Supplement

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Supplemental Methods

Counterfactual life expectancy and years of life lost

In general, the impact of a particular cause of death on LE can be estimated by finding the difference between the real LE and the counterfactual LE (what the life expectancy would have been in the absence of the cause). The counterfactual life expectancy is derived in the cause-eliminated life table (sometimes referred to as cause-deleted life table), which estimates the mortality experience of a population in the hypothetical scenario in which the cause of death in question were completely eliminated from the population.

We derive the life tables for the scenario in which all opioid-related deaths in the US are eliminated, following the method in the textbook Demography: Measuring and Modeling Population Processes.[1] We start with all-cause life tables from the NVSS (given by race/ethnicity and sex, or state, and by year). We first abridge them into age groups matching the death counts data (<1 years, 1-4 years, and 5-year age groups from 5-100 years), using standard methods.[2] Note that when estimating the years of life lost by sex and year for Figure 1, we used single year age groups, so we don't abridge the NVSS life tables.

We derive the cause-eliminated life table from the all-cause life table, using the fraction of all deaths that are not opioid-related, in each age group:

$$R_{age}^{-opioids} = \frac{D_{age} - D_{age}^{opioids}}{D_{age}}.$$

D_{age} and $D_{age}^{opioids}$ are the number of all-cause and opioid-related deaths in each age group, respectively. These are obtained from CDC WONDER for each year (2019, 2020, 2021, and 2022), by 5-year age group and demographic group. However, when estimating years of life lost stratified by sex only, we accessed death counts by single year ages.

With this scaling factor, the cause-eliminated life table values (labeled as *-opioids*) can be calculated from the all-cause life table values, according to the following equations (see Preston, Heuveline and Guillot textbook for more details).

Here *n* refers to the width of the age groups. For the first age group, *n*=1, for the second, *n*=4, and for all subsequent age groups *n*=5. The probability of survival is scaled up to account for removing this cause of death:

$$p_{age}^{-opioids} = (p_{age})^{R}$$

The number of people surviving at each age is:

$$l_{age+n}^{-opioids} = l_{age}^{-opioids} \times p_{age}^{-opioids}$$

The probability of death within the age interval is:

$$q_{age}^{-opioids} = 1 - p_{age}^{-opioids}$$

And the number of individuals who die within the age interval is:

$$d_{age}^{-opioids} = q_{age}^{-opioids} \times l_{age}^{-opioids}$$

For each age, the difference between the real (rLE_{age}) life expectancy from the all-cause life table and the counterfactual (cLE_{age}) life expectancy from the cause-eliminated life table reveals the impact of opioid mortality on life expectancy:

$$\Delta LE_{age} = cLE_{age} - rLE_{age}$$

Thus, we estimate the reduction in life expectancy at birth due to opioid overdose deaths for the entire US population and by demographic group, using opioid-specific and all-cause death counts, stratified by age, from the CDC WONDER database and life tables from the NVSS.

We can calculate years of life lost (YLL) due to a cause of death by multiplying the number of deaths at each age due to this particular cause ($D_{age}^{opioids}$) by the remaining counterfactual LE in the absence of this cause of death. Deaths are occurring throughout the age group, rather than all at the start of the age group, so we average between the remaining counterfactual LE at the start of the current age group (cLE_{age}) and at the start of the next age group (cLE_{age+n}). Total YLL are obtained by summing over all ages:

$$YLL = \Sigma_{age}(D_{age}^{opioids} \times \frac{1}{2}(cLE_{age} + cLE_{age+n}))$$

State life tables:

When estimating the state-specific cause-eliminated life tables, we used the state-specific all-cause life tables from NVSS for the years 2019 and 2020. However, the state-specific life tables are unfortunately not yet available for the years 2021 and 2022, as they are typically released more than 3 years delayed. In order to best approximate the state-specific mortality experiences in 2021 (and 2022), we calculated the change in age-specific probabilities of death (the *q* values in the life tables) from 2020 to 2021 (and the changes from 2020 to 2022) from the national US population life tables.

$$\Delta q_{age}(2021) = q_{2021,age} - q_{2020,age}$$
$$\Delta q_{age}(2022) = q_{2022,age} - q_{2020,age}$$

This gives us a measure of how much the probability of death at each age changed. We then apply this shift to the 2020 state-specific, age-specific probabilities of death.

$$q_{state,2021,age} = q_{state,2020,age} + \Delta q_{age}(2021)$$
$$q_{state,2022,age} = q_{state,2020,age} + \Delta q_{age}(2022)$$

From these new *q* values we then re-calculate our new estimate for the 2021 (and 2022) state-specific life tables.

The absolute value of the changes in age-specific probabilities of death between the 2020 and 2021 US population life tables was between 0% and 21% of the 2021 values, with 72/100 ages having a change of <10%. The absolute value of the changes in age-specific probabilities of death between the 2020 and 2022 US population life tables was between 0% and 28% of the 2022 values, with 88/100 ages having a change of <10%.

Redistribution of suppressed death counts

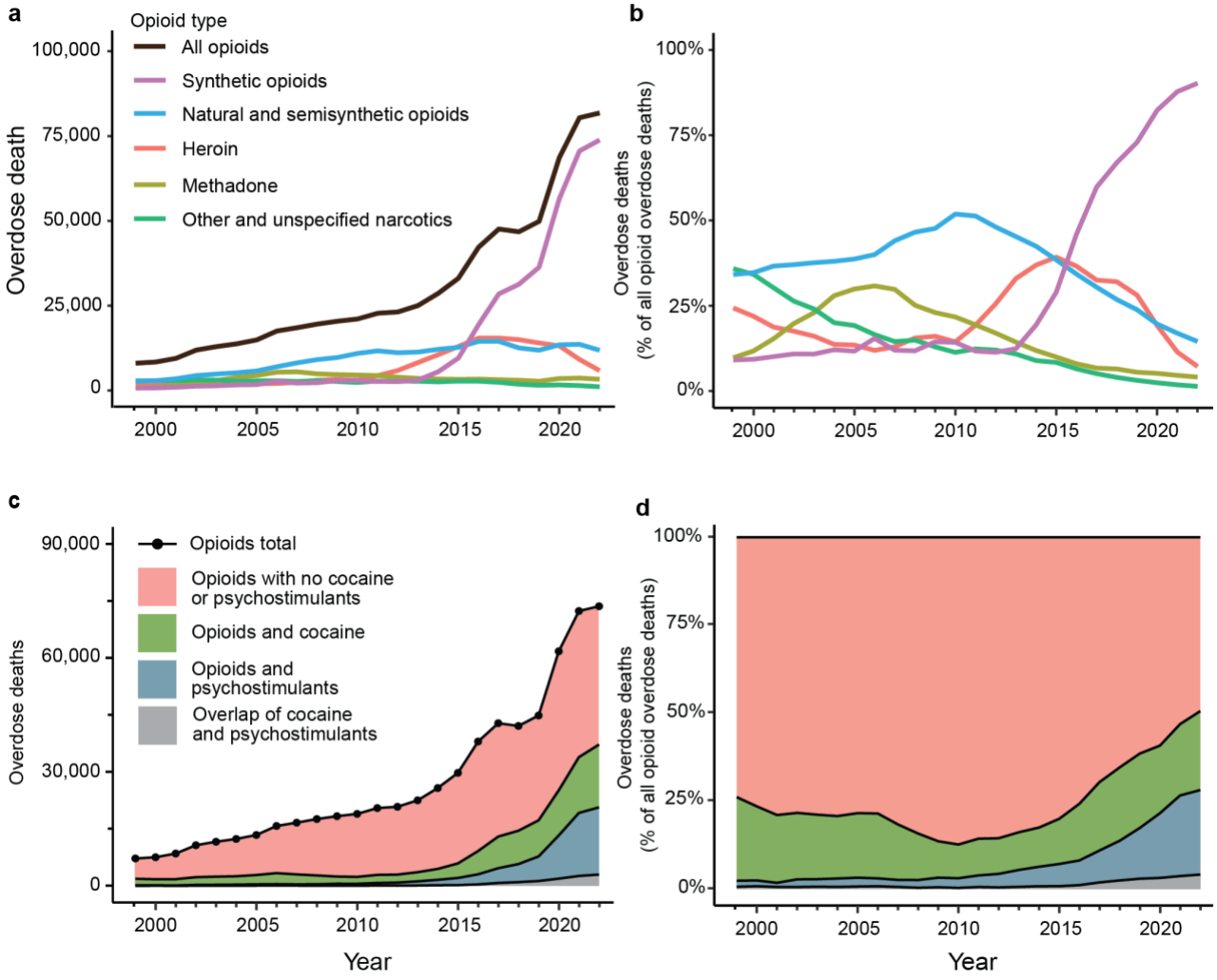
In order to minimize the effects of the data suppression that occurs for death counts <10 (see Methods), we also separately download the total number of opioid-related deaths for each group. From this, we calculate how many deaths were suppressed, and redistribute them across the age groups with suppressed death counts, using a multinomial distribution. We set event probabilities according to the national age distribution of opioid overdose deaths.

When calculating our cause-eliminated life tables by race/ethnicity and sex, or by state, we repeat this redistribution of suppressed death counts 100 times. At each iteration, we estimate the age-dependent scaling factor R, based on the resulting redistributed opioid death age distribution and calculate the cause-eliminated life table. From this we find a distribution of values for the years of life lost and the loss of life expectancy. Throughout the text we report the mean of this distribution. The resulting 95% confidence intervals are vanishingly small (varying in width from 0.4% to 0.0002% of the mean).

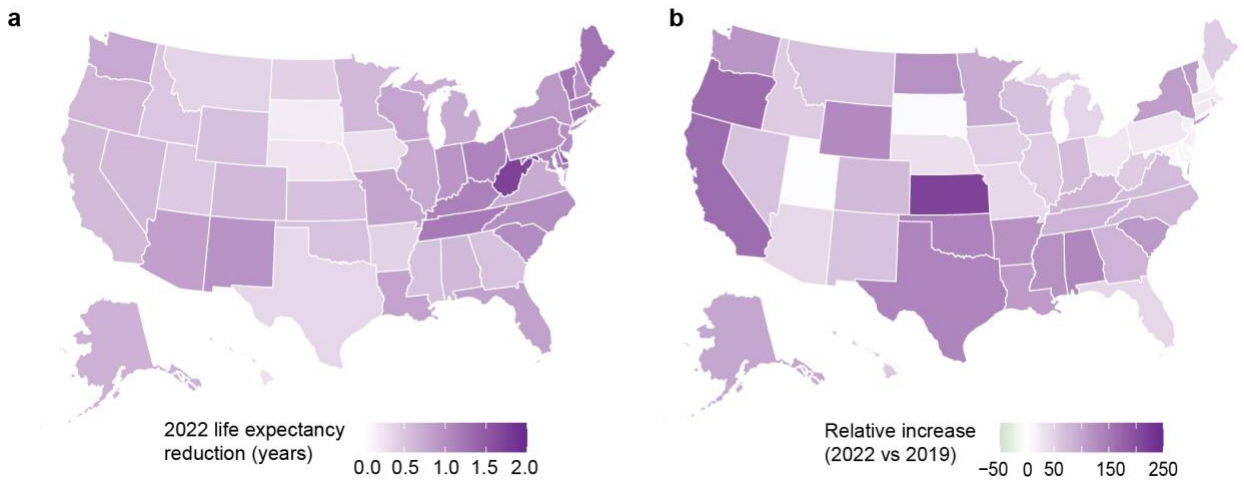
Data

States throughout the US have different protocols for reporting sex on birth certificates, in terms of whether certifiers have the authority to determine the decedent's sex listed on the death certificate, or whether there are laws protecting decedents' gender identity and thus requiring that their self-identified gender be included on the death certificate. Throughout, we use the term 'sex,' in agreement with the National Vital Statistics System's terminology in analyzing the same death certificates data.

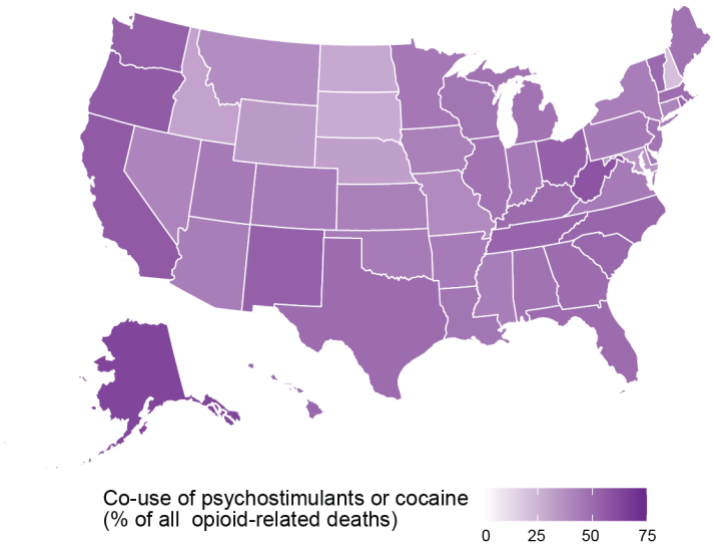
Supplemental Figures



Supplement Figure 1: Trends in opioid overdose deaths in the United States from 1999 to 2022. A) Total number of opioid overdose deaths each year, also showing the number of deaths by opioid type. B) Percentage of yearly opioid overdose deaths by opioid type. C) Total number of opioid overdose deaths each year, showing the subset of deaths also involving either cocaine or psychostimulants with abuse potential (e.g. methamphetamines). D) Percentage of yearly opioid overdose deaths by stimulant co-use. Note that some deaths involve more than one type of opioid. Synthetic Opioids include, for example, drugs such fentanyl (and its derivatives) and tramadol, but excludes methadone. Natural and Semisynthetic Opioids include, for example, oxycodone, hydrocodone, and morphine. Heroin is categorized separately although it is also a semisynthetic opioid. Methadone, a synthetic opioid prescribed to treat opioid use disorder, is categorized separately. Other and Unspecified Narcotics include deaths due to opioid or cocaine-like substances, or mixtures thereof, that were not further sub-categorized on the death certificate. Data shown here are death counts from the CDC WONDER Multiple Cause of Death database (see Methods for ICD codes used).



Supplement Figure 2: US loss of life expectancy by state, 2019-2022. A) Life expectancy reduction to opioid overdose deaths in 2022, by state and B) relative increase in loss of life expectancy between 2019 and 2022, by state. Life expectancy reductions are estimated by comparing real life expectancies to estimated counterfactual life expectancies, describing a scenario in which opioid-related mortality is eliminated.



Supplement Figure 3: Opioid and stimulant co-involvement in the US. Percentage of opioid-related deaths involving either psychostimulants with abuse potential or cocaine in 2022, by state.

Supplemental Tables

	Sex	AI/AN	Asian	Black	Hispanic	White
2022 Loss in Life Expectancy	F	1.0	0.13	0.53	0.31	0.55
	M	1.5	0.20	1.1	0.82	0.96
2021 Loss in Life Expectancy	F	0.90	0.083	0.43	0.24	0.50
	M	1.0	0.13	0.96	0.73	1.0
2020 Loss in Life Expectancy	F	0.63	0.12	0.32	0.25	0.49
	M	0.83	0.22	0.78	0.57	0.94
2019 Loss in Life Expectancy	F	0.43	0.084	0.27	0.19	0.36
	M	0.62	0.087	0.59	0.31	0.76
2022 Years of Life Lost	F	14,300	6,500	150,200	97,900	622,300
	M	23,200	25,100	349,000	358,600	1,271,000
2021 Years of Life Lost	F	13,000	5,700	140,400	92,000	640,200
	M	16,300	18,700	303,800	305,500	1,305,700
2020 Years of Life Lost	F	9,200	5,200	106,700	69,200	578,900
	M	13,000	19,800	240,100	253,200	1,196,300
2019 Years of Life Lost	F	6,800	3,200	74,600	48,900	461,500
	M	8,600	12,300	159,200	189,000	921,200
2022 Years of Life Lost per capita	F	1,170	61.7	688	312	630
	M	1,940	257	1,730	1,110	1,300
2021 Years of Life Lost per capita	F	1,050	55.8	646	297	646
	M	1,350	198	1,510	963	1,340
2020 Years of Life Lost per capita	F	742	51.1	494	227	580
	M	1,090	214	1,210	819	1,230
2019 Years of Life Lost per capita	F	551	31.9	348	163	461
	M	714	136	809	618	947

Supplement Table 1: Years of life lost in the US due to opioids from 2019 to 2022. Years of life lost (top) and loss of life expectancy (bottom) due to opioid overdose deaths in 2019, 2020, 2021, and 2022, by race and ethnicity, and by sex. We only report the years of life lost and the reduction in life expectancy for the 5 largest race and ethnicity groups. There was not enough data from the Native Hawaiian and Other Pacific Islanders group to estimate the years of life lost or the reduction in life expectancy (see Methods).

	Sex	AI/AN	Asian	Black	Hispanic	White
Loss in Life Expectancy to psychostimulant co-use	F	0.46	0.10	0.11	0.14	0.22
	M	0.61	0.064	0.18	0.24	0.32
Loss in Life Expectancy to cocaine co-use	F	0.18	0.10	0.27	0.14	0.16
	M	0.23	0.067	0.47	0.28	0.19
Loss in Life Expectancy to both psychostimulant and cocaine co-use	F	0.55	0.11	0.31	0.19	0.30
	M	0.75	0.10	0.60	0.44	0.47
Years of life lost to psychostimulant co-use	F	6,100	1,600	18,900	26,800	205,500
	M	8,800	6,000	59,600	84,300	414,800
Years of life lost to cocaine co-use	F	1,800	1,600	68,700	24,700	126,800
	M	2,700	6,500	146,400	102,000	249,400
Years of life lost to both psychostimulant and cocaine co-use	F	7,400	2,900	80,900	47,700	303,900
	M	10,900	11,600	189,300	176,700	615,300
Years of life lost per capita to psychostimulant co-use	F	495	15.0	86.5	85.5	208
	M	736	61.3	295	261	425
Years of life lost per capita to cocaine co-use	F	149	15.6	315	78.7	128
	M	225	66.2	724	316	256
Years of life lost per capita to both psychostimulant and cocaine co-use	F	602	27.4	370	152	308
	M	909	119	936	547	631

Supplement Table 2: Years of life lost and life expectancy reduction to polysubstance use in 2022 in the US. Loss in life expectancy (top), Years of life lost (middle), and Years of life lost per capita (bottom) due to co-involvement of opioids and stimulants in 2022, by race/ethnicity and sex.

State	2019 Years of Life Lost	2022 Years of Life Lost	2019 Years of Life Lost per 100,000	2022 Years of Life Lost per 100,000	2019 Loss in Life Expectancy	2022 Loss in Life Expectancy
Alabama	15,300	39,000	311	768	0.265	0.587
Alaska	3,400	7,200	465	985	0.348	0.641
Arizona	54,000	75,400	742	1,020	0.594	0.792
Arkansas	7,400	14,000	244	460	0.181	0.377
California	131,200	291,900	332	748	0.234	0.558
Colorado	26,200	48,400	455	828	0.352	0.573
Connecticut	43,300	48,400	1,210	1,330	0.963	1.08
Delaware	15,800	17,800	1,620	1,750	1.23	1.30
D.C.	7,700	9,900	1,090	1,480	0.855	1.20
Florida	149,700	211,800	697	952	0.574	0.771
Georgia	32,200	75,400	303	691	0.289	0.492
Hawaii	2,100	4,000	150	279	0.164	0.235
Idaho	5,400	11,100	303	570	0.315	0.444
Illinois	83,200	112,400	657	894	0.487	0.692
Indiana	49,200	78,000	730	1,140	0.541	0.876
Iowa	6,300	9,300	200	290	0.192	0.264
Kansas	7,200	20,100	246	686	0.171	0.499
Kentucky	37,500	62,400	840	1,380	0.617	1.07
Louisiana	20,200	48,200	435	1,050	0.379	0.764
Maine	12,700	23,700	945	1,710	0.799	1.13
Maryland	78,900	79,000	1,310	1,280	1.01	1.04
Massachusetts	79,800	86,000	1,160	1,230	0.889	0.961
Michigan	66,900	85,700	670	854	0.512	0.690
Minnesota	18,500	42,600	328	745	0.327	0.560
Mississippi	8,600	18,800	288	639	0.243	0.512
Missouri	42,500	60,700	692	983	0.568	0.760
Montana	2,800	5,100	258	453	0.232	0.357
Nebraska	2,700	5,000	137	257	0.185	0.224
Nevada	13,300	24,100	432	757	0.359	0.552
New Hampshire	15,400	16,800	1,130	1,200	0.883	0.888
New Jersey	99,000	93,800	1,110	1,010	0.847	0.912
New Mexico	15,200	27,000	726	1,280	0.582	0.915
New York	115,700	190,100	595	966	0.432	0.812
North Carolina	73,700	141,600	703	1,320	0.556	0.927
North Dakota	1,700	4,200	221	537	0.188	0.370
Ohio	132,700	154,500	1,130	1,310	0.877	1.04

Oklahoma	9,700	28,300	246	704	0.218	0.488
Oregon	12,700	37,200	301	878	0.238	0.567
Pennsylvania	119,700	145,300	935	1,120	0.764	0.896
Rhode Island	9,600	12,300	903	1,130	0.673	0.871
South Carolina	32,800	66,700	637	1,260	0.481	0.963
South Dakota	1,600	1,800	180	196	0.162	0.167
Tennessee	58,000	110,200	850	1,560	0.647	1.12
Texas	58,400	127,000	202	423	0.149	0.323
Utah	15,200	16,700	473	495	0.446	0.416
Vermont	4,700	9,500	747	1,470	0.591	1.12
Virginia	50,900	80,900	596	932	0.432	0.679
Washington	32,200	80,800	423	1,040	0.352	0.676
West Virginia	24,800	39,500	1,390	2,220	1.11	1.66
Wisconsin	36,500	55,000	626	934	0.474	0.725
Wyoming	1,800	3,200	309	544	0.235	0.506

Supplement Table 3: Burden of opioid mortality by state in 2019 and 2022. Years of life lost, years of life lost per 100,000 and loss in life expectancy (years) to opioid related deaths in 2019 and 2022, by US state.

References

1. Preston S, Heuveline P, Guillot M. Demography: Measuring and Modeling Population Processes | Wiley [Internet]. [cited 2022 Jul 25]. Available from: https://www.wiley.com/en-us/Demography%3A+Measuring+and+Modeling+Population+Processes-p-9781557864512
2. Arias E. United States Life Tables, 2021.