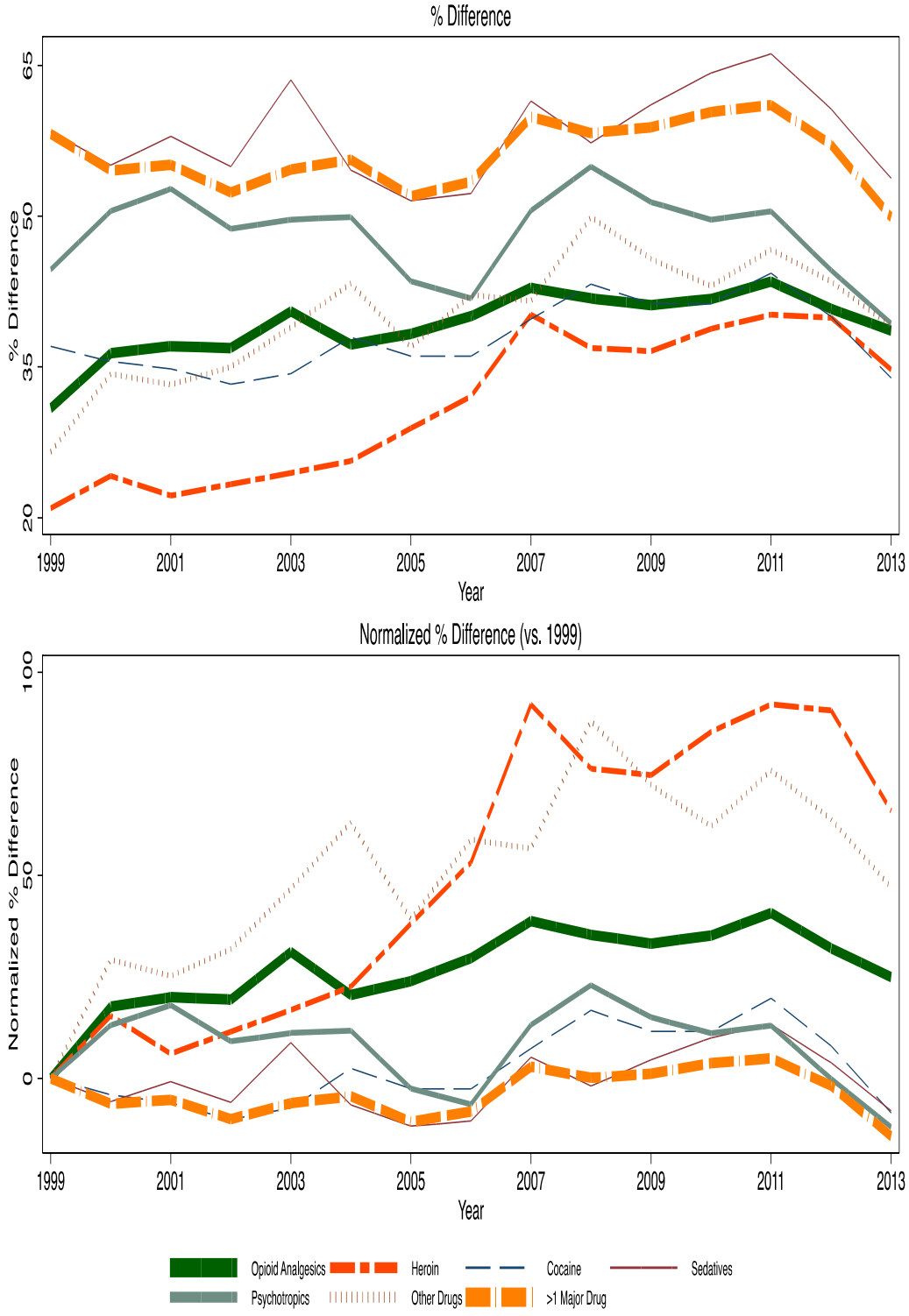


Figure 6: Percent Difference Between Adjusted and Reported Prevalence or Number of Deaths



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

Figure 7: Difference Between Adjusted and Reported Prevalence or # Deaths

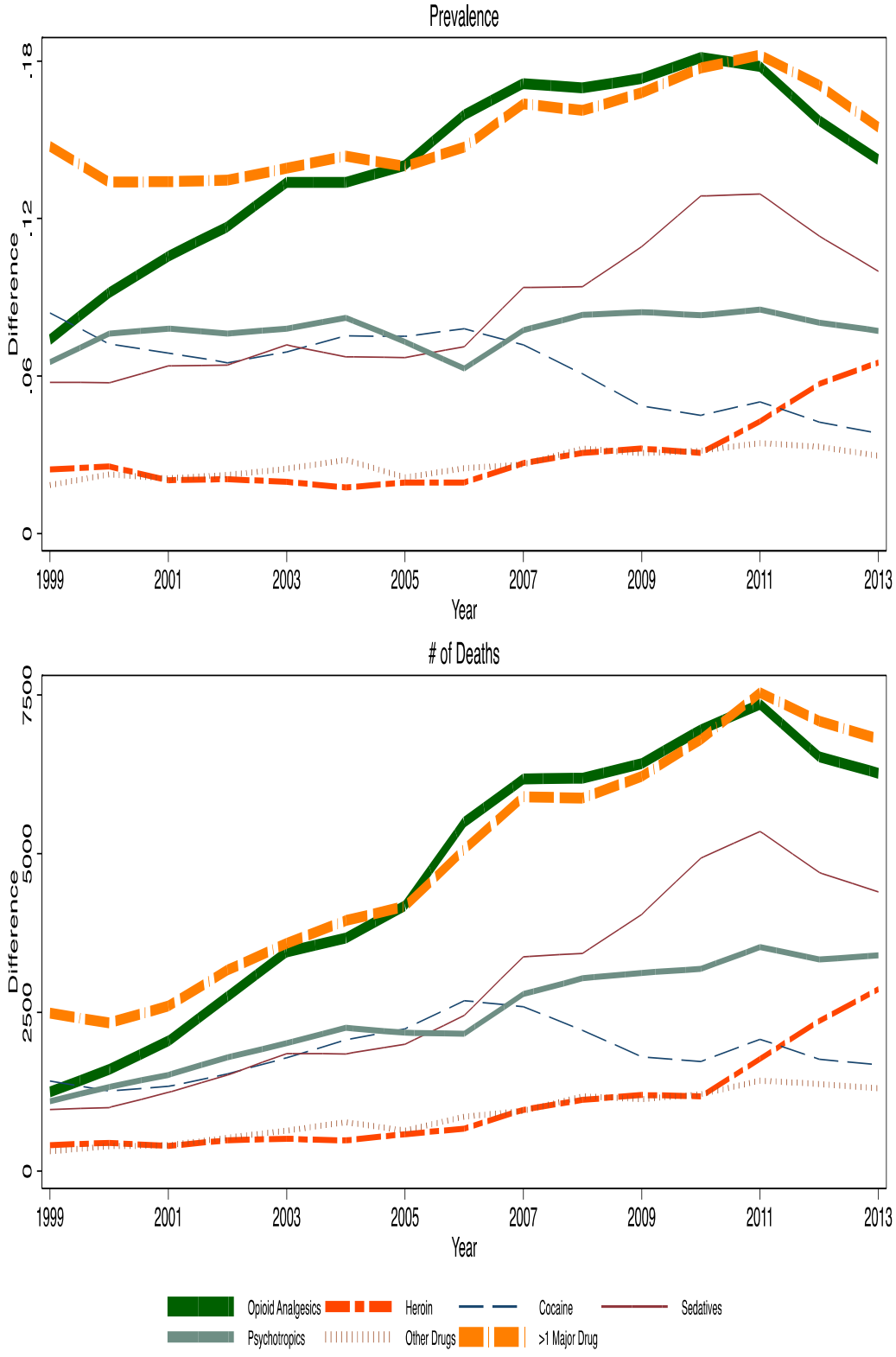


Figure 8: Change in Overdose Deaths Accounted For: 1999 through Stated Year

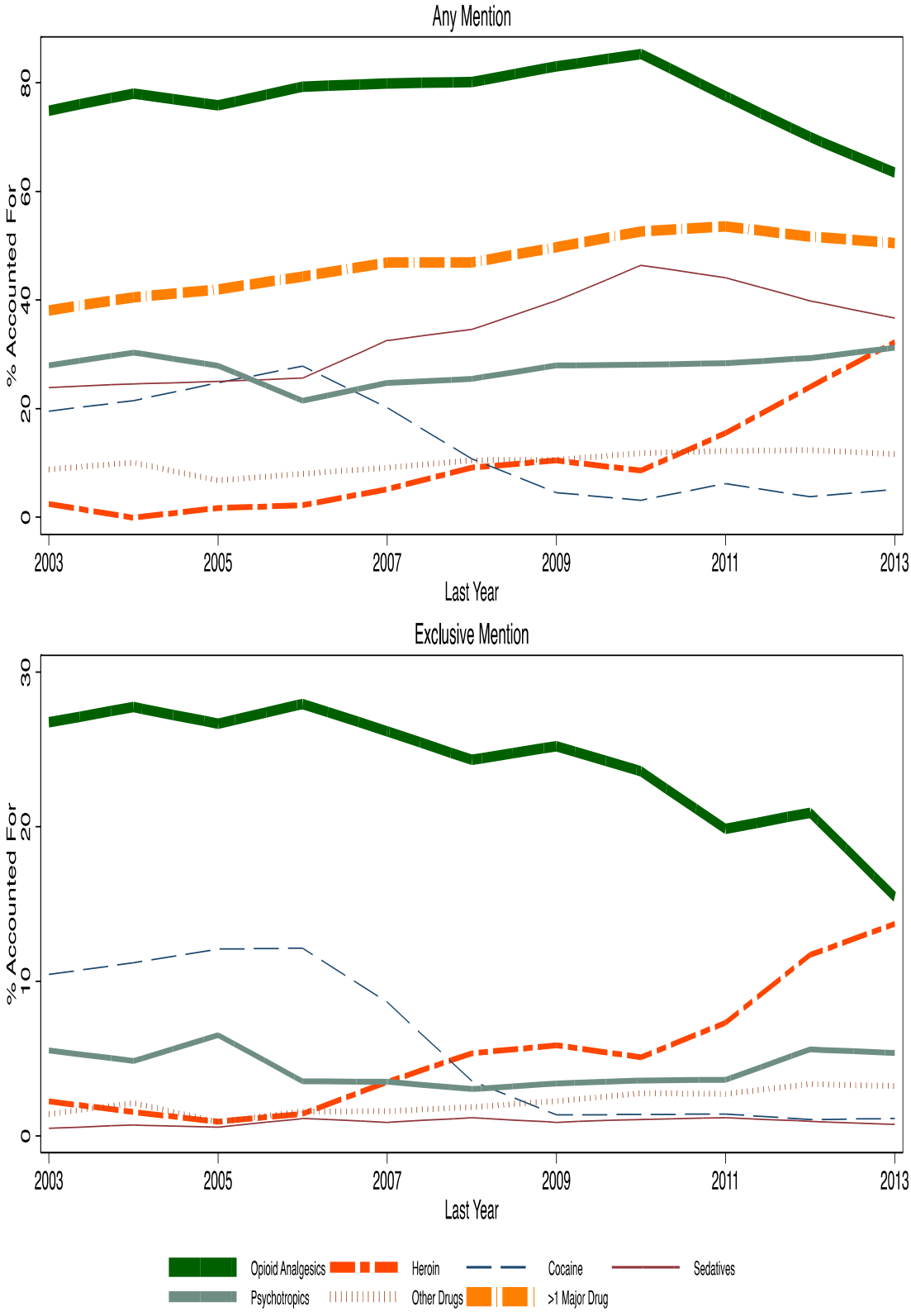
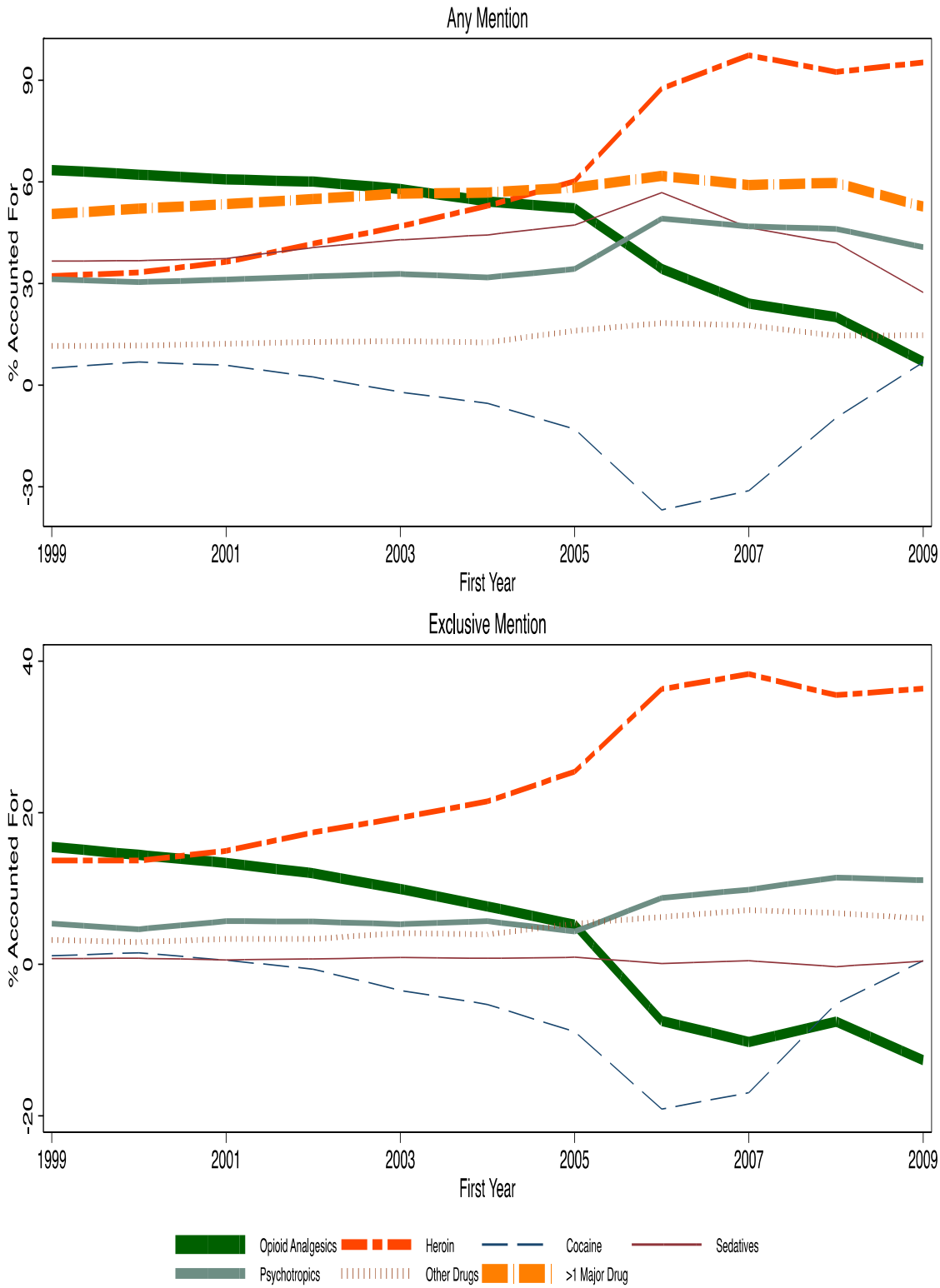


Figure 9: Change in Overdose Deaths Accounted For: Stated Year through 2013



Appendix

Table A.1. Characteristics of Low and High Diagnosis Counties, 2013

Characteristic	Low Diagnosis Counties	High Diagnosis Counties
Female	40.7%	37.1%
Black	7.5%	11.4%
Other Nonwhite	1.5%	2.2%
Hispanic	6.2%	7.2%
Married	26.5%	24.6%
< High School Grad	19.3%	18.8%
High School Grad	47.0%	46.0%
Some College	23.1%	21.8%
College Grad	8.8%	9.2%
Age: <20	2.3%	2.7%
Age: 21-30	17.3%	17.6%
Age: 31-40	20.9%	20.7%
Age: 41-50	26.0%	25.7%
Age: 51-60	24.1%	24.1%
Age: 61-70	6.9%	7.0%
Age:71-80	1.6%	1.4%
Age:≥80	1.0%	0.8%
Type of Death		
Accidental	81.6%	80.4%
Intentional	11.3%	11.4%
Undetermined	6.9%	7.9%
Homicide	0.2%	0.2%
Autopsy Performed	72.3%	79.3%

Note: See note on Table 2.

Table A.2: 2013 Adjusted Prevalences Using Alternative Specifications

Drug Mentions	Method of Adjusting Prevalence: Basic	Linear Probability Model	No Covariates	Supple-mentary Covariates
	(1)	(2)	(3)	(4)
Opioid Analgesics	51.2%	49.6%	50.6%	50.9%
Heroin	25.3%	24.6%	25.6%	25.2%
Cocaine	15.0%	14.7%	15.8%	15.0%
Sedatives	28.6%	26.8%	27.7%	28.3%
Psychotropics	27.4%	26.0%	27.0%	27.1%
Other Specified	10.5%	10.0%	10.5%	10.5%
Unspecified	38.4%	39.1%	36.7%	38.4%
>1 Major Drug Class	46.5%	44.1%	46.1%	46.2%

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: Predicted Number of Conditions Listed, 2013 Drug Poisoning Deaths

	Estimate	Standard Error
SOME Not Controlled For		
SPECIFY = actual value	3.206	0.046
SPECIFY= 0	1.729	0.089
SPECIFY=1	3.628	0.054
SOME Controlled For		
SPECIFY & SOME = actual value	3.206	0.046
SPECIFY = 0, SOME = actual value	2.083	0.096
SPECIFY = 1, SOME = actual value	3.527	0.054
SPECIFY = 0, SOME =0	1.767	0.089
SPECIFY = 1, SOME =0	3.212	0.065
SPECIFY = 1, SOME =1	4.283	0.102

Note: Table shows predicted number of conditions listed on 2013 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.4: Estimates of Drug Involvement in Drug Poisoning Deaths, 1999 and 2023

	Based on Reported # of Deaths				Based on Adjusted # of Deaths			
Drug Mentions	1999	2013	Δ	% Total Δ	1999	2013	Δ	% Total Δ
All Deaths	16,849	43,982	27,133	100.0%	16,849	43,982	27,133	100.0%
Any Mention								
Opioid Analgesic	4,030	16,235	12,205	45.0%	5,275 [4808-6143]	22,501 [21641-23361]	17,276 [15498-18953]	63.5% [57.1-69.9%]
Methadone	*784*	*3,591*	*2,807*	*10.3%*	1,320 [1080-1561]	5,050 [4711-5390]	3,730 [3150-4310]	13.7% [11.6-15.9%]
Other Opioid Anal	*3,360*	*13,547*	*10,187*	*37.5%*	4,235 [3363-5106]	19,037 [18185-19888]	14,802 [13079-16526]	54.6% [48.2-60.9%]
Heroin	1,960	8,257	6,297	23.2%	2,370 [1707-3033]	11,123 [10231-12015]	8,753 [7198-10308]	32.3% [26.5-38.0%]
Cocaine	3,822	4,944	1,122	4.1%	5,237 [4684-5791]	6,619 [6023-7215]	1,381 [232-2531]	5.1% [0.9-9.3%]
Other Narcotic	2,931	2,971	40	0.1%	4,389 [3583-6094]	3,922 [3377-4466]	-917 [-2717-883]	-3.4% [-10.0-3.3%]
Sedatives	1,662	8,179	6,517	24.0%	2,633 [2253-2253]	12,575 [11807-13343]	9,942 [8795-11090]	36.6% [32.4-40.9%]
Bezodiazepines	*1,135*	*6,973*	5,838	21.5%	1,925 [1588-2261]	10,855 [10149-11562]	8,931 [7888-9974]	32.9% [9.1-36.8%]
Psychotropics	2,466	8,642	6,176	22.8%	3,568 [3093-4043]	12,039 [11251-12828]	8,472 [7209-9735]	31.2% [26.6-35.9%]
A*ntidepressants*	*1,749*	*4,458*	*2,709*	*10.0%*	2,748 [2371-3125]	6,923 [6452-7394]	4,175 [3327-5024]	15.4% [12.3-18.5%]
Antipsychotics	*321*	*1,474*	*1,153*	*4.2%*	542 [413-671]	2,330 [2068-2592]	1,788 [1397-2179]	6.6% [5.1-8.0%]
Psychostimulants	*547*	*3,627*	*3,080*	*11.4%*	656 [490-822]	4,471 [3903-5039]	3,815 [3081-4549]	14.1% [11.4-16.8%]
Other Specified	1,171	3,336	2,165	8.0%	1,482 [1260-1704]	4,638 [4317-4960]	3,156 [2613-3700]	11.6% [9.6-13.6%]
Unspecified	8,477	22,726	14,249	52.5%	5,970 [5406-6894]	16,890 [15491-18289]	10,920 [8596-13243]	40.2% [31.7-48.8%]
Exclusive Mention								

Opioid Analgesic	1065	4475	3,410	12.6%	1,271 [969-1573]	5,468 [4999-5936]	4,197 [3427-4967]	15.5% [12.6-18.5%]
Methadone	*218*	*966*	*748*	*2.8%*	317 [223-410]	1,145 [1000-1291]	828 [590-1067]	3.1 [2.2-3.9%]
Other Opioid Anal	*827*	*3,347*	*2,520*	*9.3%*	934 [659-1209]	4084 [3276-4442]	3,150 [2517-3783]	11.6% [9.3-13.9%]
Heroin	592	3,353	2,761	10.2%	647 [453-8421]	4,369 [3831-4907]	3,721 [1989-4454]	13.7% [11.0-16.4%]
Cocaine	1,240	1,493	253	0.9%	1,496 [1239-1754]	1,802 [1469-2135]	306 [-285-896]	1.1% [-1.0-3.3%]
Sedatives	268	428	160	0.6%	316 [243-390]	522 [453-591]	205 [63-348]	0.8% [0.2-1.3%]
Psychotropics	683	1999	1,316	4.9%	776 [581-971]	2,232 [1934-2530]	1,456 [963-1949]	5.4% [3.6-7.2%]
Antidepressants	*425*	*426*	*1*	*0.0%*	516 [386-646]	522 [448-596]	6 [-198-210]	0.0% [-0.7-0.8%]
Antipsychotics	*41*	*101*	*60*	*0.2%*				
Psychostimulants	*197*	*1425*	*1,228*	*4.5%*	205 [115-294]	1538 [1269-1807]	1333 [975-1692]	4.9% [3.6-6.2%]
Other Specified	588	1301	713	2.6%	613 [496-730]	1,487 [1365-1610]	875 [635-1114]	3.2% [2.3-4.1%]
Unspecified	3690	9782	6,092	22.5%	724 [653-795]	1,613 [1498-1729]	889 [702-1075]	3.3% [2.6-4.0%]
>1 Major Drug	4,270	13,645	9,375	34.6%	6,755 [6310-7199]	20,542 [19659-21245]	13,698 [12460-14935]	50.5% [45.9-55.0%]

Note: Adjusted number of deaths calculated by multiplying adjusted prevalence by the number of deaths in the specified year. Δ in # Deaths is the difference between 2013 and 1999 deaths involving the specified drug. 95 percent confidence intervals (CI) are shown in brackets. For Δ, the lower (upper) threshold of the confidence interval is calculated by subtracting the lower (upper) threshold of the 2013 CI from the upper (lower) threshold of the 1999 CI. Adjusted prevalence could not be calculated for exclusive mentions of antipsychotics due to the small numbers of deaths from this source.