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What is the prevalence of and trend in opioid use disorder in the United States from 2010 to 2019? Using multiplier approaches to estimate prevalence for an unknown population size

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Abstract

Opioid-related overdose deaths have increased since 2010 in the U.S., but information on trends in opioid use disorder (OUD) prevalence is limited due to unreliable data. Multiplier methods are a classical epidemiological technique to estimate prevalence when direct estimation is infeasible or unreliable. We used two different multiplier approaches to estimate OUD prevalence from 2010 to 2019. First, we estimated OUD in National Survey on Drug Use and Health (NSDUH), and based on existing capture-recapture studies, multiplied prevalence by 4.5x. Second, we estimated the probability of drug poisoning death among people with OUD (Meta-analysis indicates 0.52/100,000), and divided the number of drug poisoning deaths in the US by this

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Katherine M. Keyes: Conceptualization, Methodology, Writing – original draft, Supervision. **Caroline Rutherford:** Data curation, Software, Visualization. **Ava Hamilton:** Data curation, Methodology. **Joshua A. Barocas:** Methodology, Writing – review & editing. **Kitty H. Gelberg:** Methodology, Writing – review & editing. **Peter P. Mueller:** Methodology, Writing – review & editing. **Daniel J. Feaster:** Methodology, Writing – review & editing. **Nabila El-Bassel:** Methodology, Writing – review & editing. **Magdalena Cerdá:** Conceptualization, Methodology, Writing – review & editing.

Declaration of competing interest

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Supplementary materials

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probability. Estimates were weighted to account for increase in drug-related mortality in recent years due to fentanyl. Estimated OUD prevalence was lowest when estimated in NSDUH with no multiplier, and highest when estimated from vital statistics data without adjustment. Consistent findings emerged with two methods: NSDUH data with multiplier correction, and vital statistics data with multiplier and adjustment. From these two methods, OUD prevalence increased from 2010 to 2014; then stabilized and slightly declined annually (survey data with multiplier, highest prevalence of 4.0% in 2015; death data with a multiplier and correction, highest prevalence of 2.35% in 2016). The number of US adolescent and adult individuals with OUD in 2019 was estimated between 6.7–7.6 million. When multipliers and corrections are used, OUD may have stabilized or slightly declined after 2015. Nevertheless, it remains highly prevalent, affecting 6–7 million US adolescents and adults.

1. Introduction

Since the mid-1990s (Jalal et al., 2018), there has been exponential growth in drug overdose in the United States (US) (Hedegaard et al., 2020; Jalal et al., 2018; Mattson et al., 2021), with 70,630 Americans dying of overdose in 2019 (Mattson et al., 2021) and more in 2020 (Centers for Disease Control and Prevention, 2020a), amplified by the downstream consequences of the SARS-CoV-2 pandemic. Opioids are implicated as the main contributor to fatal and non-fatal overdose in the US, with prescription opioids driving the epidemic of the 1990s and early 2000s, then heroin and synthetic opioids such as unregulated fentanyl in the 2010s (Cerdá et al., 2021). Opioid use disorder (OUD) is a chronic condition that is defined in DSM-5 (American Psychiatric Association, 2013) to include frequent use of and tolerance to opioids, symptoms of withdrawal upon cessation, unsuccessful efforts to quit or cut down, failure to fulfill role obligation and giving up activities for drug use. OUD can be a chronic and destabilizing health condition that can lead to multiple morbidities and mortality, including but not limited to overdose.

Estimating the prevalence of OUD in the US is important for a variety of reasons including assessing unmet treatment and service needs, tracking the impact of prevention and intervention efforts, and allocating resources. Evidence indicates that racial disparities in overdose are emerging, with greater increases among Black and Latinx people, suggesting the need for health equity interventions (Furr-Holden et al., 2021). However, while opioid-related death has been escalating for two decades, trends in OUD have been more difficult to quantify. Evidence suggests that OUD increased in the US population with expanded accessibility of prescription opioids in the 2000s (Dart et al., 2015; Paulozzi et al., 2012). While prescription opioid distribution declined in the US in the past decade (Centers for Disease Control and Prevention, 2020b), heroin initiation began increasing, which may underlie further increases in OUD (Han et al., 2020; Martins et al., 2017a); synthetic opioid-involved deaths are now a major contributor to mortality as well (Mattson et al., 2021). However, it remains unknown whether the size of the OUD population has increased or remained stable.

The true prevalence of OUD is difficult to ascertain as population-level surveys often miss populations at high risk (due to higher rates of survey refusal among individuals who use

drugs, and due to underreporting of those who participate), and do not routinely include individuals who are incarcerated, experiencing homelessness, or hospitalized (Han et al., 2017; Martins et al., 2017b; Parker and Weinberger, 2020). Administrative claims data, another typical source for counting people, likely miss people with OUD due to both under-diagnosis in claims and lack of access to healthcare, and these biases likely result in underestimation of disparities by race and social class. Thus, a conundrum common in surveillance for many disorders in psychiatric epidemiology emerges: how do we count cases?

A variety of indirect estimation methods exist to estimate the size of hidden populations, including those with OUD (Hickman et al., 2002). Among these, multiplier methods are often a foundational method when complete information is unavailable (Hickman et al., 2002). The general framework of a multiplier method is to identify an unbiased event in a benchmark data source that involves the target population, and a multiplier that indicates how often those in the target population experience the event. An advantage of multipliers in estimating prevalence is that they do not require primary data collection or direct data linkages, and thus can be estimated from existing data sources as well as harnessing estimates from the empirical literature.

The use of multipliers is common in the epidemiological literature estimating drug use and OUD prevalence for specific geographic areas, including in local areas within the US and for single years (De Angelis et al., 2004; Fischer et al., 2018; Mallow et al., 2019; McNeely et al., 2012). Similar types of multiplier approaches have been used to estimate opioid and injection drug use cross-nationally (Aceijas et al., 2006; De Angelis et al., 2004; Degenhardt et al., 2016; Fischer et al., 2018; Kraus et al., 2003), and opioid use in New York City (McNeely et al., 2012) as well as in other areas (Brady et al., 2008; Cooper et al., 2008; Pouget et al., 2012; Prejean et al., 2011). Data inputs to inform multiplier methods such as survey, medical record, and mortality sources are widely available, and an important foundational approach to estimating OUD population size across the US. However, to date, multiplier methods have not been used to estimate longitudinal OUD prevalence in the US.

In summary, estimating the prevalence of, and trends in, OUD in the general population of the US is a critical public health surveillance task, and existing general population surveys underestimate true prevalence. Approaches such as multiplier methods leveraging existing data can augment general population surveys to provide a more accurate assessment of true prevalence. Because each approach makes specific assumptions and has inherent limitations, using multiple approaches is more reliable to triangulate the range of estimates that plausibly capture the underlying population. We used a multi-modal approach in two benchmark datasets—National Survey on Drug Use and Health (NSDUH) and the National Vital Statistics System (NVSS)—along with various multipliers to estimate OUD prevalence in the US, by year, from 2010 to 2019.

2. Methods

2.1. Benchmark data source #1: National survey on drug use and health

NSDUH is an annually conducted in-person survey of US civilian, non-institutionalized populations aged 12 and older (Substance Abuse and Mental Health Services Administration, 2021). Sampling is via a complex multi-stage probability design, with approximately 70,000 respondents per year. Individuals aged 12–17 are oversampled, as are other groups, requiring sample weights for population-level inference. OUD is assessed via a fully structured interview with algorithms for DSM diagnoses. There was a change in questionnaire methodology in 2015, thus pre-and post-2015 rates are not directly comparable.

2.2. Multiplier correction for national survey on drug use and health

NSDUH data underestimates the prevalence of many health conditions, including drug use. The actual extent of the underestimation is unknown but can be estimated. To estimate the amount of underestimation in NSDUH, we relied on a state-level capture-recapture estimate of OUD to establish a multiplier (Barocas et al., 2018). Capture-recapture is a common method to estimate the size of difficult-to-estimate populations. Briefly, to estimate the number of a certain group, one takes a sample of that group from one source ('capture'), and then resamples from an independent source ('recapture') to determine overlap. The total number in the population can then be estimated as the number captured multiplied by the number recaptured, divided by the number captured in both samples. This method has been applied in the context of estimating the size of many 'hidden' populations including people using opioids and other drugs (Hickman et al., 2002, 1999).

We relied on a Massachusetts study, Barocas et al., as an estimate to approximate a multiplier correction (Barocas et al., 2018), as other US capture-recapture studies examined smaller geographic areas and single years. Barocas et al. uses the Massachusetts All Payer Claims data linked across 6 sources to multiply capture individuals with OUD. We compared the prevalence of past-year OUD in Massachusetts state-level NSDUH (2015–2018) to Barocas et al. (2011–2015) (Center for Behavioral Health Statistics and Quality, 2016). In the overlapping year 2015, the capture-recapture OUD prevalence estimate was 4.6% (Barocas et al., 2018); this is 4.49 times higher than the NSDUH estimate. We applied this multiplier to all years of NSDUH data for the US, which assumes that the average across states is accurately captured and that the OUD prevalence estimate from Barocas et al. is a valid estimate, but also has strengths as it is an evidence-based assessment of under-ascertainment of OUD prevalence. We relied on a single state, Massachusetts, for the capture-recapture multiplier because it is largest geographic area for which a capture-recapture estimate was available in the US in the general population. This multiplier assumes that the difference between the NSDUH estimate of OUD prevalence and the true general population OUD prevalence in Massachusetts is similar in other states; given that the NSDUH sampling frame and data collection methods are similar in other states as in Massachusetts, it is a reasonable assumption that, while the prevalence of OUD differs across states, the relative underestimation of NSDUH is, on average, similar.

2.3. Benchmark data source #: Drug poisoning deaths with multiplier

For comparison, we also used a different benchmark dataset to estimate OUD, focusing on mortality data. We used two parameters for this multiplier. First, we estimated the number of individuals in the US who died of drug poisoning death for all ages from National Vital Statistics Surveillance System, including underlying cause of death codes X40-X44, X60-X64, X85, Y10–14, and multiple cause of death codes T36-T50. Note that this multiplier does not assume that all individuals who die of drug poisoning have OUD (which is not the case (Johnson et al., 2013; Peterson et al., 2018)); rather, it utilizes the estimate of the drug poisoning death rates among those with OUD as a benchmark estimator from which OUD prevalence can be derived.

Second, we identified the estimated drug poisoning mortality rate among individuals with OUD from Larney et al. (Larney et al., 2019), a meta-analysis of death rates of individuals who use opioids. For drug-related deaths, Larney et al. meta-analyze 56 studies that reported drug poisoning, opioid poisoning, or drug-related death rates among individuals with OUD (heretofore referred to as ‘drug poisoning deaths’); the overall annual pooled estimate of 0.52 per 100 person-years (95% C.I. 0.46–0.59).

We intentionally used the death rate for all drug poisoning deaths, rather than exclusively opioid-related poisoning deaths. Only three estimates in the Larney et al. meta-analysis focused on opioid-related deaths exclusively, and estimates were more widely variable; thus, all drug poisoning deaths offered more reliability. The multiplier method does not require that the outcome be exclusively linked to the exposure (OUD), rather that the event rate (drug poisoning deaths) can be reliably estimated within the OUD population. Given that the Larney et al. meta-analysis is an average across countries, weighted based on sample size across > 50 studies of drug poisoning deaths among populations with OUD, the event estimate for the population of interest is reliable for our estimation purpose.

For the estimate of OUD prevalence in the US, we used two different estimates from the Larney et al. meta-analysis. First, we used the pooled annual estimate from the meta-analysis. This estimate has the advantage of combining data across many studies of heterogeneous underlying populations, thus averages across different types of biases in how individuals with OUD may be selected into samples. However, it also averages across many countries, which may be less generalizable to the US. We also re-estimated the OUD prevalence using the average of the two US studies (Lopez-Quintero et al. 2015; Vlahov et al. 2008) that estimated drug poisoning death rates for individuals who use opioids from the general population. The advantage of this estimate is that it does not select for treatment utilization, however, it does select for heroin and injection drug use rather than all OUD.

2.4. Multiplier correction for drug poisoning deaths

The multiplier method applied to death data described above assumes that the probability of drug poisoning death given OUD has remained relatively constant over time, and the time periods underlying the studies in the meta-analysis represent a weighted average of years from 1967 to 2017. Yet the death rate in the US has increased in recent years, largely due to expanded use of highly potent synthetic opioids (Mattson et al., 2021). We thus

applied a correction to the mortality data multiplier to account for national changes in the event rate in recent years. Synthetic opioid deaths began increasing the national drug poisoning death rate after 2015 (Mattson et al., 2021). While the use of synthetic opioids was heterogeneous across the US (increasing mostly in the east beginning in 2015; and expanding west beginning in 2017/2018) (Mattson et al., 2021), in order to calculate a national prevalence of OUD, we used the national totals which would average across US states in two steps.

First, we estimated a revised event rate of drug poisoning death among the OUD population. Nationally, the opioid overdose death rate increased approximately three times from 2014 to 2016, the time period in which synthetic opioids were first reported as increasing drug poisoning deaths in some areas of the US (see Appendix Fig. 1 from (Dowell et al., 2017)). Thus, using 2015 as the interruption of the time series of opioid drug poisoning, we estimated that the drug poisoning mortality rate among those with OUD increased approximately three-fold immediately preceding versus following the introduction of synthetic opioids into the US drug supply. While a 3-fold increase in lethality is an estimate (given that the actual change in lethality at a population level is an unknown number), it is a reasonable proxy, which we additionally varied in sensitivity analysis. Note that, below, we also consider the proportion of the population exposed to synthetic opioids; the 3x multiplier is limited to estimating the increased lethality. Given the uncertainty in this multiplier, we conducted sensitivity analyses with multiplier corrections ranging from 1.5 to 4 times. Expressed as an equation, the multiplier method without the correction:

$$y = \frac{d}{0.0052}$$

where y is the size of the OUD population, and d is the number of drug poisoning deaths.

Second, we weighted by the proportion of drug poisoning deaths for which synthetic opioids are a contributing cause. For example, in 2015, 18% of drug poisoning deaths included synthetic opioids as a contributing cause leaving 82% that did not. Thus, the denominator of the multiplier was $0.0052 \times 82\%$ (the proportion of the OUD deaths not involving synthetic opioids times the OUD death rate from Larney et al.), plus $(3 \times 0.0052 \times 18\%)$ (the proportion of the OUD deaths involving synthetic opioids times the OUD death rate from Larney et al., times the multiplication factor of 3). By 2019, 52% of drug poisoning deaths included synthetic opioids as a contributing cause, thus the denominator of the multiplier was $0.0052 \times 48\%$, plus $3 \times 0.0052 \times 52\%$. This weighting factor also resolves the issue of differing synthetic opioid death rates in different years across states (and even within state, in different local communities); a hypothetical state with 0 synthetic opioid deaths in a given year would resolve to the multiplier from Larney et al. with no correction.

Expressed as an equation, the multiplier method with the correction:

$$y = \frac{d}{0.0156p + 0.0052(1 - p)}$$

where y is the size of the OUD population, d is the number of drug poisoning deaths, and p is the proportion of deaths that involved a synthetic opioid. We used LOESS regression to smooth uncertainties across years.

3. Results

Fig. 1 shows the estimated prevalence of OUD four ways: 1) General population (NSDUH survey data) as benchmark without multiplier correction; 2) General population data with a multiplier correction; 3) Drug poisoning deaths as benchmark data with multiplier; and 4) Drug poisoning deaths as benchmark data with correction to multiplier. Each of these estimates are presented in Fig. 1 in order to enhance visual interpretability. Exact values that are graphed in Fig. 1 are provided in Supplementary Table 1.

3.1. General population survey data as benchmark without multiplier correction

Uncorrected results from the NSDUH general population survey for 2009 through 2019 estimate a past-year OUD prevalence ranging from 0.62% in 2019 to 0.90% in 2015. Overall, however, rates of OUD as estimated by NSDUH are largely stable over time, with evidence of decreases in recent years. Table 1 indicates the number of people 12 and older in the US who have OUD as estimated by the NSDUH prevalence: in 2019, this method estimates that 1.7 million individuals in the US have OUD.

3.2. General population data with a multiplier correction

When a constant multiplier (4.5) is applied to the NSDUH data, the underlying prevalence of OUD increases by the amount of the multiplier (but the trend over time does not change as the correction is constant). Thus, the minimum and maximum of the prevalence remain in the same years, with a maximum prevalence of 4.04% in 2015 and a minimum of 2.77% in 2019, with evidence of annual declines in prevalence from 2015 to 2019. Using this multiplier, the estimated number of individuals 12 and older with OUD in the US in 2019 was 7.6 million.

3.3. Drug poisoning deaths as benchmark data with multiplier

The estimated rate of OUD using the mortality data is higher than the uncorrected survey estimate and lower than the multiplier-adjusted survey estimate, for all years from 2010 to 2015 (Supplementary Table 1). The estimated prevalence for those years increased monotonically from 2.36% to 3.13%. After 2015, there is cross-over wherein the mortality data estimate is higher than the multiplier-adjusted survey estimate, and increases through 2019. The estimated prevalence of OUD using this method is 4.16% by 2019, indicative of 13.6 million individuals in the US with OUD.

3.4. Drug poisoning deaths as benchmark data with correction to multiplier

As described in the methods section, we used a correction to the basic multiplier from Larney et al. The resulting trend in OUD is approximately at the mid-point of the three other methods, with a small but stable increase in prevalence from 2009 through 2016 (2.04% in 2009 to a maximum of 2.35% in 2016), and minimal but present decreases in prevalence

thereafter (from 2.29% in 2017 through 2.04% in 2019). This method estimates that there were approximately 6.7 million individuals with OUD in the US population in 2019.

3.5. Sensitivity analyses

We conducted two sensitivity analyses. First, given that the Larney et al. meta-analytic estimate relies on data from many countries and underlying target populations, we used only the two US studies that were drawn from the general population for the event rate (Supplementary Table 2). Prevalence of OUD was generally higher. Second, we assumed that the drug poisoning death rate was 1.5x and 4x higher when synthetic opioids are in the distribution, and again weighted that increase for the proportion of deaths nationally that involve synthetic opioids (Supplementary Table 3). Prevalence of OUD was higher when at 1.5x, and lower at 4x; however, the prevalence estimates were within the bounds of the other corrected multipliers. The prevalence of OUD in 2019 would be estimated to be between 1.63% and 4.08% across sensitivity analyses.

4. Discussion

We estimated the prevalence of OUD in the US from 2009 to 2019 using different benchmark data sources and various multipliers. Two approaches yielded estimates that were comparable in trend and magnitude; the general population survey as a benchmark source with a multiplier, and drug poisoning deaths as a benchmark source with a multiplier and correction. If the multiplier assumptions that we used in our primary analysis are robust, these two approaches yielded what may be considered a reasonable range within which the true prevalence and burden of OUD likely lies and indicate that OUD prevalence generally increased from 2010 through 2015/2016. From 2016 to 2019, we estimate that OUD was relatively stable or decreasing. Nevertheless, the burden of disease remains high. For example, in 2019, under these two approaches, the prevalence of OUD is estimated to be between 2.04% to 2.77% had OUD—approximately 6.7 million to 7.6 million people.

Results from three out of four methods suggest that there were declines in OUD prevalence after approximately 2015/2016. It is worth noting that at the same time that OUD prevalence estimates were decreasing, OUD treatment admissions were increasing. (Arfken et al., 2020). Thus, the factors that caused an increase in treatment admissions (e.g. increases in medical for opioid use [MOUD] providers and access (Solomon et al., 2022)) may be independent of factors that cause decrease initiation of new OUD cases. Increases in treatment admissions coupled with decreases in OUD prevalence could also be indicative of declines in length of OUD episodes decline due to effective treatment and/or recovery and death.

If a range of 6.7 to 7.6 million individuals in the US with OUD is a reasonable estimate given available information, then it still indicates a grave unmet need for capacity building around services for individuals with OUD. While not all individuals with OUD may utilize or need treatment services (Frank et al., 2021), the lack of available and accessible services, including medication for opioid use disorder and harm reduction services, across the US is well documented (Alinsky et al., 2020; Bagley et al., 2020; Hadland et al., 2017; Krawczyk et al., 2017; Larochelle et al., 2019; Morgan et al., 2018), including lower rates of availability in rural areas (Haffajee et al., 2019; Rosenblatt and Andrilla, 2015), and

racial/ethnic inequalities in services (Banks et al., 2021; Krawczyk et al., 2017). In 2017, 46.4% of US counties lacked any publicly listed MOUD provider (Haffajee et al., 2019). While MOUD treatment has increased since 2017, the large unmet treatment need continues to be a major public health issue in addressing OUD in the US.

The present study relied on survey estimates and basic multiplier methods to estimate OUD prevalence. Multiplier methods are useful in settings where more comprehensive individual-linked data are not available, such as the US, but can be augmented and expanded with additional data and methods as more information becomes available. Bayesian evidence syntheses (Ades and Cliffe, 2002; Ades and Sutton, 2006; De Pretis et al., 2019) are possible when multiple data sources are linked, including to estimate drug use prevalence (Tan et al., 2018), which may become more possible in coming years for national US prevalence estimation. At a more local level, other methods include venue-based sampling (Muhib et al., 2001; Ott et al., 2018; Verdery et al., 2019), network methods, and respondent driven sampling (Feehan and Salganik, 2016; Johnston et al., 2015), including in conjunction with venue-based sampling (Crawford et al., 2018; Fearon et al., 2017; Handcock et al., 2014; Johnston et al., 2017; Verdery et al., 2019). As individual-level data linkages are more robustly developed and made available for research, increasingly accurate estimation of OUD prevalence and other relevant public health indicators will be possible, and investment in these data resources should be a priority.

Limitations to the present study included that the multipliers used are subject to assumptions. For the multiplier of the NSDUH estimate, we relied on a capture-recapture study in a single state. While this capture-recapture has the advantage of including the general population in a large geographic area, it is possible that the multiplier would vary in other states. Conducting capture-recapture and other prevalence estimation methods in other states would improve surveillance estimates and allow for assessment of these potential differences. Further, for the multiplier used in the death data we relied on a meta-analysis that included a range of countries, time periods, and underlying populations; while this is a strength given that the meta-analysis is thus an average of a wide range of studies, it assumes that the meta-analytic estimate accurately captures the mortality rates in the US OUD population. However, the US studies included in the meta-analysis were consistent with the average estimate across all countries. The correction to the multiplier to account for increased lethality in recent years is also subject to assumptions; additional surveillance of the OUD population in the US is critical to improving assessment of drug lethality.

In summary, the present study documents variation in estimation of the prevalence and size of the OUD population in the United States. The methods described here are foundational epidemiological methods for prevalence estimation when available data to inform the size is limited. Additional development of new data resources, linkages, and prevalence estimation techniques will add to the literature in this area; for example, more states are now allowing for All Payer and linked data sources for research purposes, and techniques such as Bayesian estimation are becoming more widely developed (Jones et al., 2020). Importantly, research using general population studies such as NSDUH should consider including correction factors for underestimated prevalence, or be more explicit about the limitations of these data sources for prevalence estimation. Overdose and its underlying drivers have shifted in the

US over the course of the 21st century (Cerdá et al., 2021; Mattson et al., 2021). While tertiary prevention including dissemination and access to naloxone and other overdose death prevention efforts remain vital for public health (Lee et al., 2021), primary prevention of OUD is additionally critical to reduce morbidity and mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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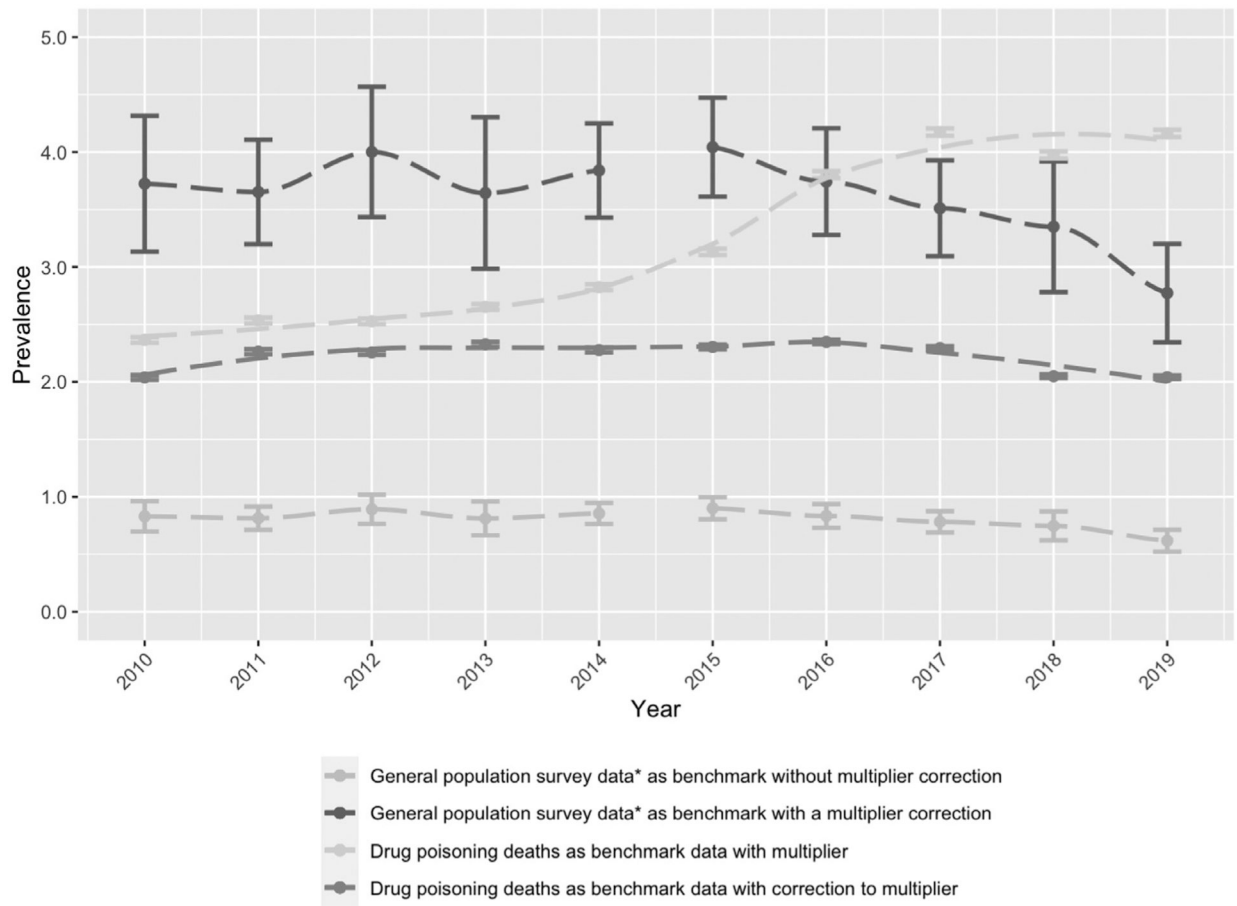


Fig. 1. Annual estimates with 95% confidence intervals and LOESS smoothing of opioid use disorder (OUD) prevalence in the US population from 2010 to 2019 using four different approaches.

Table 1

Estimated OUD population size by year, data source, and multiplier method.

Year	Survey data	Survey data, multiplier	Mortality data, multiplier	Mortality data, multiplier with correction
2010	2105,757	9448,532	7301,238	6294,171
2011	2097,321	9410,679	7897,057	7050,944
2012	2319,213	10,406,309	7931,159	7081,392
2013	2130,957	9561,604	8384,710	7355,008
2014	2269,135	10,181,609	9003,420	7260,822
2015	2412,106	10,823,120	10,070,299	7404,632
2016	2247,523	10,084,636	12,290,652	7586,822
2017	2129,367	9554,470	13,595,644	7470,134
2018	2044,469	9173,532	13,005,535	6703,884
2019	1700,870	7631,804	13,664,233	6698,153