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Trends in Black and White Opioid Mortality in the United States, 1979–2015

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Background: Recent research on the US opioid epidemic has focused on the white or total population and has largely been limited to data after 1999. However, understanding racial differences in long-term trends by opioid type may contribute to improving interventions.

Methods: Using multiple cause of death data, we calculated age-standardized opioid mortality rates, by race and opioid type, for the US resident population from 1979 to 2015. We analyzed trends in mortality rates using joinpoint regression.

Results: From 1979 to 2015, the long-term trends in opioid-related mortality for Earlier data did not include ethnicity so this is incorrect. It is all black and all white residents in the US. blacks and whites went through three successive waves. In the first wave, from 1979 to the mid-1990s, the epidemic affected both populations and was driven by heroin. In the second wave, from the mid-1990s to 2010, the increase in opioid mortality was driven by natural/semi-synthetic opioids (e.g., codeine, morphine, hydrocodone, or oxycodone) among whites, while there was no increase in mortality for blacks. In the current wave, increases in opioid mortality for both populations have been driven by heroin and synthetic opioids (e.g., fentanyl and its analogues). Heroin rates are currently increasing at 31% (95% confidence interval [CI] = 27, 35) per year for whites and 34% (95% CI = 30, 40) for blacks. Concurrently, respective synthetic opioids are increasing at 79% (95% CI = 50, 112) and 107% (95% CI = −15, 404) annually.

Conclusion: Since 1979, the nature of the opioid epidemic has shifted from heroin to prescription opioids for the white population to increasing of heroin/synthetic deaths for both black and white populations. See video abstract at, http://links.lww.com/EDE/B377.

Keywords: Opioids, Racial disparities, Joinpoint analysis, Substance abuse

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Since 1979, the opioid mortality rate has increased 22-fold in the United States, resulting in over 33,000 deaths in 2015 alone, drawing national attention and becoming an important part of the political agenda.[1,2] The continuous intensification of fatal overdoses is unique to opioids, as the rate of all nonopioid drug overdoses, though doubling from 1979 to 2006, has remained constant since then (eFigure 1; http://links.lww.com/EDE/B356 and eTable 1; http://links.lww.com/EDE/B356).

In the 1990s and 2000s, the epidemic was driven by prescription opioids[3,4] as part of aggressive marketing tactics by the pharmaceutical industry and changing medical standards in diagnosis and treatment of chronic pain.[5,6] However, clinical behaviors (i.e., prescription patterns and pain management) differ markedly by race,[7,8] with much lower opioid prescription rates in the black population than in the white population.[9,10] In addition, the extent of racial bias in prescribing patterns has been found to vary by physician characteristics such as gender and race.[11,12] This differential clinician behavior is important because prescription opioid misuse is a substantial risk factor for heroin use.[13] Recent research has suggested that rates of heroin use and prescription opioid misuse in blacks and whites have begun to converge in recent years.[14–16] However, the convergence and divergence of opioid mortality rates by race over longer time periods have not been explored.

Recent research describes the opioid epidemic as having been initially driven by prescription opioids starting in the mid-1990s, followed by a continuing rise in the number of

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All code to download and analyze the publicly available data, as well as to reproduce all tables and plots, is available at https://github.com/mkiang/opioid_trends.

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TABLE 1. Joinpoint Regression Results by Race and Broad Opioid Type, 1979–2015

	Observed Value[a]											
	1979		2015		Average APC		Trend 1			Trend 2		
	Rate	95% CI	Rate	95% CI	AAPC	95% CI	Years	APC	95% CI	Years	APC	95% CI
Rate ratio[b]	0.71	0.58, 0.84	1.9	1.8, 1.9	3	2, 4	1979–1993	−1	−3, 1	1993–2010	9	8, 10
All opioids												
White	0.44	0.41, 0.47	12	12, 12	10	9, 11	1979–1989	8	5, 12	1989–2006	13	12, 13
Black	0.62	0.52, 0.72	6.6	6.3, 6.8	6	5, 7	1979–1994	11	9, 13	1994–2011	0	0, 1
Heroin												
White	0.14	0.12, 0.15	4.8	4.7, 4.9	12	10, 14	1979–1998	12	10, 13	1998–2005	1	−4, 6
Black	0.33	0.25, 0.40	3.1	2.9, 3.3	7	6, 9	1979–1995	8	6, 10	1995–2010	0	−2, 1
Methadone												
White	0.053	0.042, 0.063	1.2	1.2, 1.2	2	−1, 4	1979–1988	−2	−6, 3	1988–1998	−9	−15, −4
Black	0.036	0.0080, 0.063	0.58	0.51, 0.65	0	−5, 3	1979–1987	2	−9, 14	1987–1999	−13	−20, −4
Other												
White	0.25	0.23, 0.28	8.2	8.0, 8.3	9	4, 15	1979–1990	8	2, 14	1990–1993	23	−30, 118
Black	0.26	0.19, 0.33	4.2	4.0, 4.4	7	5, 10	1979–1994	15	10, 19	1994–2013	0	−2, 1

[a]All observed values are expressed as rates per 100,000 except the rate ratio.
[b]Rate ratio is the white opioid mortality rate divided by the black opioid mortality rate.
AAPC indicates average annual percent change; APC annual percent change; CI, confidence interval.

heroin deaths starting in the mid-2000s, concurrently fueled by illicitly manufactured synthetic opioids such as fentanyl, starting around 2013.[17–19] However, these studies have largely been limited to opioid mortality in the total or white population after 1999, with only more recent work focusing on the opioid epidemic in the black population.[20] We aim to supplement the current literature by describing black- and white-specific opioid mortality trends from 1979 to 2015. To date, this is the longest period of analysis of opioid mortality in the United States, contributing an expanded perspective on trends over time and allowing for the examination of mortality by race and opioid type to understand the factors behind these trends.

METHODS

Multiple Cause of Death Data

We used a publicly available microlevel dataset with multiple causes of death derived from all the death certificates collected in the United States by the National Center for Health Statistics from 1979 to 2015.[21] For death certificates related to fatal overdoses, state laws require all contributing substances be identified, and where possible, a single agent to be specified as the underlying cause of death. In addition, up to 20 other contributory causes can be listed on the death certificate. The presence of a drug is not sufficient for the drug to be deemed the underlying cause; therefore, both the underlying and contributory causes must be considered when identifying deaths from drug overdose.[4,22]

Death certificates are coded by the National Center for Health Statistics to produce multiple cause of death data.[21] Over the period 1979–1998, deaths were classified according to the Ninth Revision of the International Classification of Diseases (ICD-9),[23] while the Tenth Revision (ICD-10)[24] has been implemented since 1999.

Defining Opioid-Related Deaths

We defined overdoses involving opioids as specified in the *Consensus recommendations for national and state poisoning surveillance* (eTable 2; http://links.lww.com/EDE/B356).[25] Specifically, for 1979–1998, an opioid overdose was defined as a death with at least one of the following ICD-9 codes for either the underlying cause or for one of the contributory causes: E850.0 (heroin), E850.1 (methadone), E850.2 (other pharmaceutical opioid), or N965.0 (undetermined/unknown opioid).

For 1999–2015, all opioid overdoses were defined by a combination of specific codes for the underlying cause and at least one relevant contributory cause code. The ICD-10 codes for the underlying cause corresponding to overdoses are X40–X44, X60–X64, X85, and Y10–Y14. In addition, for a death to be defined as opioid related, it has to include one or more of the following ICD-10 codes: opium (T40.0); heroin (T40.1); other natural and semi-synthetic (T40.2) such as codeine, morphine, hydrocodone, or oxycodone; methadone (T40.3); other synthetic (T40.4) such as tramadol, fentanyl, and fentanyl derivatives; or unspecified (T40.6).

Statistical Analysis

Using the multiple cause of death data, we tabulated deaths from opioid overdose for the total, black, and white resident populations by five-year age groups (i.e., 0–4, 5–9, …, 85+). In addition, we tabulated these deaths by type of opioid. Due to the changes in the coding of opioid types from

Trend 3			Trend 4			Trend 5			Trend 6		
Years	**APC**	**95% CI**	**Years**	**APC**	**95% CI**	**Years**	**APC**	**95% CI**	**Years**	**APC**	**95% CI**
2010–2015	−6	−9, −3									
2006–2013	5	3, 6	2013–2015	15	6, 25						
2011–2015	16	10, 23									
2005–2010	12	3, 22	2010–2015	31	26, 36						
2010–2015	33	27, 40									
1998–2003	43	37, 49	2003–2006	20	12, 30	2006–2011	−5	−7, −3	2011–2015	−8	−11, −6
1999–2006	24	18, 29	2006–2009	−9	−25, 19	2009–2015	−2	−5, 2			
1993–2010	9	8, 10	2010–2013	−1	−17, 18	2013–2015	18	1, 39			
2013–2015	34	2, 77									

ICD-9 to ICD-10, we defined three temporally stable opioid categories as (a) opioid deaths involving heroin, (b) opioid deaths involving methadone, and (c) opioid deaths involving an opioid other than (but not excluding) heroin or methadone. We refer to these categories as "heroin", "methadone", and "other" throughout the text; however, note that multiple opioids could be listed on death certificates coded with the ICD-10, and thus these categories are not mutually exclusive. The "other" category covers natural/semisynthetic, synthetic, and unspecified opioid types. For the ICD-10 years (1999–2015), we additionally tabulated deaths by type of opioid using the more specific ICD-10 categories defined above. To estimate the denominator of the rates, we used national race- and age-specific annual population estimates from the US Census Bureau's Population Estimates Program. All rates are expressed as the number of deaths per 100,000 people and directly age-standardized to the US 2000 population. Standard errors for the rates were obtained using a Poisson approximation.[26,27] We calculated the opioid rate ratio as the rate for whites divided by the rate for blacks and estimated standard errors for the ratio using the delta approximation.[28]

We used joinpoint regression to examine trends in the age-standardized rates and rate ratio calculated as described above via the Joinpoint Regression Program version 4.5.0.1.[29] Using a segmented weighted least squares regression, the program iteratively adds joinpoints and finds the model with the optimal number of joinpoints, between zero and five, selecting the model that best fits the data. Model fit is evaluated using a permutation test.[30] To account for the ICD-9 to ICD-10 coding change, an indicator variable was used for years ≥1999 for models spanning the entire period (see eTables 3–8; http://links.lww.com/EDE/B356 for full joinpoint model results). For the best model in each case, we report the annual percent change as well as the average annual percent change for the entire period under analysis. The average annual percentage change is defined as the weighted average of the annual percentage changes, with weights equal to the number of years in each time segment. Summary results are presented in Table 1 and Table 2. The code to reproduce tables and figures are available online (eText 1; http://links.lww.com/EDE/B356). This study was reviewed by the Harvard TH Chan School of Public Health institutional review board and did not require full review because it uses publicly available, retrospective, de-identified data.

RESULTS

From 1979 to 2015, the opioid mortality rate for whites increased from 0.44 to 12, corresponding to an average increase of 10% (95% confidence interval [CI] = 9, 11) per year. Over the same period, the rate for blacks increased from 0.62 to 6.6 for an average annual increase of 6% (95% CI = 5, 7). While the rate for whites increased steadily over the whole period, the rate for blacks remained stable in 1994–2011 (Table 1 and Figure 1). This differential growth is reflected in changes in the rate ratio (white to black mortality) through three successive waves. The rate ratio was approximately 0.71 from 1979 to 1993, then increased by 9% (95% CI = 8, 10) per year to over 2 by 2010 and declined thereafter by −6% (95% CI = −9, −3) annually to reach 1.9 in 2015 (Figure 1).

We examined trends in mortality by broad opioid category (heroin, methadone, and other) to identify the drivers of change in the rate ratio. Both blacks and whites experienced

TABLE 2. Joinpoint Regression Results by Race and ICD-10 Opioid Type, 1999–2015

	Observed Value[a]														
	1999		2015		Average APC		Trend 1			Trend 2			Trend 3		
	Rate	95% CI	Rate	95% CI	AAPC	95% CI	Years	APC	95% CI	Years	APC	95% CI	Years	APC	95% CI
Heroin															
White	0.74	0.71, 0.78	4.8	4.7, 4.9	13	10, 16	1999–2005	1	−4, 5	2005–2010	12	5, 21	2010–2015	31	27, 35
Black	0.83	0.73, 0.93	3.1	2.9, 3.3	9	7, 11	1999–2010	−1	−3, 2	2010–2015	34	30, 40			
Methadone															
White	0.31	0.29, 0.34	1.2	1.2, 1.2	9	7, 12	1999–2003	43	34, 52	2003–2006	21	8, 36	2006–2015	−6	−7, −5
Black	0.21	0.16, 0.26	0.58	0.51, 0.65	6	4, 8	1999–2006	22	17, 27	2006–2015	−5	−6, −3			
Natural															
White	1.1	1.1, 1.2	4.6	4.5, 4.7	9	8, 10	1999–2010	13	12, 14	2010–2015	1	−2, 3			
Black	0.62	0.54, 0.71	2.1	2.0, 2.3	8	8, 9	1999–2015	8	8, 9						
Synthetic															
White	0.30	0.28, 0.32	3.6	3.5, 3.7	17	13, 21	1999–2006	18	11, 24	2006–2013	3	−2, 8	2013–2015	79	50, 112
Black	0.12	0.078, 0.15	2.1	2.0, 2.2	15	1, 32	1999–2013	6	−6, 19	2013–2015	107	−15, 404			
Unspecified															
White	0.96	0.92, 1.0	1.0	1.0, 1.0	0	−1, 0	1999–2015	0	−1, 0						
Black	2.1	1.9, 2.2	0.59	0.52, 0.67	−8	−9, −7	1999–2015	−8	−9, −7						

[a]All observed values are expressed as rates per 100,000.
AAPC indicates average annual percent change; APC, annual percent change; CI, confidence interval; ICD, International Classification of Diseases.

an increase in heroin and other opioid mortality over the full period (Table 1 and Figure 2). In 1979, the heroin mortality rate was 0.14 for whites and 0.33 for blacks. By 2015, the heroin mortality rates had risen to 4.8 for whites and 3.1 for blacks, resulting in average annual increases of 12% (95% CI = 10, 14) for whites and 7% (95% CI = 6, 9) for blacks. The general pattern of increase in heroin mortality was similar for both populations: the rates first grew relatively slowly up to the 1990s, reaching a plateau in 1995 for blacks and 1998 for whites, before accelerating after 2005 for whites and 2010 for blacks. Between 2010 and 2015, the annual percent change in heroin mortality reached over 30% for both populations.

The mortality rate from other opioids increased from approximately 0.25 for each of the two populations to 8.2 for whites and 4.2 for blacks. In contrast to heroin mortality, the trends in other opioid mortality over the period differ markedly by race. For whites, the rate increased substantially in 1993–2010, while for blacks, it remained stable during this period. However, during 2013–2015, mortality due to other opioids increased substantially for both populations, at an

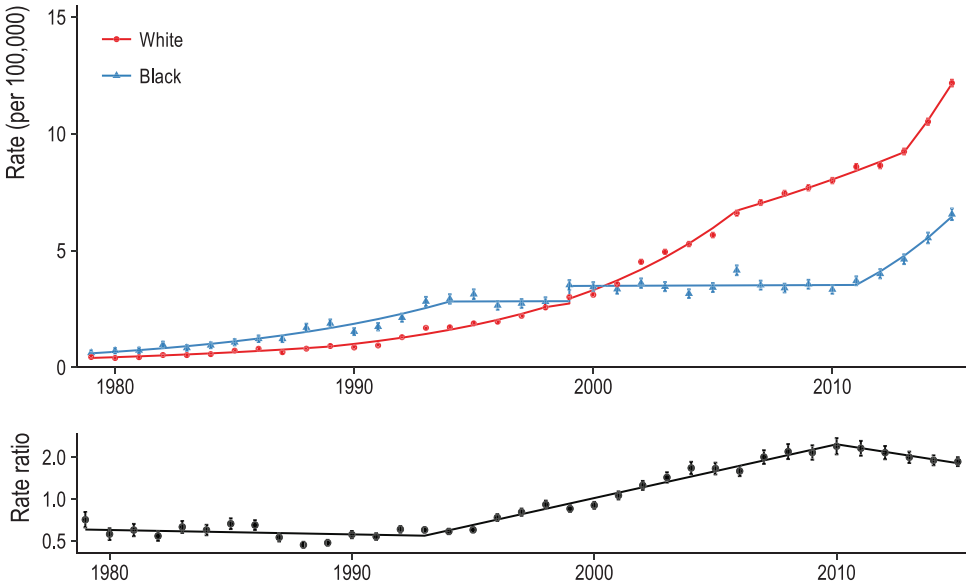

FIGURE 1. A, Age-standardized opioid mortality rate for the white (red) and black (blue) US resident populations, 1979–2015. B, Rate ratio (white/black) of opioid mortality rates. Dots are estimated rate. Vertical bars represent 95% confidence interval. Solid lines are joinpoint model fits.

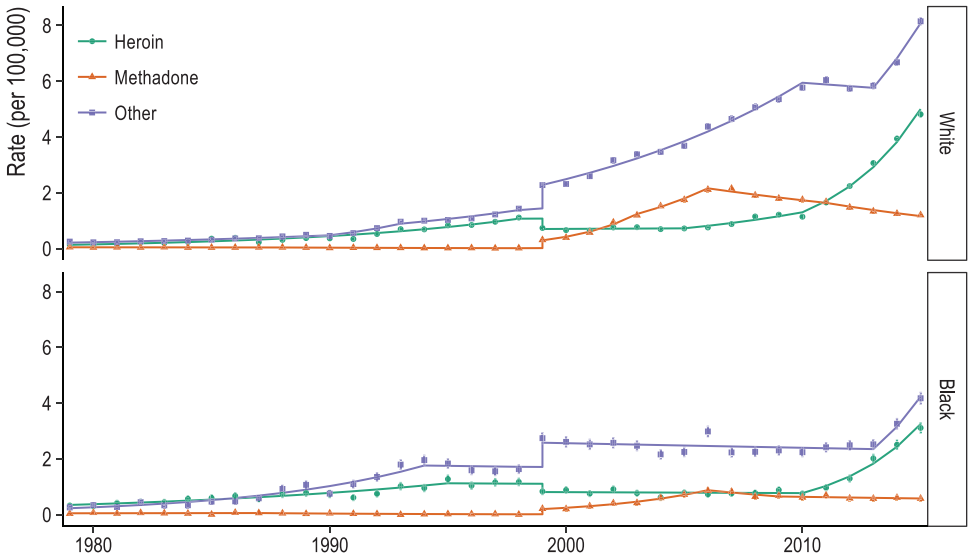

FIGURE 2. Age-standardized opioid mortality rates by general type of opioid: heroin (green), methadone (orange), or other opioid (violet) for white (top) and black (bottom) US resident populations, 1979–2015. Vertical bars are 95% confidence intervals. Solid lines are joinpoint model fits.

annual rate of 18% (95% CI = 1, 39) for whites and 34% (95% CI = 2, 77) for blacks.

Opioid types can be further disaggregated during the period 1999–2015, due to the ICD-10 coding details (Table 2 and Figure 3). In addition to heroin and methadone, the ICD-10 also identifies opium (not analyzed due to low counts), natural/semi-synthetic opioids (e.g., oxycodone and hydrocodone), synthetic opioids other than methadone (e.g., fentanyl and tramadol), and unspecified opioids. The "other" opioid category defined above mainly consists of natural and semi-synthetic opioids and non-methadone synthetic opioids.

Trends in mortality due to natural/semi-synthetic opioids differ by race. By 2015, the natural opioid mortality rate for whites was more than double that for blacks, at 4.6 compared to 2.1. The rate for blacks increased steadily by 8% (95% CI = 8, 9) per year from 1999 to 2015. The white rate increased by 13% (95% CI = 12, 14) per year in 1999–2010, then leveled out in 2010–2015 at 1% (95% CI = −2, 3). The differential increase in natural opioid mortality by race explains the increase in the rate ratio from 1999 to 2010.

The synthetic opioid mortality rate was 0.30 for whites and 0.12 for blacks in 1999 and increased an average of 17% (95% CI = 13, 21) for whites and 15% (95% CI = 1, 32) for blacks. For whites, the synthetic mortality rate increased 79% per year (95% CI = 50, 112) from 2013 to 2015, largely due to fentanyl, often taken in combination with heroin.[31] While the confidence interval is wide and imprecise, the synthetic mortality rate for blacks was 107 (95% CI, −15, 404).

DISCUSSION

The opioid epidemic can be divided into three waves between 1979 and 2015. During the first wave, from 1979 to the mid-1990s, opioid mortality was higher for the black population, but rates of increase were similar for both populations and largely driven by heroin. During the second wave, from the mid-1990s to 2010, the opioid epidemic expanded quickly within the white population while opioid mortality remained stable in the black population. As a consequence, the racial gradient of risk reversed in 2000, and by 2010, the opioid mortality rate were over 2 times higher for whites than for blacks. During this period, the opioid epidemic was driven largely by non-heroin and non-methadone opioids (i.e., prescription painkillers). Lastly, from about 2010 to 2015, the opioid mortality rate grew rapidly for both the black and white populations. This third wave has similarities to the first wave, as the mortality increase has been driven by heroin, and more recently synthetic opioids, in both populations. However, recent death rates due to heroin and synthetic opioids have reached unprecedented levels, increasing by an average of at least 30% per year since 2010, with further acceleration since 2013.

As reported in previous literature,[4] the acceleration in the mortality increase for whites since 1990 has been closely tied to an increase in the number of prescription drugs and the use of opioid pain medication, prompting several initiatives to curb the improper use of these painkillers. For example, in 2010, OxyContin was reformulated to be less easily abused. In addition, there have been other government-led initiatives such as Prescription Drug Monitoring Programs, Medicaid

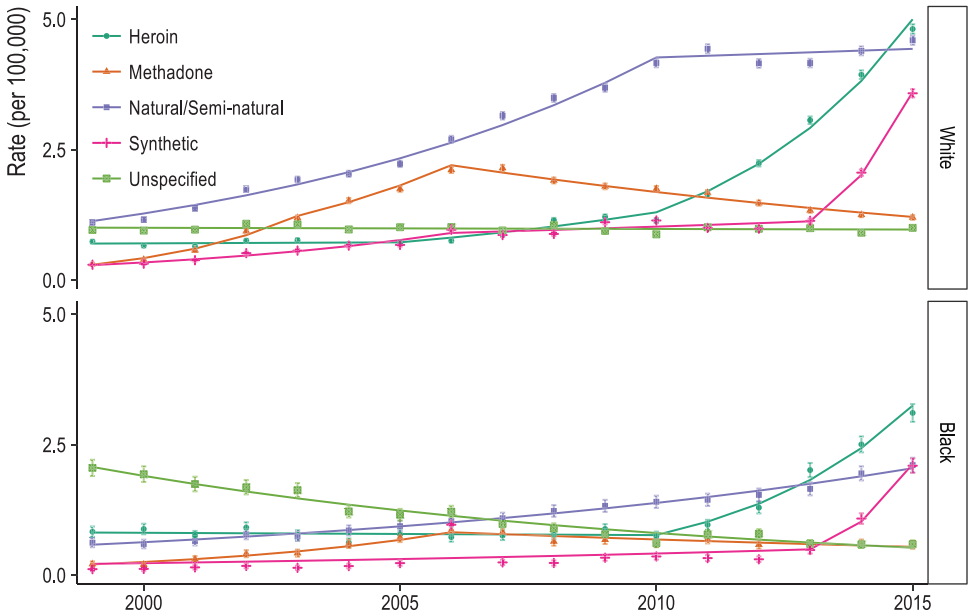

FIGURE 3. Opioid mortality rates for International Classification of Diseases (ICD)-10 years (1999–2015) by type for white (top) and black (bottom) US resident populations. Opioid types include heroin (green), methadone (orange), natural/semi-natural opioids (purple), synthetic opioids (pink), and unspecified opioids (light green). Vertical bars are 95% confidence intervals. Solid lines are joinpoint model fits.

Lock-in programs and pain clinic laws, which sought to limit access and deter overuse of prescription opioids. These initiatives may explain the leveling of the natural/semi-synthetic opioid mortality rate that is observed since 2010.

The focus on restricting the supply of prescription opioids without concurrently reducing demand, however, appears to be associated with a shift from prescription painkillers to heroin and other illicit opioids. In recent years, the supply of both heroin and illegally manufactured fentanyl has increased in the United States.[32,33] The increased availability and affordability of illicit opioids has led to many users substituting heroin/fentanyl for prescription opioids. Previous research has demonstrated a clear pathway of addiction from prescription opioids to heroin.[34] The Centers for Disease Control and Prevention reported that those addicted to opioid painkillers are 40 times more likely to be also addicted to heroin.[35]

However, the substitution of heroin for prescription opioids does not explain the recent rapid increase in the heroin and synthetic opioid mortality rates seen in the black population. Indeed, our findings show that the opioid mortality rate for blacks more than doubled in 5 years, even without a history of high prescription opioid mortality. Increased heroin mortality in more recent years is likely to be partly a consequence of the increased availability and affordability of heroin since 2010.[36] However, more recent increases in overdoses are likely to be driven by the increased potency of heroin, which is now often mixed with fentanyl.[34]

In addition to physician training and restrictions to the supply of prescription opioids, recent policies to curb the opioid epidemic have included comprehensive efforts such as harm reduction and early addiction treatment.[37] For example, access to naloxone, a drug designed to rapidly reverse the effects of opioid overdose, has been shown to reduce opioid mortality when expanded in settings where overdoses are more likely to occur.[38,39] Local interventions have expanded naloxone access by equipping law enforcement officers,[40] schools,[41] and libraries.[42] Similarly, there has been renewed interest in safe injection sites, where opioid users inject under the supervision of medical personnel,[43] which have been shown to reduce opioid overdose deaths[44] without an increase in drug trafficking or crime.[45] Effectively addressing the epidemic will continue to require a better understanding of social and economic determinants of opioid use and the impact of both supply-side and demand-side interventions.[46,47]

Our work contributes to the existing literature on understanding the opioid epidemic in three main ways. First, we presented an analysis of opioid mortality over an extended time frame, analyzing an additional 20 years of data prior to 1999, when published studies usually begin. This longer time series highlights similarities between historical conditions and the most recent wave of the epidemic. Second, we focused our analysis on differences in opioid mortality by race, whereas previous research tends to focus on trends in the total population, or in the white population only, thereby omitting some key racial differences in the epidemic over time. Finally, examining trends by type of opioid provides evidence of shifts in the epidemic from heroin to prescription drugs to heroin and fentanyl.

The current opioid epidemic in the United States is unprecedented compared to previous drug crises, in terms of the number of people affected and the rate of increase in overdose deaths. Our findings show that the nature of the epidemic has changed substantially over the past 35 years, shifting from relatively low heroin mortality, to a prescription drug problem in the white population, and more recently to a heroin/fentanyl epidemic affecting both the black and the white populations. In particular, since 2010, increases in mortality have been similar in both populations. The different patterns in the opioid epidemic by race suggest the need for targeted policy interventions to account for the distinctive pathways to addiction. A better understanding of racial differences and how they relate to the use of other drugs, place of residence, and socioeconomic status is necessary to improve health interventions and rehabilitation programs across the country.

Limitations

This study has several limitations. First, differences in cause of death reporting between blacks and whites could affect estimates of the rate ratio. Recent research has indicated that opioid mortality is underreported by about 24% nationally and that the extent of underreporting varies by geography.[48] In particular, increases in heroin mortality were underreported in southern states such as Louisiana and Alabama, with large black populations, which may affect estimates of heroin mortality among the black population, especially if this geographic effect is aggravated by further differential reporting by race. For example, if medical examiners are more likely to classify deaths of whites as due to an "unspecified drug" (ICD-10 code T50.9) rather than to opioids, the rate ratio estimate may be too conservative. Conversely, classifying black opioid deaths as an "unspecified drug" would make our rate ratio estimate too higher. The misclassification of race on death certificates could also affect the calculation of opioid mortality. However, although no validation studies have been carried out to examine the accuracy of coding of opioid deaths by race, an analysis of all causes of death showed that the effect on mortality of the misclassification of race on death certificates is small.[49]

Second, the jump joinpoint model assumes that the underlying trend remains the same during the ICD-9 to ICD-10 transition. While there are no validation studies on the effect of the ICD change on opioid deaths specifically, the comparability ratio of accidental injuries (under which accidental overdose—the overwhelming case of overdoses—is categorized) is estimated to be 1.03, which suggests that death classifications are reasonably comparable.[50] Unfortunately, the classification change occurred as the epidemic was accelerating, and so quantifying this effect is difficult without further validation.

Last, it is important to note that fentanyl mortality rates may be underestimated, as a specific toxicology test must be requested by the coroner to determine the drug's presence. Indeed, the observed increase in fentanyl deaths since 2013 is likely attributable, at least in part, to improved detection through post-mortem investigations due to increased awareness in the medical community.[51]

CONCLUSION

Over the period 1979 to 2015, age-standardized opioid mortality rates increased for both the white and the black populations. Although rates of increase were initially similar in the two populations and driven by heroin, the period 1993–2010 saw a rapid increase in opioid mortality for whites, largely due to prescription painkillers. Since 2010, opioid mortality has been increasing rapidly in both groups, largely driven by increases in heroin and synthetic opioids.

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