

# Premature mortality from all causes and drug poisonings in the USA according to socioeconomic status and rurality: an analysis of death certificate data by county from 2000–15



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## Summary

**Background** Increasing premature mortality among some groups of Americans has been largely driven by increases in drug poisoning deaths. However, to our knowledge, a formal descriptive study by race and ethnicity, socioeconomic status, rurality, and geography has not been done. In this study, we examined US trends in premature all-cause and drug poisoning mortality between 2000 and 2015 at the county level among white, black, and Latino people.

**Methods** We used US mortality data for the period Jan 1, 2000, to Dec 31, 2015, including underlying cause of death and demographic data, collected from death certificates by the Centers for Disease Control and Prevention National Center for Health Statistics, and ascertained county attributes from the 2011–15 Census American Community Survey. We categorised counties into quintiles on the basis of the percentage of people unemployed, the percentage of people with a bachelor's degree, median income, and rurality. We estimated premature (ie, deaths in those aged 25–64 years) age-standardised mortality for all causes (by race and ethnicity) and drug poisoning, by county, for the periods of 2000–03 and 2012–15. We estimated annual percentage changes in mortality (2000–15) by county-level characteristics.

**Findings** Premature mortality declined from 2000–03 to 2012–15 among black and Latino people, but increased among white people in many US counties. Drug poisoning mortality increased in counties throughout the country. Significant increases between 2000 and 2015 occurred across low and high socioeconomic status and urban and rural counties among white people aged 25–64 years (annual percentage change range 4·56% per year [95% CI 3·56–5·57] to 11·51% per year [9·41–13·65]), black people aged 50–64 years (2·27% per year [0·42–4·16] to 9·46% per year [7·02–11·96]), Latino women aged 25–49 years (2·43% per year [1·18–3·71] to 5·01% per year [3·80–6·23]), and Latino men aged 50–64 years (2·42% per year [0·53–4·34] to 5·96% per year [3·86–8·11]). Although drug poisoning mortality increased rapidly in counties with the lowest socioeconomic status and in rural counties, most deaths during 2012–15 occurred in the largest metropolitan counties (121395 [76%] in metropolitan counties with  $\geq 250\,000$  people vs 2175 [1%] in the most rural counties), reflecting population size.

**Interpretation** Premature mortality has declined among black and Latino people in the USA, and increased among white people, particularly in less affluent and rural counties. Increasing drug poisoning mortality was not limited to poor white people in rural areas. Rapid increases have occurred in communities throughout the USA regardless of race and ethnicity, socioeconomic status, or rurality. Widespread public health interventions are needed to address this public health emergency.

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## Introduction

In 2016, life expectancy at birth in the USA decreased for the second year in a row, an unexpected trend for a high-income country.<sup>1,2</sup> These trends largely reflect increasing mortality among young and middle-aged white people over the past two decades, due in part to increases in drug poisonings, with additional contributions from suicide and chronic liver disease.<sup>3,4</sup> Premature mortality has also increased substantially among American Indians and Alaska Natives, but declines in premature mortality occurred among black and Latino people and Asian and

Pacific Islanders over the same period.<sup>4</sup> Mortality and life expectancy are known to vary substantially between and within US states,<sup>4,6</sup> with widening gaps reported in life expectancy between rich and poor Americans.<sup>7–9</sup> However, the effect of diverging national trends in premature mortality by race and ethnicity on county-level disparities in mortality is unclear. A common narrative surrounding recent increases in drug poisoning mortality often focuses on poor, rural, white Americans in regions of high unemployment. Although drug poisonings are particularly high in rural counties with economic distress,<sup>10</sup> other data

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### Research in context

#### Evidence before this study

Reports have shown declines in US life expectancy in 2015 and 2016. These trends largely reflect increasing mortality among young and middle-aged white Americans over the past two decades, due in part to increases in drug poisonings, with additional contributions from suicide and chronic liver disease. The narrative surrounding recent increases in drug poisoning mortality often focuses on poor, rural, white Americans in regions of high unemployment. However, other data increasingly suggest that increases in drug poisonings are more widespread, impacting all races and ethnicities and urban areas. To our knowledge, variation in premature all-cause and drug poisoning mortality over time by race and ethnicity, geography, and socioeconomic status has not been thoroughly interrogated. Although previous studies have examined geographical heterogeneity in all-cause and drug poisoning mortality, these studies were not stratified by racial or ethnic group, an important consideration given diverging patterns among white people compared with black and Latino people.

#### Added value of this study

In this study, we examined US trends in total premature and drug poisoning mortality from 2000 to 2015 at the county level among white, black, and Latino people. We also examined

trends by county-level measures of rurality and socioeconomic status (ie, education, income, and unemployment), identifying communities most impacted by increasing mortality. Our analyses provide insights into the combination of demographic, socioeconomic, and geographical distributions of the premature and drug poisoning mortality epidemics in the USA. Although progress has been made in reducing premature mortality among black and Latino people throughout the USA, mortality has increased among white men and women in many areas, with the largest increases occurring in less affluent and rural counties. Rapid increases in drug poisoning mortality occurred in both high and low socioeconomic status counties and in both urban and rural counties.

#### Implications of all the available evidence

Mortality from drug poisonings is a pressing concern across race and ethnicity, geographical region, and socioeconomic status, with the largest number of deaths occurring in large metropolitan counties. Alarming increases in drug poisoning deaths have impacted communities throughout the USA and, despite increased awareness, the most recent data show that death rates are accelerating. Widespread public health interventions are urgently needed to stem these adverse trends and prevent future premature deaths.

suggest that increases in drug poisonings might be more widespread, affecting urban areas and all races and ethnicities.<sup>4,11–16</sup>

In this study, we examined US trends in premature all-cause and drug poisoning mortality between 2000 and 2015 at the county level among white, black, and Latino people. County-level analysis enabled the evaluation of trends by macro-level measures of rurality and socioeconomic status (ie, education, income, and unemployment). These analyses provide insights into the combination of demographic, socioeconomic, and geographical distributions of the current epidemics of premature and drug poisoning mortality. This information could help identify potential underlying causes and target populations in the greatest need of public health interventions.

## Methods

### Data sources

We used US mortality data for the period of Jan 1, 2000, to Dec 31, 2015, including underlying cause of death and demographic data, collected from death certificates by the Centers for Disease Control and Prevention (CDC) National Center for Health Statistics. Our analysis focused on all-cause and drug poisoning deaths, classified on the basis of International Classification of Diseases, Tenth Revision codes (X40–X44, X60–X64, X85, and Y10–Y14) to capture all drug poisoning deaths, including accidents (78% of all poisoning deaths), suicide (13%), homicide (0.1%), and deaths with unknown

intent (9%). We considered all poisoning deaths because of the possibility of misclassification of intent by medical examiners, which varies substantially by region, and to remain consistent with CDC definitions.<sup>17,18</sup> Race and ethnicity of all decedents was also ascertained from death certificates and classified as non-Hispanic white (ie, white), non-Hispanic black or African American (ie, black), and Hispanic or Latino (ie, Latino). We ascertained specific population data by county for age, sex, and race and ethnicity from the US Census intercensal populations. Our analyses were restricted to people aged 25–64 years to focus on premature death.<sup>4</sup> Data are publicly available, thus, institutional review board approval was not needed.

### County attributes

We ascertained county attributes from the 2011–15 Census American Community Survey (ACS).<sup>19</sup> For our county-level analysis we used three macro-level county attributes reflecting socioeconomic status—the percentage of people unemployed (ie, percentage of civilians aged ≥16 years in the labour force who are unemployed), the percentage of people with a bachelor's degree (based on the population aged ≥25 years), and the median household income in the past 12 months (measured in 2015 inflation-adjusted US\$). We classified these variables in quintiles on the basis of population distribution across counties. The weighted  $\kappa$  statistics comparing county-level quintiles between the ACS administered in 2000 and 2011–15 were 0.42 for the

	2000–03		2012–15	
	Counties (n=3144)	Person-years	Counties (n=3145)	Person-years
Analysis of total premature mortality				
White population	3056 (97.2%)	424 919 009/425 093 952 (>99.9%)	3071 (97.6%)	429 723 754/429 811 317 (>99.9%)
Black population	1398 (44.5%)	69 732 746/70 600 504 (98.8%)	1481 (47.1%)	83 181 283/84 165 742 (98.8%)
Latino population	732 (23.3%)	68 360 639/71 342 674 (95.8%)	987 (31.4%)	103 843 825/107 197 290 (96.9%)
Analysis of drug poisoning mortality	997 (31.7%)	509 530 430/599 328 938 (85.0%)	1700 (54.1%)	630 446 469/667 918 632 (94.4%)

Table shows data included in maps of county-level mortality (ie, counties with ten or more deaths per calendar period per ethnic group for total premature mortality, and ten or more drug poisoning deaths per calendar period for drug poisoning mortality), as a percentage of the total data available

**Table: Data from county-level analyses presented on maps**

percentage of people unemployed, 0.83 for the percentage with a bachelor's degree, and 0.67 for median income. We also categorised counties by the 2013 Rural–Urban Continuum codes that were developed by the United States Department of Agriculture.<sup>20</sup> The weighted  $\kappa$  statistic comparing counties by Rural–Urban Continuum codes from 2003 to 2013 was 0.91.

### Statistical analysis

We estimated age-standardised total premature mortality (stratified by race and ethnicity) and drug poisoning mortality for each US county for two calendar periods (2000–03 and 2012–15) by standardising to the 2000 US population in 5-year age groups. For county-specific analyses, we restricted our analysis to counties with ten or more deaths per calendar period by racial or ethnic group. We estimated rate ratios (RRs) by comparing county-specific age-standardised mortality for the periods between 2012–15 and 2000–03, limited to counties with ten or more deaths in both periods.

We estimated age-standardised overall and drug poisoning mortality for the periods of 2000–03 and 2012–15 by age group (25–49 years and 50–64 years) separately for white, black, and Latino people. Next, we aggregated counties across quintiles of percentage unemployment (0–6.39%, 6.40–7.55%, 7.56–8.69%, 8.70–9.99%, and 10.00–29.43%), percentage with a bachelor's degree (1.89–20.13%, 20.14–27.27%, 27.28–31.04%, 31.05–37.57%, and 37.58–78.77%), median income (\$19 330–44 240, \$44 250–50 940, \$50 950–56 190, \$56 200–67 310, and \$67 320–123 450), and a collapsed version of the Rural–Urban Continuum (metropolitan areas with  $\geq 1$  million people, metropolitan areas with 250 000 to <1 million people, metropolitan areas with <250 000 people, urban areas with  $\geq 20 000$  people, urban areas with 2500 to <20 000 people, and completely rural populations with <2500 people). Because we aggregated across counties for these analyses, we included all counties regardless of population size and number of deaths.

Additionally, to assess time trends in mortality, we estimated annual percentage changes in age-standardised mortality per year between 2000 and 2015 for each county

attribute (ie, examined separately across quintiles of percentage of people with bachelor's degrees, quintiles of percentage of people unemployed, quintiles of median income, and six categories of rurality). In sensitivity analyses, we restricted drug poisonings to those classified as unintentional intent (ie, accidental drug poisonings) and defined quintiles of county-level unemployment using county attributes from 2000 as opposed to 2012–15. Unemployment was selected for this analysis because it had the poorest agreement with quintiles defined with 2012–15 data. Notably, annual percentage changes were not estimable in some categories among black and Latino people when there were no drug poisoning deaths in at least one calendar year. All analyses were done using SEER\*Stat software (version 8.3.4).

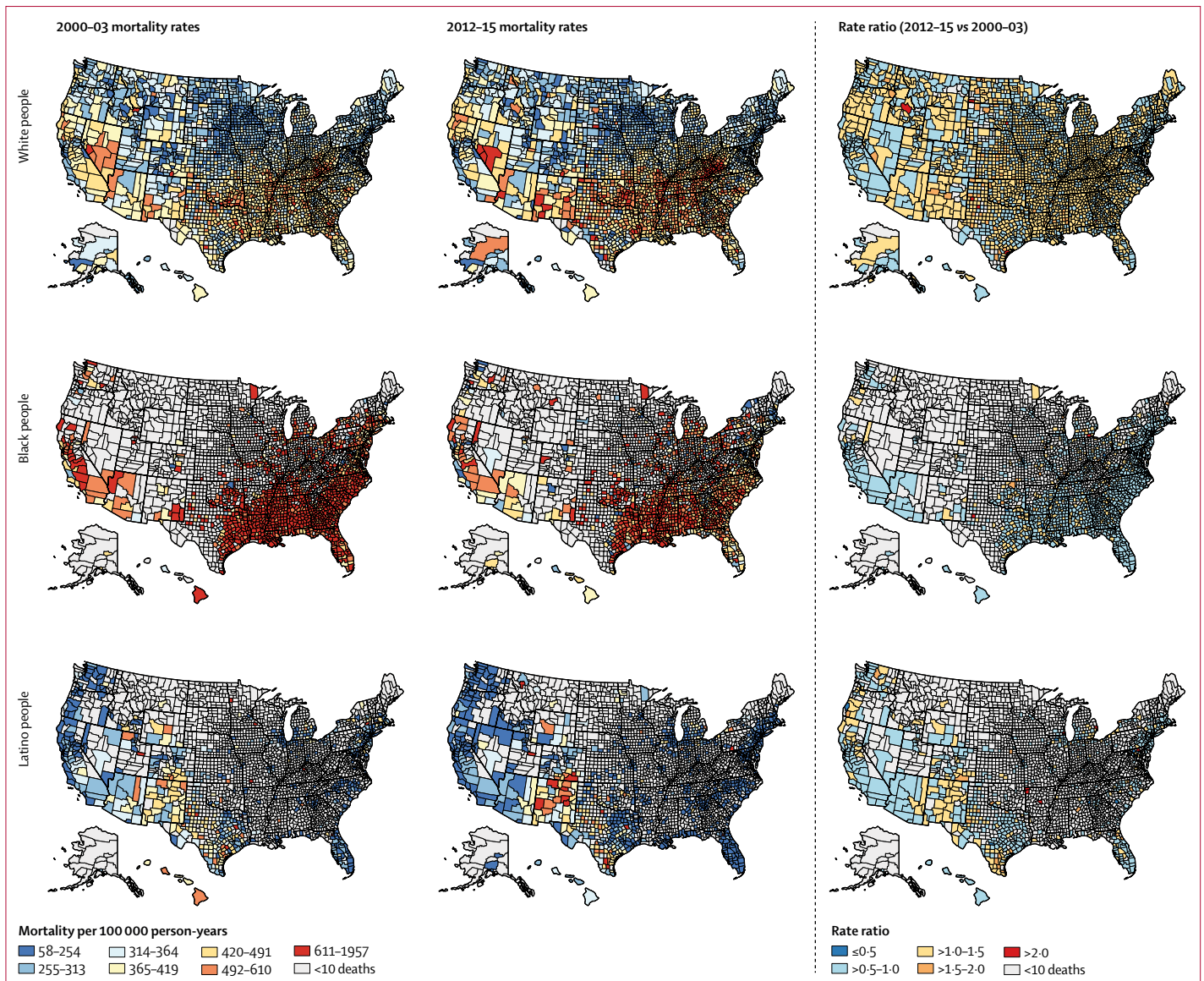
### Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report, but did approve a final version of the manuscript. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

### Results

Between 2000 and 2015, 9.5 million premature deaths occurred among people in the USA aged 25–64 years (age-standardised rate 341.5 per 100 000 person-years). 2205 280 premature deaths occurred in the period of 2000–03 (1555 690 in white people, 420 419 in black people, and 158 057 in Latino people), and 2553 491 premature deaths occurred in the period of 2012–15 (1775 231, 452 354, and 224 708, respectively). For drug poisoning mortality, these figures were 74 088 deaths (56 914 in white, 9697 in black, and 5867 in Latino people) in 2000–03 and 159 471 deaths (128 427, 14 894, and 11 886, respectively) in 2015. We captured all drug poisoning deaths, including accidents, suicide, homicide, and deaths with unknown intent.

For total premature mortality, the counties with data included on our maps (ie, counties with ten or more deaths per category) represented more than 99.9% of the white population for 2000–03 and 2012–15, 98.8% of the



**Figure 1: Age-standardised all-cause premature mortality and rate ratios comparing 2012–15 with 2000–03 by US county and race and ethnicity**  
 Data represent those aged 25–64 years. All rates are expressed per 100 000 person-years and data are not included for counties with less than 10 deaths.

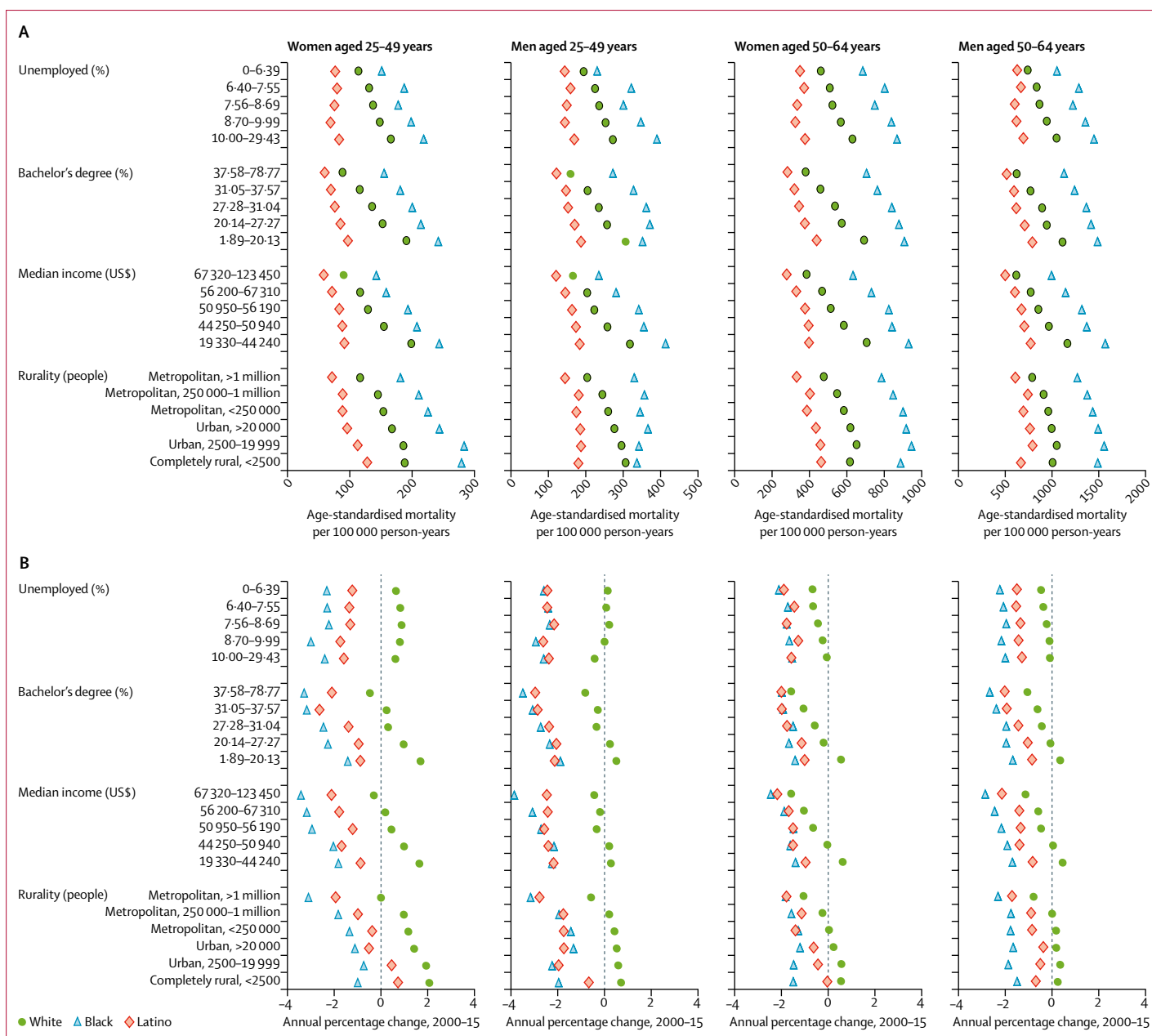
black population for 2000–03 and 2012–15, and 95·8% and 96·9% of the Latino population for 2000–03 and 2012–15, respectively (table). For drug poisoning mortality, counties included in our analysis represented 85·0% of the US population between 2000 and 2003 and 94·4% of the US population between 2012 and 2015 (table).

Broadly speaking, all-cause mortality was highest in black people, lower in white people, and lowest in Latino people for the periods of 2012–15 and 2000–03 (appendix). Within each racial or ethnic group, substantial between-county differences were observed. From 2000–03 to 2012–15, all-cause premature mortality in black and Latino people declined across most counties, with some

exceptions where increases occurred. Such trends were widespread and occurred throughout the country (figure 1, appendix), including in counties with both low and high mortality. By contrast, premature all-cause mortality increased among white people in most counties from 2000–03 to 2012–15, and these increases were not limited to specific states or regions (figure 1, appendix).

We additionally examined whether all-cause mortality and trends varied across aggregated county-level socioeconomic factors (unemployment, education, and median income) or rurality. As expected, all-cause premature mortality for the period of 2012–15 was consistently lower in more affluent counties across all categories of race and ethnicity, sex, and age group

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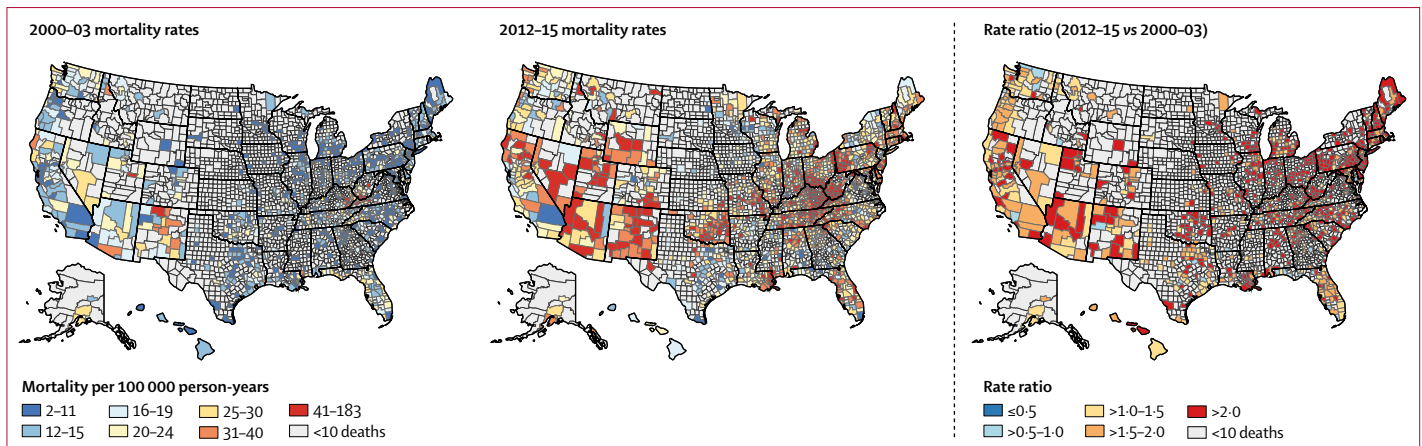


**Figure 2: County-level age-standardised all-cause mortality and annual percentage change in mortality**  
 (A) Age-standardised all-cause mortality, 2012–15 and (B) annual percentage changes in mortality, 2000–15, by age, sex, race and ethnicity, and county attributes.

(figure 2, appendix). Premature mortality was also generally lower in urban counties than in rural counties across all racial and ethnic groups, except in younger black men (aged 25–49 years) and older Latino men (aged 50–64 years), among whom mortality was similar in the most urban and most rural counties (appendix). Overall, among both men and women, all-cause mortality was generally highest among black people, followed by white and Latino people across these county-level characteristics.

When we examined yearly trends in all-cause premature mortality from 2000 to 2015, mortality among

black and Latino men and women declined over time in both age groups (24–49 years and 50–64 years) and across all types of counties, regardless of county-level unemployment, education, income level, or rurality (figure 2, appendix). By contrast, all-cause mortality among white women aged 25–49 years increased significantly across the majority of socioeconomic groups and in urban areas (range of annual percentage change 0.31% per year [95% CI 0.02–0.60] to 2.07% per year [1.62–2.52]), except for those living in the largest metropolitan counties (population >1 million) and those



**Figure 3: Age-standardised drug poisoning premature mortality and rate ratios comparing 2012–15 with 2000–03 by US county**

Data represent those aged 25–64 years. All rates are expressed per 100 000 person-years and data are not included for counties with less than ten deaths.

in the highest quintiles of median income or education. All-cause mortality also increased significantly among white men aged 25–49 years in counties with the lowest levels of income and education, and across urban and rural counties (range of annual percentage change 0.22% per year [95% CI 0.00–0.45] to 0.69% per year [0.31–1.07]), but not in the largest metropolitan counties. Among white men and women aged 50–64 years, all-cause mortality declined significantly or remained stable across most county attributes (appendix). However, all-cause mortality increased significantly in the lowest income and education quintiles, and in smaller urban (<20 000 people) counties (range of annual percentage change 0.35% per year [95% CI 0.02–0.68] to 0.60% per year [0.23–0.98]); appendix). All-cause mortality also increased significantly among white women aged 50–64 years living in rural areas (annual percentage change 0.53% per year [95% CI 0.16–0.91]).

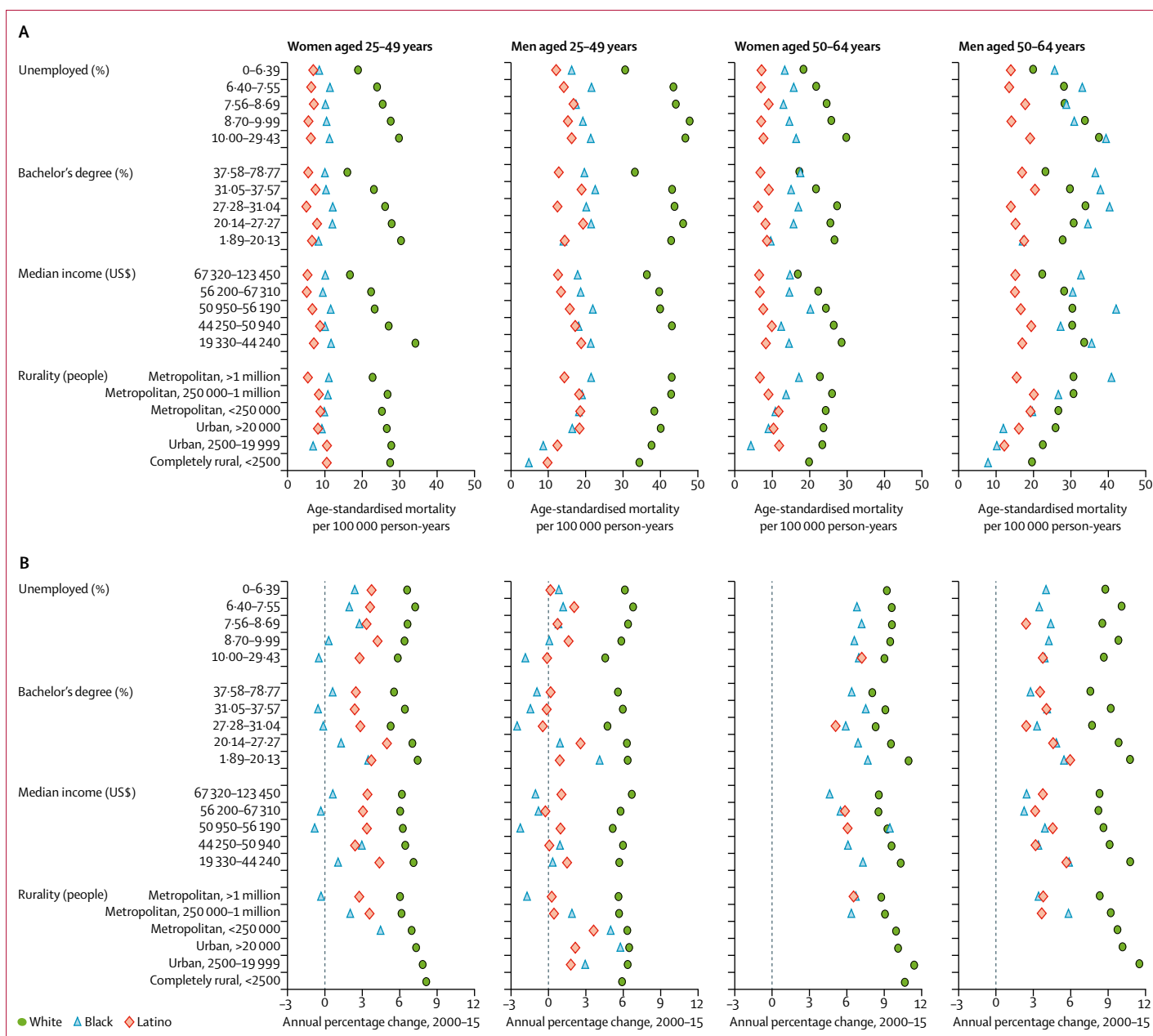
As drug poisoning deaths are a primary contributor to increasing premature mortality over time among some groups in the USA,<sup>3,4</sup> we examined county-level trends in drug poisoning mortality between the periods of 2000–03 and 2012–15. There were 474 439 premature drug poisoning deaths between 2000 and 2015 (age-standardised mortality 18.9 per 100 000 person-years). In 2012–15, drug poisoning mortality was generally highest among white people, with the exception of men aged 50–64 years, in whom mortality was highest among black men (appendix). We found substantial variation in drug poisoning mortality across US counties (figure 3, appendix). Nevertheless, counties with increasing drug poisoning mortality were scattered across the country rather than localised to any particular region. Increases were substantial—drug poisoning mortality doubled in more than 500 counties and quintupled in more than 30 counties (appendix).

Among white men and women aged 25–49 years and white women aged 50–64 years, drug poisoning mortality between 2012 and 2015 was far higher than mortality

in black and Latino people across county attributes (unemployment, education, median income, and rurality) (figure 4, appendix). However, among people aged 50–64 years, black men generally had higher or similar drug poisoning mortality compared with white men across quintiles of unemployment, education, and median income (figure 4). In this age group, black men had higher drug poisoning mortality than did white men in the largest metropolitan counties, whereas white men had higher drug poisoning mortality in smaller metropolitan, urban, and rural counties. Drug poisoning mortality generally followed a socioeconomic gradient across quintiles of unemployment, education, and median income among white men and women (ie, highest rates in areas with the highest unemployment, lowest level of education, and lowest income), but these patterns were not evident among black or Latino men and women (figure 4).

When we examined drug poisoning premature mortality for all racial and ethnic groups combined, age-standardised mortality was similar across rurality (22.6–27.4 per 100 000 person-years for 2012–15; figure 5). However, when we examined the absolute number of deaths, 85 209 (53%) drug poisoning deaths occurred in metropolitan counties with populations greater than 1 million people and 36 186 (23%) occurred in counties with populations of 250 000–999 999 people, while only 2175 (1%) drug poisoning deaths occurred in completely rural areas (figure 5).

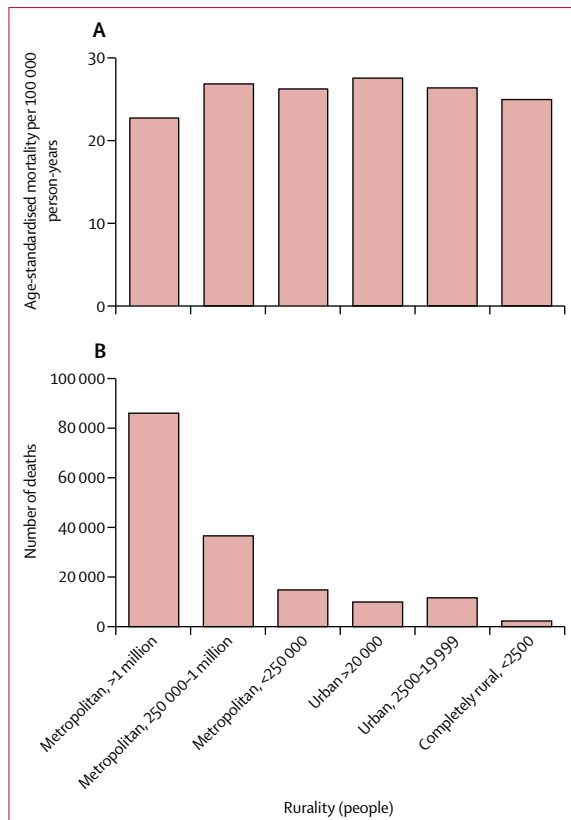
In white people, drug poisoning mortality increased across county attributes and among all age groups (figure 4, appendix). These annual increases between 2000 and 2015 ranged from 4.56% per year (95% CI 3.56–5.57) to 8.17% (5.78–10.62) among those aged 25–49 years, and from 7.58% per year (5.75–9.43) to 11.51% (9.41–13.65) among those aged 50–64 years, regardless of county socioeconomic status or rurality. Among black men and women and Latino men, drug poisoning mortality increased significantly in some categories of county



**Figure 4: County-level age-standardised drug poisoning mortality and annual percentage change in mortality**  
 (A) Age-standardised drug poisoning mortality, 2012-15 and (B) annual percentage changes in drug poisoning mortality, 2000-15, by age group, sex, race and ethnicity, and county attributes. Annual percentage changes were not estimable in groups with at least one calendar year with no deaths.

attributes among those aged 25-49 years and remained stable in most others. However, among Latino women aged 25-49 years, Latino men aged 50-64 years, and black men and women aged 50-64 years, drug poisoning mortality increased significantly in less affluent and more affluent counties, and in larger metropolitan counties (appendix). Estimated annual percentage changes were high, ranging from 2.27% per year (95% CI 0.42-4.16) to 9.46% per year (7.02-11.96) among black men and women, 2.42% per year (0.53-4.34) to 5.96% per year

(3.86-8.11) among Latino men aged 50-64 years, and 2.43% per year (1.18-3.71) to 5.01% per year (3.80-6.23) among Latino women aged 25-49 years. Data were generally too sparse to evaluate in more rural counties, and likewise we could not evaluate annual percentage changes for many of the county characteristics among Latino women aged 50-64 years. Inferences were the same when restricted to unintentional drug poisonings and when unemployment quintiles were based on 2000 county characteristics (appendix).



**Figure 5: Age-standardised drug poisoning mortality and number of drug poisoning deaths**  
 (A) Age-standardised drug poisoning mortality and (B) number of drug poisoning deaths.

## Discussion

In this nationwide analysis of US death certificate data, we have shown that premature mortality has increased in some US populations since 2000, while drug poisoning mortality has increased broadly across racial and ethnic groups, geography, and county-level characteristics. This finding builds on previous research showing that trends in premature mortality in the USA in the early 21st century have diverged, with death rates for 25–64 year-olds increasing among white people and decreasing among black and Latino people.<sup>4</sup> The current analysis shows that this pattern has been widespread, occurring in counties throughout the country. By contrast, increases in drug poisoning mortality occurred broadly among white, black, and Latino men and women. Rapid increases in drug poisoning mortality occurred in both high and low socioeconomic status counties and in both urban and rural counties. Although rural counties have had rapid increases in drug poisoning mortality,<sup>10</sup> we found that 75% of these deaths occurred in large, metropolitan counties compared with only 1% in the smallest rural counties for the period of 2012–15, reflecting the larger populations of metropolitan counties. Therefore, our findings are inconsistent with

the narrative that increases in premature deaths due to drug overdoses have been restricted to specific populations, such as white people living in rural areas with high unemployment.

All-cause premature mortality was generally highest in counties with the highest unemployment, lowest attained education and income, and in more rural locations. Additionally, premature mortality declined more rapidly in counties with higher socioeconomic status and in more urban counties, indicating increasing disparities over time, as previously reported.<sup>7–9</sup> Health disparities by socioeconomic status have been well established for several diseases in the USA, including cancer, heart disease, and HIV.<sup>21–23</sup> Certain risk factors for premature mortality are more prevalent among poorer US counties, which might contribute to these disparities, including smoking, obesity, physical inactivity, and fewer physicians.<sup>24</sup>

Among white people, progress against cancer and heart disease mortality in some age groups has been countered by rapidly increasing mortality from drug poisonings, deaths by suicide, and chronic liver disease and cirrhosis.<sup>3,4</sup> Declining trends in premature mortality among black and Latino men and women reflect progress in decreasing cancer, heart disease, and HIV deaths.<sup>4</sup> To date, increases in drug poisoning deaths have not yet negated progress against other causes of death in these groups of people, although increasing drug poisoning deaths among black and Latino people are concerning.<sup>12,25</sup>

We showed that increases in drug poisoning deaths affect all racial and ethnic groups in many counties across the USA, regardless of socioeconomic status. We included all drug poisonings, regardless of intent (ie, accidental, intentional, assault, and undetermined) in our analysis, as there is notable geographical variability in the classification of intent on death certificates; however, results were similar when restricted to accidental deaths. Although white men and women have had the most rapid increases in drug poisoning mortality, rates have increased in some groups of 25–49-year-old black and Latino men and women, and across county-level characteristics among those aged 50–64 years. Black men aged 50–64 years had higher drug poisoning mortality than white men, consistent with our previous work, which showed that increases in drug poisoning deaths were most pronounced among black people aged 50 years and older (by comparison with white people, in whom deaths have increased sharply during the ages of 20–64 years). Notably, drug poisoning deaths have also increased among white, black, and Latino people aged 20–24 years.<sup>26</sup>

The increases in drug poisoning deaths are caused by several contributing drugs. When drug-specific death rates were previously compared during 2012–15, heroin caused the largest increases among white, black, and Latino men and women.<sup>12</sup> Although heroin is the most common cause of drug-related death among white and Latino men and prescription opioids are the most



common cause of drug-related death among white and Latino women, cocaine remains the largest contributor to drug-related deaths among black men and women.<sup>12,16</sup> Increases in drug overdoses probably reflect increases in both the prevalence of use and the degree of risk per use, for example, the number of people prescribed opioids in the USA increased considerably in the first decade of this century, and there have also been reports of increasing heroin use.<sup>27</sup> Additionally, contamination of heroin and cocaine with fentanyl and its analogues is making these products more dangerous.<sup>28,29</sup>

Between 2012 and 2015, premature mortality due to drug poisonings was generally highest among people residing in counties with the highest unemployment and lowest educational attainment and median income, although this pattern was stronger in white people than in black and Latino people. This observation is consistent with studies that found positive associations between county poverty and drug poisoning deaths.<sup>10,30</sup> The geographical heterogeneity of drug poisoning deaths will probably continue, as drug availability, prescribing patterns, and resources to combat overdose vary by region. For example, although opioid prescribing has declined in recent years, many US counties still averaged more than one prescription per resident in 2016.<sup>31</sup> Furthermore, law enforcement encounters with fentanyl, a potent synthetic opioid, increased rapidly between 2010 and 2015, with the largest increases observed in the eastern half of the country.<sup>32</sup> Nevertheless, there have been strong increases in drug poisoning deaths throughout the country and, while there are certain geographical areas in which drug poisoning death rates are particularly high,<sup>10,15</sup> this epidemic is geographically extensive. The magnitude of these increases is alarming, with county-level drug poisoning death rates increasing by as much as 17-times between the periods of 2000–03 and 2012–15, and as high as 11% per year among white people aged 50–64 years in the most rural and poorest counties. It is also important to note that drug poisoning death rates have increased in both urban and rural areas, and more than half of all drug poisoning deaths occur in the largest metropolitan areas, compared with 1% in completely rural areas. Thus, widespread public health efforts to combat the drug overdose epidemic are needed in communities throughout the USA, including increases in access to medication-assisted treatments, increases in drug treatment for inmates, better health care coverage of non-opioid approaches to pain management, and increased access to naloxone to prevent deaths when overdoses occur.<sup>33</sup>

The main strength of our study was the use of nationwide death certificate data and nationally representative county-level characteristics from the American Community Survey to assess premature all-cause mortality and drug poisoning mortality, which enabled us to study death rates and trends over time by age, sex, race and ethnicity, county, and county-level characteristics.

However, the use of death certificates when ascertaining race and ethnicity of decedents and the use of self-reported race and ethnicity in the Census for population counts might have resulted in a small amount of racial or ethnic misclassification, particularly for Latino decedents.<sup>34</sup> In our geographical analysis, results were restricted to those counties with ten or more deaths, limiting our ability to assess county-specific mortality trends in more sparsely populated areas, although these counties contribute very little to overall mortality. Although previous studies have used statistical modelling to estimate poisoning rates for sparsely populated counties,<sup>15</sup> given that our approach included most of the US population, as well as 88% of drug poisoning deaths between 2000 and 2003 and 94% of drug poisoning deaths between 2012 and 2015, we chose not to model rates for counties with less than ten deaths. Among larger counties, within-county variation in mortality probably occurs, which is not captured in our analysis. Additionally, our assessment of education, income, and unemployment was made at the county level and does not represent the socioeconomic status of the specific individuals that died in those counties, or represent quintiles in each stratum of age, sex, and race and ethnicity. Furthermore, socioeconomic metrics were assigned to counties on the basis of the 2011–15 estimates, and some counties changed quintiles over time; however, we believe that the most recent classification of county-level socioeconomic status is the most relevant to current rates and trends. Moreover, sensitivity analyses using quintiles on the basis of county-level unemployment estimates from 2000 showed similar results. Our estimates of annual percentage changes in mortality assumed linear changes over the time period. It is possible that non-linear trajectories occurred, however, annual percentage changes are a straightforward way to compare overall trends during a time period across different groups. Finally, we were unable to include data on American Indians, Alaska Natives, and Asian or Pacific Islanders in our analysis because of the small size of these populations.

Although progress has been made in reducing county-level premature mortality among black and Latino people in the USA, mortality has increased among white men and women in many areas of the country, particularly among less affluent and rural counties. Rapid rises in drug poisoning mortality have largely driven these increases. Nevertheless, the current drug poisoning epidemic is not limited to any one group on the basis of race and ethnicity, geography, or socioeconomic status, contrasting with the perception that this is largely a problem of white, rural, poor Americans. Indeed, alarming increases in drug poisoning deaths have affected communities throughout the USA and are accelerating, despite increased awareness.<sup>18,35</sup> Our results highlight the urgent need for widespread public health interventions to prevent future premature deaths.

**Contributors**

MSS, ABdG, and NDF designed the study, analysed and interpreted the data, drafted the manuscript, provided crucial revisions, and approved the final version of the manuscript. AFB, YC, PC, PH, SQK, EJP-S, EJR, SS, DAT, and DW interpreted the data, provided crucial manuscript revisions, and approved the final version of the manuscript.

**Declaration of interests**

We declare no competing interests.

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