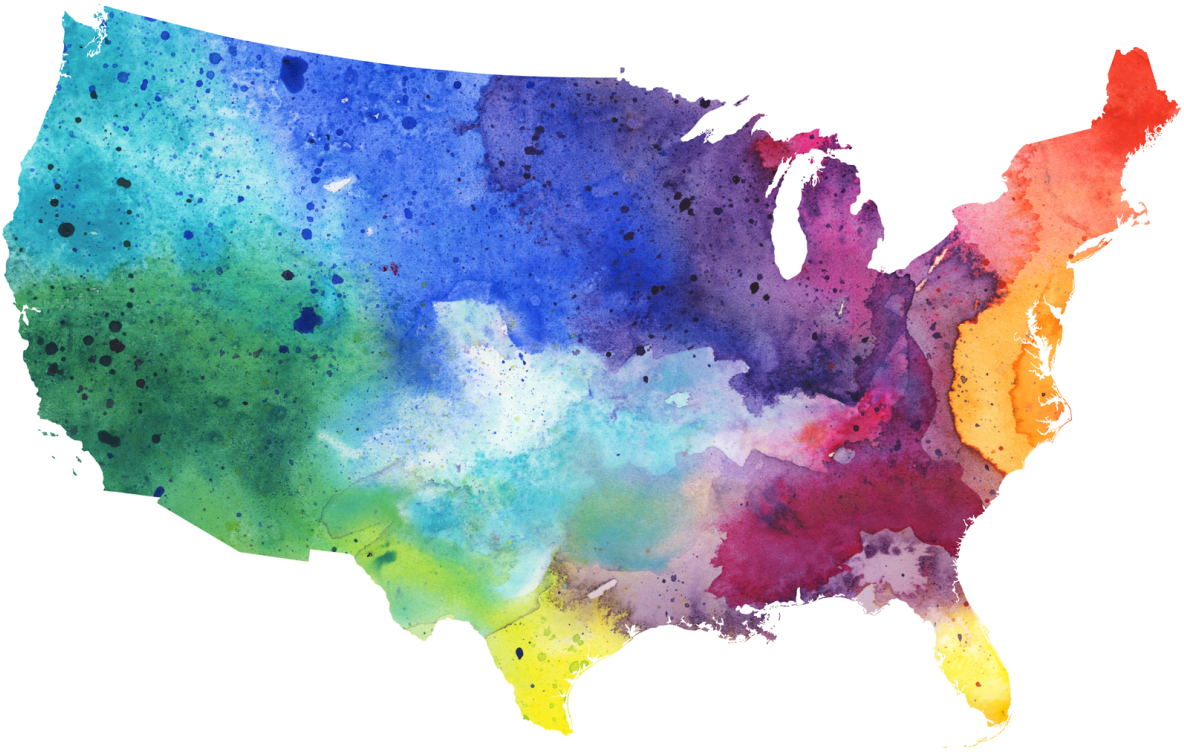
Geographic Patterns and Disparities in Health-related Behaviors and Outcomes in the United States



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Geographic Patterns and Disparities in Health-related Behaviors and Outcomes in the United States

Geografische patronen en verschillen in gezondheidsgerelateerde gedragingen en uitkomsten in de Verenigde Staten

Thesis

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Chapter 1

Introduction

BACKGROUND

Risk exposures (e.g., smoking, physical inactivity), health outcomes, and longevity have long been known to vary substantially from country to country.[1,2] Recent research has highlighted substantial regional variation in risk exposures, health outcomes, and longevity within a wide range of countries.[3–8] In the United States of America (US), differences in risk exposures, health outcomes, and longevity have been well documented at the state level.[9,10] Previous research at the county level has consistently found an even greater degree of variation among counties than among states, much of which occurs within state borders.[11–14] However, variation in risk exposures, health outcomes, and longevity has not been as thoroughly described at this level as for more aggregate geographies.

County-level measurement of risk exposure, health outcomes, and longevity is important for at least three reasons. First, local information is valuable to public health practitioners and policy-makers. Most local public health departments in the US are organized by county,[15] making county-level information particularly important. Geographically precise information on risk factors, for example, can help public health officials and policy-makers better target prevention and treatment efforts and to allocate limited resources to the most pressing local needs. Second, geographic differences in health outcomes may indicate avoidable health disparities. Fine-grained, local-level measurement of health outcomes facilitates identifying these avoidable disparities so that they may be addressed. Moreover, tracking changes in geographic differences in health outcomes overtime is critical (though not, by itself, sufficient) to ensuring that future health gains are equitably distributed. Third, an understanding of how specific health outcomes vary on a fine-scale geographically may lead to new or deeper insights into the underlying drivers of ill health and variation in outcomes. In some cases, maps of health outcomes may suggest particular mechanisms which deserve further study; in other cases, this information could be used in ecological analyses to provide further support of (or contradict) existing hypotheses.

The purpose of this thesis is to develop methods for estimating exposure to risks, health outcomes, and longevity at the county level in the US, to use the resulting estimates to evaluate whether geographic disparities in health at the county level are increasing or decreasing over time, and to explore the drivers of variation in longevity among counties. The remainder of this chapter focuses on a discussion of geographic disparities in the US and an overview of the methodological challenges of estimating exposure to risks, health outcomes, and longevity at the county level. The chapter concludes with the specific research questions for this thesis and an overview of the remaining chapters.

GEOGRAPHIC DISPARITIES IN HEALTH IN THE US

Disparities in health outcomes have long been recognized among different regions and states in the US. Routine tracking of mortality and cause of death statistics by the federal government dates to the early 20th century (although not all states participated until the 1930s) and has consistently shown substantial differences in fatal health outcomes among states and large cities.[16,17] Growing recognition of regional differences in risk exposure, the prevalence of chronic conditions such as diabetes, cardiovascular diseases, and respiratory diseases, and of functional limitations led to the establishment in the early 1980s of health surveys designed to track these health-related indicators at the state level.[18]

At the county level, life expectancy is the best described measure of health outcomes, although there are limitations to the methods that have been used, to date, to estimate county-level trends in life expectancy. Murray et al.[19] first estimated county-level differentials in life expectancy in the late 1990s, and identified counties along the southern half of the Mississippi river, throughout much of the southeast, in central Appalachia, and in counties in South and North Dakota with Native American reservations where life expectancy was substantially lower than the national average for both men and women. Overall, Murray et al. reported that life expectancy varied by up to 16.5 years for men and 13.0 years for women among counties in 1990. Subsequent analyses by Ezzati et al.[20] and Kulkarni et al.[21] also found similar spatial patterns and large geographic disparities in life expectancy among counties, while an analysis by Wang et al.[14] confirmed these earlier findings and presented evidence that county-level geographic disparities in life expectancy have increased in recent decades. Existing analyses of cause-specific mortality rates,[22–27] chronic conditions,[11,28,29] and risk factors[12,13] have also found substantial geographic disparities among counties, both within and across state borders, though spatial patterns differ among different risk factors and outcomes.

Quantifying and tracking temporal trends in geographic disparities

Geographic differences in risk factor prevalence, health outcomes, and longevity may indicate the presence of avoidable health disparities. *Healthy People 2020*, which describes national health goals for the US, includes "Achieve health equity, eliminate disparities, and improve the health of all groups" as one of its four overarching goals, and explicitly recognizes disparities by geographic location in addition to disparities by race, ethnicity, gender, sexual identity and orientation, and disability status.[30] County-level estimation of health indicators can facilitate monitoring trends in geographic disparities and progress towards achieving better, more equitable health outcomes as envisioned by the *Healthy People 2020* framework.

Several researchers[14,20] have previously described increases in geographic disparities in life expectancy among counties in recent decades, but temporal trends in county-level

geographic disparities in the US for other health outcomes or for exposure to risks have not been described. Moreover, recent research[31] on socioeconomic disparities in survival has highlighted different trajectories for different age groups, but no similar analysis has been undertaken with respect to geographic disparities.

Drivers of variation in health outcomes

Some of the variation in health outcomes at the county level is almost certainly due to differences in the prevalence of individual-level risk factors for disease and death. This includes more proximal risks, such as smoking, excessive alcohol use, insufficient physical activity, poor diet, and risky sexual practices, but also more distal risk factors such as poverty, lack of education, immigrant status, or membership in a disadvantaged racial or ethnic group.[32–34] Contextual, ecological factors are likely also implicated in county-level differences in health outcomes.[35,36] These include many of the same social and economic factors that operate at the individual level: for example, an individual's health may be impacted not only by her own income, but also by the overall wealth of her community, as well as the distribution of wealth within her community. Physical and environmental features of the county[37–39]—such as altitude, sunlight, air pollution, and other environmental toxins—and features of the built environment[40,41]—such as building quality, transportation infrastructure, and the food landscape—may also play a role in determining health outcomes. Similarly, differences in health outcomes may be partially attributable to differences in public policies and regulatory structures[42,43]—such as public health funding; taxes and regulations related to smoking, alcohol, and sugar-sweetened beverages; and enforcement of traffic laws—as well as differences in access to and quality of health care.[44,45]

There is potentially considerable (and complex) interplay among these different factors, including within the individual level (e.g., education status may impact smoking behavior[46]), within the contextual level (e.g., public policy may impact the prevalence of environmental risks or the quality of the built environment[47]), and between these two levels (e.g., features of the built environment may impact an individual's level of physical activity[48]). Moreover, many of these factors are not static and individuals may move from one county to another in a way that either diminishes or increases apparent geographic disparities in health.[49] Taken together, these dynamics dramatically complicate efforts to describe the relative importance of drivers leading to county-level differences in health.

A number of previous studies have examined county-level correlates of life expectancy or some other measure of survival. These studies have found positive correlations at the county level between longevity and income, education, other measures of socioeconomic status, and access to quality health care and negative correlations at the county level between longevity and concentration of minority populations, prevalence of environmental expo-

sures, and prevalence of behavioral and metabolic risk factors.[38,39,50–52] Only a few studies have considered the cumulative effect of a wider range of potential drivers of county-level variation in longevity, however.[53–55] The most comprehensive analysis of potential drivers of county-level variation in longevity found that between 72% and 86% (depending on sex and race) of the variation among counties in survival to age 70 could be explained by a suite of 22 socioeconomic and environmental variables and that among a subset of counties where data on risk factor prevalence were available, 86% to 90% of the variation in survival could be explained by variation in these same socioeconomic and environmental variables as well as variation in risk factor prevalence.[53] None of these previous county-level studies systematically considered the relative importance of different potential drivers of geographic disparities in longevity, however.

METHODOLOGICAL CHALLENGES

There are a number methodological challenges related to generating, utilizing, and interpreting county-level estimates of risk exposures, health outcomes, and longevity. This section describes the data sources available for county-level analyses in the US and the main challenges related to generating estimates from these data that are addressed in this thesis.

Data sources

Health data that can be used to describe county-level trends are limited. Most national health surveys do not sample respondents in all (or even most) counties, and many do not make geographic identifiers available due to privacy concerns. This thesis makes use of two data sources that are uniquely well suited to county-level analyses as well as a third that can be used in combination with county-level data.

The National Vital Statistics System (NVSS) collects death certificate data from all US states and territories and includes information on effectively every death that occurs in the US, including age at death, sex, place of residence, and underlying cause of death for each decedent.[56] County-level identifiers for NVSS data can be requested from the National Center for Health Statistics. In this thesis, NVSS data are used to estimate county-level trends in cause-specific mortality rates as well as county-level trends in life expectancy.

The Behavioral Risk Factor Surveillance System (BRFSS) is an annual telephone survey conducted in all US states and coordinated by the Centers for Disease Control and Prevention (CDC).[57] The BRFSS collects information on behavioral and metabolic risk factors and chronic diseases as well as demographic data from between 100,000 and 500,000 thousand individuals each year and includes respondents in most counties. Until 2013, county-level identifiers

were publically available for BRFSS data, though this variable was suppressed in small counties. In this thesis, BRFSS data are used to estimate county-level trends in smoking, excessive alcohol use, diabetes, and self-reported health.

The National Health and Nutrition Examination Survey (NHANES) is a household survey of approximately 5,000 respondents per year conducted in bi-annual cycles by the CDC.[58] While publically available NHANES datasets lack geographic identifiers and cannot be used directly for county-level estimation, the NHANES includes detailed biometric data not available from most other data sources. In this thesis, NHANES data are used in conjunction with BRFSS data to estimate county-level trends in diabetes prevalence, including undiagnosed diabetes.

Small area estimation

In cases where appropriate data for measuring risk factor exposure or health outcomes at the county level exist, a main barrier to producing precise estimates is the statistical challenges posed by small numbers. Standard statistical techniques for estimating population parameters rely on large sample sizes to reduce the influence of random fluctuations (i.e., stochastic "noise"). Most counties are relatively small, however, a problem that is compounded when working with survey data where only a fraction of the population of each county is sampled. In these cases, using only the data available for each county leads to highly imprecise estimates, making it difficult to discern true differences between counties or time periods.

Early research on county-level patterns of risk exposure or health outcomes typically employed one of two methods to overcome the issues posed by small numbers: synthetic estimates, or pooling data. Synthetic estimates are constructed by first estimating a quantity of interest using all available data (i.e., data from all locations) stratified by relevant demographic features (e.g., sex, race), and then weighting these estimates by the observed demographic characteristics in each smaller area.[59] This approach accounts for variation in the outcome of interest that is related to variation in the stratifying variables included in the construction of these estimates, but does not account for any other sources of variation and therefore likely often underestimates true variation. The second approach is more straightforward: data are pooled over multiple years to increase the available sample size, mitigating the effects of small numbers. The main limitation of this approach is that estimates constructed in this way do not refer to a specific, limited time period and are not useful for examining county-level temporal trends or changes in the magnitude of geographic disparities among counties over time. Moreover, estimates constructed this way in many cases are still based on a relatively small sample size and may not be sufficiently reliable in smaller counties.

More recently, researchers have used small area estimation (SAE) to address the challenges posed by small numbers.[28,60,61] SAE utilizes mixed effects models that allow for "borrowing

strength" to increase the effective sample size available for each individual location and thus improve the precision of the estimates. These models typically borrow strength spatially (i.e., from neighbors or nearby areas) and often also borrow strength temporally and from external sources of information. Borrowing strength spatially and temporally is conceptually related to simply pooling data by aggregating areas or combining multiple years of data, but in an SAE framework the pooling is partial and the strength of the spatial and temporal relationships are estimated based on the data. Borrowing strength from external information relies on the observation that many demographic and environmental characteristics of counties are already precisely known from censuses or other administrative data sources, and that these characteristics are often related to health outcomes of interest. Thus this external information can be incorporated into SAE in the form of covariates.

In the US, researchers have previously used some form of SAE to generate estimates of life expectancy,[14,21,51] mortality from select causes of death (e.g., drug overdose,[25] heart disease,[27,62] and cancer[26,63]), prevalence of behavioral and metabolic risk factors (e.g., hypertension,[12] obesity and physical activity[13]), and chronic conditions (e.g., COPD[29]) at the county level. Model specification has varied widely, however, and not all approaches have been validated. Srebotnjak et al.[28] describe a framework for validating county-level SAE models which could be used to assess model performance and aid in developing more precise methods for SAE in the US.

Data quality

In addition to the challenges posed by small numbers, there are several issues specific to the data sources identified for county-level analyses. The primary concern related to NVSS deaths data relates to the quality of information available about the underlying cause of death for each decedent. Underlying cause of death is coded according to the *International Classification of Diseases and Related Health Problems (ICD)*.[64,65] Previous research[66,67] has identified a number of potential misuses of ICD codes as they relate to underlying causes of death, particularly codes that refer to an intermediate or immediate cause of death instead of an underlying cause (e.g., cardiopulmonary arrest) and codes that are insufficiently specific (e.g., malignant neoplasms of other and ill-defined sites). Collectively, these cause of death codes have been referred to in the literature as 'garbage codes,' recognizing their limited use for public health analyses.[66] The likelihood that a death will be assigned a garbage code varies over time and by location as well as by true underlying cause of death, compromising the reliability of comparisons made across locations, years, or causes. Methods for redistributing garbage codes to likely true underlying causes of death have been developed for the Global Burden of Disease (GBD) project,[1,67] but have not been previously utilized for county-level analyses.

BRFSS data are subject to a different set of limitations. Response rates are relatively low—in 2012, they ranged from 27.7% to 60.4% among states[68]—raising the possibility of non-response bias due to differences in the quantity of interest between respondents and non-respondents. For national and state-level estimates, survey weights are used to mitigate the effects of non-response, however these survey weights are not calibrated for county-level estimates. For similar reasons, non-coverage bias is also a concern for the BRFSS, particularly with respect to individuals who can only be reached by mobile phone: prior to 2011, the BRFSS only sampled landlines and thus excluded both individuals without any phone (a relatively small population) as well as individuals with only a mobile phone (more than a quarter of the adult population in 2010[69]). This compromises the integrity of estimates derived from data prior to 2011 and in some cases introduces substantial discontinuities between estimates in 2010 and 2011 that likely reflect these methodological changes rather than true changes in the population.[70] Finally, the self-reported nature of the data poses challenges: in some cases, respondents may not accurately report, whether due to intentional misreporting (e.g., under-reporting weight[71]), misunderstanding of the questions (e.g., interpreting 'average' to mean 'mode' rather than 'mean' when asked about average number of alcoholic beverages consumed[72]), or lack of information (e.g., respondents with undiagnosed chronic conditions will not report those conditions[73]).

Quantifying geographic disparities

Many different metrics for quantifying disparities have been proposed that vary in terms of what aspects of a distribution are measured and whether comparisons are absolute or relative.[74,75] These choices can have a substantive impact on the conclusions drawn from such analyses, impacting, for example, whether disparities appear to increase or decrease over time. To date, investigations of county-level geographic disparities in life expectancy in the US have focused on absolute measures of inequality, specifically the standard deviation or the range.[14,20,51] Given the potential sensitivity of these conclusions to the metric used, more thorough consideration of various alternatives is warranted.

RESEARCH QUESTIONS

This thesis has three specific research questions:

1. Can methods be developed that both address small numbers issues and also account for known biases in available data, allowing for sufficiently precise estimates of health-related risk factors and mortality for US counties?
2. To what extent does the prevalence of health-related risk factors and health outcomes vary among counties in the US, and are inequalities increasing or decreasing over time?

3. What proportion of the variation observed in mortality rates at the county level can be explained by variation in socioeconomic factors, behavioral and metabolic risk factors, and access to and quality of health care?

The remainder of this thesis is divided into seven chapters. Chapters 2–4 focus on county-level variation in risk factors, specifically smoking (chapter 2), excessive alcohol use (chapter 3), and diabetes (chapter 4). Chapters 5–7 focus on county-level variation in health outcomes, including cause-specific mortality rates (chapter 5), life expectancy (chapter 6), and self-reported health (chapter 7). Chapters 2–5 explicitly address the first research question, developing and validating county-level small area estimation models and corrections for various biases in the underlying data sources utilized in these analyses. All chapters consider the second research question, describing and, in various ways, quantifying county-level geographic disparities in health. The third research question is specifically addressed in chapter 6. Finally, chapter 8 contains a general discussion of the findings and implications of this thesis and proposes next steps.

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Chapter 2

Cigarette smoking prevalence in US counties: 1996–2012

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ABSTRACT

Background

Cigarette smoking is a leading risk factor for morbidity and premature mortality in the United States, yet information about smoking prevalence and trends is not routinely available below the state level, impeding local-level action.

Methods

We used data on 4.7 million adults age 18 and older from the Behavioral Risk Factor Surveillance System (BRFSS) from 1996 to 2012. We derived cigarette smoking status from self-reported data in the BRFSS and applied validated small area estimation methods to generate estimates of current total cigarette smoking prevalence and current daily cigarette smoking prevalence for 3,127 counties and county equivalents annually from 1996 to 2012. We applied a novel method to correct for bias resulting from the exclusion of the wireless-only population in the BRFSS prior to 2011.

Results

Total cigarette smoking prevalence varies dramatically between counties, even within states, ranging from 9.9% to 41.5% for males and from 5.8% to 40.8% for females in 2012. Counties in the South, particularly in Kentucky, Tennessee, and West Virginia, as well as those with large Native American populations, have the highest rates of total cigarette smoking, while counties in Utah and other Western states have the lowest. Overall, total cigarette smoking prevalence declined between 1996 and 2012 with a median decline across counties of 0.9% per year for males and 0.6% per year for females, and rates of decline for males and females in some counties exceeded 3% per year. Statistically significant declines were concentrated in a relatively small number of counties, however, and more counties saw statistically significant declines in male cigarette smoking prevalence (39.8% of counties) than in female cigarette smoking prevalence (16.2%). Rates of decline varied by income level: counties in the top quintile in terms of income experienced noticeably faster declines than those in the bottom quintile.

Conclusions

County-level estimates of cigarette smoking prevalence provide a unique opportunity to assess where prevalence remains high and where progress has been slow. These estimates provide the data needed to better develop and implement strategies at a local and at a state level to further reduce the burden imposed by cigarette smoking.

INTRODUCTION

Tobacco consumption is a leading risk factor for morbidity and premature mortality in the United States (US).[1–4] While cigarette smoking prevalence has been declining at the national level, there is substantial variation across states within the US and reason to believe that even more variation may exist at local levels, such as counties.[5–7]

Evidence-based and cost-effective strategies for reducing the burden of tobacco are available.[8,9] States have differed in their uptake of these strategies, however, and have also seen varying degrees of success in reducing the prevalence of cigarette smoking and the associated disease burden, deaths, and costs to the health care system.[10] In the US, local jurisdictions have the ability to implement their own tobacco control policies and programs. Further, state-level policies may not be implemented or enforced evenly across all jurisdictions. Consequently it is essential that local estimates of current cigarette smoking prevalence are available for identifying areas that need further attention, for tracking progress, and for evaluating the effectiveness of control measures.

The US Centers for Disease Control and Prevention (CDC) routinely reports current cigarette smoking prevalence at the state level using data from the Behavioral Risk Factor Surveillance System (BRFSS).[10,11] More local assessments have been published for some, but not all, jurisdictions.[12–15] The County Health Rankings & Roadmaps program[14] incorporates county-level estimates of current cigarette smoking prevalence into their annual rankings of counties based on selected health outcomes and health behaviors. These estimates use BRFSS data but are averages over long time periods and do not provide the means to look at estimates for specific years or trends over time. The National Cancer Institute has produced estimates of current cigarette smoking prevalence for health service areas and counties for two periods, 1997–1999 and 2000–2003, but these estimates have not been updated to include data from the last decade.[16] Indeed, to our knowledge there has been no recent, comprehensive assessment of trends in current cigarette smoking prevalence at the county level using a consistent statistical methodology applied to all counties. In this study, we develop county-level measurements of cigarette smoking prevalence for all counties in the United States annually from 1996 to 2012.

METHODS

Data

We utilize county-level data on cigarette smoking from the BRFSS. The BRFSS is a telephone survey in which trained interviewers in each state collect data on a large number of health-

related behaviors and conditions for the noninstitutionalized adult population. The BRFSS is operated by state health departments in collaboration with the CDC, and all states implement the same core questionnaire. Beginning in 2011, the BRFSS incorporated cell phones into the sampling frame in addition to landlines in order to capture the growing segment of the population that only receives calls on a cell phone. Details on BRFSS methodology are available elsewhere,[17,18] and questionnaires and data are available at www.cdc.gov/brfss. Alaska conducts a supplemental BRFSS using the same methodology as the standard BRFSS;[19] data from the Alaska supplemental BRFSS on cigarette smoking were included from 2004 to 2012 in addition to data from the standard BRFSS.

Cigarette smoking status was assessed using two questions from the BRFSS.[20] Respondents were first asked, "Have you smoked at least 100 cigarettes in your entire life?" If a respondent answered yes, he or she was then asked, "Do you now smoke cigarettes every day, some days or not at all?" We used the responses to these two questions to classify respondents into three groups: nonsmokers (those who answer "no" to the first question or "not at all" to the second question), nondaily current smokers (those who answer "some days" to the second question), and daily current smokers (those who answer "every day" to the second question). We estimate the prevalence of current total cigarette smoking (both nondaily and daily combined; hereafter referred to as "total cigarette smoking prevalence") as well as the prevalence of current daily cigarette smoking only (hereafter referred to as "daily cigarette smoking prevalence").

Small area estimation models

We applied previously described small area models to estimate the prevalence of cigarette smoking for US counties.[21–23] In brief, we constructed a family of logistic hierarchical mixed effects regression models for each outcome, stratified by sex. These models incorporate spatial and temporal smoothing and a series of county- and state-level covariates to improve predictions for all counties, including those with limited data available in a given year from the BRFSS. More details on the regression models and the county- and state-level data sources incorporated in the models can be found in Additional files 1 and 2. These models allowed us to generate annual estimates of total and daily cigarette smoking prevalence for male and female adults (age 18 and older) in all US counties and county equivalents. All estimates were age-standardized following the age structure of the 2000 census.[24] The uncertainty of the prevalence estimates was assessed using simulation methods.[25]

Model validation and performance assessment

We also used previously developed validation methods[21–23] to select the best-performing model among a number of different plausible models. Our approach was as follows: for each sex we selected counties with at least 900 survey respondents between 2006 and 2010 (the

"validation set"); 900 was selected in previous investigations based on simulation studies as the number that generated sufficiently precise estimates for a wide range of outcomes. Using the pooled data for this time period, we calculated a "gold standard" estimate of cigarette smoking prevalence for each county in the validation set. We then created new datasets by generating random samples from counties in the validation set of size 10, 50, and 100 respondents per year. Next, we used these "sampled-down" datasets to fit each model and compared the resulting prevalence estimates for counties in the validation set with the gold standard. We measured model performance using the concordance correlation coefficient, which is a measure of the agreement between the model predictions and the gold standard, and the root mean squared error, a measure of the magnitude of the deviation between the model predictions and the gold standard, expressed in the same units as the predictions.

Bias correction for wireless-only households

In 2011 cell phones were introduced into the BRFSS sampling frame in order to capture the growing share of the adult population that is "wireless-only" (36.5% as of the second half of 2012)[26] and cannot be reached by landline. Previous research has suggested that cigarette smoking prevalence is different among wireless-only respondents and respondents who can be reached by landline, and that omitting wireless-only respondents from a survey will bias estimates of cigarette smoking prevalence, most likely leading to underestimates.[27,28] We used two complementary approaches to address the omission of wireless-only respondents from the BRFSS sampling frame prior to 2011. First, we incorporated a number of demographic characteristics—race, marital status, and educational achievement—that are related both to phone ownership and to cigarette smoking prevalence into the small area models. This allowed us to adjust our modeled estimates for each county to match the observed distribution of the population by these characteristics and to account for differences in the cigarette smoking prevalence between the wireless-only population and the general population that are due to differences in these factors. However, after making this adjustment, the prevalence estimates derived from the 2011 sample were higher than those derived from the 2010 sample, a marked and unlikely departure from trends observed in the recent past. Indeed, this suggested that differences in race, marital status, and education alone do not explain all of the difference in cigarette smoking prevalence between wireless-only respondents and the rest of the population. To address this bias, we fit two separate small area models: the first to data from respondents with landlines in all years (1996–2012), and the second to data from all respondents, including wireless-only respondents, in 2011 and 2012. In the second model, we included phone usage category (landline-only, dual, and wireless-only) to adjust estimates for the observed phone usage characteristics of the county. We compared the estimates for 2011 from the combined sample (the second model) to the estimates for the landline sample (the first model) to derive county-level measures of the bias introduced by not including wireless-only respondents in 2011. We assumed that this

bias has increased linearly with time from no bias in the year 2000 (when relatively few adults were wireless-only)[29–31] to the level measured in 2011 and used this assumption to calculate corrected estimates in each year from 2001 to 2010. Estimates for 1996 to 2000 were based on the first model, without correction, while estimates for 2011 and 2012 were based on the second model.

Unit of analysis

Our unit of analysis was counties or county equivalents (e.g., parishes, census enumeration areas, boroughs, and independent cities). As of 2012 there were 3,143 counties and county equivalents. To account for changes over the study period, we merged some counties to get consistent areas, for a total of 3,127 counties. There were 4,738,256 respondents age 18 and over in the BRFSS from 1996 to 2012 who had complete data for all variables of interest. In 2012 the combined response rate for cell and landline ranged from 27.7% to 60.4% with a median of 45.2% among the states. This response rate takes into account the likely number of eligible respondents among phone numbers for which eligibility could not be determined.[32] All analyses were carried out in R version 3.0.2.[33]

RESULTS

Model validation and performance

The concordance correlation for the selected model for male total cigarette smoking prevalence was 0.78, 0.83, and 0.87 at sample sizes 10, 50, and 100, respectively, compared to 0.90 when all data were included (i.e., "in sample"). For women, the corresponding figures are 0.78, 0.85, 0.88, and 0.91. The root mean squared error for the selected model for male cigarette smoking prevalence was 2.7, 2.5, 2.2, and 1.9 for sample sizes 10, 50, 100, and in sample, respectively, while for women the root mean squared error was almost identical at 2.8, 2.4, 2.2, and 1.9 for the same sample sizes. Performance of the selected model for male and female daily cigarette smoking was similar to that for total cigarette smoking.

Bias correction for wireless-only households

We compared model predictions for 2011 that incorporated respondents who could only be reached by cell phone with model predictions that did not incorporate these respondents in order to derive a correction for earlier years in which the wireless-only population was excluded. In 2011, the median difference in total cigarette smoking prevalence between modeled estimates with and without wireless-only respondents included was 1.21 percentage points for men and 1.55 percentage points for women. In 2010, the last year without cell phones, where bias due to their exclusion is expected to be greatest, we corrected 57.3% and 75.4% of counties for males and females, respectively, upward by at least one percentage

point and 4.7% and 16.3% of counties for males and females, respectively, upward by at least two percentage points for total cigarette smoking prevalence.

National total cigarette smoking prevalence

Figure 1 shows the national estimates for age-standardized total cigarette smoking prevalence derived from our models. Total cigarette smoking prevalence has declined for males by 1.3% (95% uncertainty interval: 1.2%–1.4%) per year, from 27.3% (26.9%–27.7%) to 22.2% (21.9%–22.5%), and for females by 1.4% (1.2%–1.5%) per year, from 22.2% (21.9%–22.6%) to 17.9% (17.7%–18.2%). Most of this decline took place from 2002 onwards; trends from 1996 to 2002 are relatively flat.

For comparison, direct (nonmodeled) estimates from the National Health Interview Survey (NHIS),[34] a nationally representative household survey, are also plotted. These estimates have been reweighted to account for the distribution of the population by race, marital status, and educational attainment and then age-standardized; this is for consistency with the modeled BRFSS estimates. Estimates from the NHIS for total cigarette smoking confirm the declines observed in the modeled estimates based on BRFSS data. Further, while estimates from NHIS vary noticeably from year to year, on the whole the level of total cigarette smoking suggested by the NHIS is consistent with that from our models based on BRFSS data.

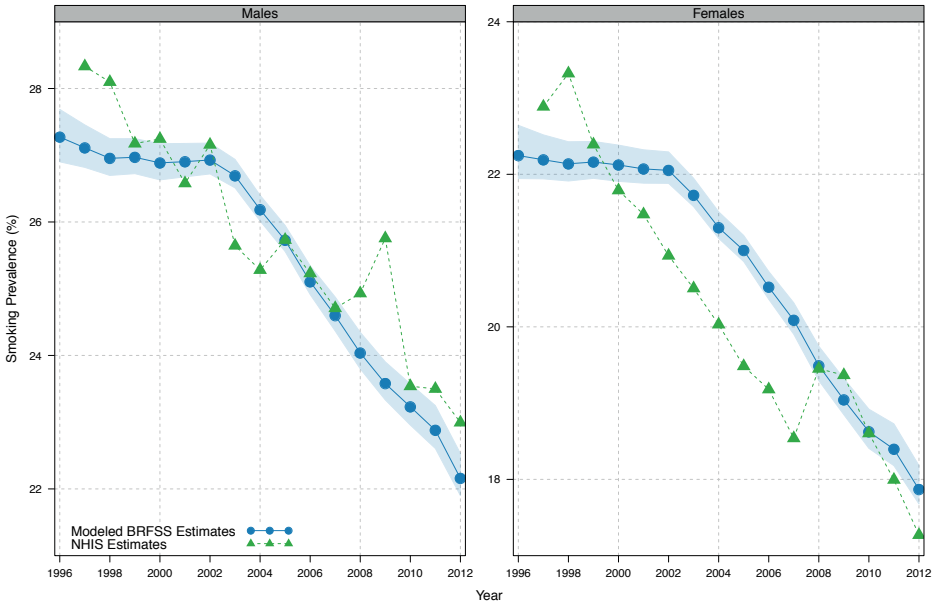

Figure 1. National age-standardized total cigarette smoking prevalence, 1996–2012.

County-level total cigarette smoking prevalence

Figures 2 and 3 show the age-standardized total cigarette smoking prevalence for males and females, respectively, in 1996 and 2012. (Estimates for the top and bottom 10 counties in 2012 are presented in Tables 1 and 2 for males and females, respectively, and estimates for all counties in all years are presented in Additional file 3.) For males, regions with high levels of cigarette smoking are observed in the South and parts of the Midwest, particularly around Kentucky. High levels are also observed in parts of Alaska, South Dakota, Nevada, and Arizona. Regions of noticeably low cigarette smoking among males are observed in Utah, Colorado, Wyoming, California, Washington, and parts of New England. For females, the highest levels of cigarette smoking are concentrated in Kentucky, West Virginia, Tennessee, Missouri, Oklahoma, Arkansas, and Louisiana; this pattern is somewhat different from the pattern among males where a much larger portion of the South experienced elevated cigarette smoking rates. Higher levels for females are also observed in parts of Alaska, Nevada, Arizona, North Dakota, and South Dakota, while the lowest levels are seen in Utah, Colorado, Wyoming, California, and along the Mexico-Texas border.

Table 1. Top- and bottom-ranked counties for male total cigarette smoking prevalence, 2012.

Rank[a]	County	Age-standardized total cigarette smoking prevalence (%)[a]
1 (1, 6)	Falls Church City, VA	9.9 (8.1, 12.0)
2 (1, 4)	Utah County, UT	9.9 (8.8, 11.3)
3 (2, 17)	Davis County, UT	11.7 (10.2, 13.6)
4 (2, 21)	Wasatch County, UT	11.8 (9.8, 14.0)
5 (2, 23)	Arlington County, VA	11.8 (9.8, 14.2)
6 (3, 32)	Summit County, UT	12.5 (10.6, 14.7)
7 (3, 37)	Howard County, MD	12.7 (10.7, 15.1)
8 (3, 46)	Whitman County, WA	12.8 (10.4, 15.4)
9 (3, 38)	Cache County, UT	12.8 (10.8, 15.0)
10 (3, 49)	Loudoun County, VA	13.1 (10.9, 15.6)
3,118 (2,866, 3,127)	Issaquena County, MS	36.8 (31.9, 42.2)
3,119 (2,809, 3,127)	East Carroll Parish, LA	37.0 (31.6, 42.4)
3,120 (2,898, 3,126)	Clay County, KY	37.2 (32.3, 42.2)
3,121 (2,859, 3,127)	Lee County, KY	37.4 (31.9, 42.2)
3,122 (2,946, 3,126)	Bethel Census Area, AK	37.5 (33.1, 42.3)
3,123 (2,875, 3,127)	Sioux County, ND	37.7 (32.1, 43.6)
3,124 (2,879, 3,127)	Shannon County, SD	37.9 (32.2, 44.1)
3,125 (2,967, 3,126)	Nome Census Area, AK	38.1 (33.1, 42.8)
3,126 (3,082, 3,127)	Wade Hampton Census Area, AK	41.2 (35.9, 46.8)
3,127 (3,089, 3,127)	Northwest Arctic Borough, AK	41.5 (35.9, 46.8)

[a]Numbers in parentheses are 95% uncertainty intervals.

In 1996, the lowest total cigarette smoking prevalence for males was observed in Utah County, UT (15.5% [13.2%–17.6%]), while the highest was found in Northwest Arctic Borough, AK (42.6% [37.0%–48.5%]), a difference of 27.1 percentage points. In 2012, Falls Church City, VA had the lowest prevalence at 9.9% (8.1%–12.0%), while the highest prevalence was still found in Northwest Arctic Borough, AK at 41.5% (35.9%–46.8%), a 31.7 percentage point difference. For females, the lowest prevalence in 1996 was found in Utah County, UT at 9.0% (7.2%–10.8%), which is 27.8 percentage points lower than the highest-observed prevalence that year in Perry County, KY at 36.8% (31.7%–42.1%). In 2012, female cigarette smoking prevalence was still lowest in Utah County, UT (5.8% [4.9%–6.8%]), which was 35.1 percentage points lower than the highest prevalence in that year, in Northwest Arctic Borough, AK (40.8% [34.8%–46.8%]).

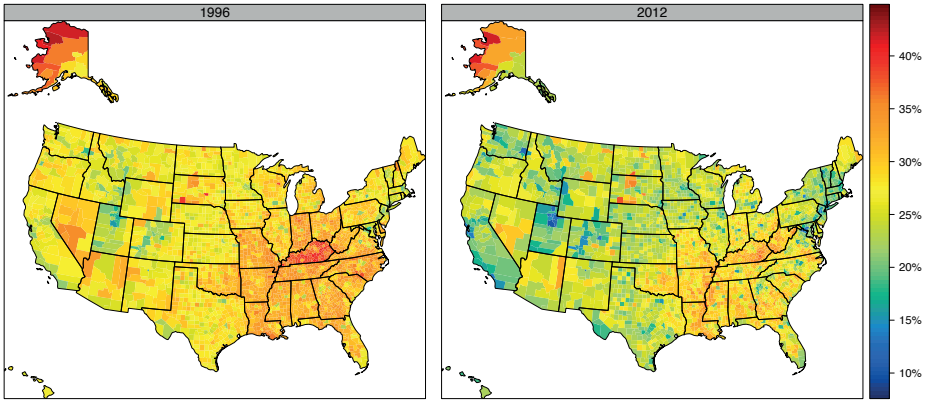

Figure 2. Age-standardized total cigarette smoking prevalence, males, 1996 and 2012.

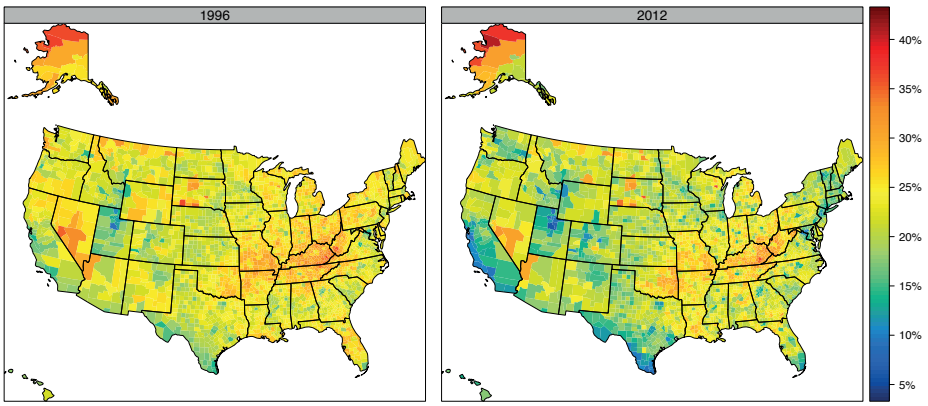

Figure 3. Age-standardized total cigarette smoking prevalence, females, 1996 and 2012.

Table 2. Top- and bottom-ranked counties for female total cigarette smoking prevalence, 2012.

Rank[a]	County	Age-standardized total cigarette smoking prevalence (%)[a]
1 (1, 2)	Utah County, UT	5.8 (4.9, 6.8)
2 (1, 8)	Wasatch County, UT	7.1 (5.7, 8.8)
3 (2, 21)	Davis County, UT	8.3 (7.1, 9.9)
4 (2, 33)	Hidalgo County, TX	8.6 (6.9, 10.8)
5 (2, 37)	San Mateo County, CA	8.7 (6.9, 10.8)
6 (2, 42)	Cameron County, TX	8.8 (6.9, 11.3)
7 (2, 37)	Summit County, UT	8.9 (7.2, 10.8)
8 (3, 36)	Santa Clara County, CA	9.0 (7.4, 10.8)
9 (3, 41)	Cache County, UT	9.1 (7.4, 11.1)
10 (7, 32)	Los Angeles County, CA	9.6 (8.6, 10.6)
3,118 (2,844, 3,126)	Elliott County, KY	34.0 (28.2, 40.7)
3,119 (2,791, 3,126)	Shannon County, SD	34.1 (27.6, 40.9)
3,120 (2,973, 3,126)	Knox County, KY	34.7 (29.8, 39.8)
3,121 (2,924, 3,127)	Buffalo County, SD	35.4 (29.2, 42.2)
3,122 (2,997, 3,126)	Nome Census Area, AK	35.8 (30.2, 41.1)
3,123 (3,002, 3,127)	Wade Hampton Census Area, AK	36.2 (30.4, 42.5)
3,124 (3,023, 3,127)	Clay County, KY	36.2 (30.8, 41.9)
3,125 (3,014, 3,127)	Menominee County, WI	36.5 (30.6, 42.5)
3,126 (3,067, 3,127)	North Slope Borough, AK	37.5 (32.2, 43.0)
3,127 (3,110, 3,127)	Northwest Arctic Borough, AK	40.8 (34.8, 46.8)

[a]Numbers in parentheses are 95% uncertainty intervals.

Even within a single state there is often substantial variation among counties. The median gap between highest and lowest cigarette smoking prevalence among counties within the same state in 2012 was 14.7 percentage points for males and 13.6 percentage points for females. The largest gap for males in 2012 was observed in Virginia, where there was a 23.6 percentage point gap in cigarette smoking prevalence for men between Sussex County (33.5% [28.6%–38.7%]) and Falls Church City (9.9% [8.1%–12.0%]). For females, the largest gap in 2012 was observed in Alaska, where there was a 25.4 percentage point gap for women between Northwest Arctic Borough (40.8% [34.8%–46.8%]) and Haines Borough (15.4% [12.3%–18.8%]).

In the vast majority of counties, males smoked cigarettes at higher rates than females (Figure 4): in 99.0% of counties in 1996 males had a higher cigarette smoking prevalence than females, while in 2012 the same was true in 96.4% of counties. The gap between male and female total cigarette smoking prevalence has changed with time, however: the median difference between male and female cigarette smoking was 5.4 percentage points in 1996 compared to 3.4 in 2012. Across all counties in 1996, the gap between male and female cigarette

smoking ranged from -3.2 percentage points in Colonial Heights City, VA, to 15.3 percentage points in Jefferson County, MS. In 2012, the gap between male and female cigarette smoking ranged from -5.7 percentage points in Menominee County, WI, to 16.5 percentage points in Sunflower County, MS. The correlation between male and female cigarette smoking prevalence was 0.75 in 1996 and 0.81 in 2012.

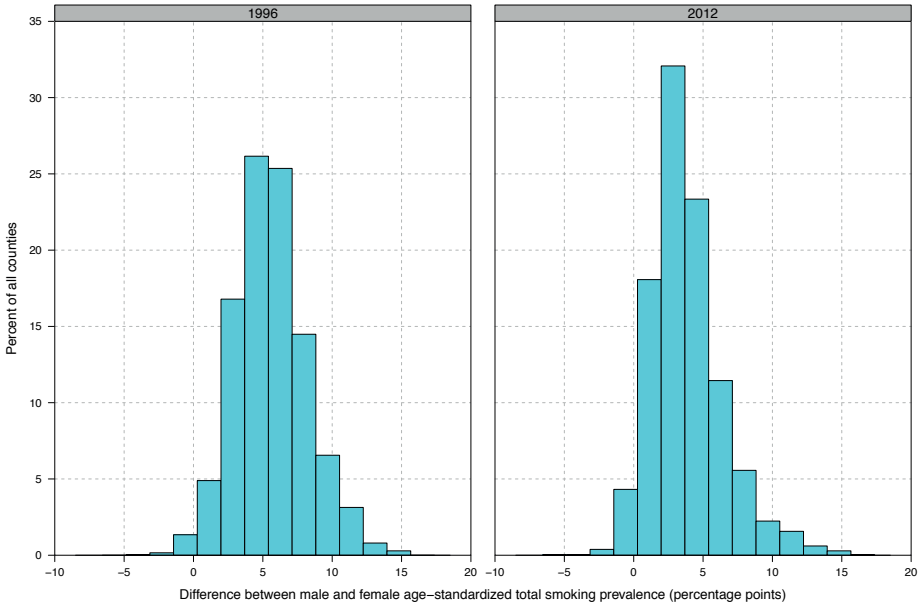

Figure 4. Difference between male and female age-standardized total cigarette smoking prevalence, 1996 and 2012.

Figures 5 and 6 show the change in age-standardized total cigarette smoking prevalence from 1996 to 2012, expressed in terms of the annualized rate of change; Tables 3 and 4 give the top and bottom 10 counties in terms of annualized rates of change. Amongst all counties, the median annualized rate of change was -0.9% for males and -0.6% for females. The greatest decline for males was 4.5% (2.6%–6.4%) per year in Falls Church City, VA, while the greatest for females was 4.1% (1.9%–6.4%) per year in Maverick County, TX. The largest increase for males was 1.1% (-0.2%–2.4%) per year in Issaquena County, MS, while the greatest increase for females was 1.7% (-0.4%–3.6%) per year in McMullen County, TX. Only 39.8% of counties for males and 16.2% of counties for females experienced statistically significant declines in cigarette smoking prevalence between 1996 and 2012, though an additional 57.3% of counties for men and 66.1% of counties for women experienced nonstatistically significant declines over this same period. Counties with statistically significant declines represent a disproportionate share of the population, however, such that 74.4% of the adult male population and 61.1% of the adult female population in 2012 lived in counties where the decline

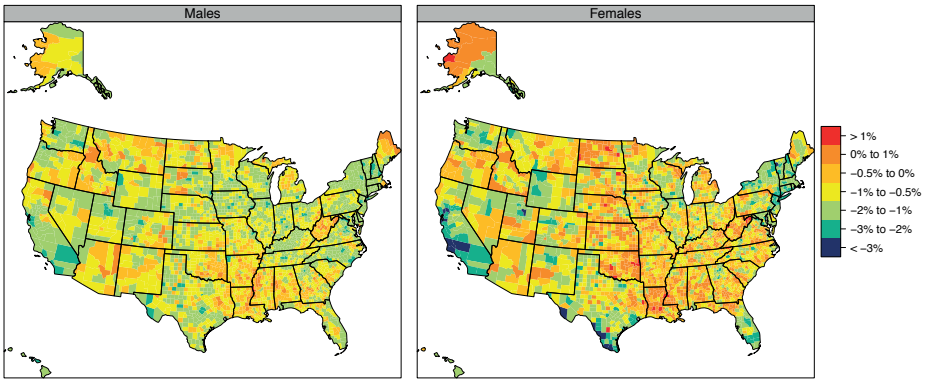

Figure 5. Annualized rate of change in age-standardized total cigarette smoking prevalence, 1996–2012.

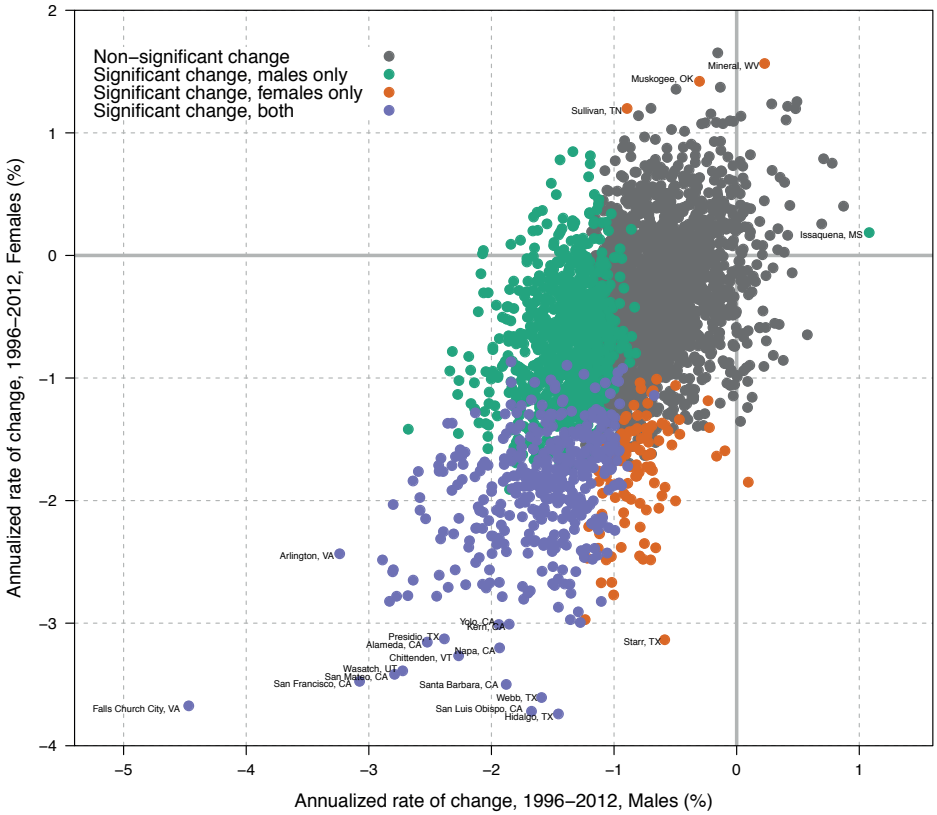

Figure 6. Annualized rate of change in age-standardized total cigarette smoking prevalence, females compared to males, 1996–2012.

Table 3. Top- and bottom-ranked counties for annualized rates of change in male total cigarette smoking prevalence, 1996–2012.

Rank[a]	County	Annualized rate of change in total cigarette smoking prevalence (%)[a]
1 (1, 87)	Falls Church City, VA	-4.5 (-6.4, -2.6)
2 (1, 555)	Arlington County, VA	-3.2 (-4.7, -1.7)
3 (1, 687)	San Francisco County, CA	-3.1 (-4.5, -1.6)
4 (2, 755)	Loudoun County, VA	-2.9 (-4.3, -1.5)
5 (2, 629)	New York County, NY	-2.8 (-4.1, -1.7)
6 (3, 745)	Orange County, CA	-2.8 (-3.9, -1.6)
7 (2, 981)	Dallas County, IA	-2.8 (-4.2, -1.3)
8 (4, 486)	Rockingham County, NH	-2.8 (-3.9, -1.8)
9 (2, 883)	San Mateo County, CA	-2.8 (-4.2, -1.4)
10 (3, 702)	Utah County, UT	-2.8 (-4.0, -1.6)
3,118 (1,795, 3,125)	Lincoln County, AR	0.4 (-0.8, 1.7)
3,119 (1,791, 3,125)	Lee County, AR	0.5 (-0.8, 1.7)
3,120 (1,625, 3,126)	Claiborne County, MS	0.5 (-0.9, 1.8)
3,121 (1,908, 3,126)	Benson County, ND	0.5 (-0.7, 1.8)
3,122 (1,784, 3,126)	Wheeler County, GA	0.6 (-0.8, 1.9)
3,123 (2,031, 3,127)	East Carroll Parish, LA	0.7 (-0.6, 2.0)
3,124 (2,321, 3,126)	Hardy County, WV	0.7 (-0.4, 1.8)
3,125 (2,177, 3,127)	Bent County, CO	0.8 (-0.5, 2.1)
3,126 (2,229, 3,127)	Meagher County, MT	0.9 (-0.5, 2.3)
3,127 (2,550, 3,127)	Issaquena County, MS	1.1 (-0.2, 2.4)

[a]Numbers in parentheses are 95% uncertainty intervals.

in total cigarette smoking prevalence was statistically significant. There were statistically significant increases in only one county for males and in only three counties for females. The correlation between male and female annualized rates of decline in the same county was moderate at 0.55. In most counties, males and females saw cigarette smoking prevalence move in the same direction (Figure 6), however, in 16.1% of counties males experienced declines while females experienced increases and, conversely, in 1.4% of counties females experienced declines while males experienced increases. For both males and females, the correlation between the level of cigarette smoking prevalence in 1996 and the rate of decline between 1996 and 2012 was low: 0.26 for males and 0.15 for females.

Total cigarette smoking prevalence as well as changes in total cigarette smoking prevalence varied between counties with different mean income levels.[35] Table 5 shows the median total cigarette smoking prevalence in 1996 and 2012 and the annualized rate of decline in total cigarette smoking prevalence over this period among counties in each income quintile (defined in terms of income in 1996). In both 1996 and 2012, the median cigarette smok-

Table 4. Top- and bottom-ranked counties for annualized rates of change in female total cigarette smoking prevalence, 1996–2012.

Rank[a]	County	Annualized rate of change in total cigarette smoking prevalence (%)[a]
1 (1, 441)	Maverick County, TX	-4.1 (-6.4, -1.9)
2 (1, 527)	Hidalgo County, TX	-3.7 (-5.6, -1.8)
3 (1, 596)	San Luis Obispo County, CA	-3.7 (-5.5, -1.7)
4 (1, 892)	Falls Church City, VA	-3.7 (-6.1, -1.3)
5 (1, 622)	Webb County, TX	-3.6 (-5.7, -1.5)
6 (1, 722)	Santa Barbara County, CA	-3.5 (-5.5, -1.5)
7 (2, 711)	San Francisco County, CA	-3.5 (-5.3, -1.5)
8 (1, 707)	San Mateo County, CA	-3.4 (-5.3, -1.5)
9 (1, 710)	Wasatch County, UT	-3.4 (-5.2, -1.5)
10 (7, 303)	Chittenden County, VT	-3.3 (-4.3, -2.2)
3,118 (2,208, 3,118)	Sullivan County, TN	1.2 (-0.1, 2.5)
3,119 (1,806, 3,124)	Adair County, OK	1.2 (-0.4, 2.8)
3,120 (2,002, 3,123)	Hampshire County, WV	1.2 (-0.2, 2.7)
3,121 (1,559, 3,125)	Grant County, WV	1.2 (-0.6, 3.0)
3,122 (1,837, 3,126)	Benson County, ND	1.3 (-0.4, 3.1)
3,123 (1,693, 3,126)	Bristol City, VA	1.4 (-0.5, 3.2)
3,124 (2,105, 3,126)	Allen Parish, LA	1.4 (-0.1, 3.1)
3,125 (2,148, 3,125)	Muskogee County, OK	1.4 (-0.1, 3.0)
3,126 (2,116, 3,126)	Mineral County, WV	1.6 (-0.1, 3.2)
3,127 (1,888, 3,127)	McMullen County, TX	1.7 (-0.4, 3.6)

[a]Numbers in parentheses are 95% uncertainty intervals.

Table 5. Total cigarette smoking prevalence and annualized rate of change by income quintile, 1996–2012.

	Income quintile, 1996	Median annualized rate of change, 1996–2012 (%)[a]	Median age-standardized total smoking prevalence, 1996 (%)[a]	Median age-standardized total smoking prevalence, 2012 (%)[a]	Counties with statistically significant declines between 1996 and 2012 (%)
Males	1st quintile	-0.5 (-2.4, 1.1)	32.1 (22.8, 40.7)	29.6 (17.5, 37.9)	14.1
	2nd quintile	-0.8 (-2.3, 0.7)	30.5 (20.4, 39.5)	27.2 (18.1, 34.8)	22.7
	3rd quintile	-0.9 (-2.4, 0.4)	29.4 (19.7, 41.5)	25.6 (14.8, 41.2)	34.6
	4th quintile	-1.1 (-2.8, 0.3)	29.0 (17.5, 37.9)	24.5 (12.8, 37.5)	52.2
	5th quintile	-1.4 (-4.5, 0.0)	27.3 (15.5, 42.6)	21.8 (9.9, 41.5)	75.4
Females	1st quintile	-0.3 (-4.1, 1.4)	24.6 (14.0, 36.8)	23.6 (8.6, 36.5)	4.2
	2nd quintile	-0.4 (-2.5, 1.6)	24.8 (14.3, 35.7)	23.2 (11.7, 32.4)	5.1
	3rd quintile	-0.5 (-2.7, 1.1)	24.4 (13.6, 33.2)	22.2 (11.8, 36.2)	8.2
	4th quintile	-0.7 (-3.0, 1.7)	23.9 (11.0, 35.1)	21.4 (9.1, 31.9)	18.4
	5th quintile	-1.2 (-3.7, 0.9)	22.5 (9.0, 36.7)	18.7 (5.8, 40.8)	45.2

[a]Numbers in parentheses are the minimum and maximum.

ing prevalence decreased as mean income in 1996 increased. Moreover, the median rate of change between 1996 and 2012 was more negative for higher income quintiles than for lower income quintiles. As a consequence, more counties in higher income quintiles experienced statistically significant declines from 1996 to 2012: for males only 14.1% of counties in the bottom income quintile experienced statistically significant declines compared to 75.4% of counties in the top income quintile; for females only 4.2% of counties in the bottom income quintile experienced statistically significant declines compared to 45.2% of counties in the top income quintile.

County-level daily cigarette smoking prevalence

Daily cigarette smoking prevalence is given for all counties in Additional file 4. When we examined the correlation between total and daily cigarette smoking it was very high: 0.95 across both sexes and all years combined. By definition, daily cigarette smoking is always less than total cigarette smoking prevalence, but the median difference between total and daily cigarette smoking among counties increased from 4.3 to 6.6 percentage points in males and 3.6 to 5.4 percentage points in females from 1996 to 2012. This was due to the fact that daily cigarette smoking prevalence has declined faster than total cigarette smoking prevalence: the median annualized rate of decline for daily cigarette smoking prevalence was 1.9% per year for males and 1.4% per year for females, compared to 0.9% per year and 0.6% per year for total cigarette smoking prevalence for males and females, respectively. Rates of decline in total and daily cigarette smoking over the period from 1996 to 2012 are highly correlated, however: 0.93 for both males and females. In 2012 the gap between daily and total cigarette smoking prevalence ranged from 2.7 (Utah County, UT) to 15.3 (Wade Hampton Census Area, AK) percentage points for males and from 1.4 (Utah County, UT) to 11.8 (Wade Hampton Census Area, AK) percentage points for females.

DISCUSSION AND CONCLUSIONS

Our study is the first to report on nationwide cigarette smoking prevalence and change in cigarette smoking prevalence at the county level from 1996 to 2012. Moreover, we derived these estimates using a systematic model selection and validation process. Additionally, we report on a novel method to adjust BRFSS estimates to take into account recent changes in the BRFSS methodology, which allows for analysis of trends both before and after these changes. The BRFSS has informed data users about these changes and their potential impact on the estimates and trends but has not provided a means to adjust the data. Our correction method provides a solution and allows for the seamless use of pre-2011 and post-2011 BRFSS data for research and policy analysis across the US. Our approach provides county health officials with reliable and comparable estimates of cigarette smoking prevalence for males

and females in their jurisdiction and, perhaps more importantly, provides an assessment of trends in the last 17 years to assess whether a county is making as much progress as other similar counties in the US.

Our study reveals dramatic differences in cigarette smoking prevalence across the country that would not be apparent from national estimates or even state-level estimates. Indeed, within-state variation in cigarette smoking sometimes rivals variation seen in the country as a whole. State-level estimates of cigarette smoking prevalence, while useful for beginning to explore differentials within the US and indispensable for informing state-level tobacco control policies, do not provide the same level of resolution as our county estimates and hence mask important local differences in both the current level of smoking prevalence and in trends.

County-level estimates of cigarette smoking prevalence reveal pockets of high-risk populations. Our results support previous studies that have shown that cigarette smoking rates are associated with income, educational achievement, and race/ethnicity.[13,36,37] We find that very high rates of cigarette smoking appear to be a particular problem for poorer communities and those with large populations of Native Americans and Alaska natives, while lower rates of cigarette smoking are found in more affluent counties and counties with large shares of Mexican immigrants. We also find considerable geographic variation, even within states, in smoking prevalence.

Our results support previously reported findings on a decline in the prevalence of cigarette smoking in the US as a whole. However, examining trends at the county level reveals that not all counties have contributed to this decline. In reality, a relatively small proportion of counties (though representing a disproportionately large share of the population) experienced statistically significant declines over this period. We find that rates of decline in smoking prevalence at the county level for men generally exceeded those for women. We also find that declines over this period were related to income: counties in higher income brackets tended to have more rapid declines than counties in lower income brackets.

These findings illustrate the importance of county-level estimates of smoking prevalence. Progress in reducing cigarette smoking will be limited as long as so many communities are left behind. A wide range of effective tobacco control policies and programs have been developed, including excise taxes, smoke-free policies, restriction of tobacco promotion activities, quitline interventions, mass-media advertising campaigns, and policies that reduce the out-of-pocket costs related to cessation treatments.[8,9,38,39] Our estimates uniquely provide the means to assess where existing state-level policies may not be adequately enforced and where new county-level policies may be called for in lieu of or in addition to action at the

state level. Further, as the tobacco industry seeks to maintain or increase sales, marketing of tobacco products is increasingly taking place at the local level.[40] Our county-level estimates provide a means of assessing and tracking the impact of such efforts.

These local, annual measurements of cigarette smoking prevalence can be an important stimulus to local public health decision-making and community engagement. Moreover, our methodology could be used to produce local estimates for other leading risk factors for the burden of disease and incorporated into a scoring system to rank counties in terms of their health performance. These kinds of county health profiles would enable local and state health officials to prioritize and target high-risk counties while spending local, state, and federal funds more wisely on prevention and treatment programs. Maintenance of health profiles over time will also allow tracking progress in confronting major risk factors. Being able to compare counties on a dollar-spent-per-point-reduction in prevalence will create positive competition and allow identification of best practices.

Recent work on global trends in daily smoking prevalence deserves mention despite the difference in definition of smoking prevalence employed (all types of tobacco, not just cigarettes as in the current study).[41] For males, the counties with the lowest daily smoking prevalence are comparable to those countries with the lowest daily smoking prevalence globally: indeed, less than 0.5% of countries have lower male daily smoking prevalence than these counties. At the same time, counties with the highest daily smoking prevalence are comparable to countries with moderately high daily smoking prevalence globally: slightly more than one-third (36.9%) of countries have higher smoking prevalence among men than these counties. For females the comparison is quite different: 48.1% of countries have lower female daily smoking prevalence than the lowest daily smoking prevalence in any county in the US. At the same time, only 1.6% of countries have higher female daily smoking prevalence than the highest daily smoking prevalence among counties in the US.

We have used the BRFSS to develop county-level measurements of cigarette smoking prevalence, and its limitations need to be taken into account when using or interpreting our results. First, the BRFSS is a telephone survey and is subject to bias as a result of excluding the population that has no phone line. This represents a relatively small proportion of the population (less than 2%),[26] however, so the potential for bias is limited. Second, the BRFSS relies on self-reported smoking status and is therefore subject to self-reporting bias, which may vary by sex and by age. Third, while CDC makes BRFSS data available for all respondents in each survey, not all county identifiers are released: in particular, the county identifier for respondents from very small counties is typically masked. In some cases we have been able to obtain data directly from states and recover the county of residence for these respondents. However, we have not been able to do this for all respondents, particularly in recent years,

and consequently are not able to make use of the entire BRFSS dataset in this analysis. Finally, the statistical models that we employ are also subject to error. While we have rigorously validated the model, this validation is internal to the dataset used for modeling—BRFSS—and cannot assess how well the model will perform in the presence of errors or biases in the BRFSS data. While estimates from the NHIS for total smoking are relatively consistent with our modeled estimates based on BRFSS data, there is still room for further research into why these two data sources are not more closely aligned. Further, while the correction method we employ for addressing the exclusion of wireless-only respondents prior to 2011 has the expected effect and brings our estimates of total smoking more closely in line with those from the NHIS, we have not been able to validate this methodology as thoroughly as we have the small area models, nor are we able to verify the assumption that bias due to exclusion of wireless-only respondents has increased linearly with time.

Over the past two decades, states and counties have introduced a number of policies and programs to address the tobacco epidemic. We find, however, that in a troublingly large number of counties there has been relatively little progress in reducing cigarette smoking prevalence. Many areas of the country are still smoking at levels found in previous decades when cigarette smoking was not yet widely recognized as a major risk factor for morbidity and premature mortality. Smoking is a leading cause of death and deserves acute attention by health and medical professionals. Public health is local, and we believe that our study provides the necessary tools to understand and measure patterns of smoking at the local level with existing data.

DECLARATIONS

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

LD-L, AHM, TS, and CJLM developed and applied the model to estimate cigarette smoking prevalence by sex, year, and county. AHM and CJLM designed the overall study and analytical strategy. AF advised on the modeling strategy to adjust for the exclusion of cell phones. AHM and LD-L wrote the first draft. AHM, LD-L, TS, AF, GH, and CJLM revised the paper. All authors have read and approved the final manuscript.

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ADDITIONAL FILE 1

Small area models

We consider four families of logistic regression models for estimating smoking prevalence in each county. The first family, which we call the "naïve" model, contains only an intercept, demographic characteristics, a linear time trend, and county-level random slopes and intercepts:

$$Y_{i,k,t} \sim \text{Binomial}(N_{i,k,t}, p_{i,k,t})$$
$$\text{logit}(p_{i,k,t}) = v_{i,k,t} = \beta^{(0)} + \beta^{(1)} \cdot t + \beta_k^{(2)} + \gamma_i^{(0)} + \gamma_i^{(1)} \cdot t$$

where i indicates county, k indicates demographic group (e.g., age, race, etc.), and t indicates calendar year. This model borrows strength by using all data to estimate the mean level ($\beta^{(0)}$), the effect of certain demographic characteristics (given by the $\beta_k^{(2)}$ terms), and the temporal trends ($\beta^{(1)}$) while still allowing for county-level variation through inclusion of the random intercept ($\gamma_i^{(0)}$) and slope ($\gamma_i^{(1)}$).

The second model family, the "covariate" model, includes everything in the naïve model as well as a series of county-level covariates:

$$\text{logit}\,(p_{i,k,t}) = v_{i,k,t} = \beta^{(0)} + \beta^{(1)} \cdot t + \beta_k^{(2)} + \boldsymbol{\beta}^{(3)} \cdot \boldsymbol{X}_{i,t} + \gamma_i^{(0)} + \gamma_i^{(1)} \cdot t$$

where $\boldsymbol{X}_{i,t}$ is a matrix of county- and state-level covariates and $\boldsymbol{\beta}^{(3)}$ is a vector of regression coefficients corresponding to these covariates. This model borrows strength from external data, making use of variables available at the county level which are related to smoking prevalence. We selected covariates for our model from among those available by performing an exhaustive search: we fit logistic regression models with all combinations of all available covariates and selected the best model based on the Akaike information criterion (AIC). For smoking prevalence, the covariates we selected were proportion of the county population that is black, proportion of the county population that is American Indian or Alaska native, proportion of the county population that is Hispanic, the proportion of the county population that holds a bachelor's degree, the proportion of the county population in poverty, the proportion of the county population that is rural, the county-level number of doctors per capita, the county-level unemployment rate, and the state-level cigarette sales per capita. For daily smoking prevalence the same variables were selected except for unemployment. Details of sources for these variables are available in table S1.

The third model family, the "geospatial" model, includes everything in the naïve model as well as an additional geospatial term which captures spatial information present in the value of the county-level random effects from the naïve model:

$$\text{logit}\,(p_{i,k,t}) = v_{i,k,t} = \beta^{(0)} + \beta^{(1)} \cdot t + \beta_k^{(2)} + \beta^{(4)} \cdot \bar{\delta}_1 + \gamma_i^{(0)} + \gamma_i^{(1)} \cdot t$$

where for each county $\bar{\delta}_1$ is the mean of the estimated $\gamma_i^{(0)}$ for all neighbors (defined by adjacency) from the naïve model. This model borrows strength spatially: we expect that smoking prevalence varies somewhat smoothly in space, so for each county the smoking prevalence of the neighbors is also informative.

The final model family, the 'full' model, includes everything in the previous three models:

$$\text{logit}\,(p_{i,k,t}) = v_{i,k,t} = \beta^{(0)} + \beta^{(1)} \cdot t + \beta_k^{(2)} + \boldsymbol{\beta}^{(3)} \cdot \boldsymbol{X}_{i,t} + \beta^{(4)} \cdot \bar{\delta}_1 + \gamma_i^{(0)} + \gamma_i^{(1)} \cdot t$$

where all variables are defined as above, except that $\bar{\delta}_1$ is calculated based on $\gamma_i^{(0)}$ from the covariate model.

Because we are considering an extended time-period (17 years, from 1996 to 2012), we do not expect that the time trends will be linear over the entire period or that the effect of covariates will necessarily be the same over the entire period. We therefore fit the models using a 'moving window' approach: each model is fit multiple times, using all data in successive, overlapping windows 5 years in length (i.e. 1996–2001, 1997–2002, …, 2008–2012). We then predict for each year using the model centered on that year except for the first two years (1996 and 1997) which use the model fit to the earliest data (1996–2000). In addition to the models fit on 5-year windows, two additional models are fit to just the data from 2011 and 2012 for the purposes of calculating a correction for the omission of cell phones in earlier years, as described in the main text: one that includes all respondents, and one that includes only respondents who can be reached on a landline phone.

We include age in all models as one of the demographic characteristics. Age is grouped into 12 bins: 18–24 years, and then 5-year bins from ages 25 to 74 (i.e. 25–29, 30–34, …, 70–74), and a final bin containing all respondents age 75 and over. We considered inclusion of three other sets of demographic characteristics: race/ethnicity (white non-Hispanic, black non-Hispanic, Hispanic, American Indian or Alaska native, and other), marital status (currently married, formerly married, and never married), and educational attainment (less than high school, high school grad, some college, and college grad). In all four cases, these variables were introduced into the model as a series of indicator covariates where one reference group was absorbed into the overall intercept (age 18–24, white non-Hispanic, formerly married,

and less than HS served as the reference groups). Using the validation methods described in the main text, we tested all four model families with all combinations of including or excluding these three sets of demographic characteristics (race, marital status, and education). The models that included education noticeably outperformed the models that excluded education; models that included race and marital status slightly outperformed models that excluded these variables. We therefore considered only models that included all three sets of demographic characteristics. In addition to these demographic characteristics, models were stratified (fit separately) by sex as smoking patterns are known to differ between males and females.

Based on the fitted values of all parameters we are able to generate predictions for every county, sex, age, race, marital status, educational attainment group in each year. We collapse these estimates to county, sex, and age, by year, by finding the weighted mean of the predictions using the county's population by race, marital status, and educational attainment as the weights (see table S1 for details on the source of these populations). Because county-level populations stratified by all these variables simultaneously are not available, we assume that within a given county, sex, and age group for a given year the distributions of the population by race, by marital status, and by educational attainment are independent of each other. Once we have collapsed the estimates to county, sex, age by year, we age-standardize the estimates using the 2000 census population. State and national estimates for each year are derived by population weighting the county-level estimates in the corresponding year. Similarly, estimates for both sexes combined are a weighted average of the male and female estimates using the observed distribution of the adult population by sex in the 2000 census.

The small area models employed require that we have data from each respondent in the BRFSS on their demographic characteristics (i.e. age, sex, race, marital status, and educational attainment), their county of residence, and their smoking status. Table S2 gives information on the total number of respondents and the number of respondents with complete data in each year of BRFSS data and Additional file 2 gives the number of respondents with complete data available in each county for each year. We perform all analyses on respondents who have complete data on all of the variables listed above.

Table S1. Data Sources.

Data	Use	Source	Notes
County changes	Determining consistent county units of analysis.	Census Bureau[a]	
County adjacencies	Determining neighborhood structure for use in geospatial and full models.	Census Bureau[b]	
Proportion Black, Hispanic, American Indian or Alaska native, and Asian (county-level)	Covariate in covariate and full models.	NCHS Bridged Race Files[c–e]	
Proportion with a college degree (county-level)	Covariate in covariate and full models.	1990 Census,[f] 2000 Census,[g] 2009–2012 American Community Survey (ACS) 5-yr estimates[h]	County-level data are available for 1990, 2000, and 2007–2010. Linear interpolation is used to fill in missing years from 1990 to 2007 and the 2010 values are used for all years after 2010.
Percent rural (county-level)	Covariate in covariate and full models.	1990 Census,[i] 2000 Census,[j] 2010 Census[k]	Linear interpolation was used to fill in intercensal years. 2010 values are used for all years after 2010.
Poverty (county-level)	Covariate in covariate and full models.	Small Area Income and Poverty Estimates (SAIPE)[l]	County-level data are available for 1989, 1993, 1995, and 1997–2012. Linear interpolation was used to fill in missing years from 1990 to 2012.
Doctors per capita (county-level)	Covariate in covariate and full models.	Area Health Resource File (AHRF)[m]	County-level data are available for 1990, 1995, 2000–2008, 2010, and 2011. Linear interpolation was used to fill in missing years from 1990 to 2011 and 2011 values were used for 2011 and 2012. The variable for 'Non-Federal MDs' was used in place of all MDs as this was available for more years.
Unemployment (county-level)	Covariate in covariate and full models.	Local Area Unemployment Statistics (LAUS)[n]	
Cigarette sales per capita (state-level)	Covariate in covariate and full models.	State Tobacco Activities Tracking & Evaluation System (STATE)[o]	
County population by age, sex, and race	Aggregation of model estimates.	NCHS Bridged Race Files[c–e]	

Table S1. Data Sources. (continued)

Data	Use	Source	Notes
County population by age, sex, and marital status	Aggregation of model estimates.	2000 Census,[p] 2009–2012 American Community Survey (ACS) 5-yr estimates[q]	County-level data are available from the census in 2000 and from the 5-year ACS estimates published in 2009–2012, corresponding to estimates in 2007–2010. We use linear interpolation to fill in years between 2000 and 2007 and we use the value in 2000 for all years before 2000 and the value in 2010 for all years after 2010.
County population by age, sex, and educational attainment	Aggregation of model estimates.	2000 Census,[r] 2009–2012 American Community Survey (ACS) 5-yr estimates[s]	County-level data are available from the census in 2000 and from the 5-year ACS estimates published in 2009–2012, corresponding to estimates in 2007–2010. We use linear interpolation to fill in years between 2000 and 2007 and we use the value in 2000 for all years before 2000 and the value in 2010 for all years after 2010.
Phone usage patterns	Aggregation of model estimates in 2011–2012.	Blumberg et al.[t]	Data are available for 2011 only, so the 2011 values are applied to 2011 and 2012. Estimates are available for 93 non-overlapping geographic areas consisting of states, counties, or groups of counties. We apply the estimate for each state, county, or group of counties to all counties in the aggregate.
Age and sex standard	Age standardizing model estimates and combining male and female estimates.	2000 Census[u]	
County and state shape files	Creating maps.	SEER*Stat Bridge[v]	

[a]US Census Bureau. Substantial Changes to Counties and County Equivalent Entities: 1970–Present. Available from: http://www.census.gov/geo/reference/county-changes.html.

[b]US Census Bureau. United States County Adjacency 2010. Available from: http://www.census.gov/geo/reference/county-adjacency.html.

[c]National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC), US Census Bureau. United States Bridged-Race Intercensal Population Estimates 1990–1999. Hyattsville, United States: National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC), 2004. Available from: http://www.cdc.gov/nchs/nvss/bridged_race/data_documentation.htm#july1999.

[d]National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC), US Census Bureau. United States Bridged-Race Intercensal Population Estimates 2000–2009. Hyattsville, United States: National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC), 2012. Available from: http://www.cdc.gov/nchs/nvss/bridged_race/data_documentation.htm#july2009.

[e]National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC), US Census Bureau. United States Vintage 2012 Bridged-Race Postcensal Population Estimates 2010–2012. Hyattsville, United States: National Center for Health Statistics (NCHS), Centers for Disease Control and Preven-

tion (CDC), 2013. Available from: http://www.cdc.gov/nchs/nvss/bridged_race/data_documentation.htm#vintage2012.

[f]US Census Bureau. 1990 US Census, Summary Tape File 3 (STF3), Table P057: Educational Attainment. Available from: http://www2.census.gov/census_1990/1990STF3.html.

[g]US Census Bureau. 2000 US Census, Summary File 3 (SF3), Table DP-2: Profile of Selected Social Characteristics. Generated using American FactFinder: http://factfinder2.census.gov.

[h]US Census Bureau. 2009–2012 American Community Survey 5-year Estimates, Table S1501: Educational Attainment. Generated using American FactFinder: http://factfinder2.census.gov.

[i]US Census Bureau. 1990 US Census, Summary Tape File 1 (STF1), Table H004: Urban and Rural. Available from: http://www2.census.gov/census_1990/1990STF1.html.

[j]US Census Bureau. 2000 US Census, Summary File 1 (SF1), Table H002: Urban and Rural. Generated using American FactFinder: http://factfinder2.census.gov.

[k]US Census Bureau. 2010 US Census, Summary File 1 (SF1), Table H2: Urban and Rural. Generated using American FactFinder: http://factfinder2.census.gov.

[l]US Census Bureau. United States Small Area Income and Poverty Estimates 1989, 1993, 1995, 1997–2012. Washington, DC, United States: US Census Bureau, 2013. Available from: http://www.census.gov/did/www/saipe/data/index.html.

[m]US Department of Health and Human Services, Health Resources and Services Administration. Area Health Resources File 2012–2013. Washington, DC, United States: US Department of Health and Human Services, Health Resource and Services Administration, 2013. Available from: http://arf.hrsa.gov/download.htm.

[n]US Bureau of Labor Statistics. Local Area Unemployment Statistics. 2013. Available from: ftp://ftp.bls.gov/pub/time.series/la/.

[o]Centers for Disease Control and Prevention (CDC). State Tobacco Activities Tracking and Evaluation System, Economics, Cigarette Sales. 2013. Available from: http://apps.nccd.cdc.gov/statesystem/TrendReport/TrendReports.aspx.

[p]US Census Bureau. 2000 US Census, Summary File 3 (SF3), Table PCT007: Sex by Marital Status by Age for the Population 15 Years and Over. Generated using American FactFinder: http://factfinder2.census.gov.

[q]US Census Bureau. 2009–2012 American Community Survey 5-year Estimates, Table B12002: Sex by Marital Status by Age for the Population 15 Years and Over. Generated using American FactFinder: http://factfinder2.census.gov.

[r]US Census Bureau. 2000 US Census, Summary File 3 (SF3), Table PCT025: Sex by Age by Educational Attainment for the Population 18 Years and Over. Generated using American FactFinder: http://factfinder2.census.gov.

[s]US Census Bureau. 2009–2012 American Community Survey 5-year Estimates, Table B15001: Sex by Age by Educational Attainment for the Population 18 Years and Over. Generated using American FactFinder: http://factfinder2.census.gov.

[t]Blumberg SJ, Luke JV, Ganesh, N, Davern ME, Boudreaux MH. Wireless Substitution: State-level Estimates from the National Health Interview Survey, 2010–2011. National Health Statistics Reports. 2012; 61. Available from: http://www.cdc.gov/nchs/data/nhsr/nhsr061.pdf.

[u]US Census Bureau. 2000 US Census, Summary File 1 (SF1), Table QTP1: Age Groups and Sex. Generated using American FactFinder: http://factfinder2.census.gov.

[v]National Cancer Institute. SEER Stat Bridge State and County FIPS Codes 2000–2004. Available from: http://gis.cancer.gov/tools/seerstat_bridge/fips_vars/#sc_2000_2004.

Table S2. BRFSS Data.

Survey year	Total respondents	Missing age	Missing race	Missing education	Missing marital status	Missing county	Missing smoking status	Total respondents included in analysis	Number counties represented
1996	122,268	506 (0.4%)	425 (0.3%)	322 (0.3%)	305 (0.2%)	1,652 (1.4%)	318 (0.3%)	119,154	2,908
1997	133,321	697 (0.5%)	602 (0.5%)	342 (0.3%)	359 (0.3%)	1,324 (1.0%)	348 (0.3%)	130,157	2,951
1998	146,992	656 (0.4%)	707 (0.5%)	409 (0.3%)	393 (0.3%)	2,104 (1.4%)	378 (0.3%)	143,055	3,068
1999	156,937	842 (0.5%)	786 (0.5%)	445 (0.3%)	408 (0.3%)	1,671 (1.1%)	451 (0.3%)	153,077	3,071
2000	180,244	1,105 (0.6%)	1,152 (0.6%)	464 (0.3%)	570 (0.3%)	2,245 (1.2%)	519 (0.3%)	175,014	3,089
2001	205,140	2,119 (1.0%)	2,197 (1.1%)	594 (0.3%)	783 (0.4%)	4,043 (2.0%)	645 (0.3%)	196,163	3,109
2002	240,735	1,883 (0.8%)	2,450 (1.0%)	542 (0.2%)	766 (0.3%)	3,726 (1.5%)	685 (0.3%)	231,936	3,106
2003	257,659	2,002 (0.8%)	2,208 (0.9%)	605 (0.2%)	832 (0.3%)	3,336 (1.3%)	693 (0.3%)	249,194	3,101
2004	299,443	1,977 (0.7%)	2,919 (1.0%)	736 (0.2%)	1,088 (0.4%)	3,868 (1.3%)	990 (0.3%)	289,367	3,106
2005	352,843	2,654 (0.8%)	3,398 (1.0%)	876 (0.2%)	1,307 (0.4%)	4,976 (1.4%)	1,525 (0.4%)	339,974	3,103
2006	349,924	3,339 (1.0%)	3,757 (1.1%)	966 (0.3%)	1,497 (0.4%)	15,942 (4.6%)	1,463 (0.4%)	325,512	2,808
2007	426,347	3,598 (0.8%)	4,211 (1.0%)	1,229 (0.3%)	1,624 (0.4%)	22,815 (5.4%)	1,792 (0.4%)	393,931	2,812
2008	409,031	3,586 (0.9%)	4,270 (1.0%)	1,237 (0.3%)	1,651 (0.4%)	28,805 (7.0%)	1,632 (0.4%)	370,996	2,406
2009	426,925	3,653 (0.9%)	4,737 (1.1%)	1,480 (0.3%)	1,872 (0.4%)	35,303 (8.3%)	2,751 (0.6%)	381,002	2,283
2010	446,200	4,160 (0.9%)	6,256 (1.4%)	1,578 (0.4%)	2,120 (0.5%)	38,949 (8.7%)	2,909 (0.7%)	394,757	2,278
2011	500,550	4,950 (1.0%)	6,102 (1.2%)	1,925 (0.4%)	2,629 (0.5%)	47,842 (9.6%)	2,546 (0.5%)	438,170	2,274
2012	471,340	4,579 (1.0%)	6,279 (1.3%)	1,913 (0.4%)	2,864 (0.6%)	46,406 (9.8%)	9,612 (2.0%)	406,797	2,277
All	5,125,899	42,306 (0.8%)	52,456 (1.0%)	15,663 (0.3%)	21,068 (0.4%)	265,007 (5.2%)	29,257 (0.6%)	4,738,256	3,127

ADDITIONAL FILE 2

BRFSS sample size by county and year, 1996–2012. Available at: https://static-content.springer.com/esm/art%3A10.1186%2F1478-7954-12-5/MediaObjects/12963_2013_235_MOESM2_ESM.xlsx

ADDITIONAL FILE 3

Age-standardized total cigarette smoking prevalence, all counties, 1996–2012. Available at: https://static-content.springer.com/esm/art%3A10.1186%2F1478-7954-12-5/MediaObjects/12963_2013_235_MOESM3_ESM.xlsx

ADDITIONAL FILE 4

Age-standardized daily cigarette smoking prevalence, all counties, 1996–2012. Available at: https://static-content.springer.com/esm/art%3A10.1186%2F1478-7954-12-5/MediaObjects/12963_2013_235_MOESM4_ESM.xlsx

Chapter 3

Drinking patterns in US counties from 2002 to 2012

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ABSTRACT

Objectives

We estimated the prevalence of any drinking and binge drinking from 2002 to 2012 and heavy drinking from 2005 to 2012 in every US county.

Methods

We applied small area models to Behavioral Risk Factor Surveillance System data. These models incorporated spatial and temporal smoothing and explicitly accounted for methodological changes to the Behavioral Risk Factor Surveillance System during this period.

Results

We found large differences between counties in all measures of alcohol use: in 2012, any drinking prevalence ranged from 11.0% to 78.7%, heavy drinking prevalence ranged from 2.4% to 22.4%, and binge drinking prevalence ranged from 5.9% to 36.0%. Moreover, there was wide variation in the proportion of all drinkers who engaged in heavy or binge drinking. Heavy and binge drinking prevalence increased in most counties between 2005 and 2012, but the magnitude of change varied considerably.

Conclusions

There are large differences within the United States in levels and recent trends in alcohol use. These estimates should be used as an aid in designing and implementing targeted interventions and to monitor progress toward reducing the burden of excessive alcohol use.

INTRODUCTION

Excessive alcohol consumption is associated with many adverse health outcomes, including cancer, heart disease, stroke, liver cirrhosis, preterm birth, fetal alcohol syndrome, and unintentional and intentional injuries.[1–7] In 2010, approximately 88,600 deaths in the United States were attributable to alcohol, and the cost of excessive drinking has been estimated to exceed $220 billion per year.[8,9] In the United States, several ongoing surveys collect information on alcohol use. Most of these surveys are designed to produce national-level estimates only, whereas the Behavioral Risk Factor Surveillance System (BRFSS) and the National Survey on Drug Use and Health are designed to produce state-level estimates. More local estimates would be useful for identifying high-risk populations and for policymaking. Below the state level, however, information on alcohol use is limited: existing estimates are generally for select metropolitan areas only[10,11] or are derived by pooling data across a large number of years, making it difficult to assess trends.[12]

We estimated trends in alcohol use at the county level. Specifically, we assessed the prevalence of any drinking (at least 1 drink of any alcoholic beverage in the past 30 days) and 2 measures of excessive alcohol use: the prevalence of heavy drinking (consuming, on average, more than 1 drink per day for women or 2 drinks per day for men in the past 30 days) and the prevalence of binge drinking (consuming at least 4 drinks for women or 5 drinks for men on a single occasion at least once in the past 30 days). We included both heavy and binge drinking because these 2 measures of excessive alcohol consumption are related to different health outcomes: binge drinking tends to increase the risk of short-term health effects (e.g., injuries[6]), whereas heavy drinking tends to increase the risk of long-term health effects (e.g., cancers,[7] liver cirrhosis[5]). Further, whereas most people who are heavy or binge drinkers according to these definitions do not suffer from an alcohol use disorder or alcohol dependence, these behaviors are associated with an elevated risk of developing these conditions.[13,14]

We used small area models to produce annual estimates of any drinking, heavy drinking, and binge drinking prevalence at the county level on the basis of BRFSS data. These models incorporate a series of corrections to account for changes in questionnaire items related to alcohol consumption and for methodological changes regarding cell phones. We also combined these measures to estimate the prevalence of heavy or binge drinking among those who use any alcohol.

METHODS

We used data on alcohol use from the 2002 to 2012 BRFSS.[15] The BRFSS is a telephone survey implemented by state health departments with support from the Centers for Disease Control and Prevention. Details on BRFSS methodology are described elsewhere.[16,17] In 2012 the median response rate among all states was 49.7% and ranged from 33.8% to 64.1%.[18]

The BRFSS includes numerous questions each year that solicit information on alcohol use in the past 30 days; however, the exact questions included vary somewhat from year to year (Figure 1). We assessed any drinking status using the DRNKANY and ALCDAY questions, which reflect whether respondents drank on at least 1 occasion within the past month and the number of days per week or per month on which alcohol was consumed, respectively. We classified respondents as "any drinkers" if they answered "yes" to the DRNKANY question in years when this question was included or if they responded 1 or more days to the ALCDAY question in other years. Estimated prevalence tends to be higher in years when reporting 1 or more days in response to the ALCDAY question is used to define any drinking status than in years when responding "yes" to the DRNKANY question is used. Alcohol use is more likely

Variable name	Year										
	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
DRNKANY	[Excluded]			During the past 30 days, have you had at least one drink of any alcoholic beverage such as beer, wine, a malt beverage or liquor?						[Excluded]	
ALCDAY	A drink of alcohol is 1 can or bottle of beer, 1 glass of wine, 1 can or bottle of wine cooler, 1 cocktail, or 1 shot of liquor. During the past 30 days, how many days per week or per month did you have at least one drink of any alcoholic beverage?			During the past 30 days, how many days per week or per month did you have at least one drink of any alcoholic beverage?						During the past 30 days, how many days per week or per month did you have at least one drink of any alcoholic beverage such as beer, wine, a malt beverage, or liquor?	
AVEDRNK	On the days when you drank, about how many drinks did you drink on the average?			One drink is equivalent to a 12-ounce beer, a 5-ounce glass of wine, or a drink with one shot of liquor. During the past 30 days, on the days when you drank, about how many drinks did you drink on the average?			One drink is equivalent to a 12-ounce beer, a 5-ounce glass of wine, or a drink with one shot of liquor. During the past 30 days, on the days when you drank, about how many drinks did you drink on the average? Note: A 40 ounce beer would count as 3 drinks, or a cocktail drink with 2 shots would count as 2 drinks.				
DRNKGE5	Considering all types of alcoholic beverages, how many times during the past 30 days did you have 5 or more drinks on an occasion?			Considering all types of alcoholic beverages, how many times during the past 30 days did you have X [X = 5 for men, X = 4 for women] or more drinks on an occasion?							
MAXDRNKS	[Excluded]			During the past 30 days, what is the largest number of drinks you had on any occasion?							

Figure 1. Behavioral Risk Factor Surveillance System survey questions on alcohol: United States, 2002–2012.

Note. Vertical lines demarcate years when question text changed. Red is used to highlight the portions of the text unique to a given version of the question.

to be underreported than overreported,[19] so we included a correction in our model to adjust estimates for years when the DRNKANY question is used for consistency with years when the ALCDAY question is used.

We assessed heavy drinking status by first calculating average daily consumption for each respondent; we then classified respondents as "heavy drinkers" if average daily consumption was more than 1 drink per day for women or more than 2 drinks per day for men. Average daily consumption is typically calculated by multiplying the average number of drinking days (reported in the ALCDAY question) by the average number of drinks per drinking day (reported in the AVEDRNK question) and then dividing by 30; however, this method tends to underestimate consumption.[19] Part of this underestimation is thought to be because the respondents reported a number closer to the mode instead of the true mean number of drinks when responding to the AVEDRNK question, effectively missing alcohol consumed on less frequent occasions when a lot of alcohol is consumed at once.

To correct for this, we implemented a method called "indexing"[20] and calculated consumption separately for typical days and for binge days according to the following formula: $(AQ \times AF + BQ \times BF)/30$. AQ represents the typical quantity consumed as given by the AVEDRNK question, whereas BQ represents the quantity consumed on binge drinking days and is given by the MAXDRNKS question. Although the MAXDRNKS question refers to the most drinks consumed in the past 30 days, rather than the average number of drinks on binge drinking days, previous research has shown these 2 quantitates to be comparable.[21] BF is the frequency of binge drinking days and is given by the DRNKGE5 question, whereas the frequency of typical drinking days (AF) is calculated by subtracting DRNKGE5 from ALCDAY.

We assessed binge drinking status using the DRNKGE5 question: we classified respondents who reported 1 or more binge drinking episodes in the past 30 days as "binge drinkers." The cutpoint for binge drinking changed for women in 2006 from 5 drinks to 4 drinks, resulting in a large apparent increase in binge drinking prevalence among women mostly unrelated to actual changes in underlying behavior.[22] To account for this, we included a correction in our model to adjust estimates for women before 2006 for consistency with estimates in later years.

We also extracted county identifiers and demographic characteristics for each respondent, including: gender, age group (21–29 years, 30–39 years, 40–49 years, 50–59 years, 60–69 years, and ≥70 years), race/ethnicity (White non-Hispanic, Black non-Hispanic, American Indian/Alaska Native non-Hispanic, other non-Hispanic, and Hispanic), marital status (formerly married, never married, currently married), and education status (less than high school, high school graduate, some college, college graduate). We excluded respondents who were miss-

ing a county identifier, any of the demographic variables, or the alcohol variables of interest. We analyzed any drinking and binge drinking prevalence for 2002 to 2012, whereas we analyzed heavy drinking prevalence for 2005 to 2012 because the MAXDRNKS question was introduced only in 2005. In 2012 there were 3,143 counties; to address historical boundary changes we combined several counties and performed the analysis on a modified set of 3,127 counties. The final analysis included 3,702,936 respondents for any drinking, 2,867,260 respondents for heavy drinking, and 3,673,679 respondents for binge drinking. (Details on missingness and sample sizes can be found as a supplement to the online version of this article at http://www.ajph.org.)

Model specification

We applied small area models to the BRFSS data to estimate county-level alcohol use prevalence. These models are specified as follows:

$$Y_{i,t,a} \sim \text{Binomial}(N_{i,t,a}, p_{i,t,a})$$

where $N_{i,t,a}$ is the number of respondents and $Y_{i,t,a}$ is the number of alcohol users among these respondents in county i, year t, age group a. The prevalence of alcohol use ($p_{i,t,a}$), the parameter of interest, is modeled as follows:

$$\text{logit}\,(p_{i,t,a}) = \beta_0 + \beta_1 \cdot t + \beta_{2,a} + \boldsymbol{\beta_3} \cdot \boldsymbol{D}_{i,t,a} + \boldsymbol{\beta_4} \cdot \boldsymbol{X}_{i,t} + \beta_5 \cdot l + \nu_i + u_i + w_t + \delta_{i,t}$$

where β_0 is an intercept, β_1 is a slope on year intended to capture large-scale time trends in alcohol use, and $\beta_{2,a}$ is an effect for each age group a (21–29 years is absorbed in the intercept). $\boldsymbol{D}_{i,t,a}$ is a vector of demographic characteristics and includes the proportion of the sample belonging to each race/ethnicity group (except White non-Hispanic), each marital status group (except formerly married), and each education group (except less than high school) as well as interactions between all these factors and age; $\boldsymbol{\beta_3}$ is the corresponding vector of parameters. We included these terms to account for the impact of these demographic factors on county-level alcohol use prevalence.

$\boldsymbol{X}_{i,t}$ is a vector of time-varying county-level variables, and $\boldsymbol{\beta_4}$ is the corresponding vector of parameters. We included county-level variables to "borrow strength" from external data sources. We selected these factors on the basis of literature documenting a relationship with alcohol use as well as availability of appropriate data sources at the county level, and we included percentage of households in rural areas,[23,24] percentage living in poverty,[25] unemployment rate,[26,27] drinking places and alcohol stores per capita,[28,29] and the percentage mainline Protestant, evangelical Protestant, Catholic, or Mormon.[30,31] We did not include state-level alcohol sales (i.e., volume sold) because these estimates are not entirely comparable between states

and over time.[32] (Details on data sources for all covariates can be found as a supplement to the online version of this article at http://www.ajph.org.) $\beta_5 \cdot I$ is included in the any drinking model and the binge drinking model for women only: I is an indicator for the preferred version of the questionnaire item for a given outcome.

The remaining terms in the model account for spatial trends, temporal trends, and space-time interactions beyond what is explained by the demographic variables and county-level covariates and allow borrowing strength over both time and space. v_i and u_i are county-level random effects: v_i is assigned an independent and identically distributed normal prior ($v_i|\sigma_v^2 \sim$ Normal$(0, \sigma_v^2)$) and is intended to capture variation that is not spatially structured, whereas u_i is assigned an intrinsic conditional autoregressive prior,

$$u_i|u_{j,j\sim i}, \sigma_u^2 \sim \text{Normal}\left(\frac{1}{n_i} \cdot \sum_{j\sim i} u_j, \frac{\sigma_u^2}{n_i}\right),$$

where $j \sim i$ indicates that county j is adjacent to county i) and is intended to capture spatially structured variation.[33] w_t is a year-level random effect assigned a first order random walk prior ($w_t|w_{t-1}, \sigma_w^2 \sim$ Normal(w_{t-1}, σ_w^2)) and is intended to capture short-scale non-linear time trends beyond what is accounted for by β_1.[34] Finally, $\delta_{i,t}$ is a county year-level random effect that allows a space-time interaction. This random effect is assigned a prior that is the interaction between an intrinsic conditional autoregressive spatial effect and a first-order random walk temporal effect.[35] (Data available as a supplement to the online version of this article at http://www.ajph.org describe the procedure used for validating this model.)

Model fitting and prediction

We fit separate models for each gender and alcohol use measure. Additionally, to make fitting the models more tractable, we fit separate models for each of 8 census divisions (we combined the middle Atlantic and New England divisions, as they each have a relatively small number of counties).[36] Consequently, 16 models were specified for each of the 3 alcohol metrics.

Models were fit using the INLA program in R version 3.0.1.[37,38] We used proper but diffuse hyperpriors for all terms. Specifically, we used Normal(0, 1,000) hyperpriors for all fixed effects and Gamma(1, 0.01) hyperpriors for the precision parameter of all random effects. We generated 1,000 draws for each county-year-age group from the approximate posterior distribution of the fitted model. For the purposes of generating these draws, we set $D_{i,t,a}$, the vector of demographic variables, at the levels observed in the population rather than in the sample to adjust for differences between the composition of the sample and the underlying population. Similarly, for the any drinking and binge drinking models, we set I to 1 to produce predictions consistent with the preferred version of the questionnaire. We collapsed these draws to the county-year level by age-standardizing using the 2000 census age standard and to the state and national level by first population-weighting the county-level draws and then age-standardizing.

We obtained final estimates by finding the mean of these draws and calculated the confidence intervals (CIs) by finding the 2.5th and 97.5th percentiles. We also estimated the proportion of all drinkers who are heavy drinkers or binge drinkers. To do this we divided the prevalence of heavy drinking and binge drinking by the prevalence of any drinking. To estimate uncertainty we carried out the same procedure using draws and found the 2.5th and 97.5th percentiles.

Accounting for wireless-only respondents

Before 2011 the BRFSS sampled only individuals who could be reached by landline, excluding the population that could be reached only by cell phone that had grown to 27.8% of adults by the second half of 2010.[39] Previous research has shown that excluding individuals who can be reached only by cell phone biases estimates of alcohol use, typically downward, even after controlling for numerous demographic variables related to phone usage patterns.[40] To address this, we applied a previously described correction[41]; in short, we fit 2 versions of every model, 1 that includes only respondents who can be reached by landline, and 1 that includes both landline and cell phone respondents. We then compared county-level estimates for 2011 between the 2 models and used these to derive estimates of the bias introduced by excluding respondents who could be reached only by cell phone. We then projected this bias backward, assuming that the wireless-only population was negligible in 2000 and has increased roughly linearly between 2000 and 2011.

RESULTS

At the national level in 2012, any drinking prevalence was 56.0% (95% CI = 55.6, 56.3), heavy drinking prevalence was 8.2% (95% CI = 8.0, 8.4), and binge drinking prevalence was 18.3% (95% CI = 18.1, 18.6). (Estimates for all counties in all years can be found as a supplement to the online version of this article at http://www.ajph.org.) There was considerable variability within the United States between counties in all 3 measures, however, with any drinking prevalence ranging from 11.0% to 78.7% (SD = 11.6); heavy drinking prevalence ranging from 2.4% to 22.4% (SD = 2.6); and binge drinking prevalence ranging from 5.9% to 36.0% (SD = 5.1). Maps of any, heavy, and binge drinking prevalence in 2012 (Figure 2) depict clear regional patterns. The prevalence of any drinking was relatively high in counties in the northern states of the West and Midwest as well as along the Pacific and in New England. By contrast, any drinking prevalence was much lower in the South and in a region of the West centered on Utah. Geographic patterns for heavy and binge drinking are broadly similar to those for any drinking, although there are localized differences. Although broad geographic patterns encompassing entire states are common, there are frequently sizeable differentials within states: the median gap between highest and lowest county-level prevalence within a state was 27.6, 6.3, and 9.8 percentage points for any, heavy, and binge drinking, respectively.

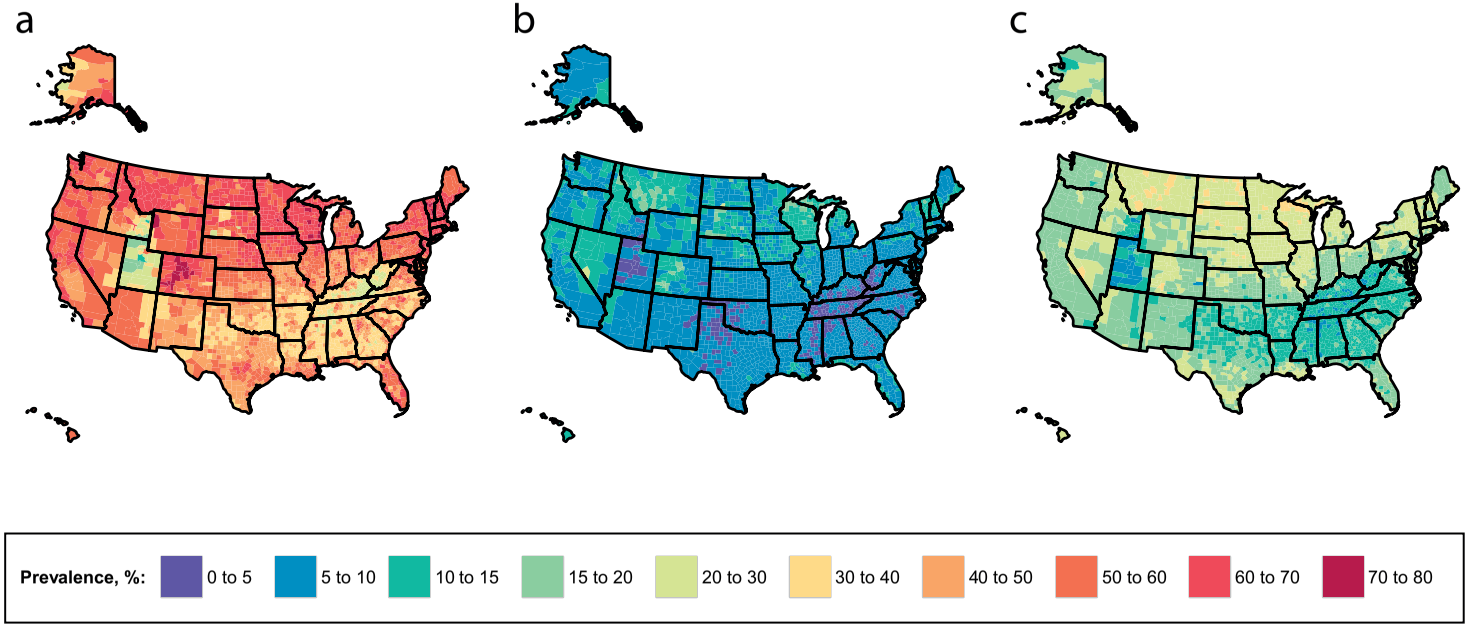

Figure 2. Age-standardized alcohol use prevalence of (a) any drinking, (b) heavy drinking, and (c) binge drinking: Behavioral Risk Factor Surveillance System, United States, 2012.

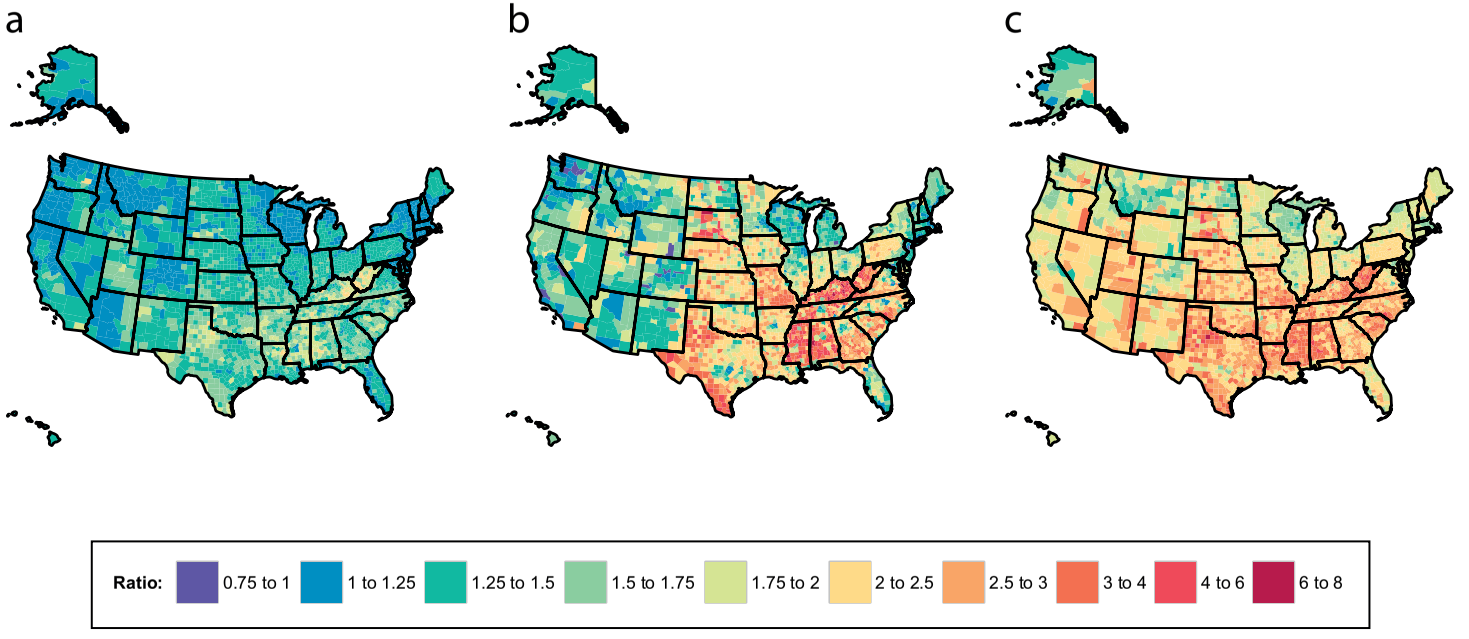

Figure 3. Ratio of male to female age-standardized alcohol use prevalence of (a) any drinking, (b) heavy drinking, and (c) binge drinking: Behavioral Risk Factor Surveillance System, United States, 2012.

By all 3 measures, alcohol use prevalence is typically higher for men than for women (Figure 3). Male and female alcohol use prevalences are most similar for any drinking: across all counties the median ratio of any drinking prevalence among men to any drinking prevalence among women in 2012 was 1.4 and ranged from 1.0 to 2.4. The difference was more dramatic, and also more variable, for heavy drinking: among all counties the median ratio of heavy drinking prevalence among men to heavy drinking prevalence among women was 2.0 and ranged from 0.8 to 7.8. This difference was even larger for binge drinking although it was somewhat less variable: across all counties, the median ratio of binge drinking prevalence among men to binge drinking prevalence among women was 2.3 and ranged from 1.1 to 6.2. In 1.4% of counties for any drinking, 50.4% of counties for heavy drinking, and 69.9% of counties for binge drinking, the prevalence of alcohol use among men was at least twice that among women in 2012.

At the national level in 2012, 14.7% (95% CI = 14.4, 15.1) of all drinkers were heavy drinkers whereas 32.8% (95% CI = 32.3, 33.3) were binge drinkers. As with the other measures of alcohol use, this proportion varies widely between counties (Figure 4), ranging from 5.9% to 66.7% for heavy drinking and 20.2% to 86.2% for binge drinking. Much of this variation occurred within state borders.

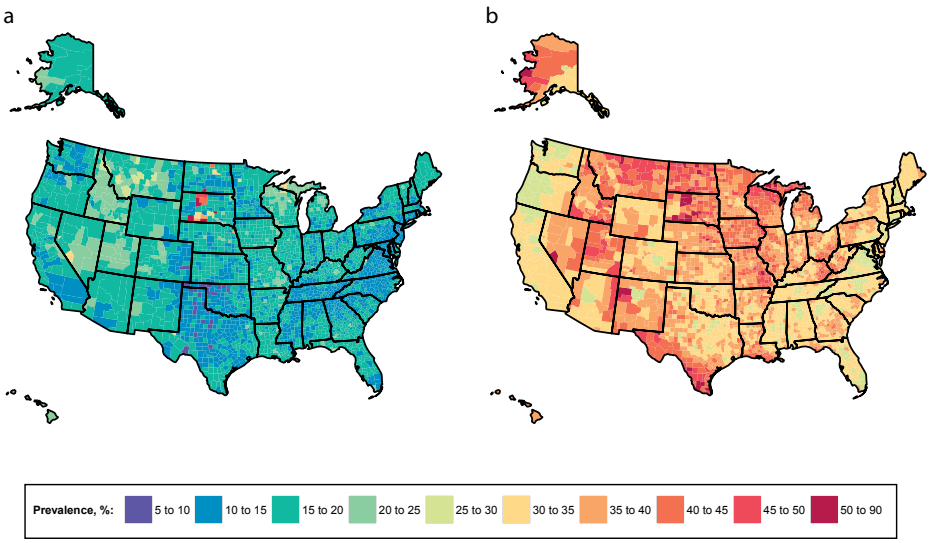

Figure 4. Age-standardized prevalence among all alcohol users of (a) heavy drinking and (b) binge drinking: Behavioral Risk Factor Surveillance System, United States, 2012.

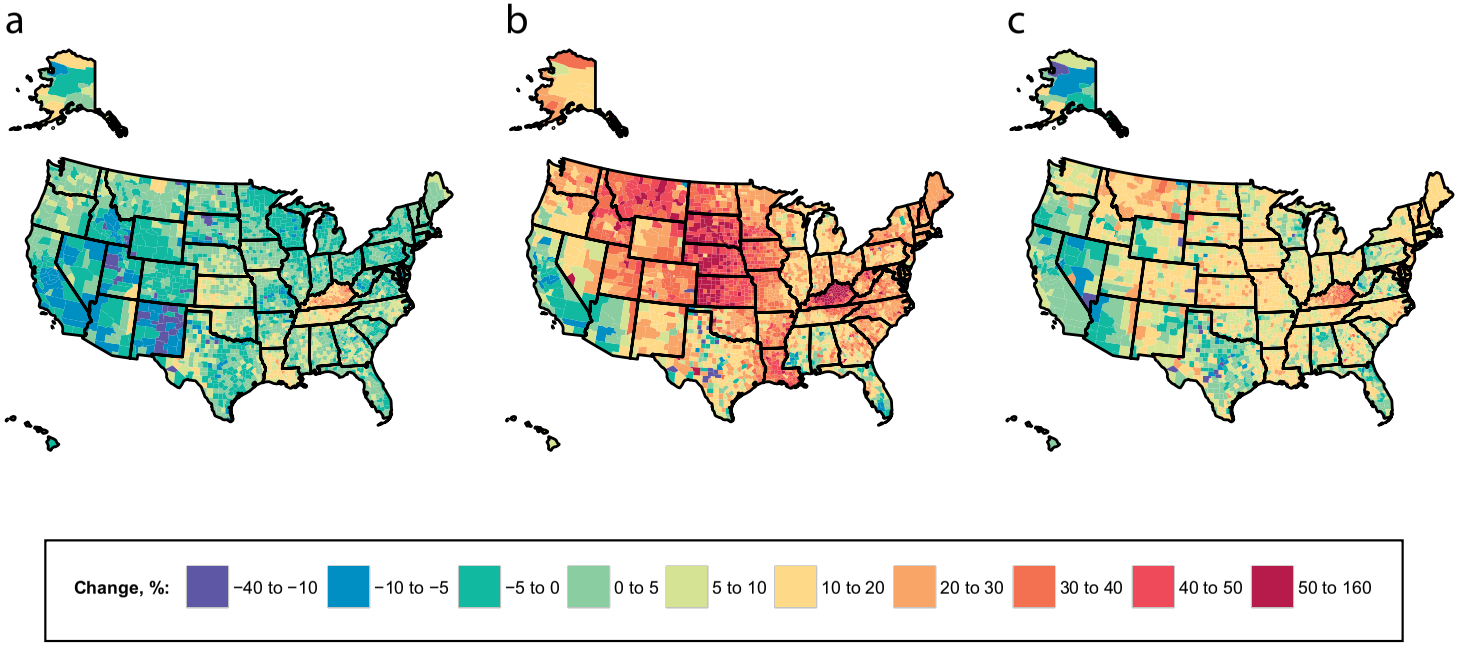

Figure 5. Change in age-standardized alcohol use prevalence of (a) any drinking, (b) heavy drinking, and (c) binge drinking: Behavioral Risk Factor Surveillance System, United States, 2005–2012.

We considered changes for all measures of alcohol use from 2005 to 2012 for consistency across measures. At the national level, we found no change in the prevalence of any drinking, but we found substantial increases for both heavy and binge drinking: a 17.2% (95% CI = 14.2, 20.3) increase from 7.0% (95% CI = 6.9, 7.2) to 8.2% (95% CI = 8.0, 8.4) for heavy drinking and an 8.9% (95% CI = 6.3, 11.6) increase from 16.8% (95% CI = 16.5, 17.2) to 18.3% (95% CI = 18.1, 18.6) for binge drinking. Trends at the county level varied widely for all 3 measures (Figure 5). Although there was little change in any drinking at an aggregate level, at the county level changes ranged from a 25.7% decrease to a 43.5% increase (SD = 6.7). These differentials are even more remarkable for heavy drinking—range −39.2% to 155.2% (SD = 15.9)—and for binge drinking—range −28.7% to 73.4% (SD = 8.3). Changes in heavy and binge drinking were positively correlated with changes in any drinking prevalence (0.48 and 0.64, respectively) and were also highly correlated with each other (0.72).

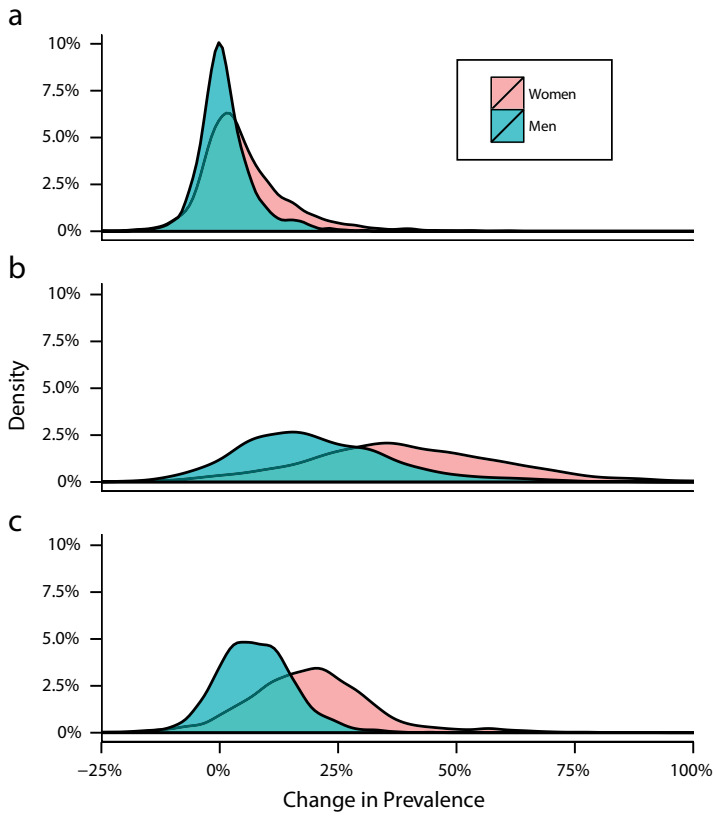

Figure 6. Change in age-standardized alcohol use prevalence, by gender, of (a) any drinking, (b) heavy drinking, and (c) binge drinking: Behavioral Risk Factor Surveillance System, United States, 2005–2012.
Note. Counties with more than 25% decline or more than 100% increase in drinking prevalence are not included.

Changes in alcohol use prevalence were not uniform for men and women. Smoothed density plots of the change from 2005 to 2012 at the county level by gender (Figure 6) demonstrate that the prevalence of all alcohol use measures, but particularly heavy and binge drinking prevalence, tended to increase more for women than for men. The median increase in female heavy and binge drinking prevalence was more than twice the median increase in male heavy and binge drinking prevalence: 38.1% and 18.3%, respectively, for heavy drinking and 18.9% and 7.3%, respectively, for binge drinking.

DISCUSSION

To our knowledge, this analysis is the first to comprehensively report on time trends in alcohol use prevalence at the county level. We found huge variations in drinking patterns among counties, even within a state. Indeed, state-level estimates would have masked the substantial variation between counties within states. Furthermore, we found huge variation among counties in the proportion of heavy or binge drinkers among all individuals who drink currently. Clearly, there is not some fixed proportion of drinkers who are binge or heavy drinkers. Further investigation into why the proportion of those who are heavy or binge drinkers varies so widely is certainly called for.

We found that although the overall prevalence of any drinking has not changed substantially in recent years, there is evidence of an increase in both heavy drinking and binge drinking. Changes in heavy and binge drinking are not evenly distributed throughout the country, however: in this study we identify areas that have experienced particularly dramatic increases in recent years and that warrant particular attention to attempt to reverse these trends. Similarly, we found that increases in heavy and binge drinking prevalence in recent years have tended to be larger for women than for men, although women have not yet caught up to men in terms of current prevalence. These findings call for interventions intended specifically to address this increase among women.

Our study has numerous limitations. The BRFSS is a telephone survey; hence it excludes individuals without a telephone and those living in institutionalized settings. BRFSS response rates are also less than ideal; although we attempted to adjust our estimates to match the demographic composition of the underlying population, there was still the potential for bias because of nonresponse. Additionally, alcohol use is self-reported and typically underreported.[19] Although we have attempted to correct for underreporting, it is likely we did not fully capture all consumption. Further, county identifiers are masked for residents of very small counties; we attempted to obtain data directly from states, but we were not able to do this for all respondents.

Finally, although this analysis does explicitly correct for changes in the questions used to elicit data on alcohol use patterns, as well as the omission of cell phones from the BRFSS sample before 2011, it is difficult to validate these corrections and results on changes over time should be interpreted with caution. However, because we attempted to bring estimates in line with the methods employed by BRFSS in 2011 and 2012, our 2011 and 2012 estimates are not subject to this limitation.

Despite these limitations, our analysis boasts numerous unique strengths. Our small area model simultaneously borrows strength spatially, temporally, and from external data sources included as covariates to improve predictions for all areas, even those with limited sample sizes. We also explicitly addressed numerous known issues with the BRFSS data on alcohol. We corrected for the underreporting of alcohol consumption, which allowed us to more accurately estimate heavy drinking prevalence. We also adjusted for the change in the cutpoint used to define binge drinking for women, which allowed us to produce estimates back to 2002 that are consistent with the currently accepted definition of binge drinking. Finally, we corrected for the bias introduced by omitting individuals who could be reached only by cell phone before 2011 from the BRFSS sampling frame. Collectively, these additional methods allowed us to improve the accuracy of our estimates and to produce a more cogent time series.

Excessive consumption of alcohol is a major risk factor for morbidity and mortality. Many effective interventions and strategies to reduce alcohol consumption and related harm are policy based and can be implemented at state and local levels.[42,43] As drinking patterns vary widely between and within states, county-level estimates are essential for identifying areas of greatest need and informing efforts to reduce excessive alcohol use. We believe that the methods and results we have presented provide an important tool to local public health officials and others seeking to reduce the loss of health and life because of excessive alcohol use.

Contributors

L. Dwyer-Lindgren, A. D. Flaxman, M. Ng, and A. H. Mokdad developed and applied the model. L. Dwyer-Lindgren, G. M. Hansen, and A. H. Mokdad performed the literature review. L. Dwyer-Lindgren and A. H. Mokdad wrote the first draft. A. D. Flaxman and C. J. L. Murray advised on the modeling strategy. C. J. L. Murray and A. H. Mokdad designed the overall study and the analytical strategy. All authors revised the article and approved the final draft.

Acknowledgments

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Human participant protection

Institutional review board approval was not required for this study because data were obtained from secondary sources.

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SUPPLEMENTAL FILES

Table S1. BRFSS Sample Size and Missingness.

Year	Respondents, age 21+[a]	Missingness							Complete observations[b]			Counties represented
		Race	Education	Marital status	County	Any drinking	Heavy drinking	Binge drinking	Any drinking	Heavy drinking	Binge drinking	
2002	232,433	2,164 (0.9%)	422 (0.2%)	550 (0.2%)	3,358 (1.4%)	1,255 (0.5%)	NA	1,851 (0.8%)	225,111 (96.8%)	NA	224,561 (96.6%)	3,104
2003	249,248	1,958 (0.8%)	492 (0.2%)	631 (0.3%)	3,001 (1.2%)	1,051 (0.4%)	NA	1,436 (0.6%)	242,581 (97.3%)	NA	242,198 (97.2%)	3,099
2004	290,960	2,595 (0.9%)	610 (0.2%)	832 (0.3%)	3,496 (1.2%)	1,761 (0.6%)	NA	1,958 (0.7%)	282,292 (97.0%)	NA	282,111 (97.0%)	3,106
2005	343,733	3,040 (0.9%)	740 (0.2%)	1,016 (0.3%)	4,500 (1.3%)	3,359 (1.0%)	13,413 (3.9%)	6,001 (1.7%)	331,823 (96.5%)	322,300 (93.8%)	329,349 (95.8%)	3,103
2006	340,690	3,284 (1.0%)	797 (0.2%)	1,096 (0.3%)	15,155 (4.4%)	5,190 (1.5%)	17,173 (5.0%)	9,184 (2.7%)	316,711 (93.0%)	305,770 (89.8%)	313,070 (91.9%)	2,808
2007	416,240	3,718 (0.9%)	1,048 (0.3%)	1,238 (0.3%)	21,855 (5.3%)	6,058 (1.5%)	19,886 (4.8%)	10,791 (2.6%)	384,573 (92.4%)	372,051 (89.4%)	380,294 (91.4%)	2,812
2008	399,648	3,753 (0.9%)	1,049 (0.3%)	1,249 (0.3%)	27,871 (7.0%)	4,041 (1.0%)	17,001 (4.3%)	8,512 (2.1%)	364,463 (91.2%)	352,887 (88.3%)	360,508 (90.2%)	2,406
2009	417,586	4,180 (1.0%)	1,277 (0.3%)	1,461 (0.3%)	33,964 (8.1%)	10,161 (2.4%)	21,814 (5.2%)	14,176 (3.4%)	370,556 (88.7%)	360,337 (86.3%)	367,069 (87.9%)	2,304
2010	436,549	5,574 (1.3%)	1,337 (0.3%)	1,639 (0.4%)	37,478 (8.6%)	6,390 (1.5%)	20,237 (4.6%)	11,362 (2.6%)	388,049 (88.9%)	375,969 (86.1%)	383,747 (87.9%)	2,298
2011	486,820	5,365 (1.1%)	1,644 (0.3%)	1,996 (0.4%)	45,501 (9.3%)	34,184 (7.0%)	44,107 (9.1%)	37,072 (7.6%)	405,371 (83.3%)	396,775 (81.5%)	402,864 (82.8%)	2,294
2012	457,002	5,482 (1.2%)	1,578 (0.3%)	2,170 (0.5%)	44,340 (9.7%)	17,304 (3.8%)	29,121 (6.4%)	21,343 (4.7%)	391,406 (85.6%)	381,171 (83.4%)	387,908 (84.9%)	2,277
Total	4,070,909	41,113 (1.0%)	10,994 (0.3%)	13,878 (0.3%)	240,519 (5.9%)	90,754 (2.2%)	182,752 (5.5%)	123,686 (3.0%)	3,702,936 (91.0%)	2,867,260 (86.9%)	3,673,679 (90.2%)	3,127

[a]This total does not include respondents with a missing value for age.

[b]These columns give the total number of usable observations for each outcome. These are respondents who have non-missing values for race, education, marital status, county, the given alcohol variable, and, for 2011–2012 only, phone usage.

Table S2. Additional Data Sources.

Data	Use	Source	Notes
County changes	Determining consistent county units of analysis	Census Bureau[a]	
County adjacencies	Determining neighborhood structure to use for spatial random effects	Census Bureau[b]	
Percent rural (county-level)	Covariate	2000 Census,[c] 2010 Census[d]	Linear interpolation was used to fill in intercensal years. 2010 values are used for all years after 2010.
Poverty (county-level)	Covariate	Small Area Income and Poverty Estimates (SAIPE)[e]	
Unemployment (county-level)	Covariate	Local Area Unemployment Statistics (LAUS)[f]	
Drinking places (county-level)	Covariate	County business patterns[g]	Businesses classified as 'Drinking Places (Alcoholic Beverages)' (NAICS code 722410). Data are available for 2002–2011. 2011 values are used for 2012.
Alcohol stores (county-level)	Covariate	County business patterns[g]	Businesses classified as 'Beer, Wine, and Liquor Stores' (NAICS code 445310). Data are available for 2002–2011. 2011 values are used for 2012.
Religious adherents (county-level)	Covariate	Religious Congregations and Membership Study[h,i]	Data are available for 2000 and 2010. Linear interpolation was used to fill in values between 2000 and 2010. 2010 values are used for all years after 2010.
County population by age, sex, and race	Prediction (adjusting for differences in demographic composition of the sample compared to the underlying population)	NCHS Bridged Race Files[j,k]	
County population by age, sex, and marital status	Prediction (adjusting for differences in demographic composition of the sample compared to the underlying population)	2000 Census,[l] 2009–2012 American Community Survey (ACS) 5-yr estimates[m]	County-level data are available from the census in 2000 and from the 5-year ACS estimates published in 2009–2012, corresponding to estimates in 2007–2010. We use linear interpolation to fill in years between 2000 and 2007 and we use the value in 2010 for all years after 2010.

Table S2. Additional Data Sources. (continued)

Data	Use	Source	Notes
County population by age, sex, and educational attainment	Prediction (adjusting for differences in demographic composition of the sample compared to the underlying population)	2000 Census,[n] 2009–2012 American Community Survey (ACS) 5-yr estimates[o]	County-level data are available from the census in 2000 and from the 5-year ACS estimates published in 2009–2012, corresponding to estimates in 2007–2010. We use linear interpolation to fill in years between 2000 and 2007 and we use the value in 2010 for all years after 2010.
Phone usage patterns	Prediction (adjusting for differences in composition of the sample compared to the underlying population)	Blumberg et al.[p,q]	Estimates are available for 93 non-overlapping geographic areas consisting of states, counties, or groups of counties. We apply the estimate for each state, county, or group of counties to all counties in the aggregate.
Age and sex standard	Age standardizing estimates and combining male and female estimates	2000 Census[r]	
County and state shape files	Creating maps	SEER*Stat Bridge[s]	

[a]US Census Bureau. Substantial Changes to Counties and County Equivalent Entities: 1970–Present. Available from: http://www.census.gov/geo/reference/county-changes.html.

[b]US Census Bureau. United States County Adjacency 2010. Available from: http://www.census.gov/geo/reference/county-adjacency.html.

[c]US Census Bureau. 2000 US Census, Summary File 1 (SF1), Table H002: Urban and Rural. Generated using American FactFinder: http://factfinder2.census.gov.

[d]US Census Bureau. 2010 US Census, Summary File 1 (SF1), Table H2: Urban and Rural. Generated using American FactFinder: http://factfinder2.census.gov.

[e]US Census Bureau. United States Small Area Income and Poverty Estimates 2002–2012. Washington, DC, United States: US Census Bureau, 2013. Available from: http://www.census.gov/did/www/saipe/data/index.html.

[f]US Bureau of Labor Statistics. Local Area Unemployment Statistics. 2013. Available from: ftp://ftp.bls.gov/pub/time.series/la/.

[g]US Census Bureau. United States County Business Patterns 2002–2011. Washington, D.C., United States: US Census Bureau. Available from: www.census.gov/econ/cbp/download/.

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Table S3. Model performance as measured by concordance correlation.

Alcohol use measure	Sex	Sample size			
		10	50	100	In sample
Any drinking	Males	0.91	0.93	0.94	0.95
	Females	0.94	0.96	0.97	0.98
Heavy drinking	Males	0.57	0.66	0.72	0.78
	Females	0.67	0.75	0.77	0.83
Binge drinking	Males	0.68	0.76	0.80	0.84
	Females	0.71	0.75	0.78	0.81

Table S4. Model performance as measured by the root mean squared error.[a]

Alcohol use measure	Sex	Sample size			
		10	50	100	In sample
Any drinking	Males	3.32	2.88	2.68	2.47
	Females	3.43	2.88	2.56	2.23
Heavy drinking	Males	2.06	1.86	1.72	1.55
	Females	1.47	1.33	1.27	1.13
Binge drinking	Males	3.11	2.70	2.50	2.22
	Females	2.08	1.90	1.80	1.68

[a]Root mean squared error is expressed in terms of percentage points.

Model validation

We used previously developed validation methods[1] to assess the performance of the small area models. Our approach was as follows: for each sex we selected counties with at least 900 survey respondents between 2006 and 2010. We refer to these counties as the "validation set". For each county in the validation set we calculated a "gold standard" estimate of alcohol use for 2008 by pooling the available data over the period 2006 to 2010. We then created new datasets by generating random samples from counties in the validation set of size 10, 50, and 100 respondents per year. Each sample size was repeated 10 times, for a total of 30 "sampled-down" datasets. The model was fit on all 30 of these sampled-down datasets and used to estimate prevalence for each county in the validation set for 2008. The resulting prevalence estimates were then compared to the gold standard. We measured model performance using the concordance correlation coefficient (table S3), which is a measure of the agreement between the model predictions and the gold standard, and the root mean squared error (table S4), a measure of the magnitude of the deviation between the model predictions and the gold standard, expressed in the same units as the predictions. In both cases, the reported value for each sample size is the median across all 10 repetitions.

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Chapter 4

Diagnosed and undiagnosed diabetes prevalence by county in the U.S., 1999–2012

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ABSTRACT

Objective

Previous analyses of diabetes prevalence in the U.S. have considered either only large geographic regions or only individuals in whom diabetes had been diagnosed. We estimated county-level trends in the prevalence of diagnosed, undiagnosed, and total diabetes as well as rates of diagnosis and effective treatment from 1999 to 2012.

Research design and methods

We used a two-stage modeling procedure. In the first stage, self-reported and biomarker data from the National Health and Nutrition Examination Survey (NHANES) were used to build models for predicting true diabetes status, which were applied to impute true diabetes status for respondents in the Behavioral Risk Factor Surveillance System (BRFSS). In the second stage, small area models were fit to imputed BRFSS data to derive county-level estimates of diagnosed, undiagnosed, and total diabetes prevalence, as well as rates of diabetes diagnosis and effective treatment.

Results

In 2012, total diabetes prevalence ranged from 8.8% to 26.4% among counties, whereas the proportion of the total number of cases that had been diagnosed ranged from 59.1% to 79.8%, and the proportion of successfully treated individuals ranged from 19.4% to 31.0%. Total diabetes prevalence increased in all counties between 1999 and 2012; however, the rate of increase varied widely. Over the same period, rates of diagnosis increased in all counties, while rates of effective treatment stagnated.

Conclusions

Our findings demonstrate substantial disparities in diabetes prevalence, rates of diagnosis, and rates of effective treatment within the U.S. These findings should be used to target high-burden areas and select the right mix of public health strategies.

INTRODUCTION

Diabetes mellitus is a leading cause of death and poor health in the U.S. In 2013, diabetes was responsible for 74.9 thousand deaths (the seventh leading cause of death) and 1.85 million years lived with disability (the eighth leading cause of disability).[1,2] Diabetes also exerts a large and rapidly increasing burden on the U.S. economy, with total costs in 2012 estimated at $245 billion.[3]

In addition to medical strategies for identifying and managing diabetes, there are a number of evidence-based public health strategies aimed at primary prevention, screening, and improved disease management.[4,5] Effectively and efficiently deploying these strategies, especially given financial constraints and competing priorities, requires detailed local information about diabetes burden. This information can be used to define the scope of the problem as well as to identify high-need areas. In particular, information about both diagnosed and undiagnosed cases is essential in order to fully appreciate the population that is in need of services. Similarly, local information about rates of diagnosis and effective treatment are important inputs for determining the right mix of strategies to address the diabetes burden of a particular community.

National trends in diabetes prevalence are typically based on the National Health and Nutrition Examination Survey (NHANES).[6] The NHANES comprises both an interview and a laboratory component, which includes collecting biomarkers for diabetes. This allows researchers to use NHANES data to describe trends in diagnosed and undiagnosed diabetes, as well as rates of diagnosis and effective treatment, but only at the national level. State and local trends,[7–9] in contrast, are typically derived from the Behavioral Risk Factor Surveillance System (BRFSS),[10] which has a much larger sample size and more comprehensive geographic coverage than the NHANES. The BRFSS does not include any biomarkers, however, and can only be used to track diagnosed diabetes prevalence.

Most local health departments are organized by county or groups of counties;[11] however; only trends in diagnosed diabetes are available at this level.[7–9] We combined NHANES and BRFSS data in order to estimate county-level prevalence of both diagnosed and undiagnosed diabetes in adults ≥20 years of age for each year from 1999 to 2012. We also calculated several derived measures, including the proportion of diabetes case patients who have received a diagnosis and the proportion of case patients who have been effectively treated.

RESEARCH DESIGN AND METHODS

Overview

For this analysis we used a two-stage approach to estimate five measures of diabetes prevalence (Table 1). In the first stage, we used NHANES data to fit a model for predicting high fasting plasma glucose (FPG) levels (≥126 mg/dL) and/or A1C levels (≥6.5% [48 mmol/mol])[12] on the basis of self-reported demographic and behavioral characteristics. We then applied this model to BRFSS data to impute high FPG and/or A1C status for each BRFSS respondent. In the second stage, we used the imputed BRFSS data to fit a series of small area models, which were used to predict the county-level prevalence of each of the five diabetes-related outcomes.

Table 1. Outcome measure definitions.

Measure	Definition
Diagnosed diabetes prevalence	The proportion of adults ≥20 years of age who report a previous diabetes diagnosis.
Undiagnosed diabetes prevalence	The proportion of adults ≥20 years of age who do not report a previous diabetes diagnosis and who have high FPG/A1C.[a]
Total diabetes prevalence	The proportion of adults ≥20 years of age who report a previous diabetes diagnosis and/or have high FPG/A1C;[a] total diabetes prevalence is equal to the sum of diagnosed and undiagnosed diabetes prevalence.
Diabetes awareness	The proportion of adults ≥20 years of age with a previous diabetes diagnosis and/or high FPG/A1C[a] who have received a diagnosis; diabetes awareness is equal to the ratio of diagnosed to total diabetes prevalence.
Diabetes control	The proportion of adults ≥20 years of age with a previous diabetes diagnosis and/or high FPG/A1C[a] who currently do not have high FPG/A1C.[a]

[a]FPG ≥126 mg/dL and/or A1C ≥6.5% (48 mmol/mol).

Data

This analysis used NHANES and BRFSS data from 1999 to 2012. Over this period, the NHANES subsample that contains FPG measurement included 17,375 respondents ≥20 years of age; 15,600 of these respondents (89.8%) had no missing values for any of the relevant variables and were incorporated into this analysis. Over the same period, the BRFSS included 4,620,693 respondents ≥20 years of age; of these, 4,107,972 respondents (88.9%) had no missing values for any relevant variable and were included in this analysis. Several additional data sources were used, either as covariates in the small area models or for poststratification of estimates, as described below. Further details on all data sources are provided in the Supplementary Data.

High FPG/A1C models

Following Danaei et al.[13] and Olives et al.,[14] we developed respondent-level logistic regression models for predicting high FPG and/or A1C status (referred to hereafter as "high FPG/A1C"). Using NHANES data, the following model was fit separately for males and females, and for individuals who had previously received a diagnosis and had not received a diagnosis:

$$Y_i \sim \text{Bernoulli}(p_i)$$
$$\text{logit}(p_i) = \beta_0 + \beta_{1,a_i} + \beta_{2,r_i} + \beta_{3,e_i} + \beta_{4,m_i} + \beta_5 \cdot BMI_i + \beta_6 \cdot BMI_i^2 + \beta_7 \cdot H_i + \beta_8 \cdot S_i$$

where Y_i is 1 if individual i has high FPG/A1C and 0 otherwise; a_i, r_i, e_i, m_i, BMI_i, and BMI_i^2 are individual i's age group (20–29, 30–39, 40–49, 50–59, 60–69, 70+ years), race/ethnicity (white, black, Hispanic, other), education status (less than high school, high school graduate, some college, college graduate), marital status (currently married, formerly married, never married), BMI, and squared BMI, respectively; and H_i and S_i are indicators for whether or not individual i has health insurance and is a current smoker, respectively.

The fitted logistic regression models were used to impute current (at the time of survey) high FPG/A1C status for each BRFSS respondent. Ten separate imputed data sets were created using simulation methods[15] to reflect the uncertainty in each BRFSS respondent's true high FPG/A1C status.

The predictive accuracy of this model was assessed using cross-validation, as described in the Supplementary Data. The model was found to have high concordance overall—it correctly predicted high FPG/A1C status for ~9 of 10 respondents—however, the sensitivity (i.e., the proportion of true case patients identified) was relatively low (11.2–13.2%, depending on sex and previous diagnosis).

Small area models

Small area models were developed to estimate county-level diagnosed diabetes prevalence, undiagnosed diabetes prevalence, and uncontrolled (diagnosed and with high FPG/A1C) diabetes prevalence based on imputed BRFSS data. These models are designed to borrow strength across space and time, and from external information in the form of covariates in order to generate more precise estimates than those calculated directly from the small samples available in most counties.

Each of these models was specified as follows:

$$Y_{j,t,a,r,m,e} \sim \text{Binomial}(p_{j,t,a,r,m,e}, N_{j,t,a,r,m,e})$$
$$\text{logit}(p_{j,t,a,r,m,e}) = \beta_0 + \beta_{1,a} + \beta_{2,r} + \beta_{3,m} + \beta_{4,e} + \boldsymbol{\beta_5} \cdot \boldsymbol{X_{j,t}} + u_j + w_t + d_{j,t}$$

where $N_{j,t,a,r,m,e}$, $Y_{j,t,a,r,m,e}$, and $p_{j,t,a,r,m,e}$ are the number of individuals sampled, the number of case patients among those sampled, and the true prevalence, respectively, in county j, year t, age group a, race/ethnicity group r, marital status group m, and education group e; β_0 is the global intercept; $\beta_{1,a}$ values are age group effects (20–29, 30–39, 40–49, 50–59, 60–69, and 70+ years); $\beta_{2,r}$ values are race/ethnicity effects (Hispanic, white non-Hispanic, black non-Hispanic, native non-Hispanic, and other non-Hispanic); $\beta_{3,m}$ values are marital status effects (currently married, formerly married, and never married); $\beta_{4,e}$ values are education effects (less than high school, high school graduate, some college, and college graduate); and $\boldsymbol{\beta_5}$ is a vector of effects for three county-year-level covariates ($\boldsymbol{X_{j,t}}$) (percentage of individuals living in poverty, percentage of rural households, and the number of doctors per capita). u_j and w_t are county- and year-level random effects, respectively, both of which are assumed to follow a conditional autoregressive distribution.[16] $d_{j,t}$ is a county-year-level random effect that is also assumed to follow a conditional autoregressive distribution.[17] Separate models were fit for males and females, and the procedure described by Dwyer-Lindgren et al.[18] was used to correct for noncoverage bias in BRFSS data prior to 2011 when a cell phone sample was introduced.[19]

Models were fit using the Template Model Builder package[20] in R version 3.2.4.[21] Simulation methods[15] were used generate 1,000 draws of diagnosed, undiagnosed, and uncontrolled diabetes prevalence from the fitted small area models. These draws were poststratified by race, marital status, and education and then age standardized. Point estimates were calculated from the mean of these 1,000 draws, whereas 95% uncertainty intervals were calculated from the 2.5th and 97.5th percentiles. Estimates of total diabetes prevalence, diabetes awareness, and diabetes control were derived from the directly modeled quantities as follows: total = diagnosed + undiagnosed; awareness = diagnosed/total; control = 1 − uncontrolled/total. State- and national-level estimates of all quantities were derived by population weighting of county-level estimates.

Finally, in order to account for the uncertainty arising from using imputed data in the models for undiagnosed and uncontrolled diabetes, the entire procedure described above was repeated for each of 10 imputed data sets. Estimates were combined across data sets, and uncertainty intervals were recalculated to take into account the variation between the imputed data sets as well as the uncertainty from the small area models.[22]

The predictive accuracy of this small area model was assessed with reference to diagnosed diabetes using empirical validation methods, as described in the Supplementary Data. In general, model predictions were found to have lower error and bias for counties with larger sample sizes. However, even for counties where only a single individual was sampled each

year, the mean error (a measure of bias) was –0.3 percentage points, while the mean absolute error (a measure of precision) was 1 percentage point.

RESULTS

Diabetes prevalence in 2012

Age-standardized diagnosed diabetes prevalence for the U.S. as a whole was 10.2% (95% uncertainty interval 10.1%, 10.4%) in 2012, whereas undiagnosed diabetes prevalence was 4.1% (3.6%, 4.5%), resulting in a total diabetes prevalence of 14.3% (13.8%, 14.7%). Among counties, diagnosed diabetes prevalence ranged from 5.6% to 20.4%, undiagnosed diabetes prevalence ranged from 3.2% to 6.8%, and total diabetes prevalence ranged from 8.8% to 26.4%. Figure 1 shows age-standardized diagnosed, undiagnosed, and total diabetes prevalence by county in 2012. Diagnosed diabetes prevalence was highest among counties in the deep South (excluding Florida), near the Texas-Mexico border, and in counties with Native American reservations in the four corners region of the Southwest and in North and South Dakota. In contrast, diagnosed diabetes prevalence was lowest among counties in the upper West and Midwest, parts of Alaska, and parts of New England. Undiagnosed diabetes prevalence similarly tended to be high among counties in the deep South, but also among counties in the Southwest and Alaska, whereas counties in New England and the upper West and Midwest tended to have lower undiagnosed diabetes prevalence. In both cases, there was significant variation among counties within as well as across states. At the county level, diagnosed and undiagnosed diabetes prevalence were positively correlated (Pearson correlation coefficient 0.77), but more so for women (0.73) than for men (0.57).

At the national level, diagnosed diabetes prevalence was marginally higher among men (10.6% [10.4%, 10.8%]) than among women (9.9% [9.7%, 10.0%]), and undiagnosed diabetes prevalence was substantially higher among men (5.0% [4.5%, 5.5%]) than among women (3.2% [2.5%, 3.8%]). Consequently, at the national level total diabetes prevalence was also higher among men (15.6% [15.1%, 16.2%]) than among women (13.0% [12.3%, 13.7%]), a pattern that was reflected in 95.1% of counties.

Nationally, diabetes awareness was 71.6% (69.5%, 73.7%) in 2012, but varied by county, ranging from 59.1% to 79.8%. Similarly, whereas at the national level 26.9% (23.3%, 30.6%) of individuals who had previously received a diagnosis of diabetes had brought their diabetes under control (i.e., FPG <126 mg/dL and A1C <6.5% [48 mmol/mol]), this ranged from 19.4% to 31.0% at the county level. Figure 2 depicts age-standardized diabetes awareness and control at the county level. Awareness was highly correlated with total diabetes prevalence (Pearson correlation coefficient 0.77) and tended to be highest in counties in the South and

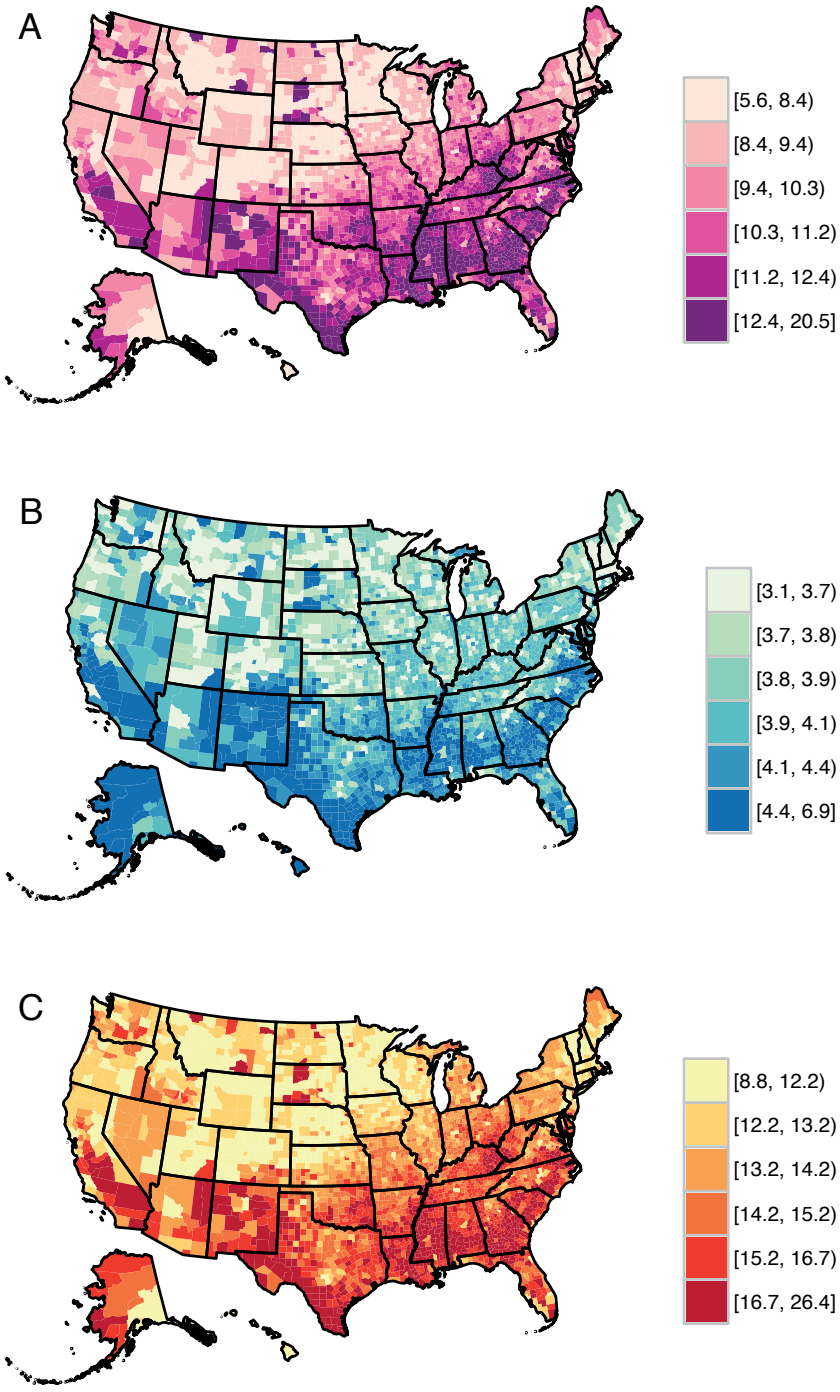

Figure 1. Age-standardized diabetes prevalence by county, 2012. A: Diagnosed diabetes prevalence. B: Undiagnosed diabetes prevalence. C: Total diabetes prevalence.

in eastern Kentucky and West Virginia; and lowest in counties in the upper West and Midwest, Alaska, and parts of New England. In contrast, there was a small negative correlation between control and total diabetes prevalence (Pearson correlation coefficient –0.08). Control tended to be highest among counties in the deep South and along the Atlantic coast; and lowest among counties in the West, Southwest, and Alaska. At the national level, both awareness and control were higher for women than for men (75.7% [72.0%, 79.4%] vs. 68.0% [65.8%, 70.1%] for awareness; 30.7% [26.5%, 35.0%] vs. 23.2% [17.6%, 28.7%] for control), a pattern that was reflected in nearly all counties.

County-level estimates of all outcomes in all years are available from the authors upon request.

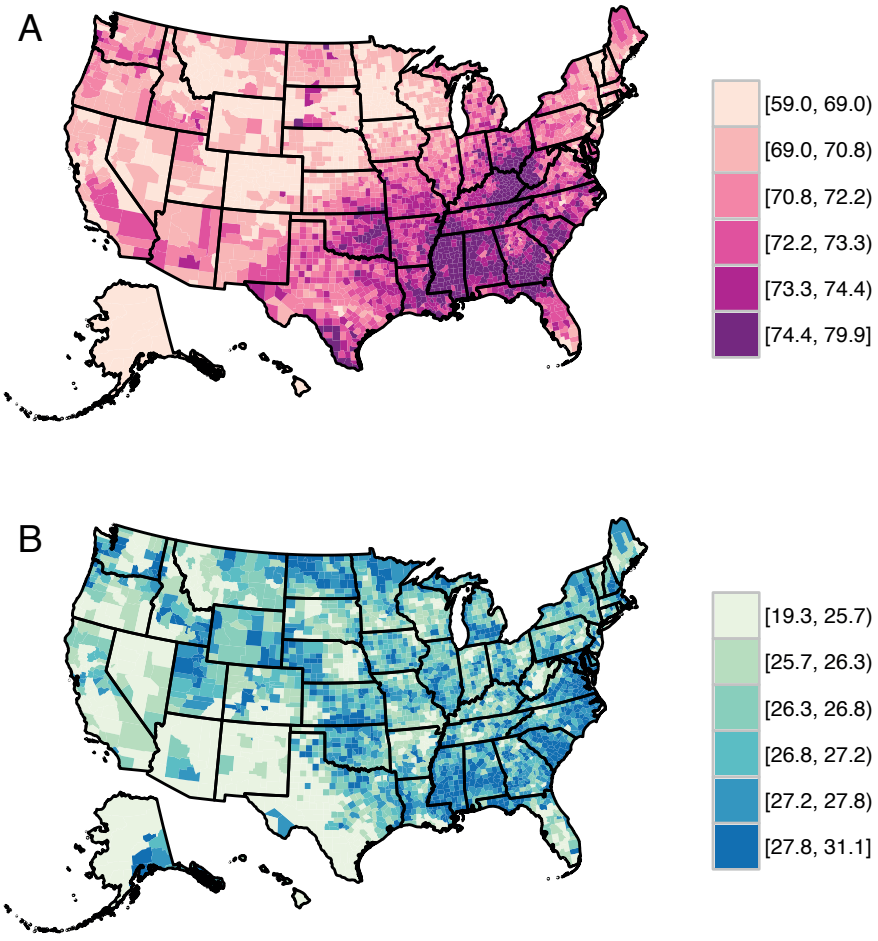

Figure 2. Age-standardized diabetes awareness and control by county, 2012. Diabetes awareness (A) and diabetes control (B).

Change in diabetes prevalence from 1999 to 2012

Between 1999 and 2012, total diabetes prevalence nationally increased by 40.0% (35.3%, 44.8%), from 10.2% (9.7%, 10.7%) to 14.3% (13.8%, 14.7%). This reflects an increase in both diagnosed and undiagnosed diabetes, but the rate of increase was larger for diagnosed than undiagnosed diabetes: 56.8% (52.3%, 61.7%) compared with 10.3% (4.8%, 15.7%). Changes in diabetes prevalence varied at the county level, however, with increases ranging from 25.2% to 117.1% for diagnosed diabetes and from 18.9% to 72.0% for total diabetes. Changes in undiagnosed diabetes prevalence ranged from a decline of 11.6% to an increase of 37.5%. We estimated a decline in undiagnosed diabetes prevalence in 0.5% of counties; however, this decline was not statistically significant in any county (one-tailed test, $\alpha = 0.05$). Figure 3 shows the percentage changes in age-standardized diagnosed, undiagnosed, and total diabetes at the county level. Counties with relatively small and relatively large increases in diagnosed diabetes are distributed throughout the country, although concentrations of counties with large increases are seen in the West, Southwest, and southern half of the Midwest, whereas a large number of counties with relatively small increases in diagnosed diabetes can be found along the Atlantic coast and parts of the deep South. Similarly, below and above average increases in undiagnosed diabetes were realized throughout the country, although in general there is a higher concentration of counties with large increases in the South and West and in Florida, and a higher a concentration of counties with small increases in the North and East and in Alaska. The map for changes in total diabetes prevalence reflects the map for changes in diagnosed diabetes, because increases in total diabetes were in large part driven by changes in diagnosed rather than undiagnosed diabetes prevalence.

Nationally, awareness increased by 12.0% (10.4%, 13.6%) between 1999 and 2012, from 63.9% (61.6%, 66.3%) to 71.6% (69.5%, 73.7%). At the same time, control has held roughly constant, increasing by 1.5% (−5.9%, 9.1%). from 26.5% (22.3%, 30.8%) to 26.9% (23.3%, 30.6%). Over this same period, we found increases in awareness for all counties, ranging from 4.8% to 38.2%. Changes at the county level in diabetes control were more mixed, however, ranging from a 12.3% decline to a 31.1% increase. Figure 4 shows the percentage changes in awareness and control at the county level. The largest gains in awareness were realized in counties in the Midwest, Southwest, Pacific Northwest, and Alaska, whereas the smallest gains were typically observed in the East and the South. Counties that increased control most dramatically tended to be clustered in and around Virginia, Oklahoma, and North Dakota, whereas those where control declined are somewhat concentrated along the coasts but also are well represented throughout the interior.

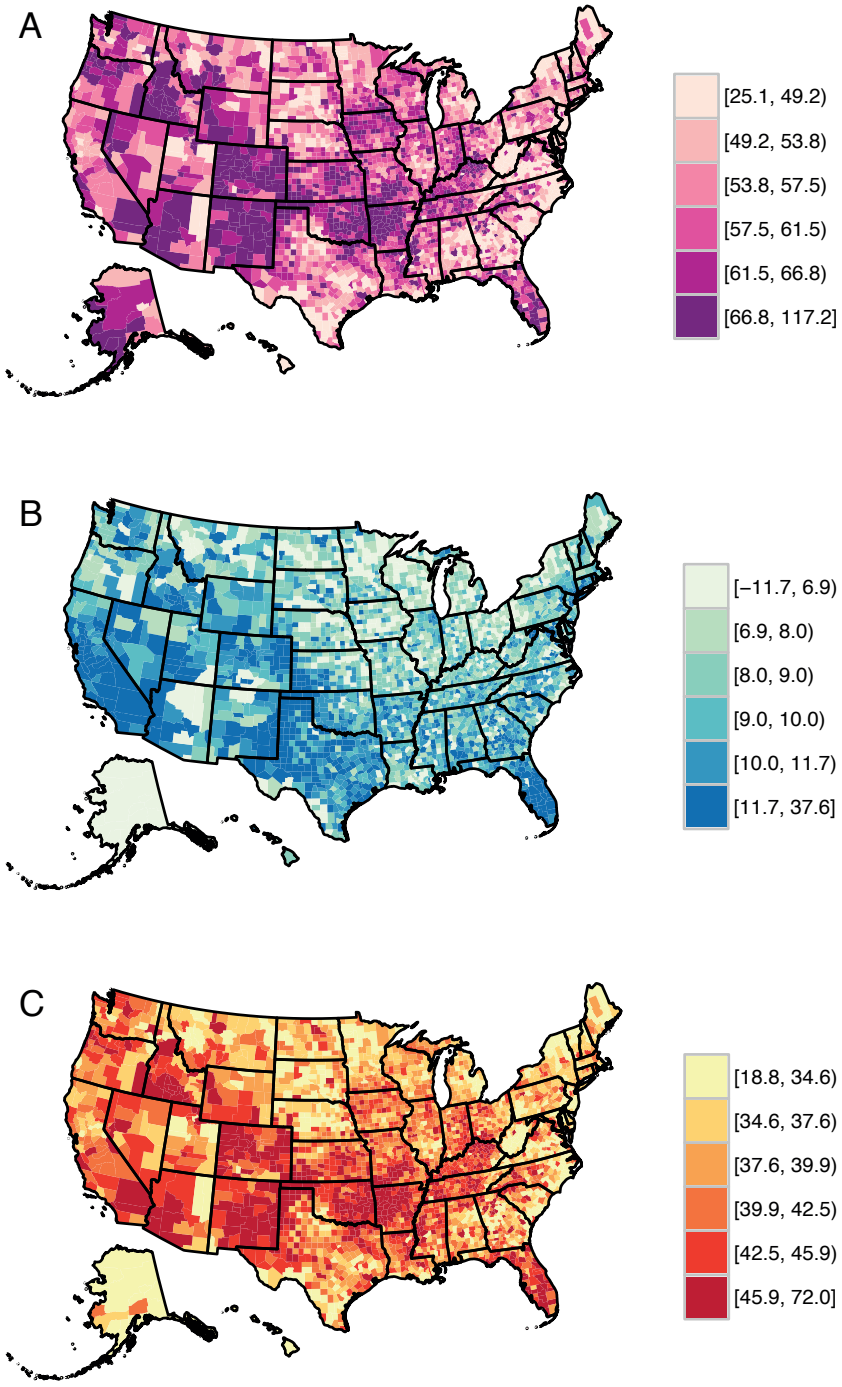

Figure 3. Percentage change in age-standardized diabetes prevalence by county, 1999–2012. A: Diagnosed diabetes prevalence. B: Undiagnosed diabetes prevalence. C: Total diabetes prevalence.

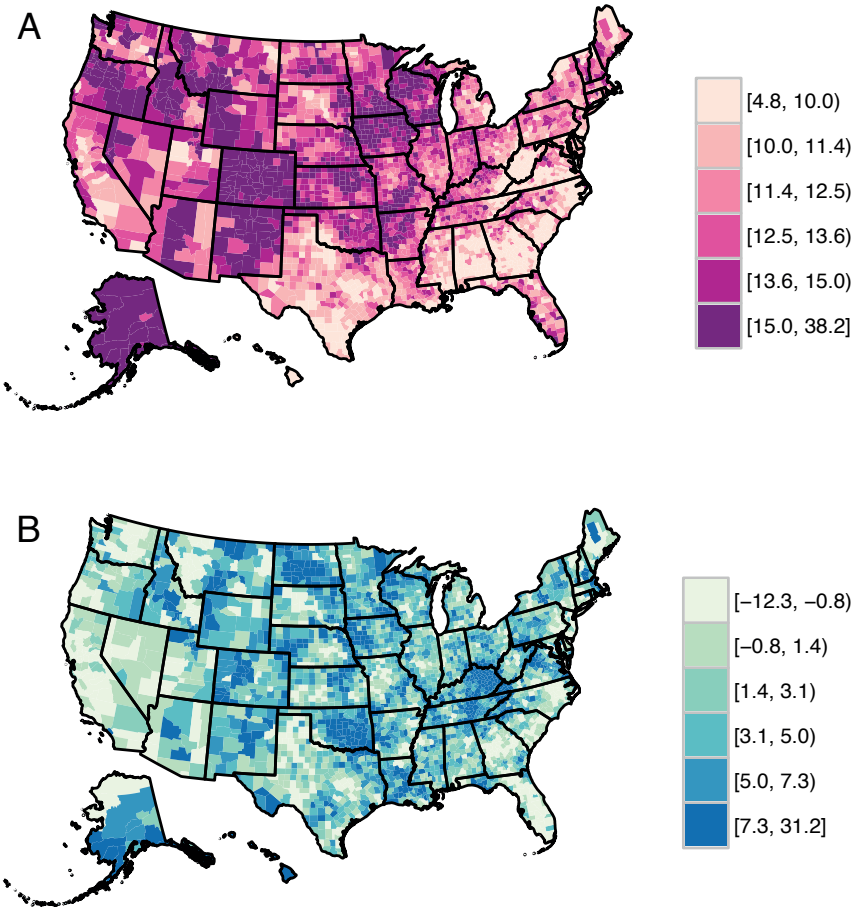

Figure 4. Percentage change in age-standardized diabetes awareness and control by county, 1999–2012. Diabetes awareness (A) and diabetes control (B).

CONCLUSIONS

The substantial and increasing health and financial burden of diabetes in the U.S. has been well documented.[1,3] Existing estimates[8,23] of county-level diagnosed diabetes have previously highlighted a dramatic variation in prevalence within the U.S. Our findings on diagnosed diabetes are very similar (for 2012, the correlation between the two sets of estimates is 0.79 for men and 0.82 for women), but we were also able to report on undiagnosed and total diabetes prevalence, as well as on diabetes awareness and control at the county level. These results reveal significant variation within the U.S. and within states not only in undiagnosed and diagnosed diabetes prevalence, but also in local capacity to address the burden of diabetes through diagnosis and successful treatment. This type of local information is essential

in order to identify the most impacted communities, and to enable public health officials to design targeted and effective intervention strategies.

This analysis is subject to a number of limitations. Most importantly, high FPG/A1C was imputed for BRFSS informants based on relevant variables shared between the BRFSS and NHANES rather than measured directly, and as a result the estimates of undiagnosed diabetes prevalence, total diabetes prevalence, diabetes awareness, and diabetes control are considerably less precise than the estimates of diagnosed diabetes prevalence, as evidenced by the much larger uncertainty intervals. Further, county-level estimates of undiagnosed and total diabetes, as well as the other measures derived from these, account for the variation in diagnosed diabetes, demographic features, BMI, smoking, and health insurance, but not for other factors. This is reflected by the relatively low sensitivity of the models for predicting high FPG/A1C—although the variables included in the model are certainly predictive of diabetes, they explain only a small portion of the individual-level variation in diabetes risk. As such, we are almost certainly underestimating the true variation in these outcomes and may be missing important outlier counties with unexpectedly high or low performance in terms of diagnosis and treatment. This analysis represents an important step forward in beginning to account for undiagnosed diabetes in addition to diagnosed diabetes, and also in exploring the variation in awareness and control, but further work on these topics is certainly needed, and will likely involve more substantial data collection at the county level.

The NHANES and BRFSS are both subject to nonresponse bias. We address this issue by explicitly incorporating many of the variables used to develop sample weights for both surveys into the small area model and poststratifying the results. Further, the BRFSS is also potentially subject to noncoverage bias because individuals without phones cannot be interviewed and a cell phone sample was only added in 2011. Previous research, however, suggests that the bias due to omission of cell phones is expected to be small for diabetes,[19] and we explicitly correct for this bias. Nonetheless, it is possible that some bias due to nonresponse or noncoverage remains.

These limitations notwithstanding, this study also has a number of strengths. Most importantly, we made efficient use of the available data, capitalizing on the strengths of the BRFSS, namely its large sample size and broad geographic coverage, as well as on the strengths of the NHANES, in particular the collection of biomarker data. This allowed us to generate a significantly more detailed picture of diabetes prevalence at the county level than has previously been available. Further, we used sophisticated small area models, which simultaneously borrow strength spatially, temporally, and from external sources of information, allowing us to generate more precise estimates for each county than is possible in a strictly design-based setting. Finally, our methods explicitly accounted for uncertainty in all modeling stages, and

the results are accompanied by 95% uncertainty intervals to convey the level of precision associated with each estimate.

The variation in total diabetes prevalence within the U.S. is staggering, with a threefold difference between the counties with the lowest prevalence and those with the highest prevalence. Some of this variation can be accounted for by socioeconomic and demographic factors, which are explicitly incorporated in our analysis of undiagnosed and total diabetes prevalence. However, our estimates of diagnosed diabetes, which are based on data directly observed at the county level, suggest that there is more variation in diabetes prevalence among counties than can be explained by socioeconomic and demographic differences alone. Further, the underlying factors driving differences between socioeconomic and demographic groups have not been entirely elucidated. Given the significant health and financial burden of high diabetes prevalence, this disparity demands further investigation into what underlying (and potentially modifiable) factors drive the exceedingly high diagnosed and total diabetes rates found in many communities.

Diabetes is both preventable and treatable. The public health system has a roll to play in increasing awareness of and screening for diabetes, connecting affected and high-risk individuals with appropriate medical care, and promoting community-level interventions that address known risk factors such as poor diet or lack of physical activity.[4,5] The results of this analysis should be considered by state and local health officials aiming to increase early detection and improve the health of impacted communities.

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Duality of interest

No potential conflicts of interest relevant to this article were reported.

Author contributions

LD-L designed the overall analytic strategy, developed the model, carried out the analyses, and drafted the manuscript. JPM, FJvL, and ADF contributed to the development of the model. AHM designed the overall analytic strategy. All authors revised the manuscript and approved the final draft. AHM is guarantor of this work and, as such, had full access to all the

data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Prior presentation

An earlier version of this analysis was presented at Spatial Statistics 2015: Emerging Patterns, Avignon, France, 9–12 June 2015.

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SUPPLEMENTARY DATA

Data

National Health and Nutrition Examination Survey (NHANES) data

We extracted reported age, sex, race/ethnicity, marital status, education status, current smoking status, current health insurance status, and diabetes diagnosis as well as measured weight, height, fasting plasma glucose (FPG), and A1C for the 17,375 individuals aged 20 years and older included in the 1999–2012 NHANES sub-sample for FPG measurements. Of these respondents, 15,600 (89.8%) had no missing values for any of these variables and were subsequently included in this analysis. BMI was calculated directly from measured weight (in kilograms) and height (in meters) as weight/height^2. Table S1 provides details on the annual NHANES sample size as well as missingness by variable.

Table S1. Sample size and missingness in NHANES data.

	Percent of respondents with non-missing:										Respondents:	
Survey year	Race	Marital status	Education	Diabetes diagnosis	FPG	A1C	BMI	Smoking status	Health plan	All	Total	Complete
1999–2000	100.0	89.3	99.6	100.0	93.4	94.9	98.6	99.9	98.4	81.1	2,188	1,774
2001–2002	100.0	99.9	99.8	100.0	95.0	95.4	94.2	99.8	98.5	89.3	2,508	2,240
2003–2004	100.0	99.9	99.8	100.0	95.3	95.9	98.4	100.0	99.3	93.0	2,247	2,089
2005–2006	100.0	100.0	99.9	99.9	94.8	94.9	98.0	99.9	99.9	92.4	2,289	2,116
2007–2008	100.0	100.0	99.9	99.9	94.5	94.5	98.2	99.9	99.9	92.0	2,776	2,555
2009–2010	100.0	99.9	99.7	99.9	95.1	89.1	99.1	100.0	99.9	87.5	2,740	2,398
2011–2012	100.0	99.9	99.9	99.9	94.1	94.8	98.6	99.8	99.9	92.4	2,627	2,428
All	100.0	98.6	99.8	99.9	94.6	94.1	97.9	99.9	99.4	89.8	17,375	15,600

Behavioral Risk Factor Surveillance System (BRFSS) data

We extracted reported age, sex, race/ethnicity, marital status, education status, current smoking status, current health insurance status, diabetes diagnosis, weight, height, and county of residence for the 4,620,693 respondents aged 20 years and older in the 1999–2012 BRFSS. 4,107,972 (88.9%) of these respondents had no missing values for any of these variables and were subsequently included in the analysis. BMI was calculated first directly from reported weight (in kilograms) and height (in meters) as weight/height^2. We then corrected for self-report bias by applying the correction factors described by Dwyer-Lindgren et al.[1] Table S2 provides details on the annual BRFSS sample size as well as missingness by variable.

Table S2. Sample size and missingness in BRFSS data.

	Percent of respondents with non-missing:											Respondents:	
Survey year	County	Race	Marital status	Education	Phone usage	Diabetes diagnosis	Height	Weight	Smoking status	Health plan	All	Total	Complete
1999	99.0	99.6	99.8	99.8	-	99.9	99.1	96.8	99.7	99.8	94.6	152,557	144,265
2000	98.8	99.5	99.7	99.8	-	99.9	99.2	96.2	99.7	99.8	93.6	175,275	164,107
2001	98.2	99.0	99.7	99.8	-	99.9	98.9	96.0	99.7	99.8	92.3	198,831	183,457
2002	98.6	99.1	99.8	99.8	-	99.9	98.9	96.2	99.7	99.8	92.8	234,589	217,621
2003	98.8	99.2	99.7	99.8	-	99.9	99.0	96.1	99.7	99.8	93.0	251,398	233,898
2004	98.8	99.1	99.7	99.8	-	99.9	98.9	96.2	99.7	99.8	93.0	293,023	272,466
2005	98.7	99.1	99.7	99.8	-	99.9	98.9	96.3	99.6	99.8	93.0	345,653	321,307
2006	95.5	99.0	99.7	99.8	-	99.9	98.8	96.1	99.6	99.8	89.7	342,488	307,339
2007	94.7	99.1	99.7	99.7	-	99.9	98.8	96.4	99.6	99.8	89.4	418,195	373,692
2008	93.0	99.1	99.7	99.7	-	99.9	98.9	96.4	99.6	99.8	87.9	401,258	352,646
2009	91.9	99.0	99.6	99.7	-	99.9	98.9	96.3	99.4	99.8	86.5	419,245	362,696
2010	91.4	98.7	99.6	99.7	-	99.9	98.8	96.1	99.4	99.8	85.7	438,078	375,261
2011	90.6	98.9	99.6	99.7	99.3	99.6	98.8	96.0	99.5	99.7	84.5	489,783	414,108
2012	90.3	98.8	99.5	99.7	99.2	99.8	98.7	96.1	98.0	99.7	83.7	460,320	385,109
All	94.6	99.0	99.7	99.7	99.9	99.9	98.9	96.2	99.4	99.8	88.9	4,620,693	4,107,972

Covariates

Three county-level covariates were included in the small area models: percent rural households, poverty rate, and doctors per capita. Percent rural households was derived from the 1990, 2000, and 2010 decennial censuses.[2] Linear interpolation was used to estimate this variable in intercensal-years and the rate of change from 2000 to 2010 was used to project this variable for 2011 and 2012. The poverty rate was obtained from the Small Area Income and Poverty Estimates (SAIPE) series.[3] Finally, the doctors per capita variable was obtained from the Area Health Resource File.[4]

Population estimates used for post-stratification

Age- and sex-specific county-level population counts by race, by marital status, by education, and by phone usage category (i.e., cell phone only, land line only, or dual) were used for post-stratifying predictions from the small area models. Population counts by race were obtained from the National Center for Health Statistics (NCHS) Bridged-Race Files.[5–7] Population counts by marital status and population counts by education status were obtained from the 1990[8,9] and 2000[10,11] decennial censuses and from the 2004–2014 American Community Survey.[12–13]

Population counts by phone usage category were obtained by applying the proportions provided by Blumberg et al.[14,15] to the population counts for all races combined from the NCHS Bridged-Race Files. Depending on population size, Blumberg et al. provides estimates for single counties, groups of counties, or at the state-level. For each county, we used the most geographically precise estimate available which included that county.

Additional data sources

We used the county adjacency file[16] from the 2010 census to define the neighborhood structure used for spatial random effects in the small area model. We used the distribution of the total population in the 2010 census[17] to derive weights used for age-standardizing outcome measures. Finally, we used census bureau records of significant county boundary changes[18] to create historically stable county units for analysis.

Model validation

High fasting plasma glucose/A1C model

We used cross-validation to assess the predictive performance of the high FPG/A1C models. First, the NHANES data was randomly split into a training set (80%) and a testing set (20%). Second, the model was fit on the training set and predictions were derived from the fitted model for respondents in the testing set. Finally, performance was assessed by comparing the predictions to the true values for respondents in the testing set. This procedure was repeated 100 times and then the concordance (the proportion of individuals correctly classified), sensitivity (the proportion of true cases that are identified as cases), and specificity (the proportion of true negatives that are identified as negative) were calculated across all repetitions.

The results of this validation exercise are given in Table S3. The high FPG/A1C models for both previously diagnosed and previously undiagnosed respondents had reasonably high specificity and overall concordance, but low sensitivity. This suggests that the variables included in this model, while predictive, do not explain all variation in risk. This is unsurprising; while we are able to capture the effect of a number of demographic characteristics as well as some basic health behaviors and resources, there are many other important factors, notably familial history and treatment (among those previously diagnosed), which we are not able to incorporate.

Small area model

We assessed the performance of the small area models using a validation framework similar to that proposed by Srebotnjak et al.[19] First, we identified counties with at least 900 male and 900 female respondents in any given 5-year period. These counties formed our 'validation set' and we calculated direct (design-based) estimates for these counties using the data pooled

over 5-years which we treated as an empirical gold standard. Second, we created testing data sets by sampling a set number of respondents from each county in the validation set to mimic smaller counties with smaller sample sizes. Specifically, we created ten testing data sets each for sample sizes of 1, 10, 50, and 100 respondents of each sex in each year. Next we fit the small area model using the testing data sets and generated predictions for all counties in the validation set. Finally, we compared the model predictions to the gold standard to assess performance. Performance was characterized in terms of the root mean squared error, mean error, mean absolute error, and correlation coefficient.

Table S3. High FPG/A1C model validation results.

Population	Sex	Specificity	Sensitivity	Concordance
Previously diagnosed	Males	93.3	12.9	87.6
	Females	95.7	11.4	91.9
	Both	94.6	12.3	89.9
Not previously diagnosed	Males	93.4	13.2	87.8
	Females	95.7	11.2	91.8
	Both	94.6	12.3	89.9

Table S4 presents the results of this validation analysis alongside the same performance metrics calculated in sample (i.e., when models are fit using all respondents). The small area models for diagnosed diabetes perform well, with minimal bias (as measured by the mean error) and reasonable precision (as measured by the root mean squared error and mean absolute error). As expected, performance, particularly in terms of precision, is better the larger the sample available.

Table S4. SAE model validation results.

Sample size	Root mean squared error	Mean error	Mean absolute error	Correlation coefficient
1	1.39	-0.33	1.04	0.75
10	1.22	-0.34	0.96	0.80
50	1.07	-0.26	0.84	0.85
100	0.99	-0.24	0.77	0.87
In sample	0.85	-0.20	0.65	0.91

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Chapter 5

US county-level trends in mortality rates for major causes of death, 1980–2014

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ABSTRACT

Importance

County-level patterns in mortality rates by cause have not been systematically described but are potentially useful for public health officials, clinicians, and researchers seeking to improve health and reduce geographic disparities.

Objectives

To demonstrate the use of a novel method for county-level estimation and to estimate annual mortality rates by US county for 21 mutually exclusive causes of death from 1980 through 2014.

Design, setting, and participants

Redistribution methods for garbage codes (implausible or insufficiently specific cause of death codes) and small area estimation methods (statistical methods for estimating rates in small subpopulations) were applied to death registration data from the National Vital Statistics System to estimate annual county-level mortality rates for 21 causes of death. These estimates were raked (scaled along multiple dimensions) to ensure consistency between causes and with existing national-level estimates. Geographic patterns in the age-standardized mortality rates in 2014 and in the change in the age-standardized mortality rates between 1980 and 2014 for the 10 highest-burden causes were determined.

Exposure

County of residence.

Main outcomes and measures

Cause-specific age-standardized mortality rates.

Results

A total of 80,412,524 deaths were recorded from January 1, 1980, through December 31, 2014, in the United States. Of these, 19.4 million deaths were assigned garbage codes. Mortality rates were analyzed for 3,110 counties or groups of counties. Large between-county disparities were evident for every cause, with the gap in age-standardized mortality rates between counties in the 90th and 10th percentiles varying from 14.0 deaths per 100,000 population (cirrhosis and chronic liver diseases) to 147.0 deaths per 100,000 population (cardiovascular diseases). Geographic regions with elevated mortality rates differed among causes: for example, cardiovascular disease mortality tended to be highest along the southern half of the Mississippi River, while mortality rates from self-harm and interpersonal violence were elevated in southwestern counties, and mortality rates from chronic respiratory disease were

highest in counties in eastern Kentucky and western West Virginia. Counties also varied widely in terms of the change in cause-specific mortality rates between 1980 and 2014. For most causes (eg, neoplasms, neurological disorders, and self-harm and interpersonal violence), both increases and decreases in county-level mortality rates were observed.

Conclusions and relevance

In this analysis of US cause-specific county-level mortality rates from 1980 through 2014, there were large between-county differences for every cause of death, although geographic patterns varied substantially by cause of death. The approach to county-level analyses with small area models used in this study has the potential to provide novel insights into US disease-specific mortality time trends and their differences across geographic regions.

INTRODUCTION

Recent research has highlighted large, long-standing, and increasing geographic inequalities in life expectancy among counties within the United States.[1,2] However, relatively little is known about geographic patterns and inequalities in mortality by underlying cause of death. Information about variation in cause-specific mortality could provide important insights into geographic inequalities and divergent trends in life expectancy. Moreover, local information about cause-specific mortality rates could be used by policy makers, clinicians, and public health professionals to inform more targeted strategies to improve health and survival and to decrease geographic inequalities in the United States.

Previous efforts[3–8] to generate country-wide county-level estimates of cause-specific mortality have generally focused on only a single cause or group of closely related causes. The cause definitions used by these analyses vary widely (ie, the specific cause of death codes included for a given cause varies by analysis) as do the periods considered and the statistical methods used. Consequently, it is difficult to compare across causes that were analyzed separately. Furthermore, to our knowledge, no previous study of county-level cause-specific mortality has attempted to correct for the presence of garbage codes, that is, cause of death codes in death registration data that are implausible or insufficiently specific.[9] The proportion of registered deaths that are assigned garbage codes varies by county, year, and underlying true cause, and a failure to appropriately redistribute these deaths may lead to erroneous conclusions about geographic patterns, time trends, and the relative burden of different causes of death.

This study presents a novel method using garbage code redistribution methods (methods for reassigning garbage codes) and small area estimation methods (statistical methods for estimating rates among small subpopulations) for estimating county-level cause-specific mortality rates.

METHODS

Data

This analysis used deidentified death records from the National Vital Statistics System provided by the National Center for Health Statistics.[10] These records covered deaths that occurred within the United States from January 1, 1980, through December 31, 2014, and included the age, sex, and county of residence at the time of death for each decedent, as well as the registered underlying cause of death, coded according to the *International Classification of Diseases, Ninth Revision* (*ICD-9*) for deaths prior to 1999 and *ICD-10* for deaths that occurred in

1999 or later.[11,12] Deaths were tabulated by age group (0, 1–4, 5–9, 10–14, …, 75–79, and ≥80 years), sex, county, year, and cause. This research received institutional review board approval from the University of Washington. Informed consent was not required because the study used deidentified data and was retrospective.

Annual county-level population counts by age, sex, and race from 1980 to 1989 provided by the US Census Bureau and annual county-level population counts by age, sex, and race/ethnicity from 1990 to 2014 provided by the National Center for Health Statistics were used in this analysis.[13–16] Population counts in both series were summed across all race/ethnicity groups to generate annual county-level population counts by age group and sex. These 2 sources were then combined to produce a time series covering 1980 through 2014 and scaled to match the total population in each year provided by the Human Mortality Database.[17]

County-level covariates on levels of education, income, race/ethnicity, Native American reservations, and population density were used in the small area estimation model. These covariates were based on data provided by the US Census Bureau and the National Center for Health Statistics. Covariates related to race and ethnicity were derived from self-reported responses to the decennial census and American Community Survey and use the categories specified by the Office of Management and Budget.[18] More details on these data sources are provided in eTable 1 in the Supplement.

In a small number of cases, county boundaries shifted between 1980 and the present. To account for these changes, several counties were merged to create historically stable units. Details on the merged county units are provided in eTable 2 in the Supplement. For simplicity, these units are referred to as counties throughout.

Cause list and garbage code redistribution

The cause list developed for the Global Burden of Disease Study (GBD)[19] was used for this analysis; it has been widely used for cause of death analyses.[20,21] The GBD cause list is arranged hierarchically in 4 levels; within each level, the cause list is designed such that all deaths are assigned exactly 1 cause. As part of the GBD study, a map has been developed that allows *ICD-9* and *ICD-10* codes to be translated to GBD causes; eTable 3 in the Supplement lists all causes in the GBD cause list and the *ICD-9* and *ICD-10* codes that contributed to each cause. This analysis focuses on the 21 causes in the second level of this hierarchy (Box). This level was selected because major causes of death (eg, neoplasms, cardiovascular diseases) are distinguished but the number of causes is still relatively small, making it possible to consider all causes.

Previous studies[9] have documented the high proportion of registered deaths for which the underlying cause of death has been assigned a garbage code, that is, a code that refers to an intermediate or immediate cause of death rather than an underlying cause of death (eg, cardiopulmonary arrest) or a code that is insufficiently specific (eg, malignant neoplasm of other and ill-defined sites). Failure to appropriately redistribute garbage codes can lead to erroneous geographic and temporal patterns (as the proportion of deaths with garbage codes varies over time and place) as well as incorrect relative rankings among causes (as the likelihood that a death is assigned a garbage code varies by true underlying cause).

To address this issue, algorithms developed for the GBD study to redistribute deaths assigned garbage codes were used.[19,21] First, specific garbage codes or groups of related garbage codes were assigned biologically plausible target causes. Second, deaths assigned garbage codes were redistributed to the target causes according to proportions derived in one of 4 ways: (1) published literature and/or expert opinion; (2) regression models linking changes in the proportion of deaths assigned to a given garbage code and those assigned to a given target code; (3) according to the proportions initially observed among the targets; and (4) for deaths with certain codes known to be related to human immunodeficiency virus (HIV)/AIDS, the mortality rate in each 5-year period was compared with that in 1980 and deaths beyond a 5% increase were assigned to HIV/AIDS, while the remainder were assigned to a different biologically plausible target. More details on each of these methods are provided in the eAppendix in the Supplement.

As an example, 62 deaths among men in King County, Washington, were coded to unspecified heart disease in 2013. Based on the garbage code redistribution algorithms, 48 of these deaths were reassigned to ischemic heart disease, 3 to hypertensive heart disease, 2 to atrial fibrillation and flutter, 3 to cardiomyopathy and myocarditis, 1 to rheumatic heart disease, 1 to endocarditis, and 4 to other cardiovascular and circulatory diseases. eFigure 1 in the Supplement depicts graphically how garbage code redistribution affects all cardiovascular diseases in King County. eFigure 2 and eFigure 3 in the Supplement show the percentage of deaths assigned garbage codes in each county and the effect of garbage code redistribution on total deaths by cause for the United States as a whole, respectively.

Mapping from *ICD-9* and *ICD-10* to the GBD cause list and redistribution of garbage codes were carried out at the lowest levels of the GBD cause hierarchy. Deaths were then aggregated to the first and second levels of the cause hierarchy.

Statistical analysis

Bayesian spatially explicit mixed-effects regression models for all-cause mortality and each cause in level 1 and level 2 of the GBD cause hierarchy were estimated separately for males

and females. The model included the following covariates: the proportion of the adult population who has graduated high school; the proportion of the population that is Hispanic; the proportion of the population that is black; the proportion of the population that is a race other than black or white; the proportion of a county that is contained within a state or federal Native American reservation; the median household income; and the population density. These covariates were chosen because they are well measured at the county level and expected to be predictive of county-level mortality rates. Further details about this model are provided in the eAppendix in the Supplement.

One thousand draws (ie, simulated values) of each model parameter were sampled from the posterior distribution and used to derive draws of the mortality rate for each county, year, and age group. To ensure internal consistency between estimates of all-cause mortality and cause-specific mortality as well as consistency with national-level estimates from the GBD study (which incorporate prevalence data for causes such as atrial fibrillation, as well as Alzheimer disease and other dementias, that cannot be used directly at the county level), the estimated mortality rates were raked (ie, scaled along multiple dimensions)[22] such that the sum across all causes equaled the estimated all-cause mortality rate and that the population-weighted average of the county-level mortality rates equaled the national-level mortality rate for each cause (further details are provided in the eAppendix in the Supplement). After raking, state- and national-level estimates of the age-specific mortality rates were derived by population weighting the county-level estimates, and estimates at the county, state, and national levels were age standardized using the US 2010 census population as the standard. Similarly, years of life lost (YLLs) were calculated for each age group by multiplying the mortality rate by population by life expectancy at the average age at death from the reference life table used in the GBD study[19] and then summed across all ages (additional details are provided in the eAppendix in the Supplement).

Point estimates for each quantity of interest were derived from the mean of the draws, while 95% uncertainty intervals (UIs) were derived from the 2.5th and 97.5th percentiles. When measuring changes over time, the change was considered statistically significant if the posterior probability of an increase (or decrease) was at least 95%, ie, if the mortality rate increased (or declined) in at least 95% of the draws.

The performance of the small area models was evaluated using an established empirical validation framework designed specifically for the United States.[23,24] This validation framework was used to compare performance of 4 variants of the model described earlier as well as 2 previously published models[1,24] in terms of bias, precision, and coverage. The selected model consistently performed as well as or better than all other models. More details about the validation methods and results are included in the eAppendix in the Supplement.

Box. Level 1 and 2 causes of death in the Global Burden of Disease hierarchy.

Communicable, Maternal, Neonatal, and Nutritional Diseases (Level 1)

HIV/AIDS and tuberculosis (level 2): tuberculosis; HIV/AIDS

Diarrhea, lower respiratory, and other common infectious diseases (level 2): diarrheal diseases; intestinal infectious diseases; lower respiratory tract infections; upper respiratory tract infections; otitis media; meningitis; encephalitis; diphtheria; whooping cough; tetanus; measles; varicella-zoster virus infection; herpes zoster

Neglected tropical diseases and malaria (level 2): malaria; Chagas disease; leishmaniasis; African trypanosomiasis; schistosomiasis; cysticercosis; cystic echinococcosis; dengue; yellow fever; rabies; intestinal nematode infections; other neglected tropical diseases; Ebola

Maternal disorders (level 2): maternal hemorrhage; maternal sepsis and other maternal infections; maternal hypertensive disorders; maternal obstructed labor and uterine rupture; maternal abortion, miscarriage, and ectopic pregnancy; indirect maternal deaths; late maternal deaths; other maternal disorders; maternal deaths aggravated by HIV/AIDS

Neonatal disorders (level 2): neonatal preterm birth complications; neonatal encephalopathy due to birth asphyxia and trauma; neonatal sepsis and other neonatal infections; hemolytic disease and other neonatal jaundice; other neonatal disorders

Nutritional deficiencies (level 2): protein-energy malnutrition; iodine deficiency; iron deficiency anemia; other nutritional deficiencies

Other communicable, maternal, neonatal, and nutritional diseases (level 2): sexually transmitted diseases excluding HIV; hepatitis; other infectious diseases

Noncommunicable Diseases (Level 1)

Neoplasms (level 2): esophageal cancer; stomach cancer; liver cancer; larynx cancer; tracheal, bronchus, and lung cancer; breast cancer; cervical cancer; uterine cancer; prostate cancer; colon and rectal cancer; lip and oral cavity cancer; nasopharynx cancer; other pharynx cancer; gallbladder and biliary tract cancer; pancreatic cancer; malignant skin melanoma; nonmelanoma skin cancer; ovarian cancer; testicular cancer; kidney cancer; bladder cancer; brain and nervous system cancer; thyroid cancer; mesothelioma; Hodgkin lymphoma; non-Hodgkin lymphoma; multiple myeloma; leukemia; other neoplasms

Cardiovascular diseases (level 2): rheumatic heart disease; ischemic heart disease; cerebrovascular disease; hypertensive heart disease; cardiomyopathy and myocarditis; atrial fibrillation and flutter; aortic aneurysm; peripheral vascular disease; endocarditis; other cardiovascular and circulatory diseases

Chronic respiratory diseases (level 2): chronic obstructive pulmonary disease; pneumoconiosis; asthma; interstitial lung disease and pulmonary sarcoidosis; other chronic respiratory diseases

Cirrhosis and other chronic liver diseases (level 2): cirrhosis and other chronic liver diseases

Digestive diseases (level 2): Peptic ulcer disease; gastritis and duodenitis; appendicitis; paralytic ileus and intestinal obstruction; inguinal, femoral, and abdominal hernia; inflammatory bowel disease; vascular intestinal disorders; gallbladder and biliary diseases; pancreatitis; other digestive diseases

Neurological disorders (level 2): Alzheimer disease and other dementias; Parkinson disease; epilepsy; multiple sclerosis; motor neuron disease; other neurological disorders

Mental and substance use disorders (level 2): schizophrenia; alcohol use disorders; drug use disorders; eating disorders

Diabetes, urogenital, blood, and endocrine diseases (level 2): diabetes mellitus; acute glomerulonephritis; chronic kidney disease; urinary diseases and male infertility; gynecological diseases; hemoglobinopathies and hemolytic anemias; endocrine, metabolic, blood, and immune disorders

Musculoskeletal disorders (level 2): rheumatoid arthritis; other musculoskeletal disorders

Other noncommunicable diseases (level 2): congenital anomalies; skin and subcutaneous diseases; sudden infant death syndrome

Injuries (Level 1)

Transport injuries (level 2): road injuries; other transport injuries

Unintentional injuries (level 2): falls; drowning; fire, heat, and hot substances; poisonings; exposure to mechanical forces; adverse effects of medical treatment; animal contact; foreign body; other unintentional injuries; environmental heat and cold exposure

Self-harm and interpersonal violence (level 2): self-harm; interpersonal violence

Forces of nature, war, and legal intervention (level 2): exposure to forces of nature; collective violence and legal intervention

Abbreviation: HIV, human immunodeficiency virus.

Inequality among counties was quantified by comparing the mortality rate in the 90th percentile with the mortality rate in the 10th percentile among all counties in a given year. Two types of inequality were considered. Absolute inequality, which represents the absolute magnitude of the gap between high- and low-mortality counties, was quantified as the difference between the mortality rates in the 90th and 10th percentiles. Relative inequality, which represents the relative difference between high- and low-mortality counties, was quantified as the ratio of the mortality rate in the 90th percentile to the mortality rate in the 10th percentile.

Garbage code redistribution was carried out in Python version 2.7.3 (Python Software Foundation) and Stata MP version 13.1 (StataCorp LP) statistical software. Small area estimation was carried out in R version 3.2.4 statistical software (R Foundation for Statistical Computing). Models were fit using the Template Model Builder Package in R.[25]

RESULTS

A total of 80,412,524 deaths among US residents were recorded from January 1, 1980, through December 31, 2014. Of these, 19.4 million deaths were assigned garbage codes. Most of these deaths (17.8 million) were assigned codes referring to intermediate or unspecified causes presumably within the same *ICD-9* or *ICD-10* chapter as the true underlying cause (9.1 million in the cardiovascular diseases chapter; 2.9 million in the respiratory diseases chapter; 1.7 million in the cancer chapter; 1.1 million in the injuries chapter; 1.0 million in the infectious diseases chapter; and 1.9 million in other chapters), while the remaining 1.7 million deaths (2.1% of all deaths) were assigned ill-defined codes. Of the 19.4 million deaths assigned garbage codes, 19.1% were reassigned using published literature, 44.7% were reassigned using regression methods, 35.6% were reassigned using observed proportions among target codes, and 0.6% were reassigned to HIV/AIDS or other targets based on comparison with 1980. As a result of merging counties to address historical boundary changes, the number of areas analyzed was 3,110 (compared with 3,142).

The Table summarizes the results for all 21 causes of death in 2014 at the national and county levels. The first section summarizes the burden of each cause at the national level: for example, there were 846.3 thousand deaths and 11,735.8 thousand YLLs from cardiovascular diseases in 2014, with a mortality rate of 252.7 deaths per 100,000 population. The second section summarizes the distribution of counties according to the age-standardized mortality rate from each cause: for example, the lowest mortality rate from neoplasms was 70.7 deaths per 100,000 population, compared with 169.5, 204.3, and 246.3 deaths per 100,000 population in counties in the 10th, 50th, and 90th percentiles, respectively, and 503.1 deaths

per 100,000 population in the county with the highest rate. This corresponds to an absolute difference of 76.8 deaths per 100,000 population between the mortality rates in counties in the 90th and 10th percentiles.

The Figures in the article show the top 10 causes (in terms of YLLs) and eFigures 4–14 in the Supplement show the other 11 causes. Estimates for all causes and years are available in an online data visualization tool (Interactive).

Neoplasms

Neoplasms (Figure 1) caused 19,511,910 deaths (24.3% of all deaths) from 1980 through 2014 and were the leading cause of YLLs and the second leading cause of deaths in 2014. The mortality rate from neoplasms varied widely among counties: counties in the 90th percentile experienced mortality rates 76.8 deaths per 100,000 population higher than those in the 10th percentile. Very high mortality rates were observed in counties along the southern half of the Mississippi River, in eastern Kentucky and western West Virginia, and in western Alaska. At the other extreme, many counties in states stretching from Idaho and Wyoming in the north to western Texas in the south had mortality rates from neoplasms much lower than average. The mortality rate from neoplasms declined by 20.1% (95% UI, 18.2%–21.4%) overall between 1980 and 2014, but the mortality rate increased during the same period in 18.5% of counties (statistically significant in 5.1% of counties). Increases in mortality from neoplasms were found primarily in south-central counties, with the largest increases observed in eastern Kentucky. In contrast, the largest decreases in mortality from neoplasms were found primarily in counties in central Colorado, southern Florida, Alaska, parts of New England, and coastal counties in California.

Cardiovascular diseases

Cardiovascular diseases (Figure 2) caused 31,992,547 deaths (39.8%) from 1980 through 2014 and were the second leading cause of YLLs and the leading cause of deaths in 2014. Cardiovascular diseases were an important contributor to mortality in every county: in 2014, cardiovascular diseases were the leading cause of death in 97.1% of counties and the top-ranked cause in terms of the age-standardized mortality rate in 98.5% of counties. However, the rate of death from cardiovascular diseases was far from uniform, with rates among counties in the 90th percentile 147.0 deaths per 100,000 population higher than rates among counties in the 10th percentile. The highest rates in 2014 were observed in counties in a band stretching from Oklahoma to Mississippi and in eastern Kentucky. Conversely, the lowest rates were observed in counties in central Colorado and near the border of Idaho, Montana, and Wyoming. Between 1980 and 2014, cardiovascular disease mortality decreased by 50.2% (95% UI, 49.5%–50.8%) overall. However, while nearly every county experienced a decline in cardiovascular disease mortality during this period (statistically significant in 99.9% of coun-

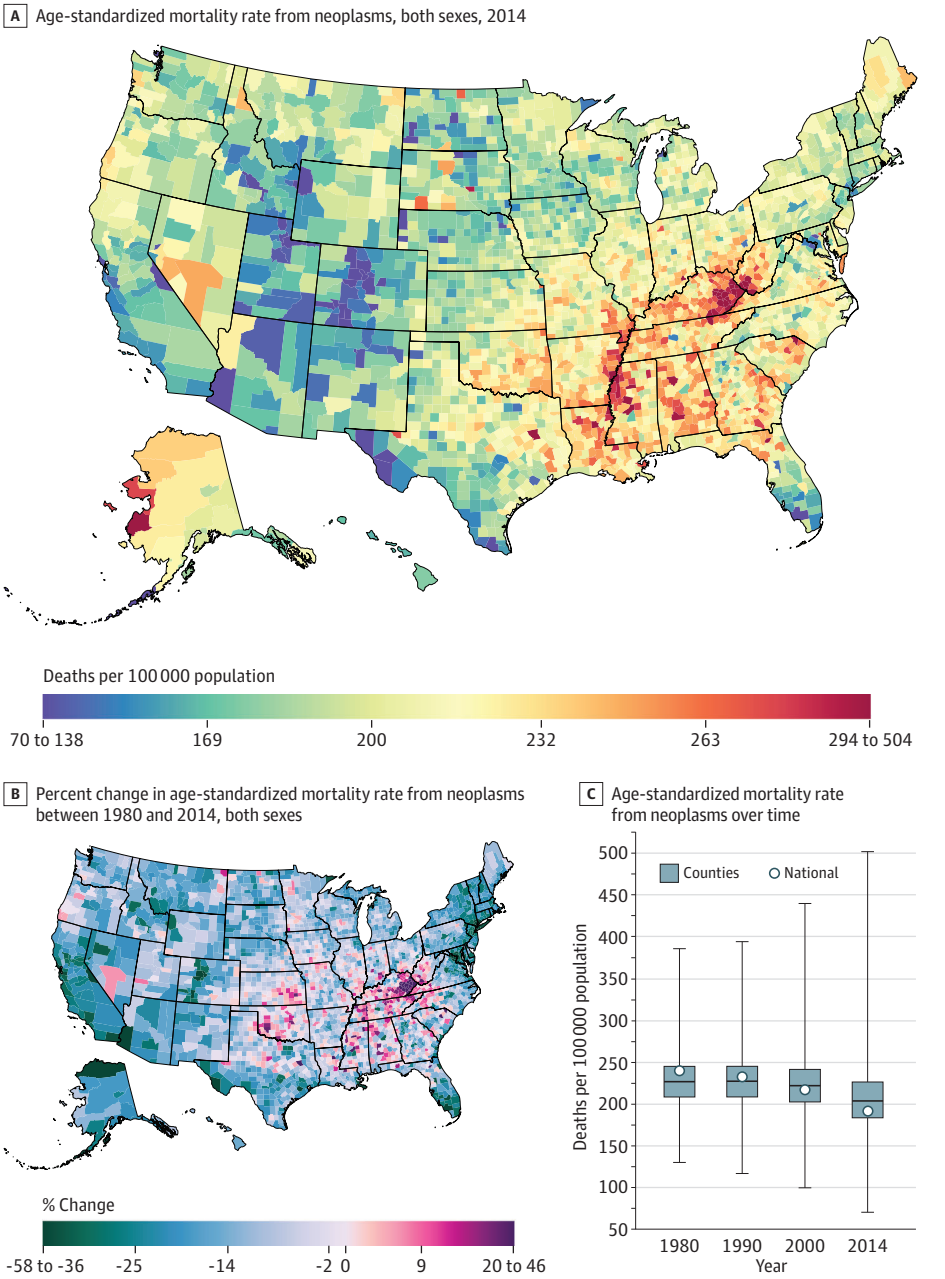

Figure 1. County-level mortality from neoplasms.

A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.

Table 1. National deaths, years of life lost, age-standardized mortality rates, and distribution of age-standardized mortality rates at the county level, 2014.

	National deaths, YLLs, and mortality rate			County-level mortality rate						
				No. of deaths/100,000 population						
Cause of death	Deaths, no. in thousands (rank)	YLLs, no. in thousands (rank)	Mortality rate, no. of deaths/100,000 population (rank)	Minimum	10th Percentile	Median	90th Percentile	Maximum	90th minus 10th percentile, no. of deaths/100,000 population (rank)[a]	90th/10th percentile, ratio (rank)[b]
Communicable, maternal, neonatal, and nutritional diseases										
HIV/AIDS and tuberculosis	8.6 (16)	316.8 (15)	2.7 (16)	0.2	0.4	0.9	3.4	65.7	3.0 (15)	8.5 (1)
Diarrhea, lower respiratory, and other common infectious diseases	100.4 (6)	1,423.7 (10)	30.0 (6)	9.1	20.9	32.2	46.7	90.8	25.8 (6)	2.2 (9)
Neglected tropical diseases and malaria	0.2 (21)	4.9 (21)	0.0 (21)	0.0	0.0	0.1	0.1	0.8	0.1 (21)	4.7 (3)
Maternal disorders	1.1 (19)	58.2 (18)	0.3 (19)	0.1	0.2	0.3	0.5	1.5	0.3 (19)	2.6 (7)
Neonatal disorders	10.4 (14)	897.2 (13)	3.3 (14)	1.2	2.1	3.1	5.2	10.9	3.1 (14)	2.5 (8)
Nutritional deficiencies	4.0 (18)	51.2 (19)	1.2 (18)	0.1	0.8	1.5	2.5	7.1	1.6 (17)	2.9 (6)
Other communicable, maternal, neonatal, and nutritional diseases	4.5 (17)	120.1 (17)	1.4 (17)	0.7	0.9	1.2	1.6	7.2	0.7 (18)	1.8 (15)
Noncommunicable diseases										
Neoplasms	646.0 (2)	12,125.5 (1)	192.0 (2)	70.7	169.5	204.3	246.3	503.1	76.8 (2)	1.5 (20)
Cardiovascular diseases	846.3 (1)	11,735.8 (2)	252.7 (1)	77.0	209.2	272.3	356.2	545.2	147.0 (1)	1.7 (18)
Chronic respiratory diseases	177.3 (5)	2,522.2 (6)	52.9 (5)	14.3	44.1	62.5	85.2	161.0	41.1 (5)	1.9 (13)
Cirrhosis and other chronic liver diseases	56.2 (9)	1,474.1 (9)	16.8 (9)	6.7	11.5	17.3	25.5	192.6	14.0 (10)	2.2 (10)
Digestive diseases	47.4 (10)	708.1 (14)	14.2 (10)	7.9	13.3	16.1	19.2	32.4	5.9 (12)	1.4 (21)

Table 1. National deaths, years of life lost, age-standardized mortality rates, and distribution of age-standardized mortality rates at the county level, 2014. (continued)

	National deaths, YLLs, and mortality rate			County-level mortality rate						
				No. of deaths/100,000 population						
Cause of death	**Deaths, no. in thousands (rank)**	**YLLs, no. in thousands (rank)**	**Mortality rate, no. of deaths/100,000 population (rank)**	**Minimum**	**10th Percentile**	**Median**	**90th Percentile**	**Maximum**	**90th minus 10th percentile, no. of deaths/100,000 population (rank)[a]**	**90th/10th percentile, ratio (rank)[b]**
Neurological disorders	318.6 (3)	2,734.0 (4)	95.4 (3)	30.8	67.5	95.5	123.2	198.9	55.7 (3)	1.8 (14)
Mental and substance use disorders	43.1 (12)	1,775.6 (8)	13.4 (12)	3.0	6.5	11.7	21.5	73.2	15.0 (9)	3.3 (4)
Diabetes, urogenital, blood, and endocrine diseases	187.1 (4)	3,085.5 (3)	55.9 (4)	11.5	43.5	61.0	84.7	203.5	41.2 (4)	1.9 (12)
Musculoskeletal disorders	9.5 (15)	184.8 (16)	2.9 (15)	1.3	2.4	3.1	4.2	10.6	1.8 (16)	1.8 (16)
Other non-communicable diseases	18.9 (13)	943.8 (12)	5.8 (13)	2.9	5.1	6.6	8.8	16.7	3.7 (13)	1.7 (17)
Injuries										
Transport injuries	44.5 (11)	1,877.4 (7)	13.8 (11)	4.5	11.9	22.3	35.0	91.6	23.1 (7)	2.9 (5)
Unintentional injuries	63.2 (7)	1,389.5 (11)	19.1 (8)	7.6	18.3	23.8	29.9	69.7	11.6 (11)	1.6 (19)
Self-harm and interpersonal violence	63.1 (8)	2,727.4 (5)	19.6 (7)	7.5	14.4	21.1	30.3	118.0	15.9 (8)	2.1 (11)
Forces of nature, war, and legal intervention	0.2 (20)	6.9 (20)	0.1 (20)	0.0	0.0	0.1	0.2	5.3	0.1 (20)	4.8 (2)

Abbreviations: HIV, human immunodeficiency virus; YLLs years of life lost.

[a]Measure of absolute geographic inequality.

[b]Measure of relative geographic inequality.

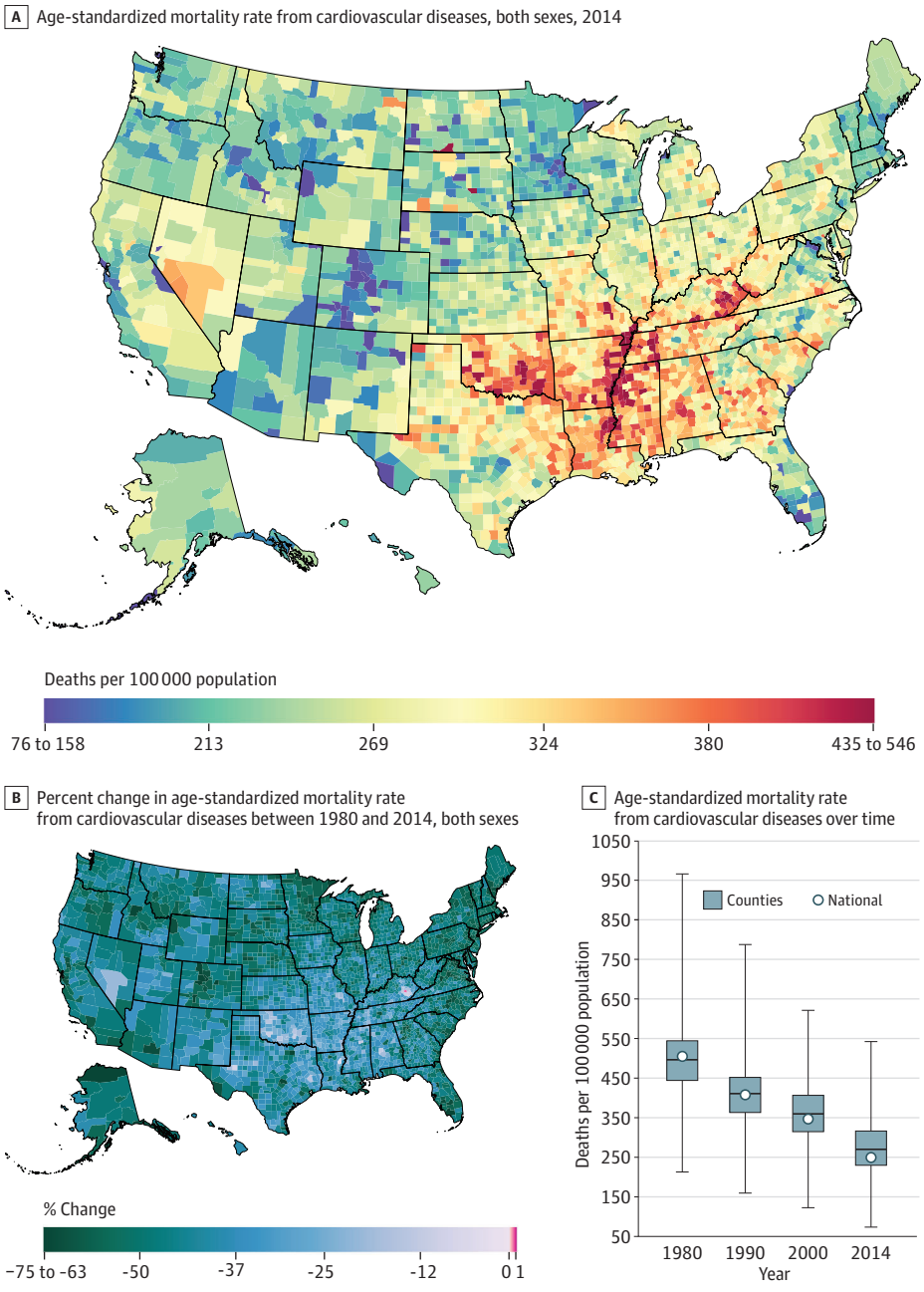

Figure 2. County-level mortality from cardiovascular diseases.

A, Age-standardized mortality rate for both sexes combined in 2014. The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. The color scale is truncated at the first percentile but not at the 99th percentile, to avoid combining counties with decreases in the mortality rate and counties with increases in the mortality rate into a single group. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.

ties), the rate of decline was highly variable. Particularly slow rates of improvement were observed in many of the same counties in the band of south-central states stretching from Oklahoma to Alabama and Kentucky that had the highest mortality rates in 2014.

Diabetes, urogenital, blood, and endocrine diseases

Diabetes, urogenital, blood, and endocrine diseases (Figure 3) caused 4,909,377 deaths (6.1%) from 1980 through 2014 and were the third leading cause of YLLs and fourth leading cause of deaths in 2014. In 2014, there was a difference of 41.2 deaths per 100,000 population in the mortality rates from these diseases between counties in the 90th and 10th percentiles. Counties throughout much of the south and mid-Atlantic had mortality rates that were higher than average. Mortality rates were particularly high in counties in Arkansas, Louisiana, and Mississippi along the Mississippi River and in counties in North Dakota and South Dakota with Native American reservations. The mortality rate from this cause increased by 21.0% (95% UI, 16.9%–24.9%) overall between 1980 and 2014. Similarly, 91.5% of counties had an increase in mortality rates from these diseases (statistically significant in 84.8% of counties). However, pockets of counties in Maryland, central Colorado, and north and western Alaska as well as individual counties throughout the rest of the country experienced declines in mortality from this cause during the same period.

Neurological disorders

Neurological disorders (Figure 4) caused 3,971,426 deaths (4.9%) between 1980 and 2014 and were the fourth leading cause of YLLs and the third leading cause of deaths in 2014. In 2014, counties in the 90th percentile had mortality rates 55.7 deaths per 100,000 population higher than counties in the 10th percentile. Compared with most of the other causes considered, broad regional geographic trends were less prominent and there was more local geographic heterogeneity: counties with relatively high and relatively low mortality rates from neurological disorders were found throughout the country. Between 1980 and 2014, the mortality rate from neurological disorders increased by 18.7% (95% UI, 15.7%–21.9%) overall. Most counties (76.2%) experienced an increase during this period (statistically significant in 61.8%), and especially large increases were observed in southern counties stretching from eastern Texas and Oklahoma to Alabama. Notable declines in mortality were found in counties in the west stretching from central Idaho and western Montana to central Colorado.

Self-harm and interpersonal violence

Self-harm and interpersonal violence (Figure 5) caused 2,049,835 deaths (2.5%) between 1980 and 2014 and were the fifth leading cause of YLLs and the eighth leading cause of deaths in 2014. In 2014, counties in the 90th percentile had mortality rates 15.9 deaths per 100,000 population higher than counties in the 10th percentile. The highest mortality rates were observed in counties in Alaska, in Native American reservations in North Dakota and

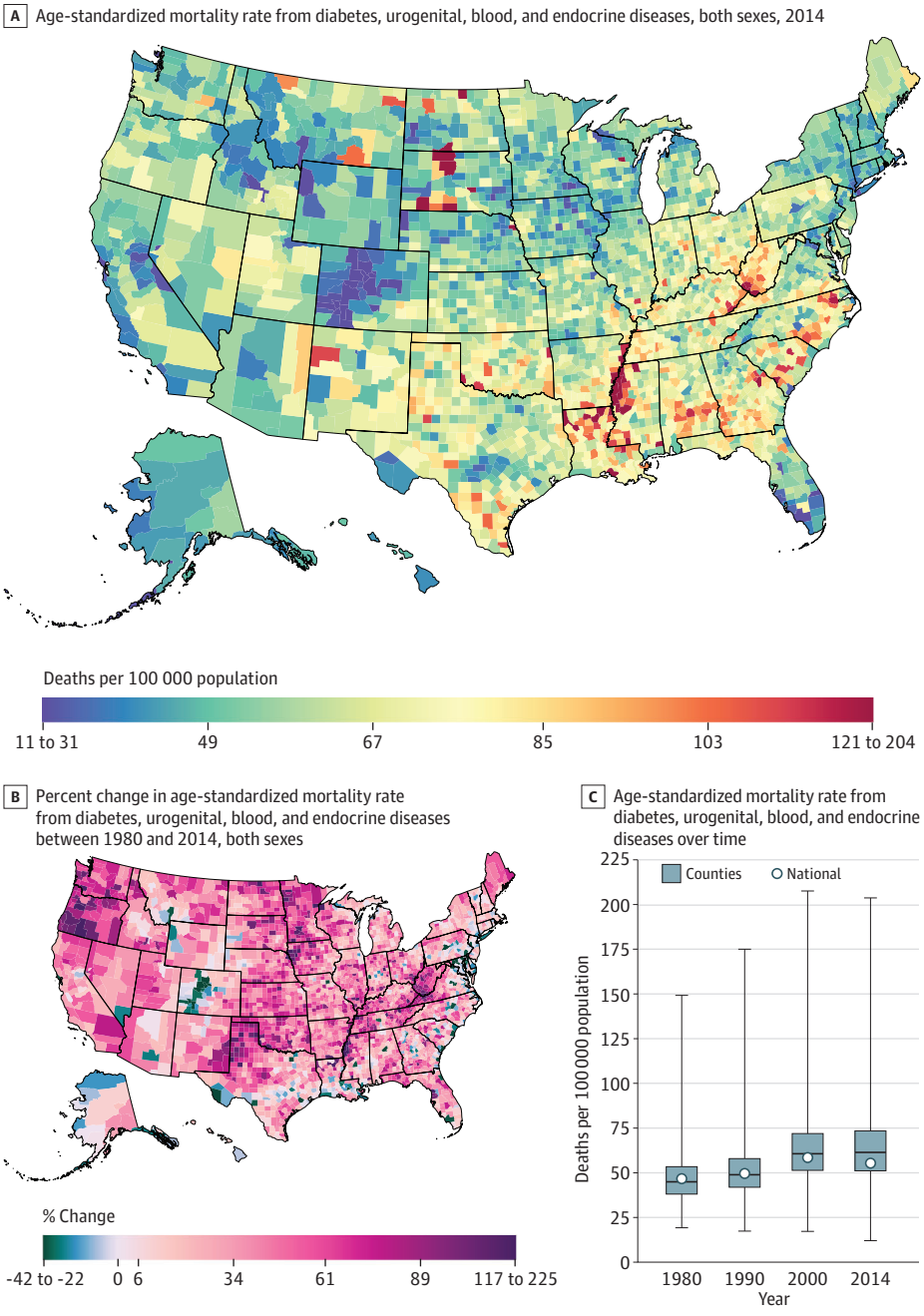

Figure 3. County-level mortality from diabetes, urogenital, blood, and endocrine diseases.

A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.

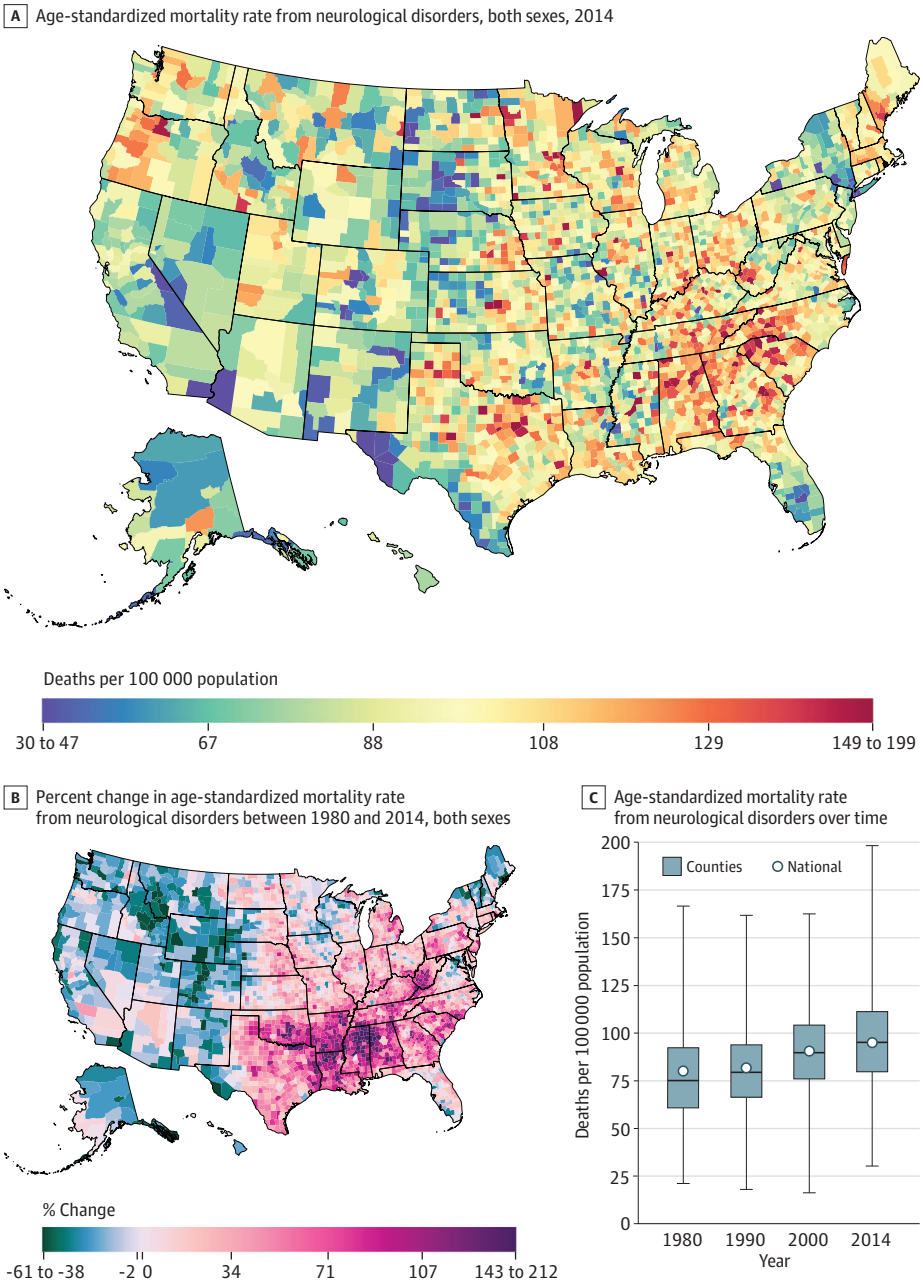

Figure 4. County-level mortality from neurological disorders.

A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.

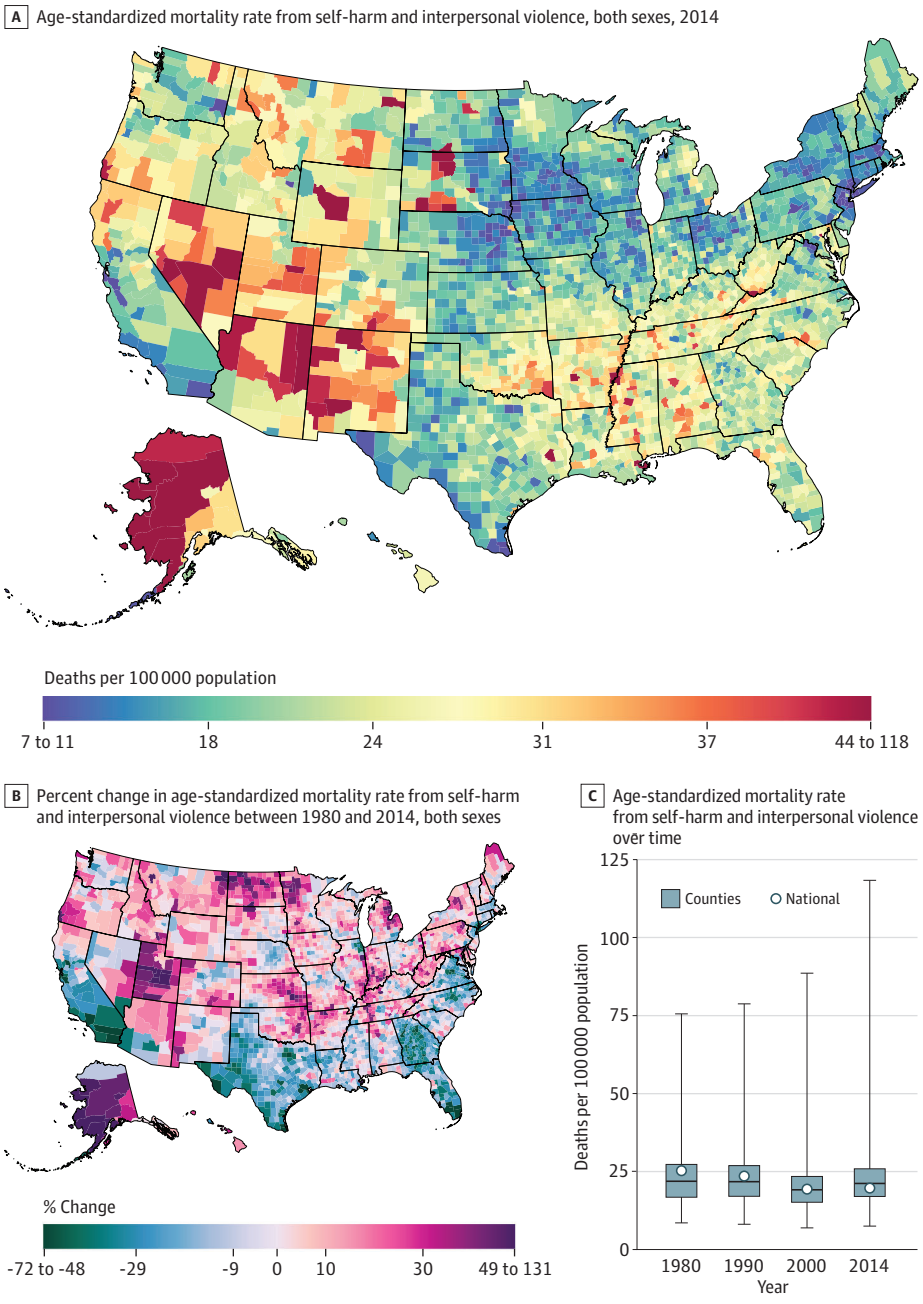

Figure 5. County-level mortality from self-harm and interpersonal violence.

A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.

South Dakota, and in states in the southwest, while lower rates were found in the upper Midwest, New England, southwestern Texas, and southern California. The mortality rate from self-harm and interpersonal violence declined by 22.1% (95% UI, 18.9%–25.3%) overall between 1980 and 2014, but changes at the county level were highly variable, with substantial declines in counties in southern California, Texas, and states along the Atlantic coast from Florida to Virginia, while counties in Utah, Oklahoma and Kansas, along the Canadian border in North Dakota and Michigan, and parts of the Midwest and New England experienced similarly substantial increases. In total, 48.8% of counties experienced declines in mortality from self-harm and interpersonal violence from 1980 to 2014, while 51.2% experienced increases (these changes were statistically significant in 29.0% and 25.7% of counties, respectively).

Chronic respiratory diseases

Chronic respiratory diseases (Figure 6) caused 4,616,711 deaths (5.7%) between 1980 and 2014 and were the sixth leading cause of YLLs and the fifth leading cause of deaths in 2014. As with other causes, there was substantial between-county variation in the mortality rate, with a difference of 41.1 deaths per 100,000 population between counties in the 90th and 10th percentiles. Elevated mortality rates were observed in a prominent cluster in eastern Kentucky and West Virginia and in a second cluster in southeastern Colorado, while the lowest mortality rates were found in the Washington, DC, area, the upper Midwest, southern Florida, southern Texas, and central Colorado. Between 1980 and 2014, mortality rates increased in a majority of counties (93.2%; statistically significant in 88.3%), with particularly sizable increases observed among counties in a band through the south from northern Texas to North Carolina and South Carolina. During the same period, a smaller number of counties, primarily along the Mexico border, in northwestern New Mexico, central Colorado, and southwestern Montana, near Washington, DC, and in eastern Pennsylvania, experienced moderate declines.

Transport injuries

Transport injuries (Figure 7) caused 1,787,070 deaths (2.2%) between 1980 and 2014 and were the seventh leading cause of YLLs and the 11th leading cause of deaths in 2014. Counties in the 90th percentile experienced mortality rates 23.1 deaths per 100,000 population higher than counties in the 10th percentile. In general, lower mortality rates were found in more urban areas, while higher mortality rates were found in more rural areas. The mortality rate from transport injuries declined for the United States as a whole by 45.4% (95% UI, 43.3%–47.5%) between 1980 and 2014. Most counties also experienced a decline during this period (98.5%; statistically significant in 93.6%), but to varying degrees. Counties in the central United States generally saw smaller improvements, while counties in the west, northern Midwest, New England, and southern Florida experienced more substantial declines.

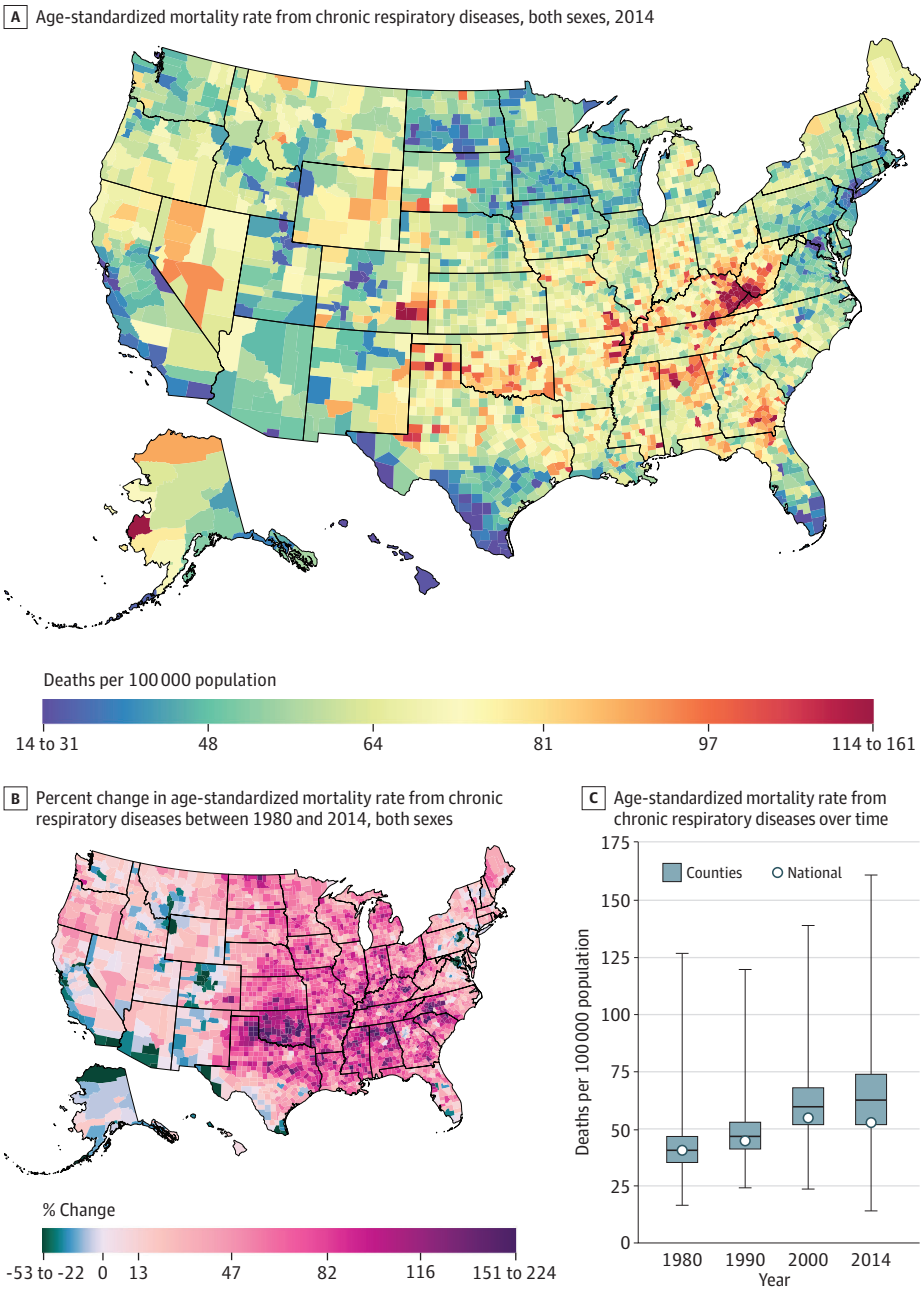

Figure 6. County-level mortality from chronic respiratory diseases.

A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.

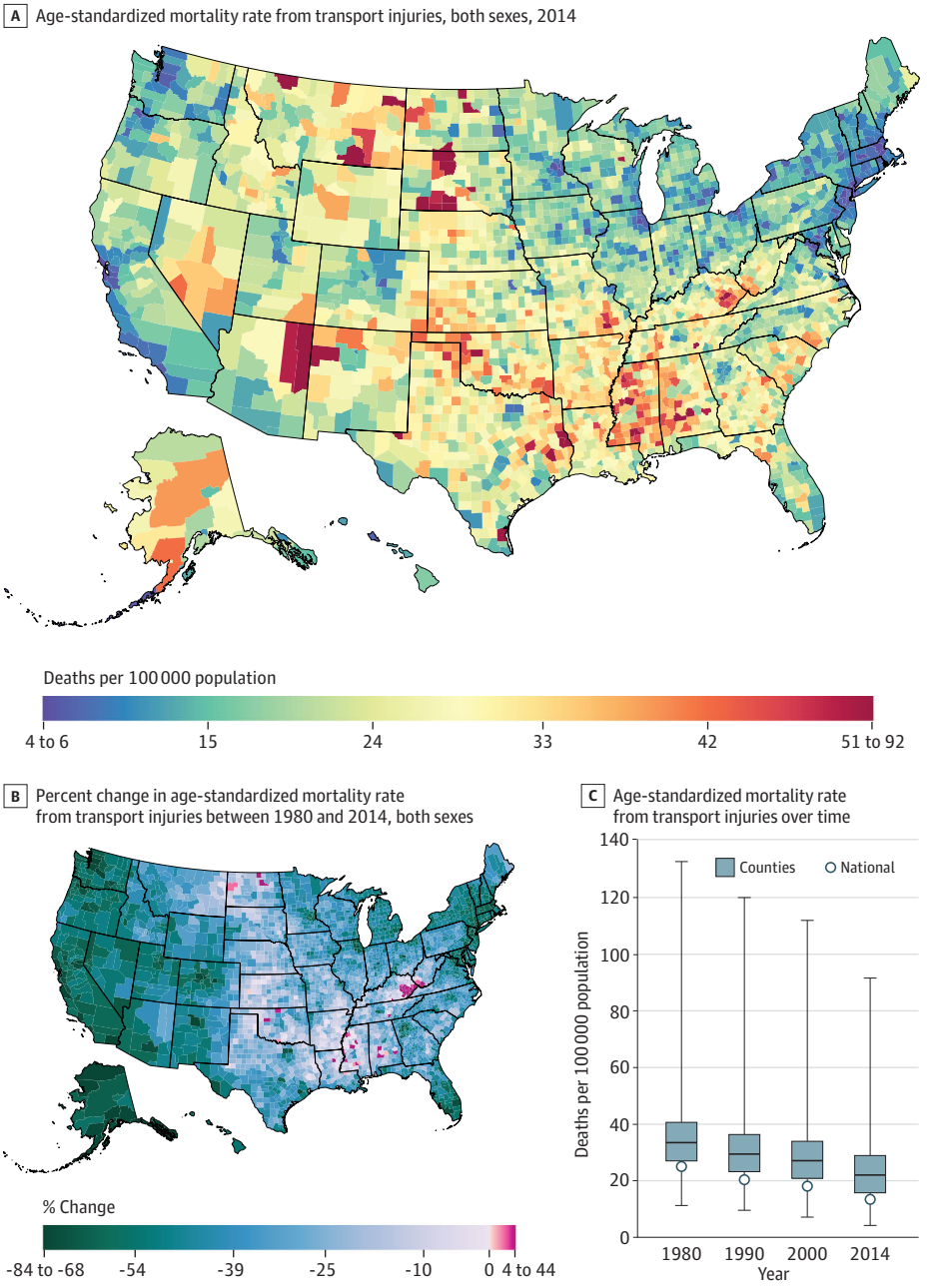

Figure 7. County-level mortality from transport injuries.

A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.

Mental and substance use disorders

Mental and substance use disorders (Figure 8) caused 814,391 deaths (1.0%) between 1980 and 2014 and were ranked eighth in terms of YLLs and 12th in terms of deaths in 2014. Mortality rates among counties in the 90th percentile were 15.0 deaths per 100,000 population higher than among counties in the 10th percentile. Exceptionally high mortality rates were found in a cluster of counties in eastern Kentucky and southwestern West Virginia; in counties in North Dakota, South Dakota, and southwestern states with Native American reservations; and in Alaska. Conversely, the lowest rates in 2014 were found primarily in counties in Nebraska, Iowa, and eastern South Dakota. The mortality rate due to mental and substance use disorders increased by 188% (95% UI, 160%–207%) overall between 1980 and 2014 and also increased in nearly every county (99.1%; statistically significant in 96.2%). However, the amount of increase varied dramatically across counties. In particular, there were several clusters of counties (in Kentucky, West Virginia, Ohio, Indiana, western Pennsylvania, and east-central Missouri) where mortality rates increased by more than 1,000% during this period.

Cirrhosis and other chronic liver diseases

Cirrhosis and other chronic liver diseases (Figure 9) caused 1,506,985 deaths (1.9%) between 1980 and 2014 and were the ninth-ranked cause of YLLs and deaths in 2014. At the county level, mortality rates in the 90th percentile were 14.0 deaths per 100,000 population higher than mortality rates in the 10th percentile. Counties in eastern Arizona, New Mexico, and south and western Texas and in selected counties in Colorado, Nevada, Wyoming, Montana, North Dakota, and South Dakota had the highest mortality rates, while counties in eastern South Dakota and Kansas as well as in Iowa and southern Minnesota had the lowest mortality rates. Between 1980 and 2014, the mortality rate from this cause declined by 15.6% (95% UI, 9.1%–26.9%) overall but increased in 69.6% of counties (statistically significant in 25.9%), with particularly large increases in southwestern Oregon and northwestern Texas.

Diarrhea, lower respiratory, and other common infectious diseases

Diarrhea, lower respiratory, and other common infectious diseases (Figure 10) were responsible for 3,234,692 deaths (4.0%) between 1980 and 2014 and were the 10th leading cause of YLLs and the sixth leading cause of deaths in 2014. Counties in the 90th percentile experienced mortality rates 25.8 deaths per 100,000 population higher than those in the 10th percentile. Mortality rates from this cause were highest in counties in southern states from Louisiana and Arkansas to Georgia, Tennessee, and Kentucky, while rates were lower than average in southern Florida, New England, the upper Midwest, central Colorado, and the Pacific Northwest. Nationally, the mortality rate from this cause declined by 22.1% (95% UI, 18.0%–26.8%) between 1980 and 2014. However, 28.3% of counties experienced increases in this mortality rate during the same period (statistically significant in 13.5%), with especially large increases found in counties in Louisiana, Arkansas, Mississippi, Alabama, southern Illinois, and eastern Kentucky.

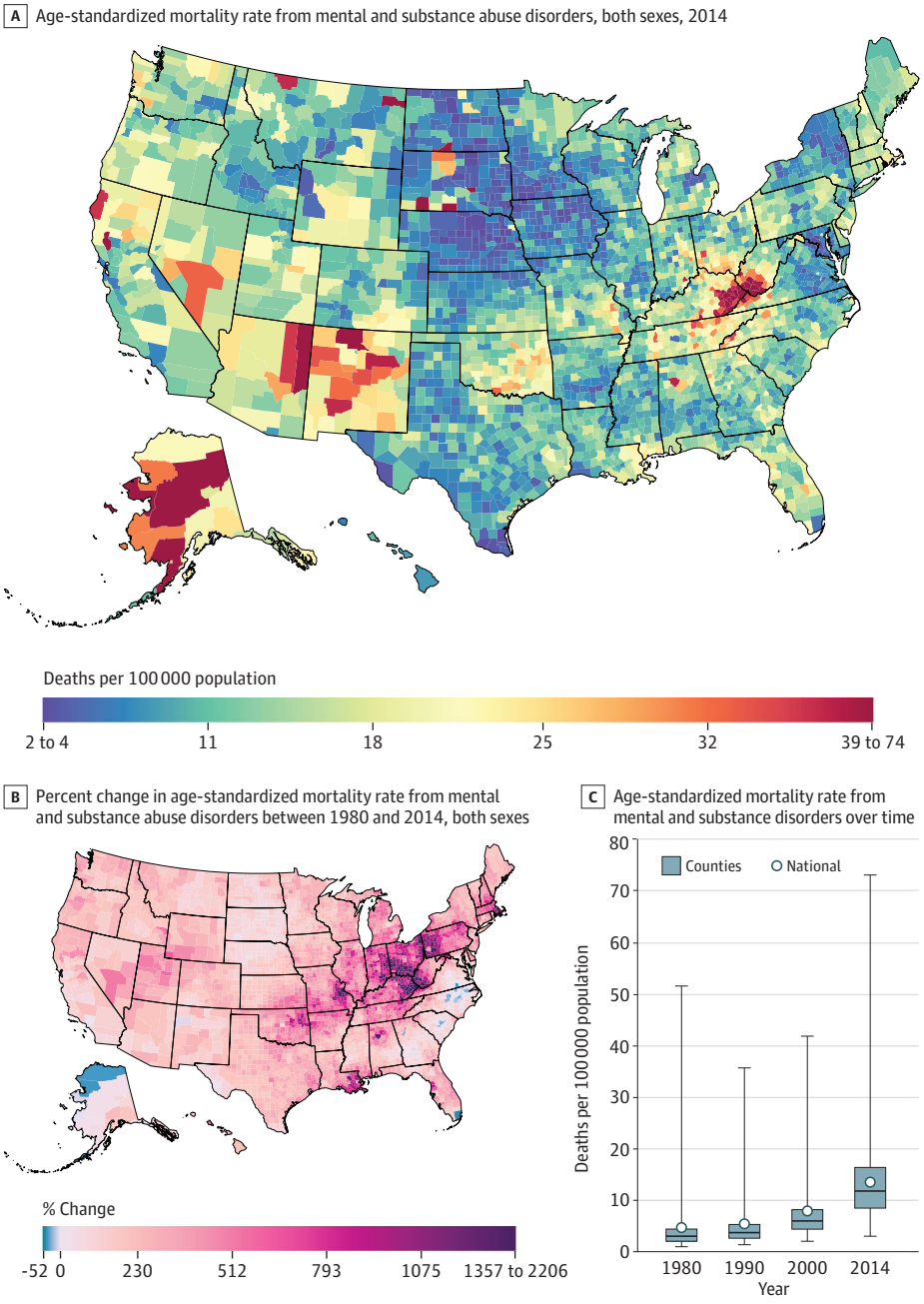

Figure 8. County-level mortality from mental and substance use disorders.

A, Age-standardized mortality rate for both sexes combined in 2014. The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. The color scale is truncated at the 99th percentile but not at the first percentile, to avoid combining counties with decreases in the mortality rate and counties with increases in the mortality rate into a single group. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.

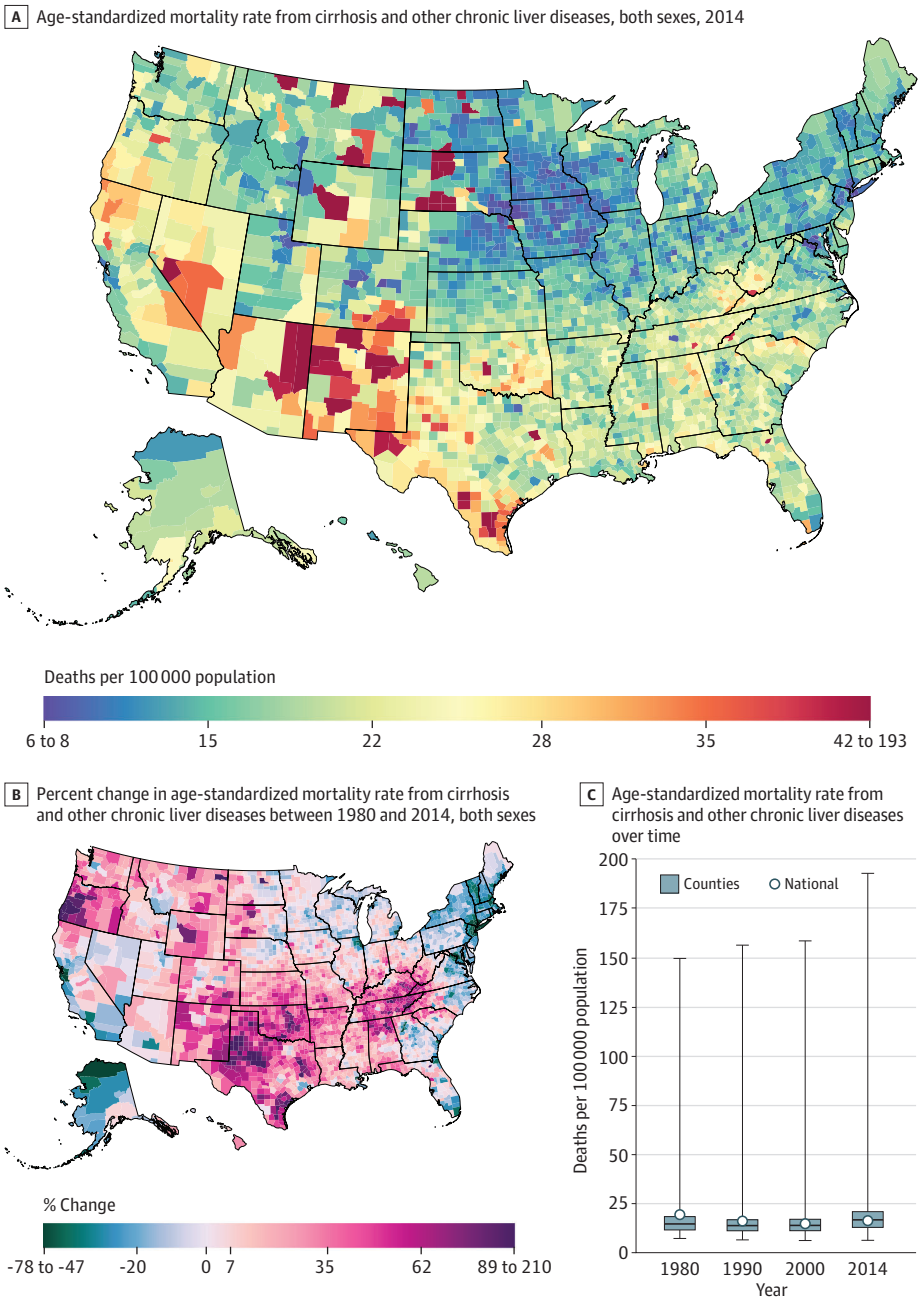

Figure 9. County-level mortality from cirrhosis and other chronic liver diseases.
A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.

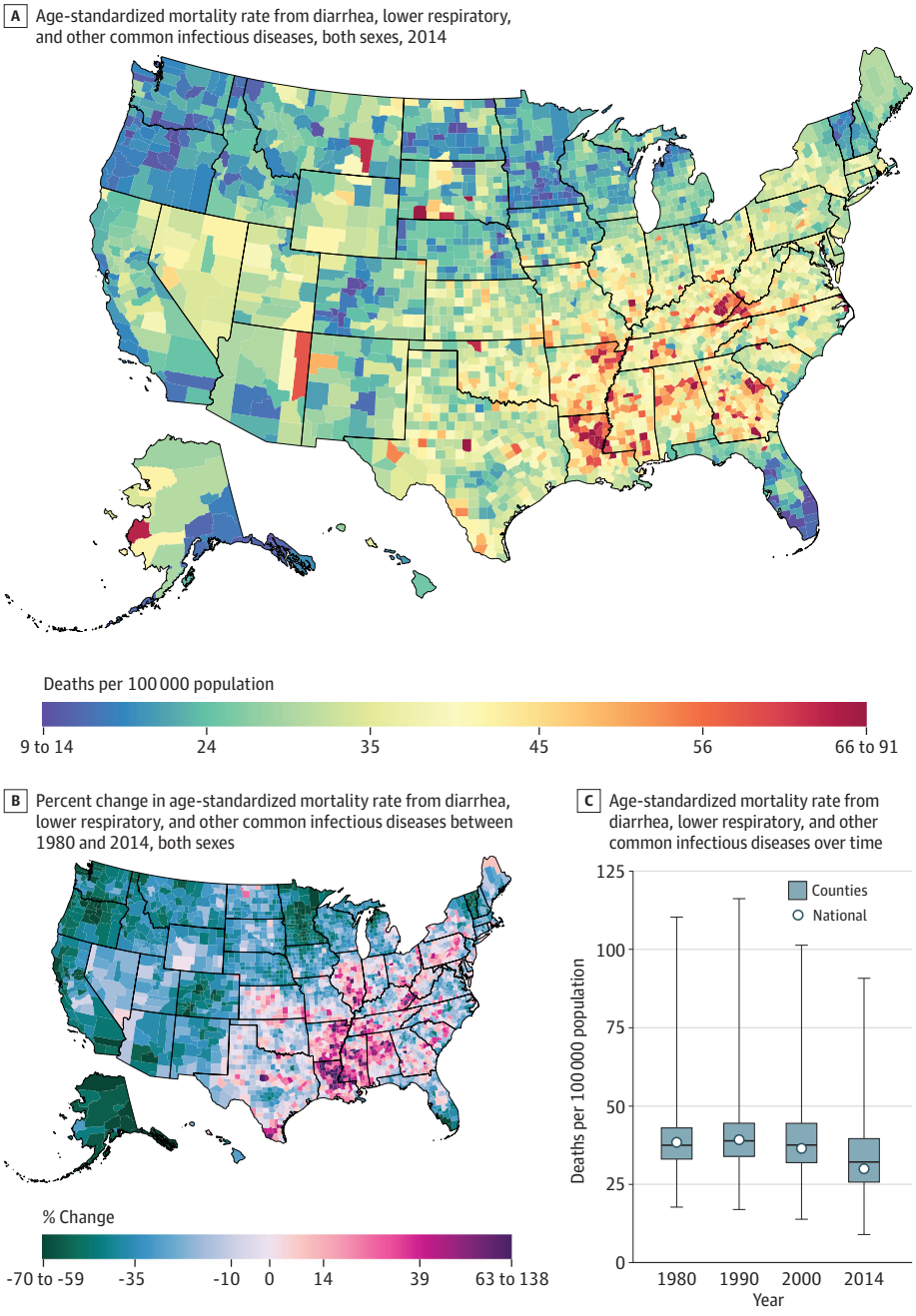

Figure 10. County-level mortality from diarrhea, lower respiratory, and other common infectious diseases. A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.

DISCUSSION

Using a novel method, this study estimated county-level mortality rates by cause for 21 major causes of death. This analysis improves on previous analyses in 3 ways. First, the scope of this analysis was much larger than in previous studies: this is the first study, to our knowledge, that considered a comprehensive set of causes over an extended period. Second, this analysis used garbage code redistribution methods to reassign deaths originally classified using insufficiently specific or implausible cause of death codes. To our knowledge, garbage code redistribution methods have not previously been used at the county level. Third, this analysis used new small area estimation methods that generated more precise estimates and more accurately quantified uncertainty compared with models previously used. As a consequence of these advances, the results of this study represent the most detailed and comprehensive accounting of county-level patterns of cause-specific mortality currently available.

Geographic patterns differed significantly across causes, underscoring the importance of considering cause-specific mortality in addition to measures of all-cause mortality such as life expectancy. For some causes (eg, cardiovascular diseases), counties in the south and Appalachia had elevated mortality, while counties in western states had mortality much lower than average, a pattern that, broadly speaking, has also been documented in maps of life expectancy as well as maps of risk factors such as smoking, physical inactivity, and obesity.[1,26,27] However, other causes had very different geographic patterns. Moreover, for some causes (eg, mental and substance use disorders), there were striking clusters of counties with very high mortality rates. Geographic patterns in changes over time were similarly variable among causes.

Information on cause-specific mortality rates and rankings among causes has long been available at the national level[19–21,28] and has been widely used for public health planning and policy making, but to our knowledge this analysis is the first to consider an exhaustive set of causes of death at the county level and to track changes over an extended period at this level. There are a number of potential uses for these estimates: state and county health departments could use county-level mortality estimates to identify pressing local needs and to tailor policies and programs accordingly; physicians could use these estimates to better understand the health concerns of the populations they serve; researchers could identify counties that have done unexpectedly well or poorly with regard to a particular cause of death and that warrant additional study to identify factors driving these trends; and communities can use these estimates as evidence when advocating for change. Further, for causes of death for which effective treatments are available, variation in mortality rates can highlight where access to treatment or quality of care is a pressing problem. Additionally, local-level estimates of mortality, and particularly cause-specific mortality, provide a mechanism for evaluating

the effect of policies and programs implemented in some, but not all, localities. More detailed cause-specific information will further enhance the utility of this type of analysis to all of these stakeholders, and in the future we plan to carry out more detailed analyses at the third and fourth levels of the GBD cause hierarchy using the framework outlined in this analysis.

This study has several important limitations. First, the death registration data do not include deaths of US residents that occurred outside the United States, although these deaths are a very small percentage of the total. Second, the population counts were based on intercensal interpolations and postcensal projections that may be subject to error. Likewise, the covariates incorporated in the small area models were based on census and other administrative data and may also be subject to error.

Third, the garbage code redistribution methods used in this analysis have not been validated against a gold standard, such as autopsy, owing to insufficient data. However, several findings support the validity of the redistribution algorithm: redistribution reduces or eliminates discontinuities in temporal trends that coincide with revisions to the *ICD* for some causes (eg, ischemic heart disease), resulting in more plausible time trends[9]; redistribution results in more plausible geographic patterns across and within countries based on existing knowledge of the distribution of risks (eg, more reasonable patterns of ischemic heart disease mortality given knowledge of the distribution of related risk factors)[29]; and in a small number of cases in which hospital linkage studies have been used to examine the cause of death in cases for which death certificates list garbage codes, the results are broadly consistent with the effect of the redistribution algorithms.

Fourth, although the garbage code redistribution methods used in this analysis may be subject to error, this uncertainty is difficult to quantify and has not been accounted for in the reported UIs. Fifth, it is possible that the large increases over time observed for some causes of deaths are driven by changing registration practices and growing recognition among physicians of these particular causes of death. This is particularly true of Alzheimer disease and other dementias.[30] However, the county-level estimates were raked to national-level estimates that incorporated prevalence data not subject to this same limitation, and this may have reduced this error. Sixth, small area models were used to more precisely estimate mortality rates, although there may be some situations in which these models were suboptimal. In particular, the models used in this analysis smoothed over time, space, and age group. As a result, unusually high or low mortality rates may have been attenuated, particularly in small counties, leading to an underestimation of geographic inequalities.

CONCLUSIONS

In this analysis of US cause-specific county-level mortality rates from 1980 through 2014, there were large between-county differences for every cause of death, although geographic patterns varied substantially by cause of death. The approach to county-level analyses with small area models used in this study has the potential to provide novel insights into US disease-specific mortality time trends and their differences across geographic regions.

ARTICLE INFORMATION

Author contributions

Dr Murray had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Dwyer-Lindgren, Bertozzi-Villa, Flaxman, Mokdad, Murray. Acquisition, analysis, or interpretation of data: Dwyer-Lindgren, Bertozzi-Villa, Stubbs, Morozoff, Kutz, Huynh, Barber, Shackelford, Mackenbach, van Lenthe, Flaxman, Naghavi, Mokdad. Drafting of the manuscript: Dwyer-Lindgren, Bertozzi-Villa. Critical revision of the manuscript for important intellectual content: Bertozzi-Villa, Stubbs, Morozoff, Kutz, Huynh, Barber, Shackelford, Mackenbach, van Lenthe, Flaxman, Naghavi, Mokdad, Murray. Statistical analysis: Dwyer-Lindgren, Bertozzi-Villa, Stubbs, Kutz, Huynh, Barber, Flaxman, Naghavi. Obtained funding: Mokdad, Murray. Administrative, technical, or material support: Morozoff, Shackelford, Mokdad, Murray. Study supervision: Mackenbach, van Lenthe, Mokdad, Murray.

Conflict of interest disclosures

All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

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EAPPENDIX

Garbage code redistribution

Garbage code redistribution methods developed for the Global Burden of Diseases, Injuries, and Risk Factors study (GBD)[1] were used in this study in order to reassign deaths to appropriate target causes. This method included four different approaches to determining the fraction of deaths assigned to each group of garbage codes that should be reassigned to a given target cause. Deaths assigned each group of garbage codes are addressed using one of these four approaches.

Both the first and second approaches used fixed proportions, i.e., the same proportions were applied to deaths assigned garbage codes regardless of which county those deaths occurred in. In the first approach, the fixed proportions were derived from relevant literature and/or expert opinion.

In the second approach, based on work by Ahern et al.,[2] the fixed proportions were derived from regression models fit to all available deaths registration data. Specifically, for a particular group of related garbage codes, the following model was fit separately for each target code and sex:

$$T_{c[r,s],t,a} = \alpha + \gamma_{1,s} + \gamma_{2,r} + (\beta_1 + \beta_{2,a} + \gamma_{3,s} + \gamma_{4,r}) \cdot G_{c[r,s],t,a} + \in_{c[r,s],t,a}$$

where:

- c indicates country, s and r indicate the super-region and region where c is located (according to the definition used by the GBD), t indicates the year, and a indicates the age group, in this case: <15 years, 15–49 years, 50–59 years, 60–69 years, 70–79 years, or 80+ years;
- $T_{c[r,s],t,a}$ is the proportion of deaths coded to the given target cause among all deaths coded either to the specified garbage code or any of its target causes, within country c, year t, and age group a;
- $G_{c[r,s],t,a}$ is the proportion of deaths coded to the specified garbage code among all deaths coded either to the specified garbage code or any of its target causes, within country c, year t, and age group a;
- α is the intercept;
- $\gamma_{1,s}$ and $\gamma_{2,r}$ are super-region- and region-level random intercepts;
- β_1 is the slope on $G_{c[r,s],t,a}$;
- $\beta_{2,a}$ is an age-group-specific slope on $G_{c[r,s],t,a}$;
- and $\gamma_{3,s}$ and $\gamma_{4,r}$ are super-region- and region-level random intercepts on $G_{c[r,s],t,a}$.

In general, an inverse relationship between $G_{c[r,s],t,a}$ and $T_{c[r,s],t,a}$ is expected: if deaths assigned to a garbage code are, in truth, due to a particular target cause, then as the overall proportion of deaths assigned garbage codes increases, the deaths assigned to a target cause should decline. This relationship may, however, vary by country or age group, so this relationship was approximated for each country and age group based on the fitted regression model $\beta_1 + \beta_{2,a} + \gamma_{3,s} + \gamma_{4,r}$. Within each country and age group, target causes where the overall effect was not negative were dropped and then the effects for the remaining targets were re-scaled to sum to 1. These re-scaled effects were used as the proportions for redistributing garbage codes to the appropriate target causes.

The third approach redistributed deaths assigned garbage codes to all relevant targets in proportion to the number of deaths observed at the state level in each target group prior to redistribution.

The fourth approach was specific to garbage codes related to Kaposi sarcoma and certain other infectious diseases and immunodeficiencies that are known to be frequently used when the underlying cause of death is HIV/AIDS. In these cases, the regional rate of change compared to 1980–84 was calculated for each set of garbage codes. The proportion of deaths assigned to these garbage codes that were due to HIV/AIDS was expected to have increased much more rapidly than the proportion due to other target causes as the HIV/AIDS epidemic expanded. Consequently, any increase greater than 5% was assumed to have been due to deaths that should have been coded as due to HIV/AIDS, while the remainder of deaths were assigned to other appropriate target codes. Separate redistribution proportions were derived by sex, age group, and 5-year time interval.

Note that the first approach is independent of the US deaths data used elsewhere in this analysis, while the third approach uses only this data in order to derive the redistribution proportions. In contrast, the second approach uses all available deaths registration data globally while the fourth uses data from countries in the same region as defined by the GBD (in this case, high income North America, i.e., the US and Canada). Regardless of how the redistribution proportions were derived, they were always applied by county such that there is no change in the total number of deaths in any county as a result of redistribution.

Deaths assigned each garbage code (or group of closely related garbage codes) were redistributed using one of the four methods described. Method 4, the HIV/AIDS method, is specific to a subset of garbage codes that are known to be commonly assigned when HIV/AIDS is the true underlying cause. Among the remaining garbage codes, the regression method (method 2), was generally used for garbage codes with a relatively small number of specified targets; this method tends to break down when there are a large number of targets because there is

often insufficient data to estimate all of the relevant relationships. For garbage codes where the regression method was not appropriate or where the results of the regression method were implausible, published literature (method 1) was used as the basis for redistribution if available, and otherwise the observed proportions among the targets (method 3) was used. Garbage codes that have little information content (e.g., 'senility') were typically redistributed to all causes using method 3.

These garbage code redistribution methods were designed to be applied at the most detailed levels of the GBD cause hierarchy (i.e., levels 3 and 4). Although this analysis does not consider these more detailed causes, redistribution was carried out at this level and deaths were then aggregated to the second level of the GBD cause hierarchy prior to applying the small area models.

SAE model

The following model was estimated separately for males and females:

$$D_{j,t,a} \sim \text{Poisson}(m_{j,t,a} \cdot P_{j,t,a})$$
$$\log(m_{j,t,a}) = \beta_0 + \boldsymbol{\beta_1} \cdot \boldsymbol{X_{j,t}} + \gamma_{1,a,t} + \gamma_{2,j} + \gamma_{3,j} \cdot t + \gamma_{4,j,t} + \gamma_{5,j} \cdot a + \gamma_{6,j,a}$$

where

- j, t, and a are indices for county, calendar year (1980–2014, renumbered sequentially from 0 to 34), and age group (0, 1–4, 5–9,… , 75–79, and 80+, recoded sequentially from 0 to 17), respectively;
- $D_{j,t,a}$ and $P_{j,t,a}$ are the number of deaths and the population count, respectively, in county j, year t, and age group a;
- $m_{j,t,a}$ is the underlying mortality rate in county j, year t, and age group a;
- β_0 is an intercept;
- $\mathbf{X}_{j,t}$ is a vector of covariates for county j and year t, and $\boldsymbol{\beta_1}$ is the associated vector of regression coefficients;
- $\gamma_{1,a,t}$ is an age group- and year-level random intercept;
- $\gamma_{2,j}$ is a county-level random intercept;
- $\gamma_{3,j}$ is a county-level random slope on year;
- $\gamma_{4,j,t}$ is a county- and year-level random intercept;
- $\gamma_{5,j}$ is a county-level random slope on age group;
- and $\gamma_{6,j,a}$ is a county- and age group-level random intercept.

γ_2, γ_3, and γ_5 were each assumed to follow a conditional autoregressive distribution[3] where the full conditional distribution is given by:

$$\gamma_j|\gamma_{k\sim j}, \sigma^2, \rho \sim \text{Normal}\left(\frac{\rho \cdot \Sigma_{k\sim j}\,\gamma_k}{n_j \cdot \rho + 1 - \rho}, \frac{\sigma^2}{n_j \cdot \rho + 1 - \rho}\right)$$

where

- $k\sim j$ indicates the set of counties k that are adjacent to county j;
- n_j is the number of counties in $k\sim j$;
- and σ^2 and ρ are variance and correlation parameters, respectively.

These random effects allow for spatial variation beyond what is already explained by the covariates in the overall level (γ_2), linear deviations from the overall time trend (γ_3), and linear deviations from the overall age pattern (γ_5). The σ^2 parameters control the amount of spatial variation in each of these dimensions while the ρ parameters, which vary between 0 and 1, determine the spatial smoothness. At the limit, as ρ goes to 0 this distribution reduces to a fully exchangeable model where the neighborhood configuration is non-informative: $\gamma_j|\sigma^2 \sim$ Normal(0, σ^2). At the other extreme, as ρ goes to 1, this distribution reduces to an intrinsic conditional autoregressive distribution where

$$\gamma_j|\gamma_{k\sim j}, \sigma^2 \sim \text{Normal}\left(\frac{\Sigma_{k\sim j}\gamma_k}{n_j}, \frac{\sigma^2}{n_j}\right)$$

indicating a high degree of spatial smoothness.

γ_1 was also assumed to follow a conditional autoregressive distribution. Specifically, this was specified as the interaction between two distributions as defined above, but for age and time, respectively, rather than county. This was specified according to the procedure described by Clayton[4] and Knorr-Held[5] (i.e., a 'Type IV' interaction). This specification allows for smoothing over age group and time simultaneously, such that the level for a given age group and year is informed both by first order neighbors (i.e., adjacent years in the same age group and adjacent age groups in the same year) as well as second order neighbors (i.e., adjacent years in adjacent age groups). For this distribution there are three hyperparameters: σ^2, which controls the overall amount of variation, and ρ_{age} and ρ_{time} which control the smoothness over age and time, respectively.

γ_4 and γ_6 were assumed to follow identical and independently distributed Normal distributions. These random effects were included in order to allow for non-linear county-level deviations in the time or age pattern (linear deviations are captured by γ_3 and γ_5).

Gamma(1, 1000) priors were specified for the inverse variance ($1 / \sigma^2$) of each random effect. Normal(0, 1.5) priors were specified for the logit-transform of the correlation parameters (ρ).

The Template Model Builder (TMB) package[6] in R version 3.2.4[7] was used to fit this model. Broadly speaking, there were three steps in this model fitting process. First, TMB was used to find the Laplace approximation to the marginal log-likelihood of the data and model parameters with respect to the hyperparameters (i.e., σ^2 and ρ terms) integrating over all fixed and random parameters (i.e., β and γ terms). Second, non-linear optimization routines in R were used to maximize this approximated marginal log-likelihood plus marginal prior for the hyperparameters and derive point estimates for all model parameters. Third, a generalized delta-method implemented in TMB was used to approximate the joint precision matrix for all model parameters.

After fitting the model, 1,000 draws from the posterior distribution were generated using a multivariate-normal approximation. Posterior draws of $m_{j,t,a}$ were derived from each posterior draw of the model parameters. Finally, point estimates and 95% uncertainty intervals for $m_{j,t,a}$ were derived from the mean and 2.5th and 97.5th percentiles, respectively, of these 1,000 draws.

Model validation

Methods

The performance of the small area models used in this analysis, several variants on this model, and two previously published models, was assessed using a framework similar to that initially described by Srebotnjak et al.[8] Broadly, there were three steps in this process.

In the first step, a 'validation set' of counties was identified. These are counties with large populations where the effect of stochastic noise is expected to be small such that the directly observed mortality rate is very close to the underlying mortality rate and can therefore be treated as a 'gold standard.' To maximize the number of counties that were eligible to be included in the validation set, populations and deaths for each county were first pooled using a three-year moving window. The dataset was then subset to only counties with non-zero death counts in every age group in each year for both males and females. For each remaining county, 1,000 draws of the mortality rate for each age group, sex, and year were simulated assuming a Poisson distribution; age groups were combined in order to generate 1,000 draws of the age-standardized mortality rate for each sex and year; and the coefficient of variation of the age-standardized mortality rate and of each age-specific mortality rate in each year and sex was calculated (i.e., the standard deviation of the draws divided by the mean of the draws). Finally, counties where the coefficient of variation was less than 1% for the age-standardized mortality rates and less than 10% for the age-specific mortality rates across all years and both sexes were selected for the validation set.

In the second step, validation data sets were created and used to fit each model and derive predictions. A total of 60 validation data sets were generated: 10 each to examine the perfor-

mance of the model for counties with a total population of 1,000, 3,000, 5,000, 10,000, 25,000, and 100,000, corresponding roughly to the 1st, 5th, 10th, 25th, 50th, and 80th percentile across all counties and years. To create each validation data set, a pre-specified number of individuals were sampled in each county in the validation dataset from the observed population age-sex distribution. Then, for each age and sex in each county in the validation dataset, deaths were sampled from a Poisson distribution with mean equal to the observed mortality rate times the sampled population size in that age group and sex. The data for all counties not in the validation dataset were included without modification. After creating the validation data sets, models were fit to these data and predictions derived in the same manner as for the observed data.

Finally, the predictions were compared to the directly observed age-standardized mortality rates. For each model corresponding to a different validation data set, and for each county-year in the validation set, the relative error ($100 \cdot (m_{gs} - m_{pred}) / m_{gs}$, where m_{gs} is the gold standard age-standardized mortality rate, and m_{pred} is the predicted age-standardized mortality rate) was calculated and whether or not the gold standard was contained by the predicted lower and upper uncertainty intervals was recorded. Across all county-years in the validation set and across all 10 validation data sets at each population level, performance was summarized in terms of the mean relative error, the mean absolute relative error (i.e., the mean of the absolute value of the relative error), and the coverage (i.e., the percent of county-years where the gold standard estimate was between the lower and upper uncertainty intervals).

A total of six models were considered.

1. The model described in the previous section.
2. As in (1), but excluding the $\gamma_{4,j,t}$ and $\gamma_{6,j,a}$ terms. This simplifies the model in (1) by only allowing for linear county-level deviations from the overall age and time trend.
3. As in (2), but also excluding $\gamma_{3,j} \cdot t$ and $\gamma_{5,j} \cdot a$ terms. This further simplifies the model in (2) by assuming that the time and age pattern is the same across all counties (beyond differences accounted for by the included covariates).
4. As in (3), but replacing $\gamma_{1,a,t}$ with separate (i.e., not interacted) age and time random effects. This simplifies the model in (3) even further by assuming no interaction between the age pattern and time pattern, i.e., that the same age pattern applies in all years and, equivalently, that the same time pattern applies to all age groups.
5. The model described by Kulkarni et al.[9] In this approach, separate mixed effects models are specified for each age group and each year and a two-stage fitting procedure is used to estimate and incorporate spatial effects.
6. The model described by Wang et al.[10] This model is an extension of the Kulkarni model that adds an additional step wherein a non-parametric temporal smoothing model is applied to the predictions in larger counties. In both the analysis by Kulkarni and the analysis by Wang, smaller counties were merged with their neighbors until all counties were part of

units with at least 5,000 males and 5,000 females. For this analysis, for comparability with models 1–4, no counties were merged beyond what was required to obtain historically stable analytic units.

Four variants on the model developed for this analysis were included in order to assess whether more complicated versions of this model allowing for more flexible interactions between age, time, and space, were appropriate, particularly for smaller populations. The previously published models were included to assess whether or not the approach developed for this analysis improves on methods that were already available. The models by Wang and Kulkarni frequently failed to converge when fit to validation sets with population size 1,000, so results from these models are not reported at this level.

This validation framework was computationally intensive as it required fitting each model and generating predictions 120 times (once for males and once for females to each of the 60 validation data sets). Consequently, applying this validation framework to each cause individually was infeasible, so instead performance overall was assessed in terms of all-cause mortality.

Results

The mean relative error for the age-standardized mortality rate is presented in eTable 4. The mean relative error is a measure of bias, i.e., whether the rates estimated by the model were systematically higher or lower than the true rates. There was no evidence of bias in either model 1 or 2, where the mean relative error never exceeded +/- 1%. For models 3 and 4, the mean relative error was similarly less than 1% at all but the smallest population size considered (1,000), where it was approximately -2.5%. The mean relative error for the other two models was more substantial: above 1% even for the largest population size, and more than 2% and 5% at maximum for the models by Kulkarni and Wang, respectively.

The mean absolute relative error for the age-standardized mortality rate is given in eTable 5. This is a measure of the overall error, i.e., how much the model estimates differ from the true estimates. As anticipated, all models performed better in this regard for larger populations. At the smallest population size, models 1–4 performed roughly equally with around 6.5–7% error, although the model used in the final analysis (1) did have the lowest error overall. For larger population sizes, models 1 and 2 outperformed models 3 and 4 by a substantial margin. The models by Kulkarni and Wang performed worse than models 1 and 2 but better than models 3 and 4 at the largest population size, however they consistently had the highest mean absolute relative error at smaller population sizes.

eTable 6 shows the coverage for the age-standardized mortality rate. Ideally, coverage should be as close as possible to 95% as this indicates that the 95% uncertainty intervals are an

appropriate reflection of an estimate's precision. Model 1 had good coverage for counties of all population sizes. Coverage for models 2–4 was generally too low, though it was better for model 2 as compared to models 3 and 4, and for small counties as compared to large counties. Coverage for the models by Kulkarni and Wang was also too low, but was better for larger populations than for smaller ones.

In summary, models 1 and 2 slightly outperformed models 3 and 4 in terms of the mean relative error and were substantially better when compared in terms of the mean absolute relative error. The models by Kulkarni and Wang performed less well in terms of both mean relative error and mean absolute relative error than all other models. In terms of coverage, model 1 was superior to all of the other models.

Raking

After the modeling steps, results were adjusted to ensure consistency across two dimensions: cause hierarchy and geography.

Adjustments by cause were needed because SAE models were run independently for all-cause mortality and each of the 24 causes in the first and second level of the GBD cause hierarchy. Thus, the cause-specific model outputs do not necessarily nest as they should; that is, summing predicted deaths from the three level 1 causes does not result in precisely the predicted all-cause death count, although generally it will be close.

Adjustments were also needed in order to ensure consistency with national-level estimates from the GBD. These estimates are based on the same death registration data but also incorporated other data sources for certain causes where registration data are known to be sub-optimal (e.g., dementias). These data were not available at the county level, so instead county-level estimates were raked to the GBD national-level estimates to capitalize on the additional information content.

To accomplish these twin goals, an algorithm known as raking, and also called iterative proportional fitting, was utilized. Given an N-dimensional table whose internal entries denote uncertain values and whose marginals denote aggregated, more certain values, raking provides a means of fitting the internal entries to the marginals while preserving some internal relationships of the table. This is accomplished simply by proportionately scaling the rows to add up to their marginal totals, then scaling the columns the same way, and repeating until the entries in the table stabilize (i.e., converge).

Consider a two-dimensional table with r rows and c columns, where $n_{i,j}$ refers to the entry in the (i,j)th cell, and N_i and N_j refer to the fixed marginal values along the rows and columns,

respectively. To illustrate, imagine that the US has only five counties, named Alpha, Bravo, Charlie, Delta, and Echo. The process below shows the raking of (synthetic) county deaths for level-1 causes (Communicable Diseases, Noncommunicable Diseases, and Injuries) to national deaths for level-1 causes and to county deaths for all-cause mortality.

Start with a table of values.

Cause	Alpha County	Bravo County	Charlie County	Delta County	Echo County	United States
Communicable	29	50	7	22	17	119
Noncommunicable	178	202	49	91	45	407
Injuries	53	67	36	26	31	203
All-Cause	200	253	97	103	82	735

In iteration 1, find new values $n_{i,j}$ such that:

$$n^1_{i,j} = n^0_{i,j} \cdot \frac{N_i}{\sum_{i=1}^{r} n^0_{i,j}}$$

Cause	Alpha County	Bravo County	Charlie County	Delta County	Echo County	United States
Communicable	27.61	47.60	6.66	20.94	16.18	119.00
Noncommunicable	128.22	145.51	35.30	65.55	32.42	407.00
Injuries	50.51	63.85	34.31	24.78	29.54	203.00
All-Cause	200.00	253.00	97.00	103.00	82.00	735.00

In iteration 2, find new values $n_{i,j}$ such that:

$$n^2_{i,j} = n^1_{i,j} \cdot \frac{N_j}{\sum_{j=1}^{c} n^1_{i,j}}$$

Cause	Alpha County	Bravo County	Charlie County	Delta County	Echo County	United States
Communicable	26.76	46.87	8.48	19.39	16.98	119.00
Noncommunicable	124.28	143.27	44.89	60.68	34.02	407.00
Injuries	48.96	62.87	43.63	22.94	31.00	203.00
All-Cause	200.00	253.00	97.00	103.00	82.00	735.00

In iteration 3, repeat iteration 1 with $n_{i,j}^{\ 2}$:

Cause	Alpha County	Bravo County	Charlie County	Delta County	Echo County	United States
Communicable	26.88	47.08	8.51	19.47	17.06	119.00
Noncommunicable	124.24	143.22	44.88	60.66	34.00	407.00
Injuries	47.46	60.95	42.30	22.24	30.05	203.00
All-Cause	200.00	253.00	97.00	103.00	82.00	735.00

In iteration 4, repeat iteration 2 with $n_{i,j}^{3}$:

Cause	Alpha County	Bravo County	Charlie County	Delta County	Echo County	United States
Communicable	27.07	47.40	8.63	19.59	17.24	119.00
Noncommunicable	125.13	144.22	45.49	61.03	34.37	407.00
Injuries	47.80	61.37	42.88	22.37	30.38	203.00
All-Cause	200.00	253.00	97.00	103.00	82.00	735.00

Continue until an additional iteration does not meaningfully change $n_{i,j}$.

Cause	Alpha County	Bravo County	Charlie County	Delta County	Echo County	United States
Communicable	27.08	47.42	8.63	19.60	17.25	119.00
Noncommunicable	125.16	144.25	45.51	61.05	34.39	407.00
Injuries	47.77	61.33	42.86	22.36	30.36	203.00
All-Cause	200.00	253.00	97.00	103.00	82.00	735.00

Raking has been shown to converge[11] if the sum of the margins are equal (i.e., $\sum_{i=1}^{r} N_i = \sum_{j=1}^{c} N_j$) and there are no zeros or negative numbers in the margins. Raking works on tables of arbitrary dimensionality, and requires only a single iteration for a one-dimensional table.

It should be noted that this algorithm was applied to mortality rates rather than death counts, and as such, an extra population-weighting step was required when raking to national estimates. There were two stages in raking. First, one-dimensional raking was applied to fit county-level all-cause estimates to national all-cause estimates. Second, two-dimensional raking was applied at each level of the cause hierarchy. That is, after raking all-cause county-level to national estimates, the following groups of causes were raked:

1. The three level 1 causes (Communicable, Noncommunicable, and Injuries) to county-level all-cause estimates and national Communicable, Noncommunicable, and Injury results.
2. The seven children of the Communicable cause to county-level Communicable estimates and national estimates for those child causes.
3. The ten children of the Noncommunicable cause to county-level Noncommunicable estimates and national estimates for those child causes.
4. The four children of the Injuries cause to county-level Injuries estimates and national estimates for those child causes.

Calculating years of life lost

Years of life lost (YLLs) were calculated for each cause as in the GBD.[1] For each age group, the number of deaths was calculated by multiplying the estimated mortality rate by the population. YLLs were then calculated for each age group by multiplying the number of deaths by

the life expectancy at the average age at death in that age group from a reference life table. The reference life table from the GBD was used in this analysis; this life table was constructed from the lowest observed mortality rate among all countries in 2013 for each age group and corresponds to a life expectancy at birth of 86.6 years.

As an example, the data in the table below show the population (column 2) and the estimated mortality rates from cardiovascular diseases (column 3) in the US in 2014. Deaths (column 4) were calculated by multiplying the population by the estimated mortality rate. Life expectancy at the average age of death within each age group (column 5) was extracted from the GBD reference life table. YLLs in each age group (column 6) were then calculated by multiplying deaths by life expectancy. Total YLLS were calculated by summing across all ages.

Age group	Population	Mortality rate	Deaths	Life expectancy	YLLs
0	3,991,801	8.3	331	86.18	28,551
1–4	16,142,348	1.1	174	84.20	14,629
5–9	21,022,679	0.4	88	79.32	6,981
10–14	20,537,438	0.6	128	73.86	9,455
15–19	21,700,738	1.6	352	69.06	24,336
20–24	22,467,579	3.6	809	64.31	52,029
25–29	21,943,503	6.7	1,471	59.43	87,389
30–34	21,222,396	12.4	2,626	54.48	143,041
35–39	19,345,592	22.0	4,262	49.53	211,091
40–44	20,432,008	40.6	8,286	44.62	369,711
45–49	22,263,758	73.9	16,443	39.80	654,382
50–54	23,899,275	125.6	30,016	35.08	1,052,861
55–59	21,541,555	193.0	41,575	30.48	1,267,073
60–64	20,198,375	279.9	56,540	25.91	1,464,742
65–69	14,333,828	420.9	60,331	21.47	1,295,080
70–74	10,102,967	671.5	67,843	17.23	1,168,681
75–79	7,298,604	1,153.5	84,191	13.28	1,117,654
80+	12,227,811	3,850.5	470,832	5.88	2,768,105
Total			846,298		11,735,793

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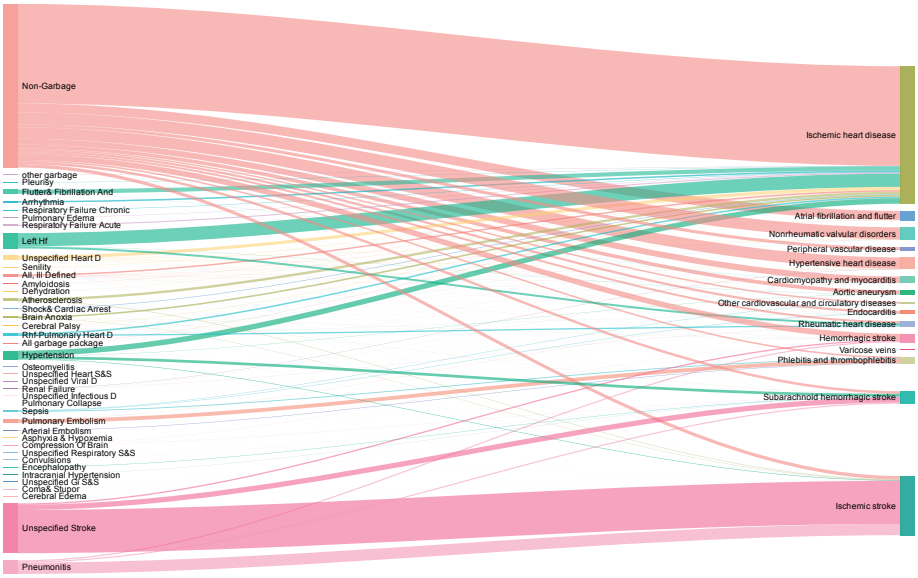
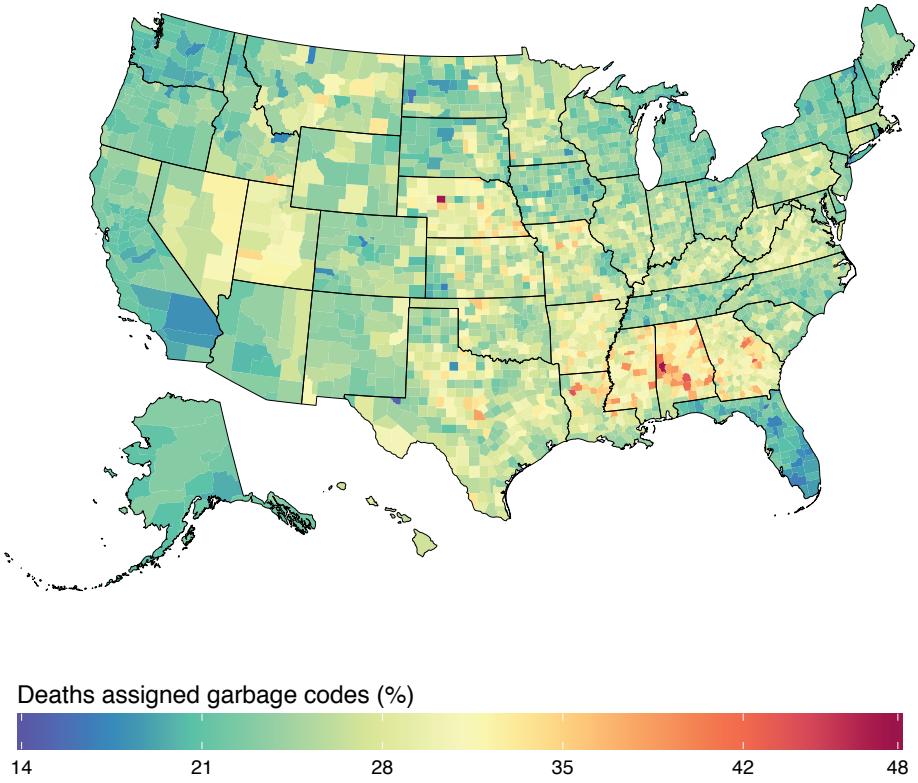
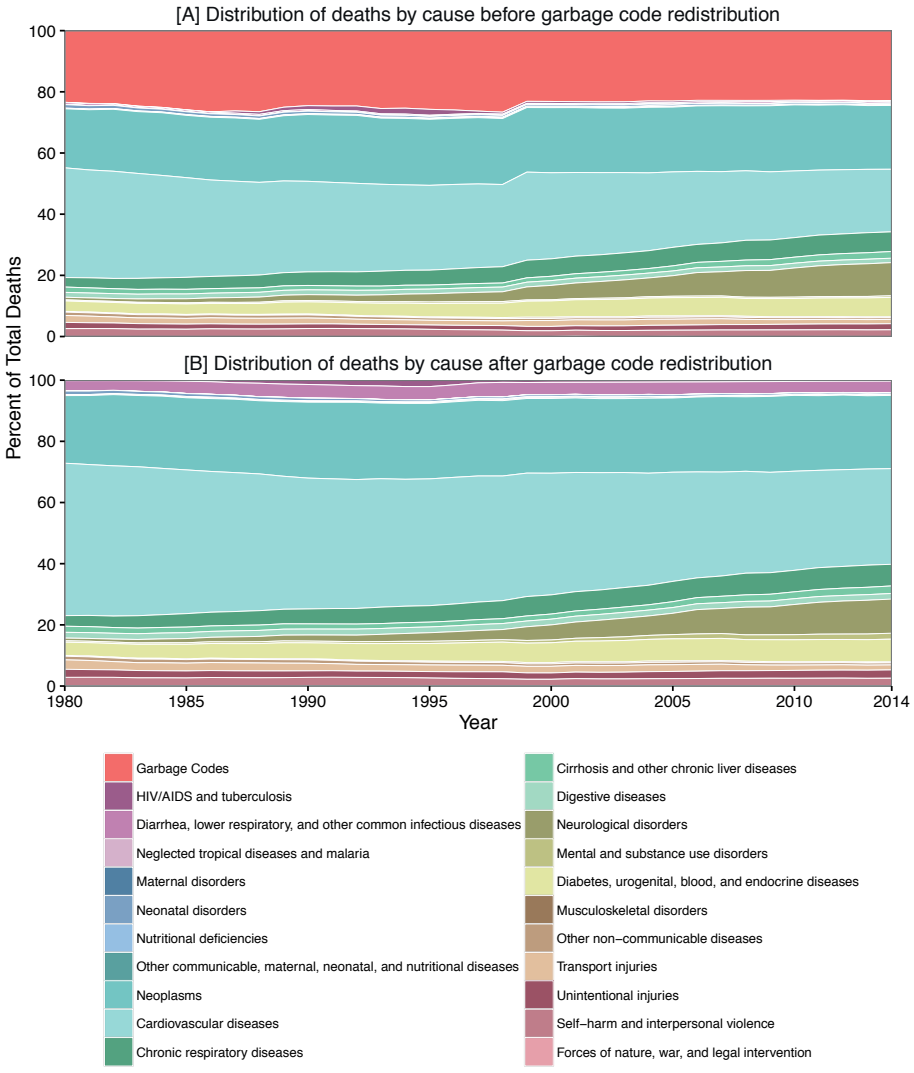
EFIGURES



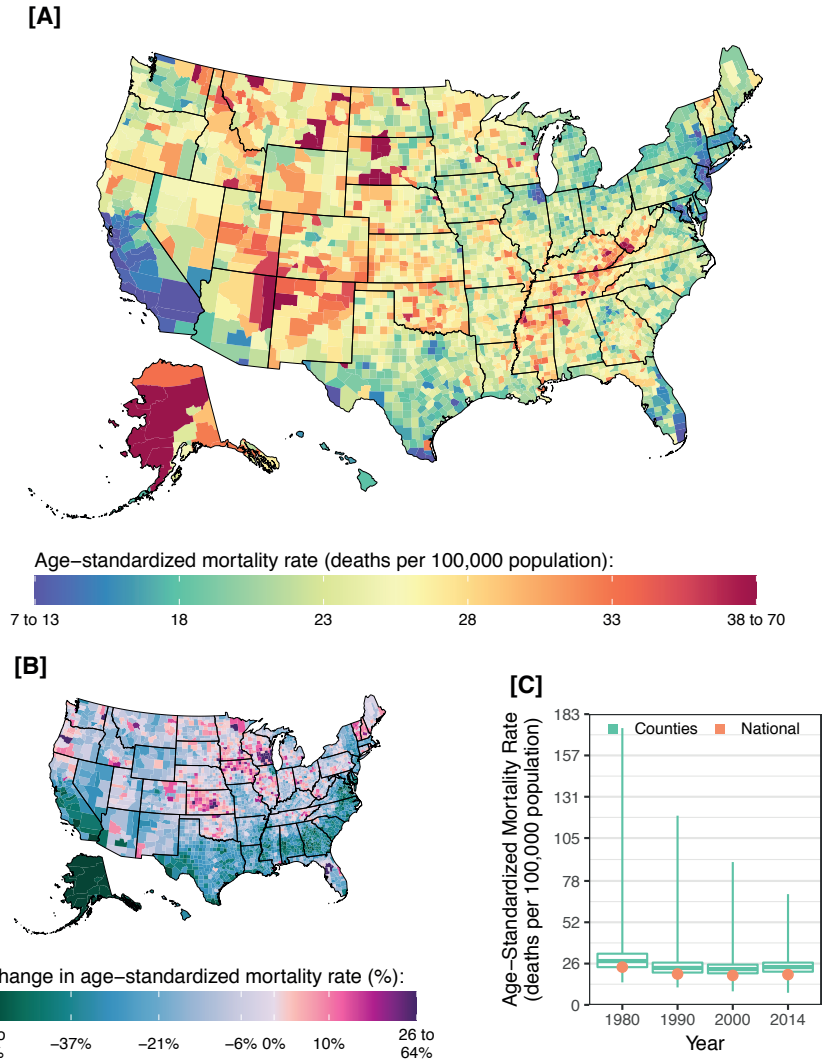
eFigure 1. Example of garbage code redistribution in King County, WA (2013).
The left axis represents ICD codes that were mapped to cardiovascular diseases in the GBD cause hierarchy and the right axis represents these cardiovascular diseases. The width of each band is proportional to the number of deaths transferred from a given set of ICD codes to a specific cardiovascular disease. Garbage codes are ICD codes which are implausible or insufficiently specific for the underlying cause of death. All categories on the left axis other than "Non-Garbage" refer to sets of garbage codes. The category "Non-Garbage" includes deaths where the original underlying cause of death code could be mapped directly to a cause in the GBD cause hierarchy.



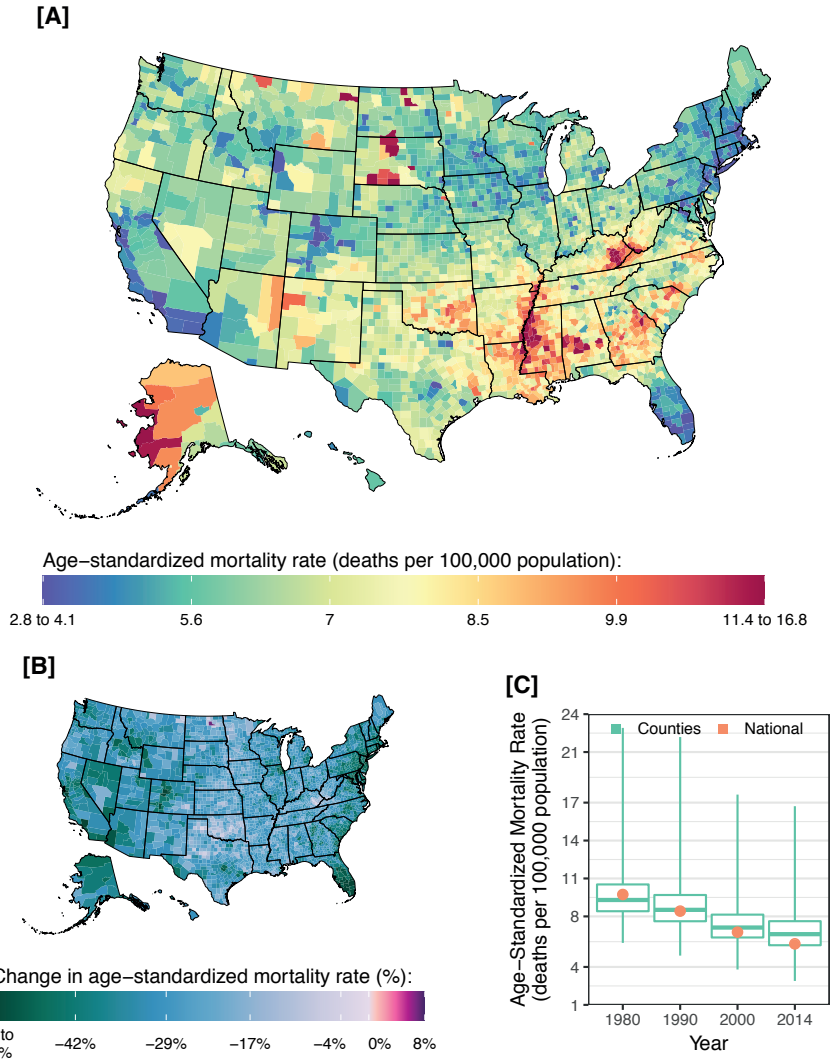
eFigure 2. Percent of deaths assigned garbage codes (1980–2014).



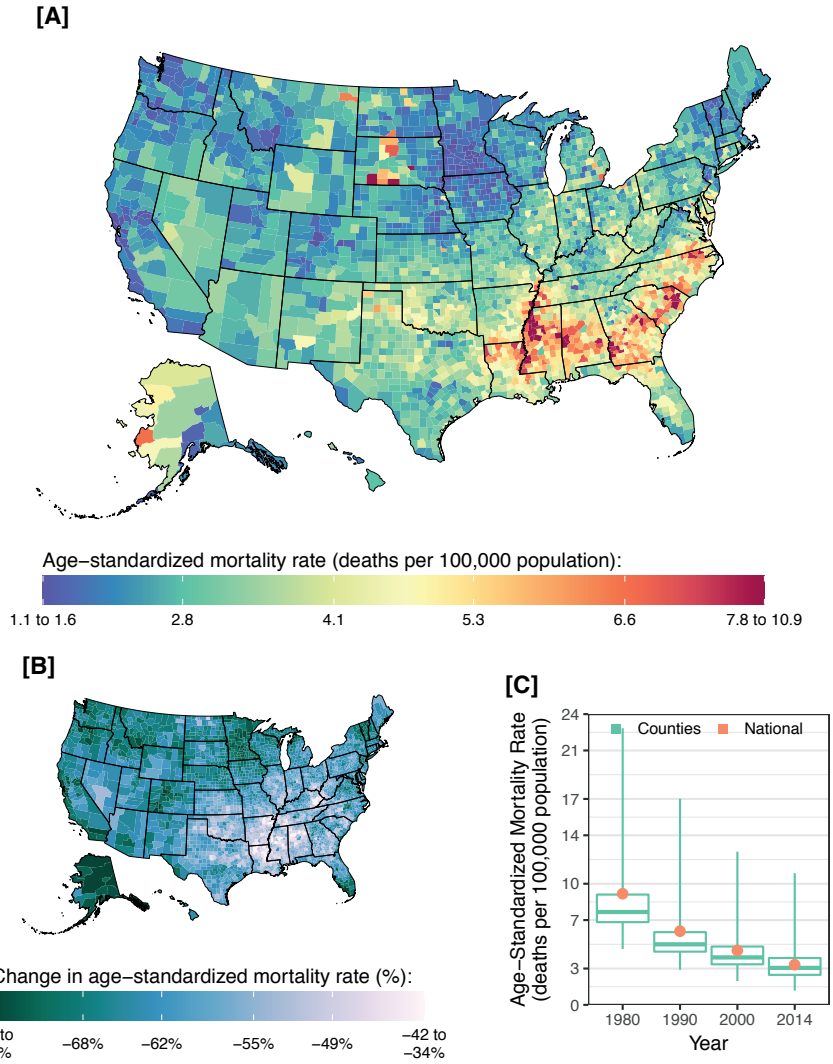
eFigure 3. Annual distribution of deaths by cause before and after garbage code redistribution (1980–2014).



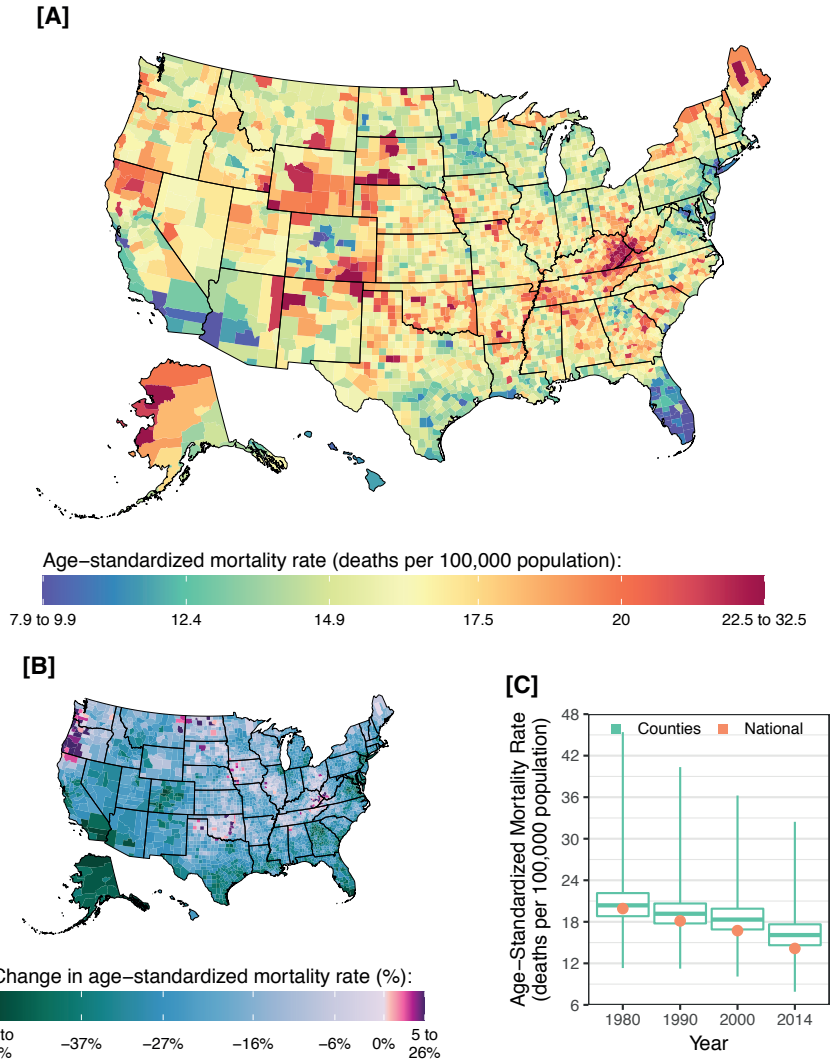
eFigure 4. County-level mortality from unintentional injuries.
A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.



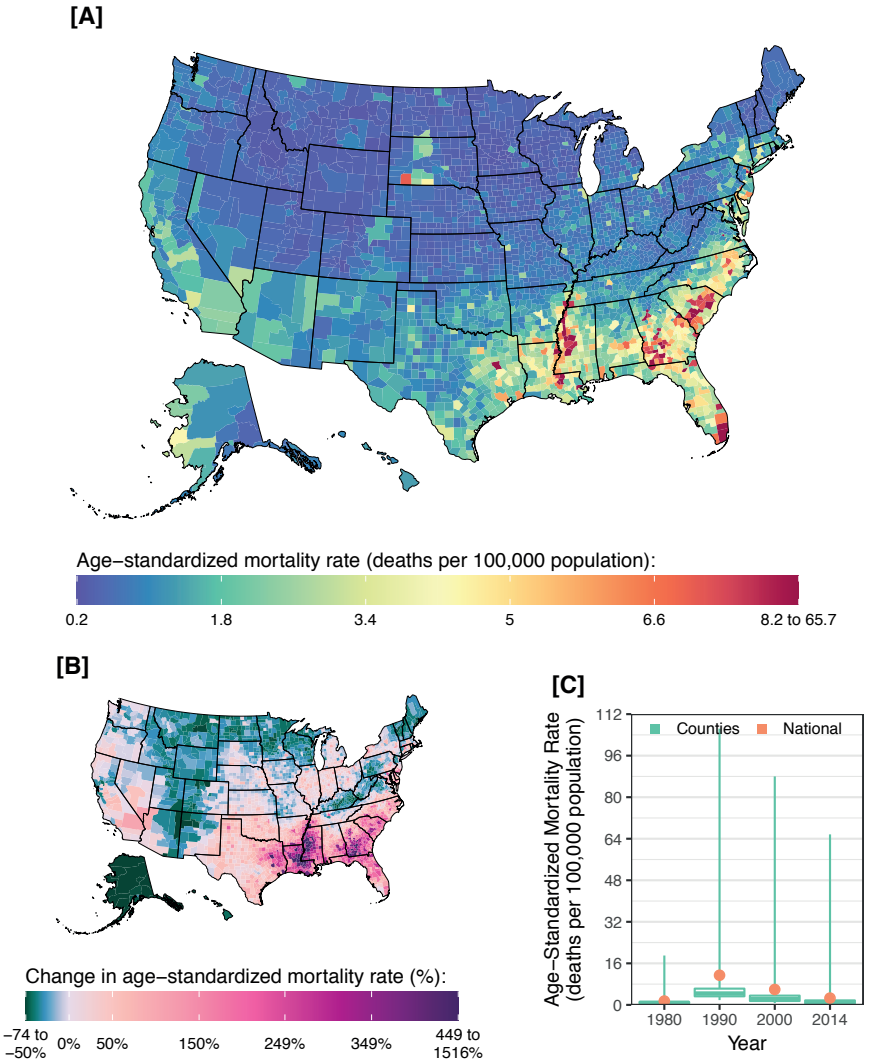
eFigure 5. County-level mortality from other non-communicable diseases.
A, Age-standardized mortality rate for both sexes combined in 2014. The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. The color scale is truncated at the first percentile but not at the 99th percentile, to avoid combining counties with decreases in the mortality rate and counties with increases in the mortality rate into a single group. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.



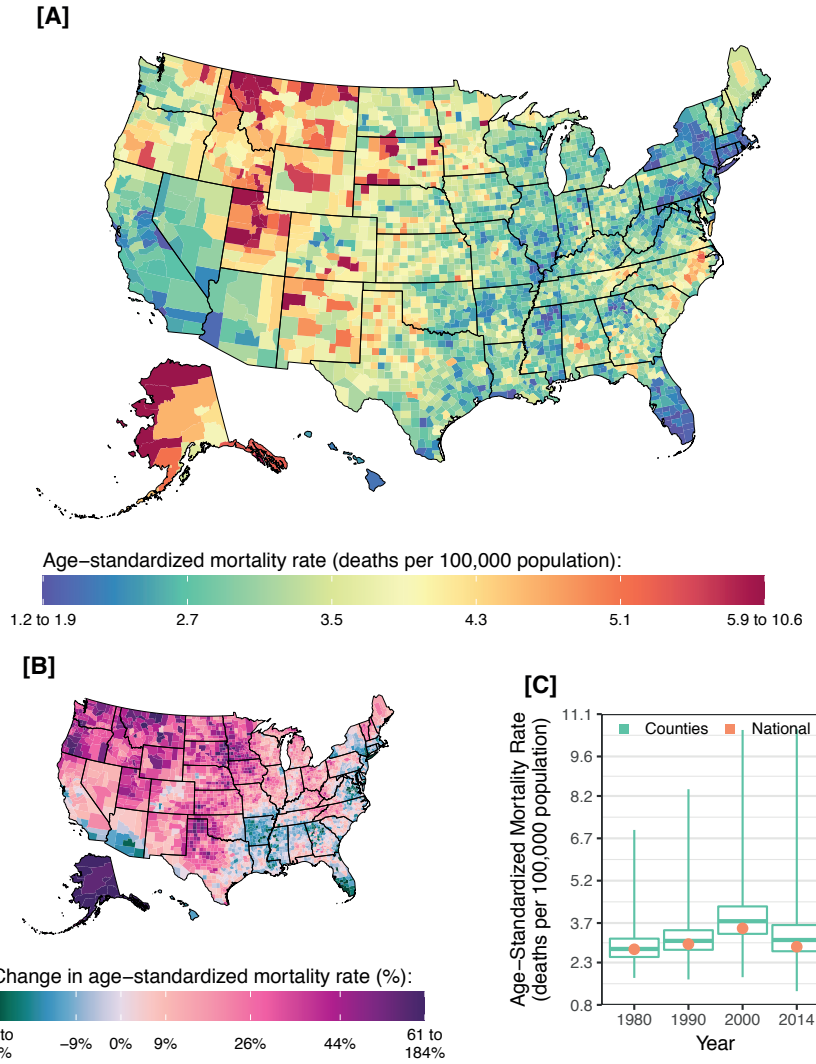
eFigure 6. County-level mortality from neonatal disorders.
A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.



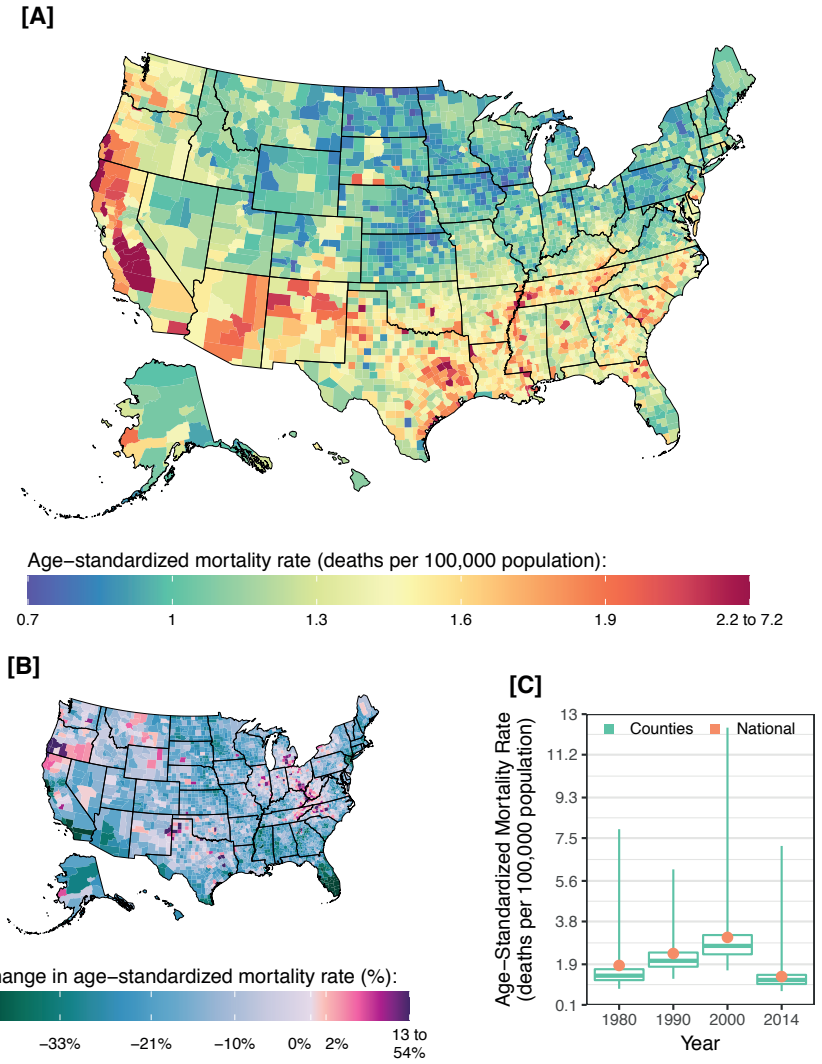
eFigure 7. County-level mortality from digestive diseases.
A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.



eFigure 8. County-level mortality from HIV/AIDS and tuberculosis.
A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.

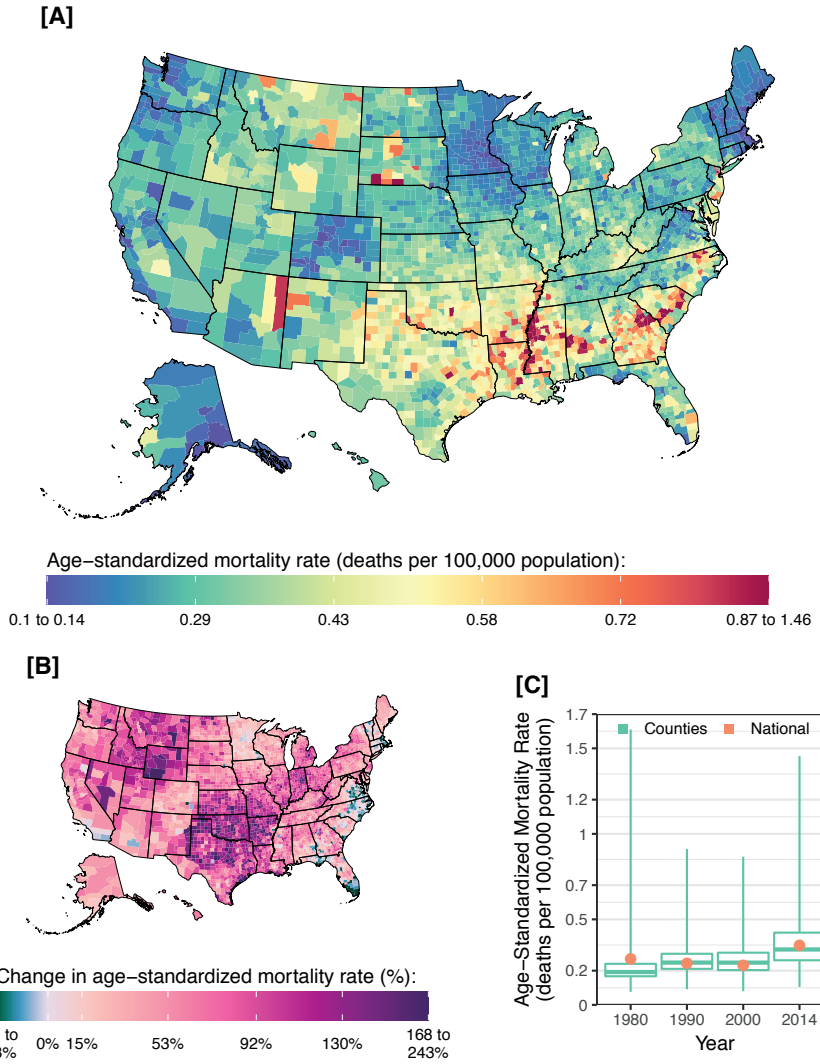


eFigure 9. County-level mortality from musculoskeletal disorders.
A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.



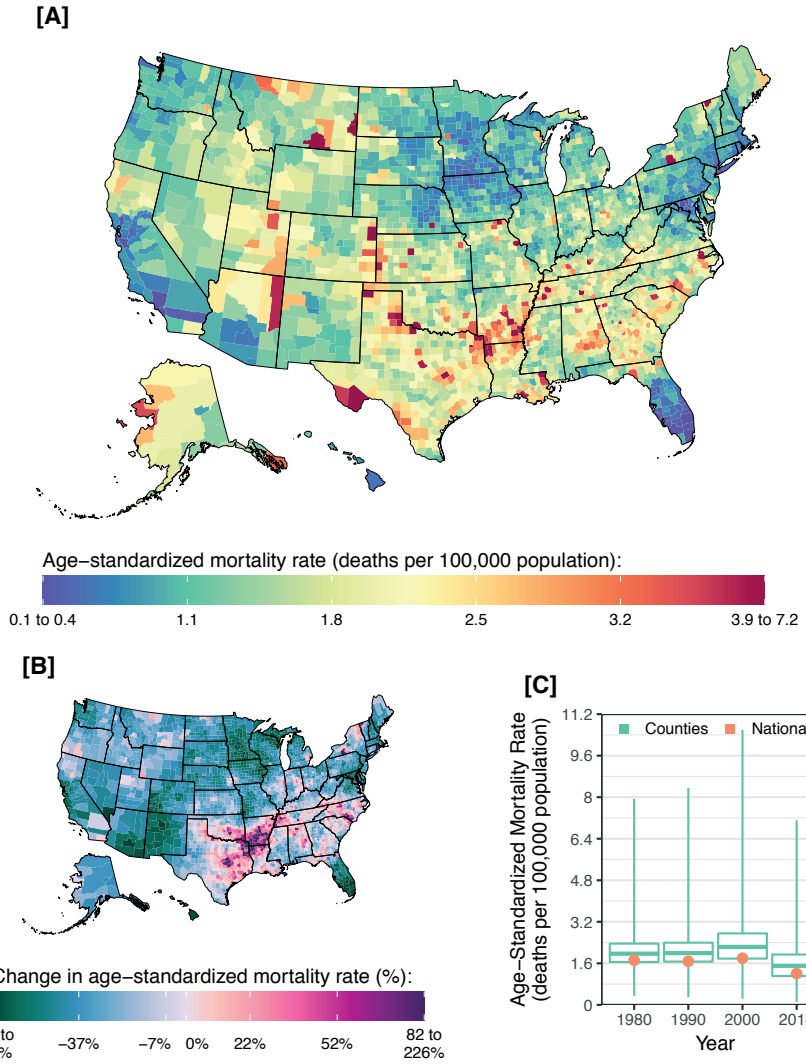
eFigure 10. County-level mortality from other communicable, maternal, neonatal, and nutritional diseases.

A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.

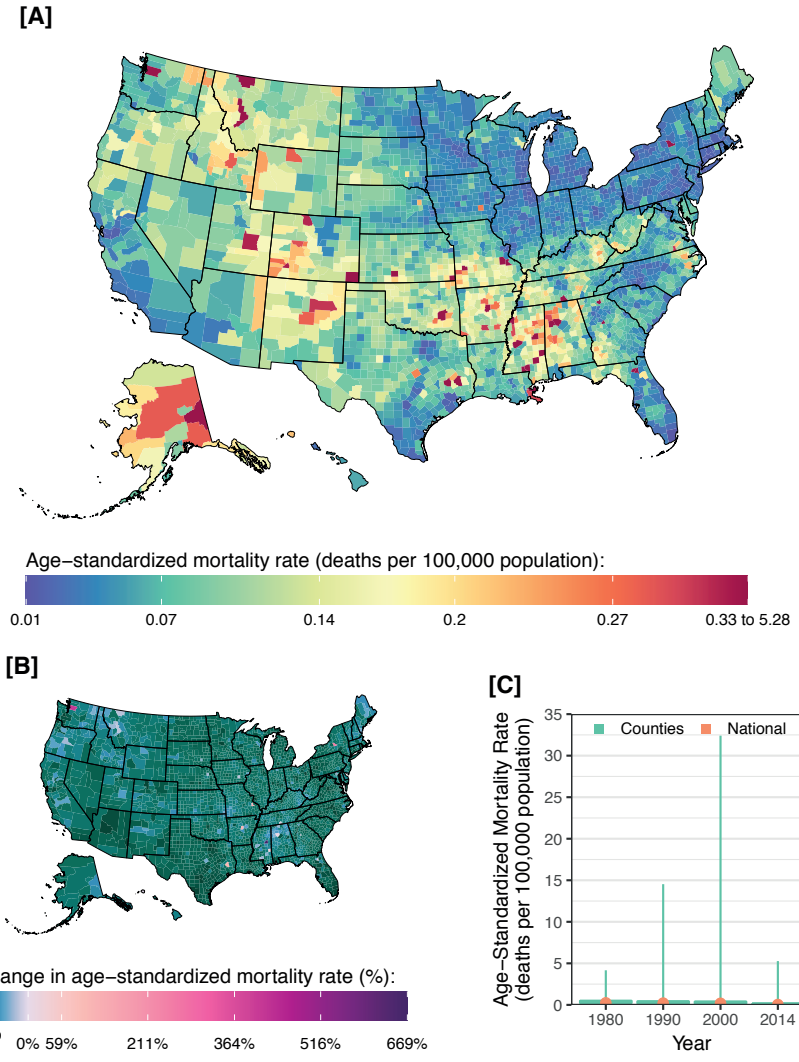


eFigure 11. County-level mortality from maternal disorders.

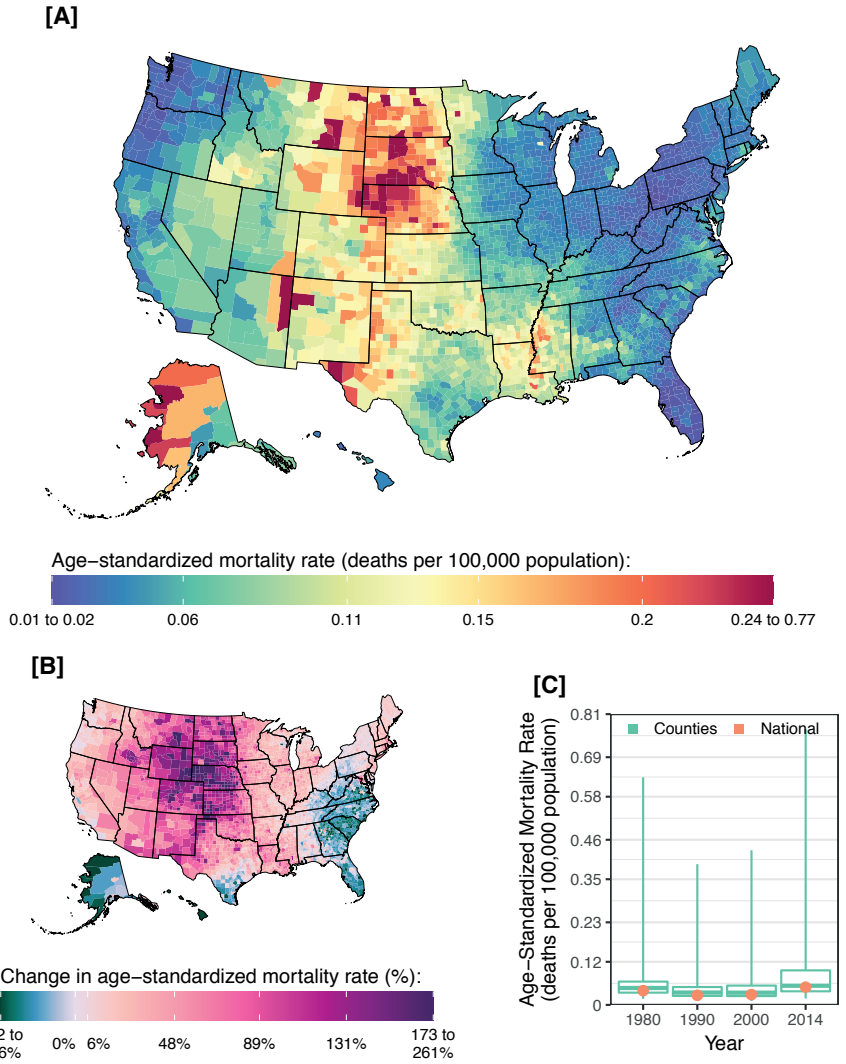
A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.



eFigure 12. County-level mortality from nutritional deficiencies.
A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.



eFigure 13. County-level mortality from forces of nature, war, and legal intervention.
A, Age-standardized mortality rate for both sexes combined in 2014. The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. The color scale is truncated at the first percentile but not at the 99th percentile, to avoid combining counties with decreases in the mortality rate and counties with increases in the mortality rate into a single group. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.



eFigure 14. County-level mortality from neglected tropical diseases and malaria.
A, Age-standardized mortality rate for both sexes combined in 2014. B, Percent change in the age-standardized mortality rate for both sexes combined between 1980 and 2014. A and B, The color scale is truncated at approximately the first and 99th percentiles as indicated by the range given in the color scale. C, Age-standardized mortality rate in 1980, 1990, 2000, and 2014. The bottom border, middle line, and top border of the boxes indicate the 25th, 50th, and 75th percentiles, respectively, across all counties; whiskers, the full range across counties; and circles, the national-level rate.

ETABLES

eTable 1. Data sources used for covariates.

Covariate	Data sources	Data processing
Percent of the population age 25 and older who have completed high school	1980 census;[a] 1990 census;[b] 2000 census;[c] 2009–2014 ACS.[d]	Linear interpolation was used fill in intermediate years between data sources. The rate of change calculated between 2007 and 2012 was applied to fill in estimates for 2013 and 2014.
Percent of the population who are Hispanic	1980 census;[e] 1990–2014 NCHS Bridged Race Files.[f,g,h]	Linear interpolation was used to fill in intermediate years between data sources.
Percent of the population who are Black and some other race	1980–1989 Census Bureau Intercensal County Estimates by Age, Sex, and Race;[i] 1990–2014 NCHS Bridged Race Files.[f,g,h]	Linear interpolation was used to fill in intermediate years between data sources.
Percent of land area in a Native American reservation	2013 Cartographic Boundary File, State-County for United States;[j] AIANNH Areas National Shapefile.[k]	Geographic boundaries of AIANNH Areas were intersected with county boundaries using ArcGIS. The area of the intersection and the area of the county were calculated using an Albers Equal Area Conic projection. The proportion of the land area that is in a reservation was generated by dividing the area of the reservation by the total area in each county.
Household median income	1980 census;[l] 1989, 1993, 1995–2014 Small Area Income and Poverty Estimates;[m] 1980–2014 Bureau of Labor Statistics, Consumer Price Index.[n]	Data were adjusted for inflation using the consumer price index, and linear interpolation was used to generate values between observed data points. Income was then log-transformed.
Population density	1980–1989 Census Bureau Intercensal County Estimates by Age, Sex, and Race;[i] 1990–2014 NCHS Bridged Race Files;[f,g,h] 2013 Cartographic Boundary File, State-County for United States.[j]	The area of each county was calculated using an Albers Equal Area Conic projection. The total population of each county was divided by the total area of the county, and was then log-transformed.

[a]Missouri Census Data Center. 1980 Census Summary Tape File 3, Table NT48A. MCDC Data Archive (Uexplore/Dexter). http://mcdc2.missouri.edu/applications/uexplore.shtml. Accessed April 22, 2013.

[b]Minnesota Population Center. 1990 Census Summary Tape File 3, Table P057. National Historical Geographic Information System: Version 2.0. Minneapolis, MN: University of Minnesota 2011. http://www.nhgis.org. Accessed July 18, 2013.

[c]U.S. Census Bureau. 2000 Census Summary Tape File 3, Table DP2; using American FactFinder; http://factfinder2.census.gov. Accessed April 18, 2013.

[d]U.S. Census Bureau. American Community Survey, 2009–2014 American Community Survey 5-Year Estimates, Table S1501; using American FactFinder; http://factfinder2.census.gov. Accessed December 8, 2015.

[e]Minnesota Population Center. 1980 Census Summary Tape File 1, Table NT8. National Historical Geographic Information System: Version 2.0. Minneapolis, MN: University of Minnesota 2011. http://www.nhgis.org. Accessed January 13, 2016.

[f]National Center for Health Statistics, Centers for Disease Control and Prevention, US Census Bureau. United States Bridged-Race Intercensal Population Estimates 1990–1999. Hyattsville, United States: National Center for Health Statistics, Centers for Disease Control and Prevention, 2004. Accessed November 21, 2011.

[g]National Center for Health Statistics, Centers for Disease Control and Prevention, US Census Bureau. United States Bridged-Race Intercensal Population Estimates 2000–2009. Hyattsville, United States: National Center for Health Statistics, Centers for Disease Control and Prevention, 2012. Accessed October 30, 2012.

[h]National Center for Health Statistics, Centers for Disease Control and Prevention, United States Census Bureau. United States Vintage 2014 Bridged-Race Postcensal Population Estimates 2010–2014. Hyattsville, United States: National Center for Health Statistics, Centers for Disease Control and Prevention, 2015. Accessed December 18, 2015.

[i]U.S. Census Bureau. Intercensal County Estimates by Age, Sex, Race: 1980–1989. http://www.census.gov/popest/data/counties/asrh/1980s/PE-02.html. Accessed January 8, 2015.

[j]U.S. Census Bureau. TIGER/Line Shapefile, 2013 Cartographic Boundary File, State-County for United States, 1:20,000,000. https://catalog.data.gov/dataset/2013-cartographic-boundary-file-state-county-for-united-states-1-20000000. Accessed February 2, 2015.

[k]U.S. Census Bureau. TIGER/Line Shapefile, 2012, Series Information File for the Nation, Current American Indian/Alaska Native/Native Hawaiian Areas (AIANNH) National Shapefile. http://catalog.data.gov/dataset/tiger-line-shapefile-2012-series-information-file-for-the-nation-current-american-indian-alaska. Accessed February 10, 2015.

[l]Minnesota Population Center. 1980 Census Summary Tape File 3, Table NT69. National Historical Geographic Information System: Version 2.0. Minneapolis, MN: University of Minnesota 2011. http://www.nhgis.org. Accessed November 12, 2015.

[m]U.S. Census Bureau. Small Area Income and Poverty Estimates. https://www.census.gov/did/www/saipe/data/statecounty/data/index.html. Accessed December 28, 2015.

[n]U.S Bureau of Labor Statistics. Consumer Price Index: All Urban Consumers History, All Items 1913–2015. http://www.bls.gov/data/. Accessed March 24, 2015.

eTable 2. Counties combined to ensure historically stable units of analysis.

State	Group	Areas
Alaska	1	Kusilvak Census Area (2158), Wade Hampton Census Area (2270)[a]
	2	Kobuk Census Area (2140),[a] Northwest Arctic Borough (2188)
	3	Aleutian Islands Census Area (2010),[a] Aleutians East Borough (2013), Aleutians West Census Area (2016)
	4	Dillingham Census Area (2070), Lake and Peninsula Borough (2164)
	5	Denali Borough (2068), Yukon-Koyukuk Census Area (2290)
	6	Hoonah-Angoon Census Area (2105), Skagway Municipality (2230), Skagway-Yakutat-Angoon Census Area (2231),[a] Skagway-Hoonah-Angoon Census Area (2232),[a] Yakutat City and Borough (2282)
	7	Ketchikan Gateway Borough (2130), Petersburg Borough (2195), Prince of Wales-Hyder Census Area (2198), Prince of Wales-Outer Ketchikan Census Area (2201),[a] Wrangell City and Borough (2275), Wrangell-Petersburg Census Area (2280)[a]
Arizona	1	La Paz County (4012), Yuma County (4027)
Colorado	1	Adams County (8001), Arapahoe County (8005), Boulder County (8013), Broomfield County (8014), Denver County (8031), Jefferson County (8059), Weld County (8123)
Florida	1	Dade County (12025),[a] Miami-Dade County (12086)
Hawaii	1	Kalawao County (15005), Maui County (15009)
Maryland	1	Montgomery County (24031), Prince George's County (24033)
Montana	1	Park County (30067), Yellowstone National Park (30113)[a]
New Mexico	1	Cibola County (35006), Valencia County (35061)
South Dakota	1	Oglala Lakota County (46102), Shannon County (46113)[a]
	2	Jackson County (46071), Washabaugh County (46131)[a]
Virginia	1	Fairfax County (51059), Fairfax City (51600)
	2	Rockingham County (51165), Harrisonburg City (51660)
	3	James City County (51095), Williamsburg City (51830)
	4	Prince William County (51153), Manassas City (51683), Manassas Park City (51685)
	5	Rockbridge County (51163), Buena Vista City (51530)
	6	Spotsylvania County (51177), Fredericksburg City (51630)
	7	Augusta County (51015), Staunton City (51790), Waynesboro City (51820)
	8	Pittsylvania County (51143), Danville City (51590)
	9	Greensville County (51081), Emporia City (51595)
	10	Albemarle County (51003), Charlottesville City (51540)
	11	Bedford County (51019), Bedford City (51515)[a]
	12	Halifax County (51083), South Boston City (51780)[a]
	13	Southampton County (51175), Franklin City (51620)
	14	Alleghany County (51005), Clifton Forge City (51560)[a]
	15	York County (51199), Newport News City (51700)

[a]County no longer exists due to boundary or name change.

eTable 3. GBD cause list and associated ICD9 and ICD10 codes.

Cause	Level	ICD9
Communicable, maternal, neonatal, and nutritional diseases	1	001–001.9, 002.0–030.9, 032–034.9, 036–036.40, 036.5, 036.8–037.9, 039–039.4, 039.8–040, 040.1–041.09, 042–066.9, 070–070.21, 070.3–070.31, 070.4–070.43, 070.49–070.53, 070.59–074.1, 074.20, 074.3–075.9, 078.4–078.7, 079–079.7, 080–083.9, 084.0–084.5, 084.7–084.9, 085.0, 086–088.9, 090–101.6, 104–104.9, 120–124.9, 125.4–125.9, 127–127.1, 128–129.0, 136–136.29, 137–139.0, 244.2, 260–263.9, 265–269.9, 280.1–280.8, 281.0–281.9, 320.0–320.89, 321–323.9, 381–383.9, 390–390.9, 392, 392.9, 461–461.9, 464.0, 464.01, 464.11–464.2, 464.21, 464.31–464.4, 464.8–464.9, 466–469, 470.0, 475–475.9, 476.9, 480–482.89, 483.0–483.9, 484.0–484.7, 487–489, 613–614.9, 630–636.92, 638–638.92, 640–679.14, 716.0–716.09, 730.4–730.6, 760–760.64, 760.8–768, 768.2–770, 770.1–775, 775.4–779.34, 779.6–779.89, 787.91
HIV/AIDS and tuberculosis	2	010–019.9, 042–044.9, 137–137.9, 138.0–138.9, 730.4–730.6
Tuberculosis	3–4	010–019.9, 137–137.9, 138.0–138.9, 730.4–730.6
HIV/AIDS	3	042–044.9
HIV/AIDS - Tuberculosis	4	
HIV/AIDS resulting in other diseases	4	042.0–042.9, 043.0–043.9, 044.1–044.9
Diarrhea, lower respiratory, and other common infectious diseases	2	001–001.9, 002.0–009.9, 032–033.9, 036–036.40, 036.5, 036.8–037.9, 047–049.9, 052–053.9, 055–055.9, 062–064.9, 073.0–073.6, 139.0, 320.0–320.89, 321–323, 323.1, 323.4–323.9, 381–383.9, 461–461.9, 464.0, 464.01, 464.11–464.2, 464.21, 464.31–464.4, 464.8–464.9, 466–469, 470.0, 475–475.9, 476.9, 480–482.89, 483.0–483.9, 484.0–484.4, 484.6–484.7, 487–489, 771.3, 787.91
Diarrheal diseases	3–4	001–001.9, 003–006.9, 007.4–007.8, 008.01–008.02, 008.04, 008.2–009.9, 787.91
Intestinal infectious diseases	3	002.0–002.9, 007–007.3, 007.9–008.00, 008.03, 008.09–008.1
Typhoid fever	4	2
Paratyphoid fever	4	002.1–002.9
Other intestinal infectious diseases	4	007–007.3, 007.9–008.00, 008.03, 008.09–008.1
Lower respiratory infections	3–4	073.0–073.6, 466–469, 470.0, 480–482.89, 483.0–483.9, 484.1–484.2, 484.6–484.7, 487–489
Upper respiratory infections	3–4	461–461.9, 464.0, 464.01, 464.11–464.2, 464.21, 464.31–464.4, 464.8–464.9, 475–475.9, 476.9
Otitis media	3–4	381–383.9
Meningitis	3	036–036.40, 036.5, 036.8–036.9, 047–049.9, 320.0–320.89, 321–322.9
Pneumococcal meningitis	4	320.1
H influenzae type B meningitis	4	320

ICD10
A00–A00.9, A01.0–A14, A15–A28.9, A30–A30.9, A32–A39.4, A39.8–A39.9, A48.1–A48.2, A48.4–A48.52, A49.1, A50–A58, A60–A60.9, A63–A63.8, A65–A65.0, A68–A70, A74, A74.8–A75.9, A77–A96.9, A98–A98.8, B00–B06.9, B10–B10.89, B15–B17.9, B19–B27.99, B29.4, B33–B33.1, B33.3–B33.8, B47–B48.8, B50–B53.8, B55.0, B56–B57.5, B60–B60.8, B63, B65–B67.99, B69–B72.0, B74.3–B75, B77–B77.9, B83–B83.8, B90–B92, B94.1–B94.2, B95–B95.5, D50.1–D50.8, D51–D52.0, D52.8–D53.9, D64.3, D86.81, E00–E02, E40–E46.9, E51–E61.9, E63–E64.0, E64.2–E64.9, F07.1, G00.0–G00.8, G03–G03.8, G04–G05.8, G14–G14.6, H70–H70.93, I00, I02, I02.9, I98.0–I98.1, J01–J01.91, J02.0, J03.0–J03.01, J04.0, J05–J05.0, J05.11, J09–J15.8, J16–J16.9, J20–J21.9, J36–J36.0, K67.0–K67.8, K74.7–K74.8, K93.0, M03.1, M12.1–M12.19, M49.0–M49.1, M73.0–M73.1, M89.6–M89.69, N70–N71.9, N73–N74.8, N96, N98–N98.9, O00–O07.9, O09–O16.9, O20–O26.93, O28–O36.93, O40–O48.1, O60–O77.9, O80–O92.79, O96–P04.2, P04.5–P05.9, P07–P15.9, P19–P22.9, P23.0–P23.4, P24–P29.9, P35–P37.2, P37.5–P39.9, P50–P61.9, P70, P70.3–P72.9, P74–P78.9, P80–P81.9, P83–P84, P90–P94.9, P96, P96.3–P96.4, P96.8–P96.89, R19.7
A10–A14, A15–A19.9, B20–B24.9, B90–B90.9, K67.3, K93.0, M49.0, P37.0
A10–A14, A15–A19.9, B90–B90.9, K67.3, K93.0, M49.0, P37.0
B20–B24.9
B20.0
B20.1–B23.9, B24.0
A00–A00.9, A01.0–A09.9, A33–A37.91, A39–A39.4, A39.8–A39.9, A48.1, A70, A83–A87.9, B01–B02.9, B05–B05.9, B94.1, D86.81, F07.1, G00.0–G00.8, G03–G03.8, G04–G05.8, H70–H70.93, J01–J01.91, J04.0, J05–J05.0, J05.11, J09–J15.8, J16–J16.9, J20–J21.9, J36–J36.0, P23.0–P23.4, P35.8, R19.7
A00–A00.9, A02–A04.1, A04.3, A04.5–A07, A07.2–A07.4, A08–A09.9, R19.7
A01.0–A01.4, A04.2, A04.4, A07.0–A07.1, A07.8–A07.9
A01.0–A01.09
A01.1–A01.4
A04.2, A04.4, A07.0–A07.1, A07.8–A07.9
A48.1, A70, J09–J15.8, J16–J16.9, J20–J21.9, P23.0–P23.4
J01–J01.91, J04.0, J05–J05.0, J05.11, J36–J36.0
H70–H70.93
A39–A39.4, A39.8–A39.9, A87–A87.9, D86.81, G00.0–G00.8, G03–G03.8
G00.1
G00.0

eTable 3. GBD cause list and associated ICD9 and ICD10 codes. (continued)

Cause	Level	ICD9
Meningococcal meningitis	4	036–036.40, 036.5, 036.8–036.9
Other meningitis	4	047–049.9, 320.2–320.89, 321–322.9
Encephalitis	3–4	062–064.9, 139.0, 323, 323.4–323.9
Diphtheria	3–4	032–032.9
Whooping cough	3–4	033–033.9, 484.3–484.4
Tetanus	3–4	037–037.9, 771.3
Measles	3–4	055–055.9, 323.1, 484.0
Varicella and herpes zoster	3–4	052–053.9
Neglected tropical diseases and malaria	2	030–030.9, 060–061.8, 065–066.9, 071–071.9, 080, 080.2–083.9, 084.0–084.5, 084.7–084.9, 085.0, 086–088.9, 120–124.9, 125.4–125.9, 127–127.1, 128–129.0
Malaria	3–4	084.0–084.5, 084.7–084.9
Chagas disease	3–4	086–086.2, 086.9
Leishmaniasis	3	85
Visceral leishmaniasis	4	85
African trypanosomiasis	3–4	086.3–086.5
Schistosomiasis	3–4	120–120.9
Cysticercosis	3–4	123.1
Cystic echinococcosis	3–4	122–122.4, 122.8–122.9
Dengue	3–4	061–061.8
Yellow fever	3–4	060–060.9
Rabies	3–4	071–071.9
Intestinal nematode infections	3	127
Ascariasis	4	127
Ebola	3–4	
Other neglected tropical diseases	3–4	065–066.9, 080, 080.2–083.9, 087–088.9, 122.5–122.7, 123–123.0, 123.2–124.9, 125.4–125.9, 127, 127.1, 128–129.0
Maternal disorders	2	630–636.92, 638–638.92, 640–679.14
Maternal hemorrhage	3–4	640–641.93, 661–661.93, 665, 666–666.9
Maternal sepsis and other maternal infections	3–4	659.3–659.33, 670–670.9

	ICD10
	A39–A39.4, A39.8–A39.9
	A87–A87.9, D86.81, G00.2–G00.8, G03–G03.8
	A83–A86.4, B94.1, F07.1, G04–G05.8
	A36–A36.9
	A37–A37.91
	A33–A35.0
	B05–B05.9
	B01–B02.9, P35.8
	A30–A30.9, A68–A68.9, A69.2–A69.9, A75–A75.9, A77–A79.9, A82–A82.9, A90–A96.9, A98–A98.8, B33.0–B33.1, B50–B53.8, B55.0, B56–B57.5, B60–B60.8, B65–B67.99, B69–B72.0, B74.3–B75, B77–B77.9, B83–B83.8, B92, P37.1
	B50–B53.8
	B57–B57.5
	B55.0
	B55.0
	B56–B56.9
	B65–B65.9
	B69–B69.9
	B67–B67.4, B67.8–B67.99
	A90–A91.9
	A95–A95.9
	A82–A82.9
	B77–B77.9
	B77–B77.9
	A98.4
	A68–A68.9, A69.2–A69.9, A75–A75.9, A77–A79.9, A92–A94.0, A96–A96.9, A98–A98.3, A98.5–A98.8, B33.0–B33.1, B60–B60.8, B67.5–B67.7, B70–B72.0, B74.3–B75, B83–B83.8, P37.1
	N96, N98–N98.9, O00–O07.9, O09–O16.9, O20–O26.93, O28–O36.93, O40–O48.1, O60–O77.9, O80–O92.79, O96–O99.91
	O20–O20.9, O43.2–O43.239, O44–O46.93, O62–O62.9, O67–O67.9, O70, O72–O72.3
	O23–O23.93, O85–O86.89, O91–O91.23

eTable 3. GBD cause list and associated ICD9 and ICD10 codes. (continued)

Cause	Level	ICD9
Maternal hypertensive disorders	3–4	642–642.94
Maternal obstructed labor and uterine rupture	3–4	652–653.93, 660–660.93, 665.0–665.34
Maternal abortion, miscarriage, and ectopic pregnancy	3–4	630–636.92, 638–638.92, 646.3–646.33
Indirect maternal deaths	3–4	646–646.24, 646.4–649.9, 674–674.94
Late maternal deaths	3–4	
Other maternal disorders	3–4	643–645.23, 650–651.93, 654–659.23, 659.4–659.93, 662–664.94, 665.4–665.94, 667–669.94, 671–673.9, 675–679.14
Neonatal disorders	2	760–760.64, 760.8–768, 768.2–770, 770.1–771, 771.4–775, 775.4–779.34, 779.6–779.89
Neonatal preterm birth complications	3–4	761.0–761.1, 765–765.9, 769–769.9, 770.2–770.9, 776.6, 777.5–777.6
Neonatal encephalopathy due to birth asphyxia and trauma	3–4	761.7–763.9, 767–768, 768.2–768.9, 770.1–770.18, 772.1–772.9, 779.0–779.2
Neonatal sepsis and other neonatal infections	3–4	771.4–771.9
Hemolytic disease and other neonatal jaundice	3–4	773–774.9
Other neonatal disorders	3–4	760–760.64, 760.8–761, 761.2–761.6, 764–764.99, 766–766.9, 770, 771, 772–772.0, 775, 775.4–776.5, 776.7–777.4, 777.7–779, 779.3–779.34, 779.6–779.89
Nutritional deficiencies	2	244.2, 260–263.9, 265–269.9, 280.1–280.8, 281.0–281.9, 716.0–716.09
Protein-energy malnutrition	3–4	260–263.9
Iodine deficiency	3–4	244.2

	ICD10
	O10–O16.9
	O32–O33.9, O64–O66.9, O71–O71.9
	N96, O00–O07.9
	O24–O25.3, O98–O99.91
	O96–O97.9
	N98–N98.9, O09–O09.93, O21–O22.93, O26–O26.93, O28–O31.8, O34–O36.93, O40–O43.199, O43.8–O43.93, O47–O48.1, O60–O61.9, O63–O63.9, O68–O69.9, O70.0–O70.9, O73–O77.9, O80–O84.9, O87–O90.9, O92–O92.79
	P00–P04.2, P04.5–P05.9, P07–P15.9, P19–P22.9, P24–P29.9, P36–P36.9, P38–P39.9, P50–P61.9, P70, P70.3–P72.9, P74–P78.9, P80–P81.9, P83–P84, P90–P94.9, P96, P96.3–P96.4, P96.8–P96.89
	P01.0–P01.1, P07–P07.39, P22–P22.9, P25–P28.9, P61.2, P77–P77.9
	P01.7, P02–P03.9, P10–P15.9, P20–P21.9, P24–P24.9, P90–P91.9
	P36–P36.9, P38–P39.9
	P55–P59.9
	P00–P01, P01.2–P01.6, P01.8–P01.9, P04–P04.2, P04.5–P05.9, P08–P09, P19–P19.9, P29–P29.9, P50–P54.9, P60–P61.1, P61.3–P61.9, P70, P70.3–P72.9, P74–P76.9, P78–P78.9, P80–P81.9, P83–P84, P92–P94.9, P96, P96.3–P96.4, P96.8–P96.89
	D50.1–D50.8, D51–D52.0, D52.8–D53.9, D64.3, E00–E02, E40–E46.9, E51–E61.9, E63–E64.0, E64.2–E64.9, M12.1–M12.19
	E40–E46.9, E64.0
	E00–E02

eTable 3. GBD cause list and associated ICD9 and ICD10 codes. (continued)

Cause	Level	ICD9
Iron-deficiency anemia	3–4	280.1–280.8
Other nutritional deficiencies	3–4	265–269.9, 281.0–281.9, 716.0–716.09
Other communicable, maternal, neonatal, and nutritional diseases	2	020–029, 034–034.9, 039–039.4, 039.8–040, 040.1–041.09, 045–046.9, 050–051.9, 054–054.9, 056–059.9, 070–070.21, 070.3–070.31, 070.4–070.43, 070.49–070.53, 070.59–070.9, 072–073, 073.7–074.1, 074.20, 074.3–075.9, 078.4–078.7, 079–079.7, 080.0, 090–101.6, 104–104.9, 136–136.29, 138, 139, 323.0–323.02, 323.2–323.3, 390–390.9, 392, 392.9, 484.5, 613–614.9, 771.0–771.2
Sexually transmitted diseases excluding HIV	3	054.1, 090–099.9, 613–614.9
Syphilis	4	090–097.9
Chlamydial infection	4	099, 099.1–099.6
Gonococcal infection	4	098–098.9
Other sexually transmitted diseases	4	099.0, 099.8–099.9
Hepatitis	3–4	070–070.21, 070.3–070.31, 070.4–070.43, 070.49–070.53, 070.59–070.9
Other infectious diseases	3–4	020–029, 034–034.9, 039–039.4, 039.8–040, 040.1–041.09, 045–046.9, 050–051.9, 054–054.0, 054.10–054.9, 056–059.9, 072–073, 073.7–074.1, 074.20, 074.3–075.9, 078.4–078.7, 079–079.7, 080.0, 100–101.6, 104–104.9, 136–136.29, 138, 139, 323.0–323.02, 323.2–323.3, 390–390.9, 392, 392.9, 484.5, 771.0–771.2

	ICD10
	D50.1–D50.8, D64.3
	D51–D52.0, D52.8–D53.9, E51–E61.9, E63–E64, E64.2–E64.3, M12.1–M12.19
	A20–A28.9, A32–A32.9, A38–A38.9, A48.2, A48.4–A48.52, A49.1, A50–A58, A60–A60.9, A63–A63.8, A65–A65.0, A69–A69.1, A74, A74.8–A74.9, A80–A81.9, A88–A89.9, B00–B00.9, B03–B04, B06–B06.9, B10–B10.89, B15–B17.9, B19–B19.9, B25–B27.99, B29.4, B33, B33.3–B33.8, B47–B48.8, B63, B91, B94.2, B95–B95.5, G14–G14.6, I00, I02, I02.9, I98.0–I98.1, J02.0, J03.0–J03.01, K67.0–K67.2, K67.8, K74.7–K74.8, M03.1, M49.1, M73.0–M73.1, M89.6–M89.69, N70–N71.9, N73–N74.8, P35–P35.3, P35.9, P37, P37.2, P37.5–P37.9
	A50–A58, A60–A60.9, A63–A63.8, B63, I98.0, K67.0–K67.2, M03.1, M73.0–M73.1, N70–N71.9, N73–N74.8
	A50–A53.9, I98.0, K67.2, M03.1, M73.1
	A55–A56.8, K67.0
	A54–A54.9, K67.1, M73.0
	A57–A58, A63–A63.8
	B15–B17.9, B19–B19.9, B94.2, P35.3
	A20–A28.9, A32–A32.9, A38–A38.9, A48.2, A48.4–A48.52, A49.1, A65–A65.0, A69–A69.1, A74, A74.8–A74.9, A80–A81.9, A88–A89.9, B00–B00.9, B03–B04, B06–B06.9, B10–B10.89, B25–B27.99, B29.4, B33, B33.3–B33.8, B47–B48.8, B91, B95–B95.5, G14–G14.6, I00, I02, I02.9, I98.1, J02.0, J03.0–J03.01, K67.8, K74.7–K74.8, M49.1, M89.6–M89.69, P35–P35.2, P35.9, P37, P37.2, P37.5–P37.9

eTable 3. GBD cause list and associated ICD9 and ICD10 codes. (continued)

Cause	Level	ICD9
Non-communicable diseases	1	035–035.9, 036.41–036.43, 036.6, 070.22–070.23, 070.32–070.33, 070.44, 070.54, 074.2, 074.21–074.23, 102–103.9, 133–133.6, 135–135.9, 136.6, 140–148.9, 150–158.9, 160–164.9, 170–175.9, 180–183.8, 184.0–184.4, 184.8, 185–186.9, 187.1–187.8, 188–188.9, 189.0–189.8, 190–194.8, 200–208.92, 209.0–209.17, 209.21–209.27, 209.31–209.57, 209.61, 209.63–209.67, 210.0–210.9, 211.0–211.8, 212.0–212.8, 213–213.9, 217–220.9, 221.0–221.8, 222.0–222.8, 223.0–223.89, 224–228.9, 229.0, 229.8, 230.1–230.8, 231.0–231.2, 232–232.9, 233.0–233.2, 233.31–233.32, 233.4–233.5, 233.7, 234.0–234.8, 235.0, 235.4, 235.6–235.8, 236.0–236.2, 236.4–236.5, 236.7, 236.91–237.3, 237.5–237.9, 238.0–238.5, 239.2–239.4, 239.6, 240–243.9, 244.0–244.1, 244.3–244.8, 245–246.9, 250–259.9, 270–273.9, 275–276, 277–277.2, 277.4–277.9, 278.0–278.8, 282–284.9, 286–286.5, 286.7–289.7, 290–292.9, 294.1–295.95, 303–303.93, 304.0–304.83, 305–305.93, 307.1, 307.51, 307.54, 327.2–327.8, 330–331.2, 331.5–337.9, 340–341.9, 345–345.91, 349–349.8, 353.6–353.9, 356–356.9, 357.0–357.7, 358–359.9, 376.0–376.1, 391–391.9, 392.0, 393–398.99, 402–404.93, 410–414.9, 416.1, 417–417.9, 420–423, 423.1–425.9, 427–427.32, 427.6–427.89, 429.0–429.1, 430–435.9, 437.0–437.2, 437.4–437.8, 441–443.9, 446–457.9, 459, 459.1–459.39, 470, 470.9–474.9, 476–476.1, 477–479, 490–504.9, 506–506.9, 508–509, 515, 516–517.8, 518.6–518.7, 518.9, 519.0–519.4, 530–536.1, 536.4–536.49, 537–537.6, 537.8–537.84, 538–543.9, 550–553.6, 555–558.9, 560–560.39, 560.8–560.9, 562–562.13, 564–564.7, 565–566.9, 569.0–569.44, 569.5–569.71, 569.84–569.85, 571–571.9, 572.3–572.9, 573.0–573.4, 573.8–577.9, 579–583.9, 585–585.9, 588–590.9, 592–593.89, 594–599.69, 599.8–599.89, 601–602.9, 604–604.99, 608.2–608.24, 610–610.9, 617–618.9, 620–620.9, 621.4–621.9, 622.3–622.7, 629–629.81, 680–689, 694–695.59, 707–707.9, 710–711.99, 714–714.33, 714.8–714.9, 728.86, 728.88, 730.1–730.19, 732–732.9, 733.0–733.19, 740–749.04, 749.2–758.9, 759.0–759.89, 760.7–760.79, 775.0–775.3, 779.4–779.5, 780.57, 780.59, 780.62–780.63, 786.03, 787.1, 788.0, 790.2–790.22, 790.3, 798–798.0, E850–E850.29, E850.9–E854.39, E860–E860.19
Neoplasms	2	140–148.9, 150–158.9, 160–164.9, 170–175.9, 180–183.8, 184.0–184.4, 184.8, 185–186.9, 187.1–187.8, 188–188.9, 189.0–189.8, 190–194.8, 200–208.92, 209.0–209.17, 209.21–209.27, 209.31–209.57, 209.61, 209.63–209.67, 210.0–210.9, 211.0–211.8, 212.0–212.8, 213–213.9, 217–217.8, 219.0, 220–220.9, 221.0–221.8, 222.0–222.8, 223.0–223.89, 224–228.9, 229.0, 229.8, 230.1–230.8, 231.0–231.2, 232–232.9, 233.0–233.2, 233.31–233.32, 233.4–233.5, 233.7, 234.0–234.8, 235.0, 235.4, 235.6–235.8, 236.1–236.2, 236.4–236.5, 236.7, 236.91–237.3, 237.5–237.9, 238.0–238.5, 239.2–239.4, 239.6, 569.0, 569.43–569.44, 569.84–569.85, 610–610.9
Lip and oral cavity cancer	3–4	140–145.9, 210.0–210.6, 235.0
Nasopharynx cancer	3–4	147–147.9, 210.7–210.9
Other pharynx cancer	3–4	146–146.9, 148–148.9
Esophageal cancer	3–4	150–150.9, 211.0, 230.1
Stomach cancer	3–4	151–151.9, 209.23, 209.63, 211.1, 230.2
Colon and rectum cancer	3–4	153–154.9, 209.1–209.17, 209.5–209.57, 211.3–211.4, 230.3–230.6
Liver cancer	3–4	155–155.9, 211.5

	ICD10
	A39.5–A39.53, A46–A46.0, A66–A67.9, B18–B18.9, B33.2–B33.24, B86, C0–C13.9, C15–C25.9, C3–C34.92, C37–C38.8, C4–C41.9, C43–C45.9, C47–C54.9, C56–C57.8, C58–C58.0, C60–C63.8, C64–C67.9, C68.0–C68.8, C69–C75.8, C81–C86.6, C88–C96.9, D00.00–D00.2, D01.0–D01.3, D02.0–D02.3, D03–D06.9, D07.0–D07.2, D07.4–D07.5, D09.0, D09.2–D09.3, D09.8, D10.0–D10.7, D11–D12.9, D13.0–D13.7, D14.0–D14.32, D15–D16.9, D22–D27.9, D28.0–D28.7, D29.0–D29.8, D30.0–D30.8, D31–D36, D36.1–D36.7, D37.01–D37.5, D38.0–D38.5, D39.1–D39.2, D39.8, D40.0–D40.8, D41.0–D41.8, D42–D43.9, D44.0–D44.8, D45–D45.9, D47–D47.0, D47.2–D47.9, D48.0–D48.62, D49.2–D49.4, D49.6, D49.81, D52.1, D55–D58.9, D59.0–D59.3, D59.5–D59.6, D60–D61.9, D63.1, D64.0, D64.4, D66–D67, D68.0–D69.8, D70–D75.89, D76–D78.89, D86–D86.8, D86.82–D86.9, D89–D89.3, E03–E07.1, E09–E14.9, E15.0, E16.0–E16.9, E20–E34.8, E36–E36.8, E65–E68, E70–E85.29, E87.71, E88–E89.9, F00–F03.91, F06.2, F10–F16.99, F18–F29.9, F50.0–F50.5, G10–G13.8, G20–G26.0, G30–G31.9, G35–G37.9, G40–G41.9, G45–G46.8, G47.3–G47.39, G61–G61.9, G70–G73.7, G90–G90.9, G93.7, G95–G95.9, G97–G97.9, H05.0–H05.119, I01–I01.9, I02.0, I05–I09.9, I11–I13.9, I20–I25.9, I27.1, I28–I28.8, I30–I31.1, I31.8–I43.9, I47–I48.92, I51.0–I51.5, I60–I61.9, I62.0–I62.03, I63–I63.9, I65–I66.9, I67.0–I67.3, I67.5–I67.7, I68.0–I68.2, I69.0–I69.398, I70.2–I70.799, I71–I73.9, I77–I89.9, I91.9, I95.2–I95.3, I97–I98, I98.2, I98.9, J30–J35.9, J37–J47.9, J60–J63.8, J65–J68.9, J70–J70.9, J82, J84–J84.9, J91–J92.9, J95–J95.9, K20–K29.91, K31–K31.89, K35–K38.9, K40–K46.9, K50–K52.9, K55–K62.9, K63.5, K64–K64.9, K66.8, K67, K68–K68.9, K70–K70.9, K71.3–K71.51, K71.7, K72.1–K74.69, K74.9, K75.2–K77.8, K80–K83.9, K85–K86.9, K90–K91.9, K92.8–K92.89, K94–K95.89, L00–L05.92, L08–L08.9, L10–L14.0, L51–L51.9, L88–L89.95, L93–L93.2, L97–L98.499, M00–M03.0, M03.2–M03.6, M05–M09.8, M30–M36.8, M40–M43.19, M65–M65.08, M71.0–M71.19, M80–M82.8, M86.3–M86.49, M87–M87.19, M88–M89.09, M89.5–M89.59, M89.7–M89.9, N00–N08.8, N10–N12.9, N14–N16.8, N18–N18.9, N20–N23.0, N25–N32.0, N32.3–N32.4, N34–N34.3, N36–N36.9, N39–N39.2, N41–N41.9, N44–N44.04, N45–N45.9, N49–N49.9, N60–N60.99, N65–N65.1, N72–N72.0, N75–N77.8, N80–N81.9, N83–N83.9, N84.0–N84.1, N87–N87.9, N99–N99.9, P04.3–P04.49, P70.0–P70.2, P96.0–P96.2, P96.5, Q00–Q07.9, Q10.4–Q18.9, Q20–Q28.9, Q30–Q36, Q37–Q45.9, Q50–Q87.89, Q89–Q89.8, Q90–Q93.9, Q95–Q99.8, R50.2, R50.82–R50.83, R73–R73.9, R78.0–R78.5, R95, X45–X45.9
	C0–C13.9, C15–C25.9, C3–C34.92, C37–C38.8, C4–C41.9, C43–C45.9, C47–C54.9, C56–C57.8, C58–C58.0, C60–C63.8, C64–C67.9, C68.0–C68.8, C69–C75.8, C81–C86.6, C88–C96.9, D00.00–D00.2, D01.0–D01.3, D02.0–D02.3, D03–D06.9, D07.0–D07.2, D07.4–D07.5, D09.0, D09.2–D09.3, D09.8, D10.0–D10.7, D11–D12.9, D13.0–D13.7, D14.0–D14.32, D15–D16.9, D22–D24.9, D26.0, D27–D27.9, D28.0–D28.1, D28.7, D29.0–D29.8, D30.0–D30.8, D31–D36, D36.1–D36.7, D37.01–D37.5, D38.0–D38.5, D39.1–D39.2, D39.8, D40.0–D40.8, D41.0–D41.8, D42–D43.9, D44.0–D44.8, D45–D45.9, D47–D47.0, D47.2–D47.9, D48.0–D48.62, D49.2–D49.4, D49.6, D49.81, K31.7, K62.0–K62.1, K63.5, N60–N60.99, N84.0–N84.1, N87–N87.9
	C0–C08.9, D00.00–D00.07, D10.0–D10.5, D11–D11.9, D37.01–D37.04, D37.09
	C11–C11.9, D00.08, D10.6, D37.05
	C09–C10.9, C12–C13.9, D10.7
	C15–C15.9, D00.1, D13.0
	C16–C16.9, D00.2, D13.1, D37.1
	C18–C21.9, D01.0–D01.3, D12–D12.9, D37.3–D37.5
	C22–C22.9, D13.4

eTable 3. GBD cause list and associated ICD9 and ICD10 codes. (continued)

Cause	Level	ICD9
Gallbladder and biliary tract cancer	3–4	156–156.9, 209.25–209.27, 209.65–209.67
Pancreatic cancer	3–4	157–157.9, 211.6–211.7
Larynx cancer	3–4	161–161.9, 212.1, 231.0, 235.6
Tracheal, bronchus, and lung cancer	3–4	162–162.9, 209.21, 209.61, 212.2–212.3, 231.1–231.2, 235.7
Malignant skin melanoma	3–4	172–172.9
Non-melanoma skin cancer	3–4	173–173.99, 222.4, 232–232.9, 238.2
Breast cancer	3–4	174–175.9, 217–217.8, 233.0, 238.3, 239.3, 610–610.9
Cervical cancer	3–4	180–180.9, 219.0, 233.1
Uterine cancer	3–4	182–182.8, 233.2
Ovarian cancer	3–4	183–183.0, 220–220.9, 236.2
Prostate cancer	3–4	185–185.9, 222.2, 236.5
Testicular cancer	3–4	186–186.9, 222.0, 222.3, 236.4
Kidney cancer	3–4	189.0–189.1, 209.24, 209.64, 223.0–223.1, 236.91
Bladder cancer	3–4	188–188.9, 223.3, 233.7, 236.7, 239.4
Brain and nervous system cancer	3–4	191–192.9
Thyroid cancer	3–4	193–193.9, 226–226.9
Mesothelioma	3–4	158.9, 163–163.9, 212.4
Hodgkin lymphoma	3–4	201–201.98
Non-Hodgkin lymphoma	3–4	200–200.9, 202–202.98
Multiple myeloma	3–4	203–203.9
Leukemia	3	204–208.92
Acute lymphoid leukemia	4	204.0–204.02
Chronic lymphoid leukemia	4	204.1–204.12
Acute myeloid leukemia	4	205.0–205.02, 205.3–205.32, 206.0–206.02, 207.0
Chronic myeloid leukemia	4	205.1–205.12, 206.1–206.12, 207.1

	ICD10
	C23–C24.9, D13.5
	C25–C25.9, D13.6–D13.7
	C32–C32.9, D02.0, D14.1, D38.0
	C33–C34.92, D02.1–D02.3, D14.2–D14.32, D38.1
	C43–C43.9, D03–D03.9, D22–D23.9, D48.5
	C44–C44.99, D04–D04.9, D49.2
	C50–C50.929, D05–D05.92, D24–D24.9, D48.6–D48.62, D49.3, N60–N60.99
	C53–C53.9, D06–D06.9, D26.0
	C54–C54.9, D07.0–D07.2, N87–N87.9
	C56–C56.9, D27–D27.9, D39.1–D39.12
	C61–C61.9, D07.5, D29.1, D40.0
	C62–C62.92, D29.2–D29.8, D40.1–D40.8
	C64–C65.9, D30.0–D30.12, D41.0–D41.12
	C67–C67.9, D09.0, D30.3, D41.4–D41.8, D49.4
	C70–C72.9
	C73–C73.9, D09.3, D09.8, D34–D34.9, D44.0
	C45–C45.9
	C81–C81.99
	C82–C86.6, C96–C96.9
	C88–C90.9
	C91–C95.92
	C91.0–C91.02
	C91.1–C91.12
	C92.0–C92.02, C92.3–C92.62, C93.0–C93.02, C94.0–C94.02, C94.2–C94.22, C94.4–C94.5
	C92.1–C92.12

eTable 3. GBD cause list and associated ICD9 and ICD10 codes. (continued)

Cause	Level	ICD9
Other neoplasms	3–4	152–152.9, 158–158.8, 160–160.9, 164–164.9, 170–171.9, 181–181.9, 182.9, 183.2–183.8, 184.0–184.4, 184.8, 187.1–187.8, 189.2–189.8, 190–190.9, 194–194.8, 209.0–209.03, 209.22, 209.31–209.43, 211.2, 211.8, 212.0, 212.5–212.8, 213–213.9, 221.0–221.8, 222.1, 222.8, 223.2, 223.8–223.89, 224–225.9, 227–228.9, 229.0, 229.8, 230.7–230.8, 233.31–233.32, 233.4–233.5, 234.0–234.8, 235.4, 235.8, 236.1, 236.99–237.3, 237.5–237.9, 238.0–238.1, 238.4–238.5, 239.2, 239.6, 569.0, 569.43–569.44, 569.84–569.85
Cardiovascular diseases	2	036.41–036.43, 036.6, 074.2, 074.21–074.23, 391–391.9, 392.0, 393–398.99, 402–402.91, 410–414.9, 417–417.9, 420–423, 423.1–425.9, 427–427.32, 427.6–427.89, 429.0–429.1, 430–435.9, 437.0–437.2, 437.5–437.8, 441–443.9, 447–454.9, 456, 456.3–457.9, 459, 459.1–459.39
Rheumatic heart disease	3–4	391–391.9, 392.0, 393–398.99
Ischemic heart disease	3–4	410–414.9
Cerebrovascular disease	3	430–435.9, 437.0–437.2, 437.5–437.8
Ischemic stroke	4	433–435.9, 437.0–437.1, 437.5–437.8
Hemorrhagic stroke	4	430–432.9, 437.2
Hypertensive heart disease	3–4	402–402.91
Cardiomyopathy and myocarditis	3–4	036.43, 036.6, 074.23, 422–422.99, 425–425.9, 429.0–429.1
Atrial fibrillation and flutter	3–4	427.3–427.32
Aortic aneurysm	3–4	441–441.9
Peripheral vascular disease	3–4	443.0–443.9
Endocarditis	3–4	036.42, 074.22, 421–421.9, 424.9–424.91
Other cardiovascular and circulatory diseases	3–4	036.41, 074.2, 074.21, 417–417.9, 420–420.99, 423, 423.1–424.8, 424.99, 427–427.2, 427.6–427.89, 442–443, 447–454.9, 456, 456.3–457.9, 459, 459.1–459.39
Chronic respiratory diseases	2	135–135.9, 136.6, 327.2–327.8, 470, 470.9–474.9, 476–476.1, 477–479, 490–504.9, 506–506.9, 508–509, 515, 516–517.8, 518.6, 518.9, 519.1–519.4, 780.57, 786.03
Chronic obstructive pulmonary disease	3–4	490–492.9, 494–494.9, 496–499
Pneumoconiosis	3	500–504.9
Silicosis	4	502–502.9, 503.0, 503.9

	ICD10
	C17–C17.9, C3–C31.9, C37–C38.8, C4–C41.9, C47–C5, C51–C52.9, C57–C57.8, C58–C58.0, C60–C60.9, C63–C63.8, C66–C66.9, C68.0–C68.8, C69–C7, C74–C75.8, D07.4, D09.2–D09.22, D13.2–D13.39, D14.0, D15–D16.9, D28.0–D28.1, D28.7, D29.0, D30.2–D30.22, D30.4–D30.8, D31–D33.9, D35–D36, D36.1–D36.7, D37.2, D38.2–D38.5, D39.2, D39.8, D41.2–D41.3, D42–D43.9, D44.1–D44.8, D45–D45.9, D47–D47.0, D47.2–D47.9, D48.0–D48.4, D49.6, D49.81, K31.7, K62.0–K62.1, K63.5, N84.0–N84.1
	A39.5–A39.53, B33.2–B33.24, D86.85, G45–G46.8, I01–I01.9, I02.0, I05–I09.9, I11–I11.9, I20–I25.9, I28–I28.8, I30–I31.1, I31.8–I43.9, I47–I48.92, I51.0–I51.5, I60–I61.9, I62.0–I62.03, I63–I63.9, I65–I66.9, I67.0–I67.3, I67.5–I67.6, I68.0–I68.2, I69.0–I69.398, I70.2–I70.799, I71–I73.9, I77–I83.93, I86–I89.9, I91.9, I98
	I01–I01.9, I02.0, I05–I09.9
	I20–I25.9
	G45–G46.8, I60–I61.9, I62.0–I62.03, I63–I63.9, I65–I66.9, I67.0–I67.3, I67.5–I67.6, I68.1–I68.2, I69.0–I69.398
	G45–G46.8, I63–I63.9, I65–I66.9, I67.2–I67.3, I67.5–I67.6, I69.3–I69.398
	I60–I61.9, I62.0–I62.03, I67.0–I67.1, I68.1–I68.2, I69.0–I69.298
	I11–I11.9
	A39.52, B33.2–B33.24, D86.85, I40–I43.9, I51.4–I51.5
	I48–I48.92
	I71–I71.9
	I70.2–I70.799, I73–I73.9
	A39.51, I33–I33.9, I38–I39.9
	A39.5–A39.50, A39.53, I28–I28.8, I30–I31.1, I31.8–I32.8, I34–I37.9, I47–I47.9, I51.0–I51.3, I68.0, I72–I72.9, I77–I83.93, I86–I89.9, I91.9, I98
	D86–D86.2, D86.89–D86.9, G47.3–G47.39, J30–J35.9, J37–J47.9, J60–J63.8, J65–J68.9, J70–J70.1, J70.8–J70.9, J82, J84–J84.9, J91–J92.9
	J40–J44.9, J47–J47.9
	J60–J63.8, J65–J65.0, J92.0
	J62–J62.9

eTable 3. GBD cause list and associated ICD9 and ICD10 codes. (continued)

Cause	Level	ICD9
Asbestosis	4	501
Coal workers pneumoconiosis	4	500–500.9, 501.0–501.9
Other pneumoconiosis	4	503, 503.1, 504–504.9
Asthma	3–4	493–493.92
Interstitial lung disease and pulmonary sarcoidosis	3–4	135–135.9, 136.6, 515, 516–516.9
Other chronic respiratory diseases	3–4	327.2–327.8, 470, 470.9–474.9, 476–476.1, 477–479, 495–495.9, 506–506.9, 508–509, 517–517.8, 518.6, 518.9, 519.1–519.4, 780.57, 786.03
Cirrhosis and other chronic liver diseases	2–4	070.22–070.23, 070.32–070.33, 070.44, 070.54, 456.0–456.21, 571–571.9, 572.3–572.9, 573.0–573.3, 573.8–573.9
Digestive diseases	2	455–455.9, 530–536.1, 537–537.6, 537.8–537.84, 538, 540–543.9, 550–551.1, 551.3–552.1, 552.3–553.6, 555–558.9, 560–560.39, 560.8–560.9, 562–562.13, 564–564.1, 564.5–564.7, 565–566.9, 569.1–569.42, 569.5, 569.7–569.71, 573.4, 574–577.9, 579–579.2, 579.4–579.9, 787.1
Peptic ulcer disease	3–4	531–534.91
Gastritis and duodenitis	3–4	535–535.9
Appendicitis	3–4	540–542.9
Paralytic ileus and intestinal obstruction	3–4	560–560.39, 560.8–560.9
Inguinal, femoral, and abdominal hernia	3–4	550–551.1, 551.3–552.1, 552.3–553.03, 553.6
Inflammatory bowel disease	3–4	555–556.9, 558–558.9, 569.5
Vascular intestinal disorders	3–4	557–557.9
Gallbladder and biliary diseases	3–4	574–576.9
Pancreatitis	3–4	577–577.9, 579.4
Other digestive diseases	3–4	455–455.9, 530–530.9, 536–536.1, 537–537.6, 537.8–537.84, 538, 543–543.9, 553.1–553.3, 562–562.13, 564–564.1, 564.5–564.7, 565–566.9, 569.1–569.42, 569.7–569.71, 573.4, 579–579.2, 579.8–579.9, 787.1

	ICD10
	J61–J61.0, J92.0
	J60–J60.0
	J63–J63.8, J65–J65.0
	J45–J46.9
	D86–D86.2, D86.89–D86.9, J84–J84.9
	G47.3–G47.39, J30–J35.9, J37–J39.9, J66–J68.9, J70–J70.1, J70.8–J70.9, J82, J91–J92, J92.9
	B18–B18.9, I85–I85.9, I98.2, K70–K70.9, K71.3–K71.51, K71.7, K72.1–K74.69, K74.9, K75.8–K76.0, K76.6–K76.7, K76.9
	I84–I84.9, K20–K29.91, K31–K31.6, K31.8–K31.89, K35–K38.9, K40–K42.9, K44–K46.9, K50–K52.9, K55–K62, K62.2–K62.6, K62.8–K62.9, K64–K64.9, K66.8, K67, K68–K68.9, K75.2–K75.4, K76.1–K76.5, K76.8–K76.89, K77–K77.8, K80–K83.9, K85–K86.9, K90–K90.9, K92.8–K92.89, M09.1
	K25–K28.9, K31, K31.1–K31.6, K31.8, K31.82–K31.89
	K29–K29.91
	K35–K37.9, K38.3–K38.9
	K56–K56.9
	K40–K42.9, K44–K46.9
	K50–K52.9, M09.1
	K55–K55.9
	K80–K83.9
	K85–K86.9
	I84–I84.9, K20–K24, K31.0, K31.81–K31.819, K38–K38.2, K57–K62, K62.2–K62.6, K62.8–K62.9, K64–K64.9, K66.8, K67, K68–K68.9, K75.2–K75.4, K76.1–K76.5, K76.8–K76.89, K77–K77.8, K90–K90.9, K92.8–K92.89

eTable 3. GBD cause list and associated ICD9 and ICD10 codes. (continued)

Cause	Level	ICD9
Neurological disorders	2	290–290.9, 294.1–294.9, 330–331.2, 331.5–337.9, 340–341.9, 345–345.91, 349, 349.2–349.8, 353.6–353.9, 356–356.9, 357.0–357.1, 357.3–357.4, 357.7, 358–359.9, 728.86, 728.88, 775.2
Alzheimer disease and other dementias	3–4	290–290.9, 294.1–294.9, 331–331.2
Parkinson disease	3–4	332–332.9
Epilepsy	3–4	345–345.91
Multiple sclerosis	3–4	340–340.9
Motor neuron disease	3–4	335–335.29, 335.8–335.9
Other neurological disorders	3–4	330–330.9, 331.5–331.9, 333–334.9, 335.3, 336–337.9, 341–341.9, 349, 349.2–349.8, 353.6–353.9, 356–356.9, 357.0–357.1, 357.3–357.4, 357.7, 358–359.9, 728.86, 728.88, 775.2
Mental and substance use disorders	2	291–292.9, 295–295.95, 303–303.93, 304.0–304.83, 305–305.93, 307.1, 307.51, 307.54, 357.5, 760.7–760.79, 780.59, 790.3, E850–E850.29, E850.9–E854.39, E860–E860.19
Schizophrenia	3–4	295–295.95
Alcohol use disorders	3–4	291–291.9, 303–303.93, 305.0–305.03, 357.5, 790.3, E860–E860.19
Drug use disorders	3	292–292.9, 304.0–304.83, 305, 305.1–305.93, 760.7–760.79, E850–E850.29, E850.9–E854.39
Opioid use disorders	4	304.0–304.03, 305.5–305.53, E850.0–E850.29
Cocaine use disorders	4	304.2–304.23, 305.6–305.63
Amphetamine use disorders	4	304.4–304.43, 305.7–305.73
Other drug use disorders	4	292–292.9, 304.1–304.13, 304.5–304.83, 305, 305.1–305.13, 305.3–305.43, 305.8–305.93
Eating disorders	3	307.1, 307.51, 307.54
Anorexia nervosa	4	307.1, 307.54
Bulimia nervosa	4	307.51
Diabetes, urogenital, blood, and endocrine diseases	2	218–219, 219.1–219.9, 236.0, 240–243.9, 244.0–244.1, 244.3–244.8, 245–246.9, 250–259.9, 270–273.9, 275–276, 277–277.2, 277.4–277.9, 278.0–278.8, 282–284.9, 286–286.5, 286.7–289.7, 349.0–349.1, 357.2, 357.6, 403–404.93, 518.7, 519.0–519.09, 536.4–536.49, 539–539.9, 551.2–551.29, 552.2–552.29, 564.2–564.4, 569.6–569.69, 579.3, 580–583.9, 585–585.9, 588–590.9, 592–593.89, 594–599.69, 599.8–599.89, 601–602.9, 604–604.99, 608.2–608.24, 617–618.9, 620–620.9, 621.4–621.9, 622.3–622.7, 629–629.81, 775.0–775.1, 775.3, 779.4–779.5, 780.62–780.63, 788.0, 790.2–790.22

	ICD10
	F00–F03.91, G10–G13.8, G20–G21.0, G21.2–G24, G24.1–G25.0, G25.2–G25.3, G25.5, G25.8–G26.0, G30–G31.1, G31.8–G31.9, G35–G37.9, G40–G41.9, G61–G61.9, G70–G72, G72.2–G73.7, G90–G90.9, G95–G95.9, M33–M33.99
	F00–F03.91, G30–G31.1, G31.8–G31.9
	G20–G21.0, G21.2–G22.0
	G40–G41.9
	G35–G35.9
	G12.2–G12.9
	G10–G12.1, G13–G13.8, G23–G24, G24.1–G25.0, G25.2–G25.3, G25.5, G25.8–G26.0, G36–G37.9, G61–G61.9, G70–G72, G72.2–G73.7, G90–G90.9, G95–G95.9, M33–M33.99
	F06.2, F10–F16.99, F18–F29.9, F50.0–F50.5, G31.2, G72.1, P04.3–P04.49, P96.1, Q86.0, R78.0–R78.5, X45–X45.9
	F06.2, F20–F23.9, F25–F29.9
	F10–F10.99, G31.2, G72.1, P04.3, Q86.0, R78.0, X45–X45.9
	F11–F16.99, F18–F19.99, P04.4–P04.49, P96.1, R78.1–R78.5
	F11–F11.99, P96.1, R78.1
	F14–F14.99, R78.2
	F15–F15.99
	F13–F13.99, F16–F16.99, F18–F19.99, R78.3–R78.5
	F50.0–F50.5
	F50.0–F50.1
	F50.2–F50.5
	D25–D26, D26.1–D26.9, D28.2, D52.1, D55–D58.9, D59.0–D59.3, D59.5–D59.6, D60–D61.9, D63.1, D64.0, D64.4, D66–D67, D68.0–D69.8, D70–D75.89, D76–D78.89, D86.8, D86.82–D86.84, D86.86–D86.87, D89–D89.3, E03–E07.1, E09–E14.9, E15.0, E16.0–E16.9, E20–E34.8, E36–E36.8, E65–E68, E70–E85.29, E87.71, E88–E89.9, G21.1–G21.19, G24.0–G24.09, G25.1, G25.4, G25.6–G25.79, G72.0, G93.7, G97–G97.9, I12–I13.9, I95.2–I95.3, I97–I97.9, I98.9, J70.2–J70.5, J95–J95.9, K43–K43.9, K62.7, K91–K91.9, K94–K95.89, M87.1–M87.19, N00–N08.8, N10–N12.9, N14–N16.8, N18–N18.9, N20–N23.0, N25–N32.0, N32.3–N32.4, N34–N34.3, N36–N36.9, N39–N39.2, N41–N41.9, N44–N44.04, N45–N45.9, N49–N49.9, N65–N65.1, N72–N72.0, N75–N77.8, N80–N81.9, N83–N83.9, N99–N99.9, P70.0–P70.2, P96.2, P96.5, R50.2, R50.82–R50.83, R73–R73.9

eTable 3. GBD cause list and associated ICD9 and ICD10 codes. (continued)

Cause	Level	ICD9
Diabetes mellitus	3–4	250–250.39, 250.5–250.99, 357.2, 775.0–775.1, 790.2–790.22
Acute glomerulonephritis	3–4	580–580.9
Chronic kidney disease	3	250.4–250.49, 403–404.93, 581–583.9, 585–585.9, 589–589.9
Chronic kidney disease due to diabetes mellitus	4	250.4–250.49
Chronic kidney disease due to hypertension	4	403–404.93
Chronic kidney disease due to glomerulonephritis	4	581–583.9
Chronic kidney disease due to other causes	4	589–589.9
Urinary diseases and male infertility	3	588–588.9, 590–590.9, 592–593.89, 594–596.81, 596.89–598.1, 598.8–599.69, 599.8–599.89, 601–602.9, 604–604.99, 608.2–608.24, 788.0
Interstitial nephritis and urinary tract infections	4	590–590.9, 595–595.9, 597–597.9, 599.0
Urolithiasis	4	592–592.9, 594–594.9, 788.0
Other urinary diseases	4	588–588.9, 593–593.89, 596–596.81, 596.89–596.9, 598–598.1, 598.8–599, 599.1–599.69, 599.8–599.89, 601–602.9, 604–604.99, 608.2–608.24
Gynecological diseases	3	218–219, 219.1–219.9, 236.0, 256.4, 617–618.9, 620–620.9, 621.4–621.9, 622.3–622.7, 629–629.81
Uterine fibroids	4	218–219, 219.1–219.9, 236.0
Polycystic ovarian syndrome	4	256.4
Endometriosis	4	617–617.9
Genital prolapse	4	618–618.9
Other gynecological diseases	4	620–620.9, 621.4–621.9, 622.3–622.7, 629–629.81
Hemoglobinopathies and hemolytic anemias	3	282–284.9
Thalassemias	4	282.4–282.49

	ICD10
	E10–E10.11, E10.3–E11.1, E11.3–E12.1, E12.3–E13.11, E13.3–E14.1, E14.3–E14.9, P70.0–P70.2, R73–R73.9
	N00–N01.9
	D63.1, E10.2–E10.29, E11.2–E11.29, E12.2, E13.2–E13.29, E14.2, I12–I13.9, N02–N08.8, N15.0, N18–N18.9
	E10.2–E10.29, E11.2–E11.29, E12.2, E13.2–E13.29, E14.2
	I12–I13.9
	N03–N06.9
	N02–N02.9, N07–N08.8, N15.0
	N10–N12.9, N15, N15.1–N16.8, N20–N23.0, N25–N32.0, N32.3–N32.4, N34–N34.3, N36–N36.9, N39–N39.2, N41–N41.9, N44–N44.04, N45–N45.9, N49–N49.9
	N10–N12.9, N15, N15.1–N16.8, N30–N30.91, N34–N34.3, N39.0–N39.2
	N20–N23.0
	N25–N29.8, N31–N32.0, N32.3–N32.4, N36–N36.9, N39, N41–N41.9, N44–N44.04, N45–N45.9, N49–N49.9
	D25–D26, D26.1–D26.9, D28.2, E28.2, N72–N72.0, N75–N77.8, N80–N81.9, N83–N83.9
	D25–D26, D26.1–D26.9, D28.2
	E28.2
	N80–N80.9
	N81–N81.9
	N72–N72.0, N75–N77.8, N83–N83.9
	D55–D58.9, D59.1, D59.3, D59.5, D60–D61.9, D64.0, D64.4
	D56–D56.9

eTable 3. GBD cause list and associated ICD9 and ICD10 codes. (continued)

Cause	Level	ICD9
Sickle cell disorders	4	282.6–282.68
G6PD deficiency	4	282.2–282.3
Other hemoglobinopathies and hemolytic anemias	4	282–282.1, 282.69–284.9
Endocrine, metabolic, blood, and immune disorders	3–4	240–243.9, 244.0–244.1, 244.3–244.8, 245–246.9, 251–256.39, 256.8–259.9, 270–273.9, 275–276, 277–277.2, 277.4–277.9, 278.0–278.8, 286–286.5, 286.7–289.7, 349.0–349.1, 357.6, 518.7, 519.0–519.09, 536.4–536.49, 539–539.9, 551.2–551.29, 552.2–552.29, 564.2–564.4, 569.6–569.69, 579.3, 596.82–596.83, 598.2, 775.3, 779.4–779.5, 780.62–780.63
Musculoskeletal disorders	2	416.1, 437.4, 446–446.9, 695.4–695.59, 710–711.99, 714–714.33, 714.8–714.9, 730.1–730.19, 732–732.9, 733.0–733.19
Rheumatoid arthritis	3–4	714–714.33, 714.8–714.9
Other musculoskeletal disorders	3–4	416.1, 437.4, 446–446.9, 695.4–695.59, 710–711.99, 730.1–730.19, 732–732.9, 733.0–733.19
Other noncommunicable diseases	2	035–035.9, 102–103.9, 133–133.6, 376.0–376.1, 680–689, 694–695.3, 707–707.9, 740–749.04, 749.2–758.9, 759.0–759.89, 798–798.0
Congenital anomalies	3	740–749.04, 749.2–758.9, 759.0–759.89
Neural tube defects	4	740–741.93, 742.0
Congenital heart anomalies	4	745–747.9
Cleft lip and cleft palate	4	749–749.04, 749.2–749.25
Down syndrome	4	758
Other chromosomal abnormalities	4	758, 758.1–758.6, 758.8–758.9
Other congenital anomalies	4	742, 742.1–744.9, 748–748.9, 749.6–757.9, 759.0–759.89
Skin and subcutaneous diseases	3	035–035.9, 102–103.9, 133–133.6, 680–689, 694–695.3, 707–707.9
Cellulitis	4	681–682.9
Pyoderma	4	035–035.9, 102–103.9, 680–680.9, 683–689
Decubitus ulcer	4	707–707.9

	ICD10
	D57–D57.219, D57.4–D57.819
	D55–D55.2
	D55.3–D55.9, D58–D58.9, D59.1, D59.3, D59.5, D60–D61.9, D64.0, D64.4
	D52.1, D59.0, D59.2, D59.6, D66–D67, D68.0–D69.8, D70–D75.89, D76–D78.89, D86.8, D86.82–D86.84, D86.86–D86.87, D89–D89.3, E03–E07.1, E09–E09.9, E15.0, E16.0–E16.9, E20–E28.1, E28.3–E34.8, E36–E36.8, E65–E68, E70–E85.29, E87.71, E88–E89.9, G21.1–G21.19, G24.0–G24.09, G25.1, G25.4, G25.6–G25.79, G72.0, G93.7, G97–G97.9, I95.2–I95.3, I97–I97.9, I98.9, J70.2–J70.5, J95–J95.9, K43–K43.9, K62.7, K91–K91.9, K94–K95.89, M87.1–M87.19, N14–N14.4, N65–N65.1, N99–N99.9, P96.2, P96.5, R50.2, R50.82–R50.83
	I27.1, I67.7, L93–L93.2, M00–M03.0, M03.2–M03.6, M05–M09.0, M09.2–M09.8, M30–M32.9, M34–M36.8, M40–M43.19, M65–M65.08, M71.0–M71.19, M80–M82.8, M86.3–M86.49, M87–M87.09, M88–M89.09, M89.5–M89.59, M89.7–M89.9
	M05–M06.9, M08.0–M08.89
	I27.1, I67.7, L93–L93.2, M00–M03.0, M03.2–M03.6, M07–M08, M08.9–M09.0, M09.2–M09.8, M30–M32.9, M34–M36.8, M40–M43.19, M65–M65.08, M71.0–M71.19, M80–M82.8, M86.3–M86.49, M87–M87.09, M88–M89.09, M89.5–M89.59, M89.7–M89.9
	A46–A46.0, A66–A67.9, B86, D86.3, H05.0–H05.119, L00–L05.92, L08–L08.9, L10–L14.0, L51–L51.9, L88–L89.95, L97–L98.499, P96.0, Q00–Q07.9, Q10.4–Q18.9, Q20–Q28.9, Q30–Q36, Q37–Q45.9, Q50–Q86, Q86.1–Q87.89, Q89–Q89.8, Q90–Q93.9, Q95–Q99.8, R95
	P96.0, Q00–Q07.9, Q10.4–Q18.9, Q20–Q28.9, Q30–Q36, Q37–Q45.9, Q50–Q86, Q86.1–Q87.89, Q89–Q89.8, Q90–Q93.9, Q95–Q99.8
	Q00–Q01.9, Q05–Q05.9
	Q20–Q28.9
	Q35–Q36, Q37–Q37.9
	Q90–Q90.9
	Q91–Q93.9, Q95–Q95.9, Q97–Q97.9, Q99–Q99.8
	P96.0, Q02–Q04.9, Q06–Q07.9, Q10.4–Q18.9, Q30–Q34.9, Q38–Q45.9, Q50–Q86, Q86.1–Q87.89, Q89–Q89.8
	A46–A46.0, A66–A67.9, B86, D86.3, L00–L05.92, L08–L08.9, L10–L14.0, L51–L51.9, L88–L89.95, L97–L98.499
	L03–L03.91
	A46–A46.0, A66–A67.9, L00–L02.93, L04–L05.92, L08–L08.9, L88, L97–L98.499
	L89–L89.95

eTable 3. GBD cause list and associated ICD9 and ICD10 codes. (continued)

Cause	Level	ICD9
Other skin and subcutaneous diseases	4	694–695.3
Sudden infant death syndrome	3–4	798–798.0
Injuries	1	E800–E800.3, E801–E801.3, E802–E802.3, E803–E803.3, E804–E804.3, E805–E805.3, E806–E806.3, E807–E807.3, E810.0–E810.7, E811.0–E811.7, E812.0–E812.7, E813.0–E813.7, E814.0–E814.7, E815.0–E815.7, E816.0–E816.7, E817.0–E817.7, E818.0–E818.7, E819.0–E819.7, E820.0–E820.7, E821.0–E821.7, E822.0–E822.7, E823.0–E823.7, E824.0–E824.7, E825.0–E825.7, E826.0–E826.4, E827.0–E827.4, E828.0– E828.4, E829.0–E829.4, E830–E838.9, E840–E849.9, E850.3–E850.89, E854.8, E856–E857.09, E860.2–E869.99, E870–E876.9, E878–E879.9, E880–E886.99, E888–E928.89, E929.1–E929.5, E930–E979.9, E990–E999.1
Transport injuries	2	E800–E800.3, E801–E801.3, E802–E802.3, E803–E803.3, E804–E804.3, E805–E805.3, E806–E806.3, E807–E807.3, E810.0–E810.7, E811.0–E811.7, E812.0–E812.7, E813.0–E813.7, E814.0–E814.7, E815.0–E815.7, E816.0–E816.7, E817.0–E817.7, E818.0–E818.7, E819.0–E819.7, E820.0–E820.7, E821.0–E821.7, E822.0–E822.7, E823.0–E823.7, E824.0–E824.7, E825.0–E825.7, E826.0–E826.4, E827.0–E827.4, E828.0–E828.4, E829.0–E829.4, E830–E838.9, E840–E849.9, E929.1
Road injuries	3	E800.3, E801.3, E802.3, E803.3, E804.3, E805.3, E806.3, E807.3, E810.0–E810.6, E811.0–E811.7, E812.0–E812.7, E813.0–E813.7, E814.0–E814.7, E815.0–E815.7, E816.0–E816.7, E817.0–E817.7, E818.0–E818.7, E819.0–E819.7, E820.0–E820.6, E821.0–E821.6, E822.0–E822.7, E823.0–E823.7, E824.0–E824.7, E825.0–E825.7, E826.0–E826.1, E826.3–E826.4, E827.0, E827.3–E827.4, E828.0, E828.4, E829.0–E829.4
Pedestrian road injuries	4	E811.7, E812.7, E813.7, E814.7, E815.7, E816.7, E817.7, E818.7, E819.7, E822.7, E823.7, E824.7, E825.7, E826.0, E827.0, E828.0, E829.0
Cyclist road injuries	4	E800.3, E801.3, E802.3, E803.3, E804.3, E805.3, E806.3, E807.3, E810.6, E811.6, E812.6, E813.6, E814.6, E815.6, E816.6, E817.6, E818.6, E819.6, E820.6, E821.6, E822.6, E823.6, E824.6, E825.6, E826.1
Motorcyclist road injuries	4	E810.2–E810.3, E811.2–E811.3, E812.2–E812.3, E813.2–E813.3, E814.2–E814.3, E815.2–E815.3, E816.2–E816.3, E817.2–E817.3, E818.2–E818.3, E819.2–E819.3, E820.2–E820.3, E821.2–E821.3, E822.2–E822.3, E823.2–E823.3, E824.2–E824.3, E825.2–E825.3
Motor vehicle road injuries	4	E810.0–E810.1, E811.0–E811.1, E812.0–E812.1, E813.0–E813.1, E814.0–E814.1, E815.0–E815.1, E816.0–E816.1, E817.0–E817.1, E818.0–E818.1, E819.0–E819.1, E820.0–E820.1, E821.0–E821.1, E822.0–E822.1, E823.0–E823.1, E824.0–E824.1, E825.0–E825.1
Other road injuries	4	E810.4–E810.5, E811.4–E811.5, E812.4–E812.5, E813.4–E813.5, E814.4–E814.5, E815.4–E815.5, E816.4–E816.5, E817.4–E817.5, E818.4–E818.5, E819.4–E819.5, E820.4–E820.5, E821.4–E821.5, E822.4–E822.5, E823.4–E823.5, E824.4–E824.5, E825.4–E825.5, E826.3–E826.4, E827.3–E827.4, E828.4, E829.4
Other transport injuries	3–4	E800–E800.2, E801–E801.2, E802–E802.2, E803–E803.2, E804–E804.2, E805–E805.2, E806–E806.2, E807–E807.2, E810.7, E820.7, E821.7, E826.2, E827.2, E828.2, E830–E838.9, E840–E849.9, E929.1
Unintentional injuries	2	E850.3–E850.89, E854.8, E856–E857.09, E860.2–E869.99, E870–E876.9, E878–E879.9, E880–E886.99, E888–E906.99, E910–E928.89, E929.2–E929.5, E930–E949.9
Falls	3–4	E880–E886.99, E888–E888.9, E929.3

	ICD10
	D86.3, L10–L14.0, L51–L51.9
	R95
	V00–V86.99, V87.2–V87.3, V88.2–V88.3, V90–V98.8, W00–W46.2, W49–W62.9, W64–W70.9, W73–W75.9, W77–W81.9, W83–W94.9, W97.9, W99–X06.9, X08–X39.9, X46–X47, X47.1–X47.8, X48–X48.9, X50–X54.9, X57–X58.9, X60–Y08.9, Y35–Y84.9, Y87.0–Y87.1, Y88–Y88.3, Y89.0–Y89.1
	V00–V86.99, V87.2–V87.3, V88.2–V88.3, V90–V98.8
	V01–V04.99, V06–V80.929, V82–V82.9, V87.2–V87.3
	V01–V04.99, V06–V09.9
	V10–V19.9
	V20–V29.9
	V30–V79.9, V87.2–V87.3
	V80–V80.929, V82–V82.9
	V00–V00.898, V05–V05.99, V81–V81.9, V83–V86.99, V88.2–V88.3, V90–V98.8
	W00–W46.2, W49–W62.9, W64–W70.9, W73–W75.9, W77–W81.9, W83–W94.9, W97.9, W99–X06.9, X08–X32.9, X39–X39.9, X46–X47, X47.1–X47.8, X48–X48.9, X50–X54.9, X57–X58.9, Y38.9–Y84.9, Y88–Y88.3
	W00–W19.9

eTable 3. GBD cause list and associated ICD9 and ICD10 codes. (continued)

Cause	Level	ICD9
Drowning	3–4	E910–E910.99
Fire, heat, and hot substances	3–4	E890–E899.09, E924–E924.99, E929.4
Poisonings	3–4	E850.3–E850.89, E854.8, E856–E857.09, E860.2–E869.99, E929.2
Exposure to mechanical forces	3	E913–E913.19, E916–E922.99, E928.1–E928.7
Unintentional firearm injuries	4	E922–E922.99, E928.7
Unintentional suffocation	4	E913–E913.19
Other exposure to mechanical forces	4	E916–E921.99, E928.1–E928.6
Adverse effects of medical treatment	3–4	E870–E876.9, E878–E879.9, E930–E949.9
Animal contact	3	E905–E906.99
Venomous animal contact	4	E905–E905.99
Non-venomous animal contact	4	E906–E906.99
Foreign body	3	E911–E912.09, E913.8–E915.09
Pulmonary aspiration and foreign body in airway	4	E911–E912.09, E913.8–E913.99
Foreign body in other body part	4	E914–E915.09
Environmental heat and cold exposure	3–4	E900–E902.99, E926–E926.99, E929.5
Other unintentional injuries	3–4	E903–E904.99, E913.2–E913.39, E923–E923.99, E925–E925.99, E927–E928.09, E928.8–E928.89
Self-harm and interpersonal violence	2	E950–E969
Self-harm	3–4	E950–E959
Interpersonal violence	3	E960–E969
Assault by firearm	4	E965–E965.4
Assault by sharp object	4	E966

	ICD10
	W65–W70.9, W73–W74.9
	X00–X06.9, X08–X19.9
	X46–X47, X47.1–X47.8, X48–X48.9
	W20–W38.9, W40–W43.9, W45.0–W45.2, W46–W46.2, W49–W52, W75–W75.9
	W32–W34.9
	W75–W75.9
	W20–W31.9, W35–W38.9, W40–W43.9, W45.0–W45.2, W46–W46.2, W49–W52
	Y38.9–Y84.9, Y88–Y88.3
	W52.0–W62.9, W64–W64.9, X20–X29.9
	X20–X29.9
	W52.0–W62.9, W64–W64.9
	W44–W45, W45.3–W45.9, W78–W80.9, W83–W84.9
	W78–W80.9, W83–W84.9
	W44–W45, W45.3–W45.9
	W88–W94.9, W97.9, W99–W99.9, X30–X32.9, X39–X39.9
	W39–W39.9, W77–W77.9, W81–W81.9, W85–W87.9, X50–X54.9, X57–X58.9
	X60–Y08.9, Y87.0–Y87.1
	X60–X84.9, Y87.0
	X85–Y08.9, Y87.1
	X93–X94.0, X94.3–X94.7, X94.9–X95.9, X96.5
	X99–X99.9

eTable 3. GBD cause list and associated ICD9 and ICD10 codes. (continued)

Cause	Level	ICD9
Assault by other means	4	E960–E964, E965.5–E965.9, E967–E969
Forces of nature, war, and legal intervention	2	E907–E909.9, E970–E979.9, E990–E999.1
Exposure to forces of nature	3–4	E907–E909.9
Collective violence and legal intervention	3–4	E970–E979.9, E990–E999.1
Garbage codes	-	000–000.9, 002, 031–031.9, 038–038.9, 039.6, 040.0, 041.1–041.9, 067–069, 076–078.3, 078.8–078.9, 079.8–079.99, 084, 084.6, 085, 085.1–085.9, 089–089.9, 105–119, 125–125.3, 126–126.9, 127.2–127.9, 130–132.9, 133.8–134.9, 136.3–136.5, 136.8–136.9, 139.1–139.9, 149–149.9, 159–159.9, 165–169, 176–179.9, 183.9–184, 184.5, 184.9, 187, 187.9, 189, 189.9, 194.9–199.9, 209, 209.2–209.20, 209.29–209.30, 209.6–209.60, 209.62, 209.69–210, 211, 211.9–212, 212.9, 214–216.9, 221, 221.9–222, 222.9–223, 223.9, 229, 229.1, 229.9–230.0, 230.9–231, 231.8–231.9, 233, 233.3–233.30, 233.39, 233.6, 233.9–234, 234.9–235, 235.1–235.3, 235.5, 235.9–236, 236.3, 236.6, 236.9–236.90, 237.4, 238, 238.6–239.1, 239.5, 239.7–239.9, 244, 244.9, 247–249.91, 264–264.9, 274–274.9, 276.0–276.9, 277.3–277.39, 278, 279–280.0, 280.9–281, 285–285.9, 286.6, 289.8–289.9, 293–294.0, 296–302.9, 304, 304.9–304.93, 306–307.0, 307.2–307.50, 307.52–307.53, 307.59–320, 320.9, 324–327.19, 328–329, 331.3–331.4, 338–339.89, 342–344.9, 346–348.9, 349.81–353.5, 354–355.9, 357, 357.8–357.9, 360–376, 376.10–380.9, 384–389.9, 399–401.9, 405–409.4, 415–416.0, 416.2–416.9, 418–419.9, 423.0, 426–426.9, 427.4–427.5, 427.9–429, 429.2–429.9, 436–437, 437.3, 437.9–440.9, 444–445.89, 458–458.9, 459.0, 459.5–460.9, 462–464, 464.00, 464.1–464.10, 464.20, 464.3–464.30, 464.5–464.51, 465–465.9, 482.9–483, 484, 484.8–486.9, 505–505.9, 507–507.9, 510–514.9, 515.0–515.9, 518–518.53, 518.8–518.89, 519, 519.8–529.9, 536.2–536.3, 536.8–536.9, 537.7, 537.89–537.9, 544–549, 553.8–553.9, 559–559.0, 560.4–560.7, 561, 562.2–563, 564.8–564.9, 567–569, 569.49, 569.79–569.83, 569.86–570.9, 572–572.2, 573, 573.5, 578–578.9, 584–584.9, 586–587.9, 591–591.9, 593.9, 599.7–599.72, 599.9–600.91, 603–603.9, 605–608.1, 608.3–609, 611–612.1, 615–616.9, 619–619.9, 621–621.35, 622–622.2, 622.8–628.9, 629.89–629.9, 637–637.92, 639–639.9, 690–693.9, 695.8–706.9, 708–709.9, 712–713.8, 714.4, 715–716, 716.1–728.85, 728.87, 728.89–730.09, 730.2–730.39, 730.7–731.9, 733, 733.2–739.9, 749.1–749.14, 759, 759.9, 770.0, 779.9–780.56, 780.58, 780.6–780.61, 780.64–786.02, 786.04–787.04, 787.2–787.9, 787.99–788, 788.1–790.1, 790.29, 790.4–797.9, 798.1–E80, E800.8–E800.9, E801.8–E801.9, E802.8–E802.9, E803.8–E803.9, E804.8–E804.9, E805.8–E805.9, E806.8–E806.9, E807.8–E810, E810.8–E811, E811.8–E812, E812.8–E813, E813.8–E814, E814.8–E815, E815.8–E816, E816.8–E817, E817.8–E818, E818.8–E819, E819.8–E820, E820.8–E821, E821.8–E822, E822.8–E823, E823.8–E824, E824.8–E825, E825.8–E826, E826.8–E827, E827.8–E828, E828.8–E829, E829.8–E83, E839, E85, E855–E855.99, E858–E859, E87, E877, E88, E887–E887.09, E928.9–E929.0, E929.8–E929.9, E980–E989

	ICD10
	X85–X92.9, X94.1–X94.2, X94.8, X96–X96.4, X96.6–X98.9, Y00–Y08.9, Y87.1
	X33–X38.9, Y35–Y38.893, Y89.0–Y89.1
	X33–X38.9
	Y35–Y38.893, Y89.0–Y89.1
	A01, A14.9, A29, A31–A31.9, A40–A45.9, A47–A48.0, A48.3, A48.8–A49.02, A49.2–A49.9, A59–A59.9, A61–A62, A64–A64.0, A71–A73, A74.0, A76, A97, A99–A99.0, B07–B09, B11–B14, B28–B29, B30–B32.4, B34–B46.9, B49–B49.9, B54–B55, B55.1–B55.9, B58–B59.9, B61–B62, B64, B68–B68.9, B73–B74.2, B76–B76.9, B78–B82.9, B83.9–B85.4, B87–B89, B93–B94.0, B94.8–B94.9, B95.6–B99.9, C14–C14.9, C26–C29, C35–C36, C39–C39.9, C42, C46–C46.9, C55–C55.9, C57.9, C59–C6, C63.9, C68, C68.9, C75.9–C80.9, C87, C97–D00.0, D01, D01.4–D02, D02.4–D02.9, D07, D07.3–D07.39, D07.6–D09, D09.1–D09.19, D09.7, D09.9–D10, D10.9, D13, D13.9–D14, D14.4, D17–D21.9, D28, D28.9–D29, D29.9–D30, D30.9, D36.0, D36.9–D37.0, D37.6–D38, D38.6–D39.0, D39.7, D39.9–D40, D40.9–D41, D41.9, D44, D44.9, D46–D46.9, D47.1, D48, D48.7–D49.1, D49.5, D49.7–D49.8, D49.89–D50.0, D50.9, D54, D59, D59.4, D59.8–D59.9, D62–D63.0, D63.8–D64, D64.1–D64.2, D64.8–D65.9, D68, D69.9, D75.9, D79–D85, D87–D88, D89.8–D99, E07.8–E08.9, E15, E16, E17–E19, E34.9–E35.8, E37–E39, E47–E50.9, E62, E64.1, E69, E85.3–E87.70, E87.79–E87.99, E90–E998, F04–F06.1, F06.3–F07.0, F07.2–F09.9, F17–F17.9, F30–F50, F50.8–G00, G00.9–G02.8, G03.9, G06–G09.9, G15–G19, G27–G29, G32–G34, G38–G39, G42–G44.89, G47–G47.29, G47.4–G60.9, G62–G69, G74–G89.4, G91–G93.6, G93.8–G94.8, G96–G96.9, G98–H05, H05.12–H69.93, H71–H99, I00.0, I03–I04, I10–I10.9, I14–I19, I26–I27.0, I27.2–I27.9, I28.9–I29.9, I31.2–I31.4, I44–I46.9, I49–I51, I51.6–I59, I62, I62.1–I62.9, I64–I64.9, I67, I67.4, I67.8–I68, I68.8–I69, I69.4–I70.1, I70.8–I70.92, I74–I76, I90, I92–I95.1, I95.8–I96.9, I98.4–I98.8, I99–J00.0, J02, J02.8–J03, J03.8–J04, J04.1–J04.31, J05.1–J05.10, J06–J08, J15.9, J17–J19.6, J22–J29, J48–J59, J64–J64.9, J69–J69.9, J71–J81.9, J83, J85–J90.9, J93–J94.9, J96–K19, K30, K31.9–K34, K39, K47–K49, K53–K54, K63–K63.4, K63.8–K63.9, K65–K66.1, K66.9, K69, K71–K71.2, K71.6, K71.8–K72.01, K75–K75.1, K78–K79, K84, K87–K89, K92–K92.2, K92.9–K93, K93.1–K93.8, K96–K99, L06–L07, L09, L15–L50.9, L52–L87.9, L90–L92.9, L94–L96, L98.5–L99.8, M04, M10–M12.09, M12.2–M29, M37–M39, M43.2–M49, M49.2–M64, M65.1–M71, M71.2–M73, M73.8–M79.9, M83–M86.29, M86.5–M86.9, M87.2–M87.9, M89.1–M89.49, M90–M99.9, N09, N13–N13.9, N17–N17.9, N19–N19.9, N24, N32.1–N32.2, N32.8–N33.8, N35–N35.9, N37–N38, N39.3–N40.9, N42–N43.42, N44.1–N44.8, N46–N48.9, N50–N59, N61–N64.9, N66–N69, N78–N79, N82–N82.9, N84, N84.2–N86, N88–N95.9, N97–N97.9, O08–O08.9, O17–O19, O27, O37–O39, O49–O59, O78–O79, O93–O95.9, P06, P16–P18, P23, P23.5–P23.9, P30–P34.2, P37.3–P37.4, P40–P49, P62–P69, P73, P79, P82, P85–P89, P96.9–P99.9, Q08–Q10.3, Q19, Q29, Q36.0–Q36.9, Q46–Q49, Q88, Q89.9, Q94, Q99.9–R19.6, R19.8–R50.1, R50.8–R50.81, R50.84–R72.9, R74–R78, R78.6–R94.8, R95.0–T71.161, T71.163–U03, U05–U99, V87–V87.1, V87.4–V88.1, V88.4–V89.9, V99–V99.0, W47–W48, W63, W71–W72, W76–W76.9, W82, W95–W97, W98, X07, X40–X44.9, X47.0, X47.9, X49–X49.9, X55–X56, X59–X59.9, Y09–Y34.9, Y85–Y87, Y87.2, Y89, Y89.9

eTable 4. Mean relative error (%) for age-standardized mortality rates derived from the SAE model.

Model	Population size					
	1,000	**3,000**	**5,000**	**10,000**	**25,000**	**100,000**
1	-0.63	-0.03	-0.04	0.15	0.09	0.13
2	-0.33	0.01	-0.05	0.08	-0.04	-0.02
3	-2.45	-0.85	-0.48	-0.00	0.14	0.28
4	-2.55	-0.69	-0.25	0.30	0.49	0.66
Kulkarni et al.	-	2.18	2.05	1.84	1.54	1.35
Wang et al.	-	3.28	4.31	5.79	4.39	1.86

eTable 5. Mean absolute relative error (%) for age-standardized mortality rates derived from the SAE model.

Model	Population size					
	1,000	**3,000**	**5,000**	**10,000**	**25,000**	**100,000**
1	6.53	4.71	4.00	3.23	2.50	1.83
2	7.17	4.86	4.05	3.27	2.54	1.94
3	6.73	5.22	4.75	4.28	3.99	3.77
4	6.81	5.19	4.70	4.24	3.95	3.75
Kulkarni et al.	-	5.97	5.72	5.21	4.33	2.86
Wang et al.	-	6.82	6.98	7.01	5.09	2.43

eTable 6. Coverage (%) for age-standardized mortality rates derived from the SAE model.

Model	Population size					
	1,000	**3,000**	**5,000**	**10,000**	**25,000**	**100,000**
1	95.43	95.15	94.75	95.20	95.63	96.68
2	93.58	92.00	90.29	87.56	80.72	64.08
3	86.30	81.10	76.24	67.61	52.20	30.91
4	85.96	81.53	76.91	68.22	52.53	30.99
Kulkarni et al.	-	63.37	64.02	65.30	68.26	73.31
Wang et al.	-	66.66	72.89	78.21	80.15	81.45

Chapter 6

Inequalities in life expectancy among US counties, 1980 to 2014: temporal trends and key drivers

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ABSTRACT

Importance

Examining life expectancy by county allows for tracking geographic disparities over time and assessing factors related to these disparities. This information is potentially useful for policy makers, clinicians, and researchers seeking to reduce disparities and increase longevity.

Objective

To estimate annual life tables by county from 1980 to 2014; describe trends in geographic inequalities in life expectancy and age-specific risk of death; and assess the proportion of variation in life expectancy explained by variation in socioeconomic and race/ethnicity factors, behavioral and metabolic risk factors, and health care factors.

Design, setting, and participants

Annual county-level life tables were constructed using small area estimation methods from deidentified death records from the National Center for Health Statistics (NCHS), and population counts from the US Census Bureau, NCHS, and the Human Mortality Database. Measures of geographic inequality in life expectancy and age-specific mortality risk were calculated. Principal component analysis and ordinary least squares regression were used to examine the county-level association between life expectancy and socioeconomic and race/ethnicity factors, behavioral and metabolic risk factors, and health care factors.

Exposures

County of residence.

Main outcomes and measures

Life expectancy at birth and age-specific mortality risk.

Results

Counties were combined as needed to create stable units of analysis over the period 1980 to 2014, reducing the number of areas analyzed from 3,142 to 3,110. In 2014, life expectancy at birth for both sexes combined was 79.1 (95% uncertainty interval [UI], 79.0–79.1) years overall, but differed by 20.1 (95% UI, 19.1–21.3) years between the counties with the lowest and highest life expectancy. Absolute geographic inequality in life expectancy increased between 1980 and 2014. Over the same period, absolute geographic inequality in the risk of death decreased among children and adolescents, but increased among older adults. Socioeconomic and race/ethnicity factors, behavioral and metabolic risk factors, and health care factors explained 60%, 74%, and 27% of county-level variation in life expectancy, respectively. Combined, these factors explained 74% of this variation. Most of the associa-

tion between socioeconomic and race/ethnicity factors and life expectancy was mediated through behavioral and metabolic risk factors.

Conclusions and relevance

Geographic disparities in life expectancy among US counties are large and increasing. Much of the variation in life expectancy among counties can be explained by a combination of socioeconomic and race/ethnicity factors, behavioral and metabolic risk factors, and health care factors. Policy action targeting socioeconomic factors and behavioral and metabolic risk factors may help reverse the trend of increasing disparities in life expectancy in the United States.

INTRODUCTION

Studies have routinely shown that life expectancy in the United States varies geographically, in some cases dramatically.[1–3] Counties are the smallest administrative unit routinely available in death registration data and represent an opportunity to explore the extent of geographic inequalities in the United States. In particular, tracking inequality at the county level over time is an important means of assessing progress toward the goal of more equitable health outcomes, as enshrined in the Healthy People 2020 objective: "Achieve health equity, eliminate disparities, and improve the health of all groups."[4] Moreover, county-level information on basic health outcomes is essential for appropriately targeting resources and designing and implementing health and social welfare policy at both the federal and state level.

Previous analyses of life expectancy at the county level have found large[2,5] and increasing[3] geographic disparities. However, these analyses either excluded or combined a large number of smaller counties, likely leading to an underestimation of geographic inequality. Moreover, recent research has highlighted the need to consider age-specific metrics of survival in addition to life expectancy overall. Case and Deaton[6] identified differential trends in mortality rates among age groups, with middle age mortality rates stagnating or even increasing for certain populations, while mortality rates among older individuals continued to decline. Similarly, Currie and Schwandt[7] identified differential trends in income-based inequalities by age, with inequalities generally declining among children and adolescents and increasing for older ages. To our knowledge, age-specific trends in geographic inequalities have not been previously described at the county level in the United States.

Beyond describing geographic variation in life expectancy, exploring what factors explain this variation might provide import insights into how to reduce inequalities and achieve more equitable health outcomes. Several previous analyses[5,8,9] have used local data on all-cause mortality to explore this question and have identified a large number of socioeconomic and race/ethnicity factors, behavioral and metabolic risk factors, and health care factors that are correlated with survival. However, these analyses have not systematically explored the extent to which county-level variation in life expectancy can be explained by the larger social and economic context of a county, the behavioral and metabolic risk profile of county residents, or the availability and quality of health care.

This analysis has 3 specific aims. First, to generate annual estimates of life expectancy and age-specific mortality risk for each county from 1980 to 2014. Second, to quantify geographic inequalities in life expectancy and age-specific mortality risks and to examine trends in geographic inequality over time. Third, to assess the extent to which variation in life expectancy is

explained by variation in socioeconomic and race/ethnicity factors, behavioral and metabolic risk factors, and health care access and quality.

METHODS

Small area models for estimating life expectancy and age-specific mortality risks

Unit of analysis

All analyses were carried out at the county level. Counties were combined as needed to create stable units of analysis over the period 1980 to 2014, reducing the number of areas analyzed from 3,142 to 3,110 (eTable 1 in the Supplement). For simplicity, these units are referred to as "counties" throughout.

Data

Deidentified death records from the National Center for Health Statistics (NCHS)[10] and population counts from the census bureau,[11] NCHS,[12–14] and the Human Mortality Database[15] were used in this analysis. Deaths and population were tabulated by county, age group (0, 1–4, 5–9, …, 80–84, and ≥85), sex, and year. County-level information on levels of education, income, race/ethnicity, Native American reservations, and population density derived from data provided by the census bureau and NCHS was also incorporated (eTable 2 in the Supplement).

Small area model

Previously described and validated Bayesian small area models for estimating age-specific mortality rates by county were used in this analysis.[16] These models incorporated 7 covariates (the proportion of the adult population who graduated high school; the proportion of the population that is Hispanic; the proportion of the population that is black; the proportion of the population that is a race other than black or white; the proportion of a county that is contained within a state or federal Native American reservation; the median household income; and the population density) and smooth mortality rates over space, time, and age to produce more stable estimates of the mortality rate in each county, year, and age group. Models were fit using the Template Model Builder Package[17] in R version 3.2.4 (R Foundation).[18] County-level estimates were scaled to ensure consistency with existing national-level estimates from the Global Burden of Disease study.[19]

Life table construction and metrics

The method described by Wang et al[20] was used to extrapolate mortality rates to older ages (5-year age groups up to age 110 years). Standard demographic methods were used to

construct period life tables for each county and year from the age-specific mortality rates estimated by the small area model.[21] Life expectancy at birth (e_0) and the probability of death for 5 age groups—0 to 5 ($_5q_0$); 5 to 25 ($_{20}q_5$), 25 to 45 ($_{20}q_{25}$), 45 to 65 ($_{20}q_{45}$), and 65 to 85 ($_{20}q_{65}$)—were extracted from these life tables.

For each measure, absolute geographic inequality was quantified as the difference between the 99th and 1st percentile level, and relative geographic inequality was quantified as the ratio of the 99th to 1st percentile level. The corresponding measures using the 90th and 10th percentile were calculated as well.

Analysis of county-level variation in life expectancy

Data

A cross-sectional data set was constructed of variables correlated with life expectancy at the county level. To maximize the number of variables included, 2009, the year with the best data coverage, was used. Three groups of variables were considered. For the first group, variables related to the broader social, economic, and demographic context of a county were identified. Specifically: the poverty rate, median household income, proportion of the adult population who graduated high school, proportion of the adult population who graduated college, the unemployment rate, proportion of the population that are black, proportion of the population that are native American, and proportion of the population that are Hispanic. For the second group, behavioral and metabolic risk factors with high attributable burden in the United States[22] for which reliable estimates were available at the county level were identified. The prevalence of obesity, leisure–time physical inactivity, cigarette smoking, hypertension, and diabetes were included. For the third group, variables related to access to health care and health care quality were identified. Three variables were ultimately included: the percentage of the population younger than 65 years who are insured, a quality index that is a composite of variables related to primary care access and quality based on Medicare data analyzed by the Dartmouth Atlas project,[23] and the number of physicians per capita. eTable 3 in the Supplement provides details about the data sources for each of these variables.

Regression models

A series of bivariate ordinary least squares regression models were fitted with life expectancy at birth in 2009 as the dependent variable and each of the variables listed above as independent variables to assess the independent relationship between each of these variables and life expectancy.

Many of the variables considered were highly correlated (eFigure 1 in the Supplement), making multivariate models including all of these factors challenging to interpret due to collinearity. Therefore, a principal component analysis[24] was conducted on each group

of variables and the first principal component from each (rescaled to run from 0 to 1) was used as a composite index representing the socioeconomic and race/ethnicity, behavioral and metabolic risk, and health care characteristics, respectively, of each county. A series of ordinary least squares regression models were fitted with life expectancy at birth as the dependent variable and each of these indices separately, and then in combination, as the independent variable(s). For all models, the estimated model coefficients and the adjusted and unadjusted R^2 were extracted. As a sensitivity analysis, the full multivariate regression models using all of the factors separately were also fitted.

RESULTS

Inequalities in life expectancy and age-specific mortality risk

There was considerable variation in mortality risk and life expectancy at the county level in all years. In 2014, life expectancy at birth for both sexes combined at the national level was 79.1 (95% uncertainty interval [UI], 79.0–79.1) years (76.7 [95% UI, 76.7–76.8] years for men,

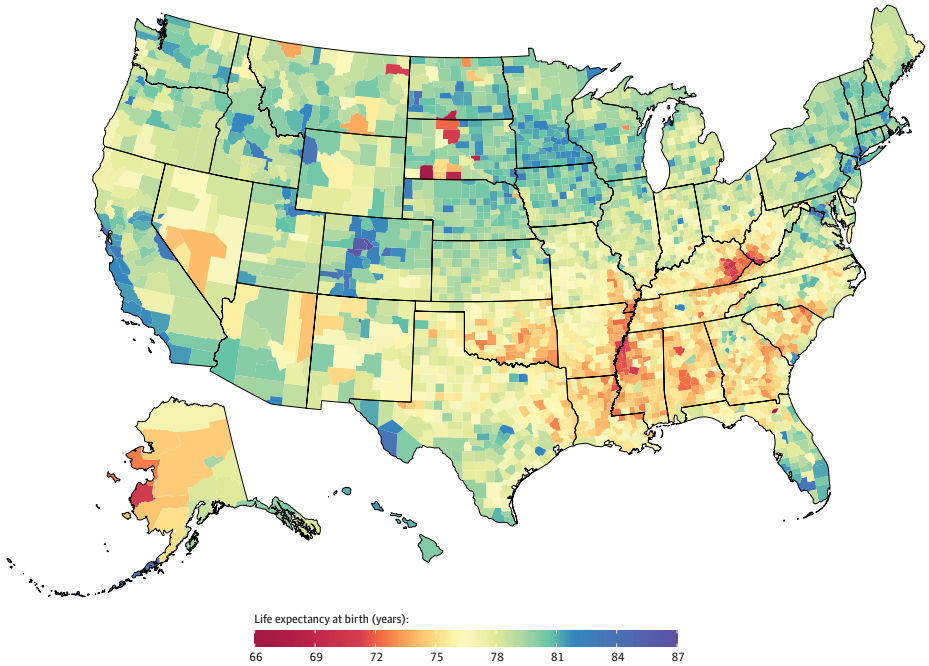

Figure 1. Life expectancy at birth by county, 2014.
Counties in South Dakota and North Dakota had the lowest life expectancy, and counties along the lower half of the Mississippi, in eastern Kentucky, and southwestern West Virginia also had very low life expectancy compared with the rest of the country. Counties in central Colorado had the highest life expectancies.

and 81.5 [95% UI, 81.4–81.5] years for women), but there was a 6.2-year gap (95% UI, 6.1–6.2) between the 10th and 90th percentile, a 10.7-year gap (95% UI, 10.5–11.0) between the 1st and 99th percentile, and a 20.1-year gap (95% UI, 19.1–21.3) between the lowest and highest life expectancy among all counties. Several counties in South and North Dakota (typically those with Native American reservations) had the lowest life expectancy, and counties along the lower half of the Mississippi and in eastern Kentucky and southwestern West Virginia also had very low life expectancy compared with the rest of the country. In contrast, counties in central Colorado had the highest life expectancies (Figure 1). Geographical patterns in mortality risk for each age group were similar, but not identical (eFigures 2–6 in the Supplement). Results by sex and for all counties and years are available in an online visualization tool.

Between 1980 and 2014, life expectancy at birth for both sexes combined in the United States increased by 5.3 (95% UI, 5.3–5.4) years, from 73.8 (95% UI, 73.7–73.8) to 79.1 (95% UI, 79.0–79.1) years (6.7 [95% UI, 6.7–6.8] years, from 70.0 [95% UI, 70.0–70.0] to 76.7 [95% UI, 76.7–76.8] for men; 3.9 [95% UI, 3.9–4.0] years, from 77.5 [95% UI, 77.5–77.6] to 81.5 [95% UI, 81.4–81.5] for women). This masks massive variation at the county level; counties

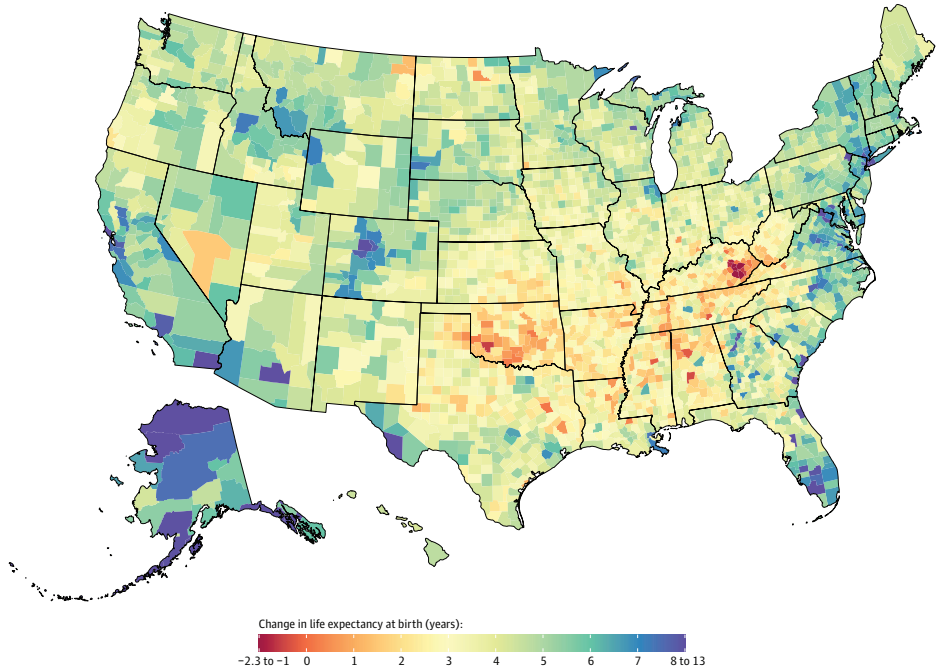

Figure 2. Change in life expectancy at birth by county, 1980 to 2014.
Compared with the national average, counties in central Colorado, Alaska, and along both coasts experienced larger increases in life expectancy between 1980 and 2014, while some southern counties in states stretching from Oklahoma to West Virginia saw little, if any, improvement over this same period.

in central Colorado, Alaska, and along both coasts experienced much larger increases, while some southern counties in states stretching from Oklahoma to West Virginia saw little, if any, improvement over this same period (Figure 2). Similarly, there was considerable variation among counties in the percent decline in the mortality risk within each age group (eFigure 7 in the Supplement). While all counties experienced declines in mortality risk for children (ages 0 to 5 years) and nearly all counties (>98%) experienced declines in the mortality risk for adolescents (ages 5 to 25 years) and older adults (ages 45 to 65 and 65 to 85 years), a significant minority of counties (11.5%) experienced increases in the risk of death between ages 25 and 45 years.

Absolute geographic inequality in life expectancy at birth increased between 1980 and 2014, with the gap between the 1st and 99th percentile increasing by 2.4 (95% UI, 2.1–2.7) years (Figure 3). However, for mortality risks, this pattern varied by age: the difference between the 1st and 99th among counties declined by 42.9% (95% UI, 40.4%–45.1%) among children (ages 0 to 5 years), by 18.9% (95% UI, 15.2%–22.7%) for adolescents (ages 5 to 25 years), and increased by 10.1% (95% UI, 6.4%–14.1%), 15.0% (95% UI, 11.6%–18.4%), and 48.2% (95% UI,

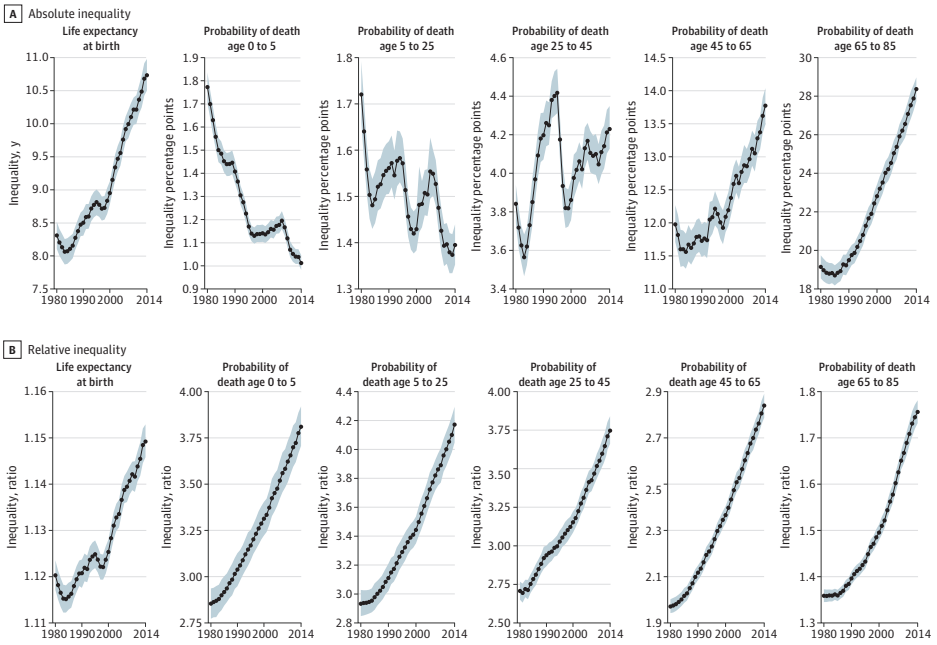

Figure 3. Absolute and relative inequality among counties in life expectancy and age-specific mortality risks, 1980–2014.

Shaded areas along the plotted data represent 95% uncertainty intervals. Absolute geographic inequality was quantified as the difference between the 99th and first percentile level, and relative geographic inequality was quantified as the ratio of the 99th to the first percentile level.

Table 1. Variables included in the regression analysis with summary statistics and bivariate regression results.

Variable	Summary statistics, mean (SD) [range]	Bivariate regression results	
		Coefficient (SE)	R^2
Socioeconomic and race/ethnicity factors			
Population below the poverty line, %	16.3 (6.4) [3.1–62.0]	-0.24 (0.005)	0.47
Median household income, log $	10.6 (0.2) [9.8–11.6]	6.06 (0.130)	0.41
Graduates, age ≥25 y, %			
High school	83.7 (7.2) [46.3–98.6]	0.20 (0.004)	0.42
College	19.2 (8.6) [4.2–72.0]	0.15 (0.004)	0.34
Unemployment rate, age ≥16 y, %	9.1 (3.2) [2.1–27.4]	-0.29 (0.011)	0.18
Black population, %	9.4 (14.7) [0.0–85.8]	-0.07 (0.002)	0.24
American Indian, Native Alaskan, and Native Hawaiian population, %	2.3 (7.9) [0.0–97.2]	-0.06 (0.005)	0.04
Hispanic population, %	8.1 (13.1) [0.0–95.9]	0.02 (0.003)	0.01
Behavioral and metabolic risk factors, %			
Obesity prevalence, age ≥20 y	37.0 (4.3) [18.0–52.0]	-0.39 (0.006)	0.54
No leisure-time physical activity prevalence, age ≥20 y	27.0 (5.2) [11.7–47.2]	-0.34 (0.005)	0.62
Cigarette smoking prevalence, age ≥18 y	24.7 (4.1) [7.7–42.1]	-0.40 (0.007)	0.54
Hypertension prevalence, age ≥30 y	39.5 (3.6) [27.9–56.4]	-0.49 (0.007)	0.62
Diabetes prevalence, age ≥20 y	14.0 (2.4) [8.1–25.5]	-0.72 (0.011)	0.59
Health care factors			
Insured population, age <65 y, %	81.7 (5.7) [57.3–96.7]	0.15 (0.007)	0.14
Quality index	70.1 (11.5) [0.0–100.0]	0.10 (0.003)	0.28
Physicians per 1,000 population, No.	1.1 (1.0) [0.0–4.4]	0.53 (0.039)	0.06

Abbreviations: SE, standard error.

42.7%–53.7%) for age groups 25 to 45 years, 45 to 65 years, and 65 to 85 years, respectively. Relative inequality rose for all age groups, likely due to the overall decrease in mortality risk over this period. Similar trends were observed when comparing the 10th and 90th percentiles (eFigure 8 in the Supplement).

Factors related to variation in life expectancy

Table 1 provides summary statistics for each of the variables included in the analysis of factors related to variation in life expectancy as well as the bivariate regression results. Statistically significant relationships with life expectancy were found for each variable. Detailed results of the principal component analysis are given in eTables 4 through 6 and eFigure 9 in the Supplement. The first principal component explained 42%, 79%, and 56% of the total variation in

Table 2. Multivariate regression results.

Variable	Model 1[a]	Model 2[a]	Model 3[a]	Model 4[a]
Intercept, coefficient (SE)	70.60 (0.10)[b]	70.40 (0.08)[b]	73.21 (0.13)[b]	70.07 (0.09)[b]
Socioeconomic and race/ethnicity factors, coefficient (SE)	13.13 (0.19)[b]	NA	NA	-0.10 (0.37)
Behavioral and metabolic risk factors, coefficient (SE)	NA	13.73 (0.15)[b]	NA	13.04 (0.33)[b]
Health care factors, coefficient (SE)	NA	NA	7.88 (0.23)[b]	1.37 (0.17)[b]
R^2	0.60	0.74	0.27	0.74
Adjusted R^2	0.60	0.74	0.27	0.74

Abbreviations: NA, not applicable or no data available; SE, standard error.
[a]Model 1 includes adjustments for socioeconomic and race/ethnicity factors (ie, poverty; income; education level; unemployment; black population; American Indian, Native Alaskan, and Native Hawaiian population; and Hispanic population); Model 2, behavioral and metabolic risk factors (ie, obesity, inactivity, smoking status, hypertension, and diabetes); Model 3, health care factors (ie, insurance, quality index, number of physicians per 1,000 people); and Model 4, combined (ie, all factors from all models).
[b]$P < .05$.

socioeconomic and race/ethnicity factors, behavioral and metabolic risk factors, and health care factors, respectively. Table 2 lists the regression results based on these three indices. Socioeconomic and race/ethnicity factors, behavioral and metabolic risk factors, and health care factors, when considered independently, explained 60%, 74%, and 27%, respectively, of the county-level variation in life expectancy. In combination, these 3 factors explained 74% of the variation. The effect size for the behavioral and metabolic risk factors index is similar in the combined model (Model 4) as in the model with just risk factors as a predictor (Model 2). In contrast, the effect size for socioeconomic and race/ethnicity factors is much reduced in the combined model (Model 4) compared with the model with just socioeconomic and race/ethnicity factors (Model 1), and is no longer statistically significant. The effect size for health care factors is also reduced in the combined model (Model 4) compared with the model with just health care factors (Model 3), but the effect is still statistically significant.

The corresponding results from the regressions using all variables separately are presented in eTable 7 in the Supplement. The overall amount of variation explained by each group of factors, both separately and in combination, is somewhat higher, but with the same ordering among the different groups of factors: 69% for socioeconomic and race/ethnicity factors, 77% for behavioral and metabolic risk factors, 31% for health care factors, and 82% for all factors combined.

DISCUSSION

This study found large—and increasing—geographic disparities among counties in life expectancy over the past 35 years. The magnitude of these disparities demands action, all the more urgently because inequalities will only increase further if recent trends are allowed to continue uncontested.

The finding that county-level geographic inequalities in life expectancy are large and increasing is consistent with earlier studies. Kulkarni et al[2] reported a 15.2-year and 12.5-year gap between counties with the lowest and highest life expectancy in 2007 for men and women, respectively, while Wang et al[3] reported a 17.8-year and 12.3-year gap in 2010 for men and women, respectively. This study estimates noticeably larger disparities: in recent years, the gap in life expectancy among counties for both sexes combined was more than 20 years. The smaller estimates in Kulkarni et al[2] and Wang et al[3] are likely due to their aggregation of smaller counties into larger merged county units (they analyze 2,356 units compared with 3,110 in this study). Chetty et al[5] also estimated county-level life expectancy for a subset of counties, with a focus on how life expectancy varies among counties for low-income compared with high-income individuals. As in this analysis, they found substantial variation in life expectancy among counties. There are several important differences in their estimation strategy as compared with the one used in this study, however. In particular, to estimate life expectancy by income level, they use death records from the social security administration rather than from NCHS. This restricts their analysis to individuals aged 40 to 76 years who reported at least some income, and introduces some uncertainty in the county of residence for decedents who relocated after reaching retirement age (62 years). Likely as a consequence of the differences in the underlying data, as well as differences in analysis methods, the correlation between the estimates from Chetty et al[5] and this analysis was lower than might be expected: between 0.38 and 0.65, depending on sex and income quartile.

This study expanded upon earlier analyses of county-level variation in longevity by examining mortality risk by age in addition to life expectancy. There were substantial geographic inequalities in the risk of death in each age group considered; however, the trajectory of inequalities over time differed by age: absolute geographic inequalities in the risk of death declined over the study period for children and adolescents, and increased for adults, especially those aged 65 to 85 years. This is broadly consistent with recent findings by Currie and Schwandt[7] who analyzed age-specific mortality rates among counties grouped by income and found that inequality among income groups decreased for children and adolescents and increased for older adults from 1990 to 2010. Further research should focus on the drivers of these divergent trends. It seems likely that increases in geographic inequality in life expectancy over the past 3 decades have been driven largely by increases in geographic inequality

in the risk of death in older ages. Consequently, these age groups are an especially important target for further research and intervention.

A large body of previous research documents a relationship between socioeconomic and race/ethnicity factors and various measures of survival.[25–28] Consistent with this research, this study found that socioeconomic and race/ethnicity factors alone explained 60% of the variation in life expectancy. At the same time, 74% of the variation was explained by behavioral and metabolic risk factors alone, while only marginally more variation was explained by socioeconomic and race/ethnicity factors, behavioral and metabolic risk factors, and health care factors combined. Furthermore, there was very little additional effect of socioeconomic and race/ethnicity factors when accounting for all 3 sets of factors simultaneously, suggesting that the association between life expectancy and socioeconomic and race/ethnicity factors at the county level is largely mediated through behavioral and metabolic risk factors.

Previous studies[8,9] examining the relationship between socioeconomic and race/ethnicity factors, behavioral and metabolic risk factors, and/or health care factors and some measure of survival at a substate level in the United States are not directly analogous because they use different measures of survival, different explanatory factors, and more aggregated geographic units or a subset of larger counties, but certain findings can still be compared. Cullen et al[8] examined the relationship between 22 socioeconomic and environmental variables and the sex-specific and race-specific probability of survival to age 70 years in 510 groups of counties. Consistent with the results of this study, they found that a large proportion of the variation in survival among counties could be explained by these variables (72%–86%, depending on the sex and race). Furthermore, in a small subset of larger counties, they found that additionally considering 8 risk and health care factors increased the amount of variation explained to 86% to 90%. Davids and Jones[9] assessed the relationship between county-level life expectancy and a small set of socioeconomic and race factors (poverty, no high school diploma, black race) and metabolic risk factors (diabetes and hypertension prevalence). As in this study, Davids and Jones[9] found an inverse relationship between life expectancy and markers of low socioeconomic status and metabolic risk factors. Their findings differ from ours, however, in that the effect of the socioeconomic and race factors was only slightly attenuated when considering risk factors concurrently, although this may be due to the much smaller number of factors considered.

The findings on factors related to variation in life expectancy have important policy implications. In particular, policies and programs that target behavioral and metabolic risk factors have the potential to improve health in all locations but especially those that are currently most at a disadvantage, consequently reducing geographic disparities. This is not to say that policies that target socioeconomic drivers of disparities would not also be effective, but

rather that there are multiple potential routes to more equitable health outcomes for federal, state, and local policy makers to consider. Furthermore, researchers now recognize that the relationship between socioeconomic status and health likely reflects causal pathways running in both directions (ie, from better health to higher socioeconomic status as well as from higher socioeconomic status to better health).[29] Thus, policies that target inequalities in health may also in the long run be effective mechanisms for addressing inequalities in socioeconomic status as well.

This study has a number of strengths. First, this analysis used recently developed and validated small area models that have been shown to generate more precise estimates than previous methodologies.[16] Second, this study did not exclude small counties or aggregate them beyond what was necessary to address historical boundary changes, allowing for a more complete accounting of geographic inequalities at the county level than previously available. Third, in addition to life expectancy, this study considered geographic inequalities in age-specific mortality risks that have not been previously explored. Fourth, this study is the first to systematically consider to what extent geographic inequalities in life expectancy at the county level can be explained by socioeconomic and race/ethnicity factors, behavioral and metabolic risk factors, and health care factors, both independently and in combination.

Limitations

This analysis also has a number of limitations. The deaths, population, and covariates data used as the basis for estimating life expectancy by county are all subject to error. The small area models are designed to smooth across counties, years, and age groups and may in some cases over-smooth, resulting in an underestimation of geographic inequalities. This study documented increasing geographic inequality in life expectancy among counties but did not assess the extent to which these trends are a reflection of increasing inequality among individuals as opposed to changes in the geographic distribution of low-risk and high-risk individuals as a result of differential migration (eg, increasing segregation of low and high risk populations).[30] In the regression analysis of factors related to county-level variation in life expectancy, the outcome variable (life expectancy) as well as the socioeconomic and race/ethnicity variables, behavioral and metabolic risk variables, and health care variables, are subject to measurement error. Moreover, all of the risk factor variables are themselves based on models that incorporated some socioeconomic factors as covariates, which may induce additional correlation between risk and socioeconomic factors in the regression analysis—this is unlikely to have a substantial effect however, because the relationship between risk factors and socioeconomic factors in the risk factor small area models is not imposed, but rather estimated from the data. A relatively small number of variables were used to represent the overall socioeconomic and race/ethnicity, behavioral and metabolic risk, and health care characteristics of a county, and consequently have likely not captured all relevant factors

within each of these groups. There are also likely factors outside of these 3 categories that are related to geographic inequality but that were not considered in this analysis. The regression analysis is cross-sectional and can be used to draw conclusions about associations but not whether these associations are causal. Similarly, it cannot be used to assess the extent to which increasing geographic inequality in life expectancy among counties is due to change in the factors considered in the regression analysis. Furthermore, if socioeconomic and race/ethnicity factors, behavioral and metabolic risk factors, and health care factors are causally related to life expectancy, this effect almost certainly plays out over the life course. However, the regression analysis only incorporates contemporaneous information about life expectancy, and these other factors and a county's current status in terms of socioeconomic and race/ethnicity, behavioral and metabolic risk, and health care factors may not perfectly represent the lifetime experience of individuals currently living and dying in that county.

CONCLUSIONS

Geographic disparities in life expectancy among counties are large and increasing. Much of the variation in life expectancy among counties can be explained by a combination of socioeconomic and race/ethnicity factors, behavioral and metabolic risk factors, and health care factors. Policy action targeting socioeconomic factors and behavioral and metabolic risk factors may help reverse the trend of increasing disparities in life expectancy in the United States.

ARTICLE INFORMATION

Author contributions

Dr Murray had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Dwyer-Lindgren, Bertozzi-Villa, Mokdad, Murray. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Dwyer-Lindgren, van Lenthe. Critical revision of the manuscript for important intellectual content: Bertozzi-Villa, Stubbs, Morozoff, Mackenbach, van Lenthe, Mokdad, Murray. Statistical analysis: Dwyer-Lindgren, Bertozzi-Villa, Stubbs, van Lenthe. Obtained funding: Mokdad, Murray. Administrative, technical, or material support: Morozoff, Mokdad, Murray. Study supervision: Mackenbach, van Lenthe, Mokdad, Murray.

Conflict of interest disclosures

None reported.

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Role of the funder/sponsor

The funders/sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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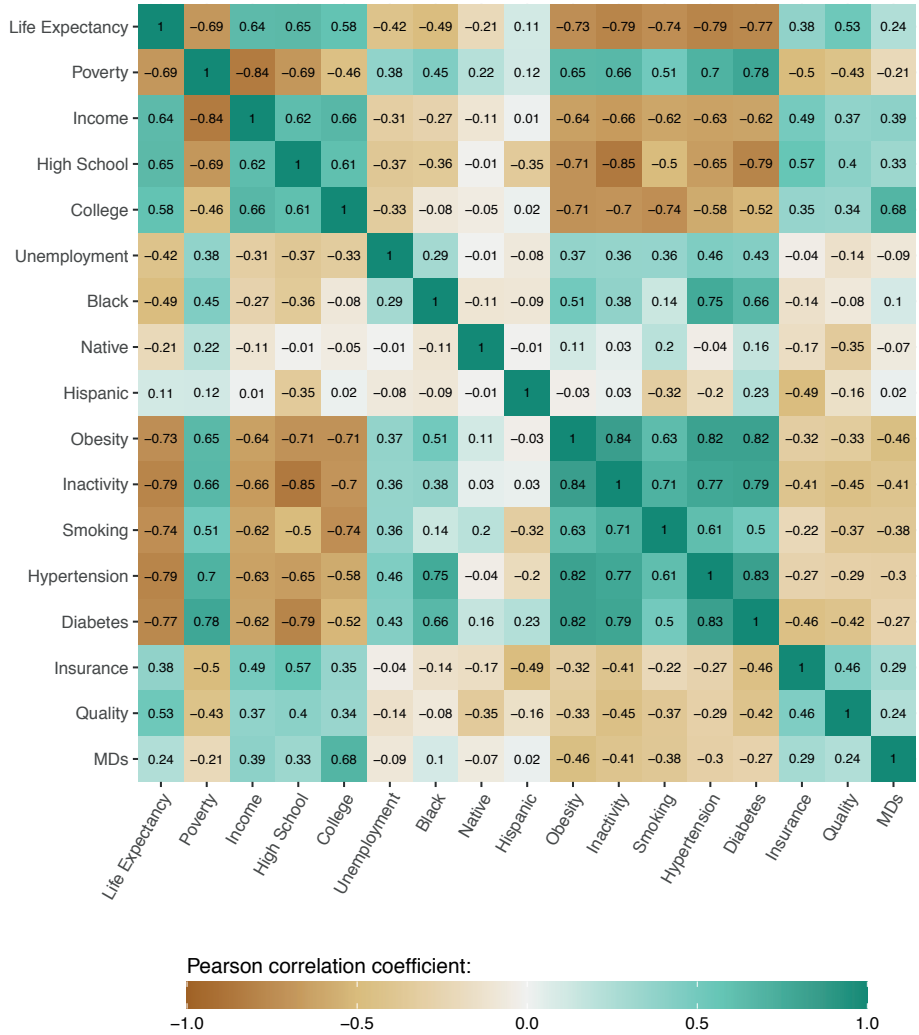
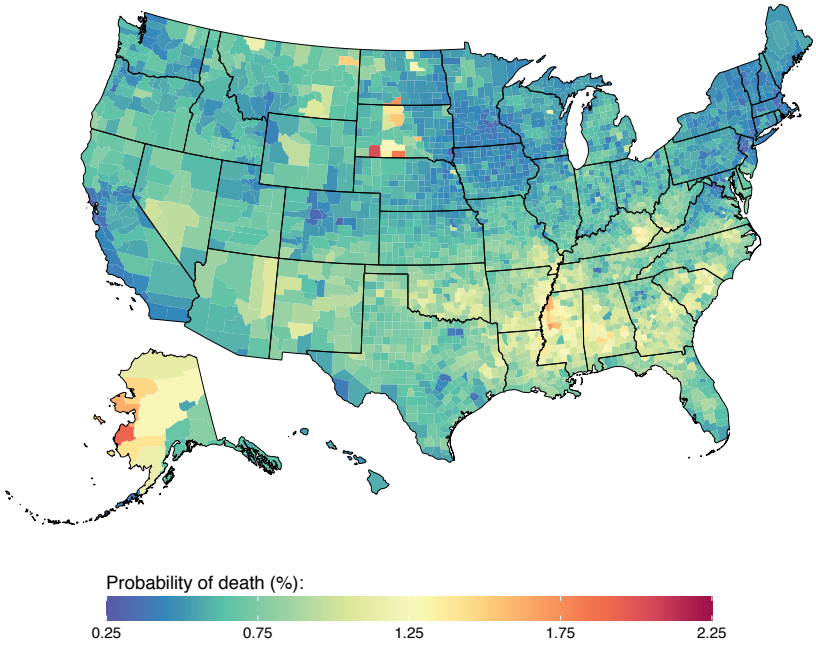
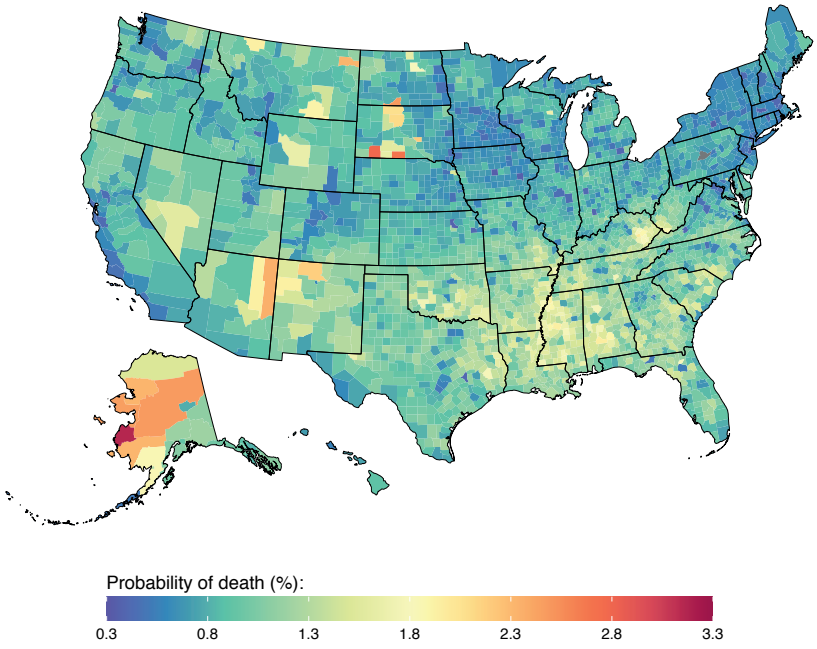
SUPPLEMENT



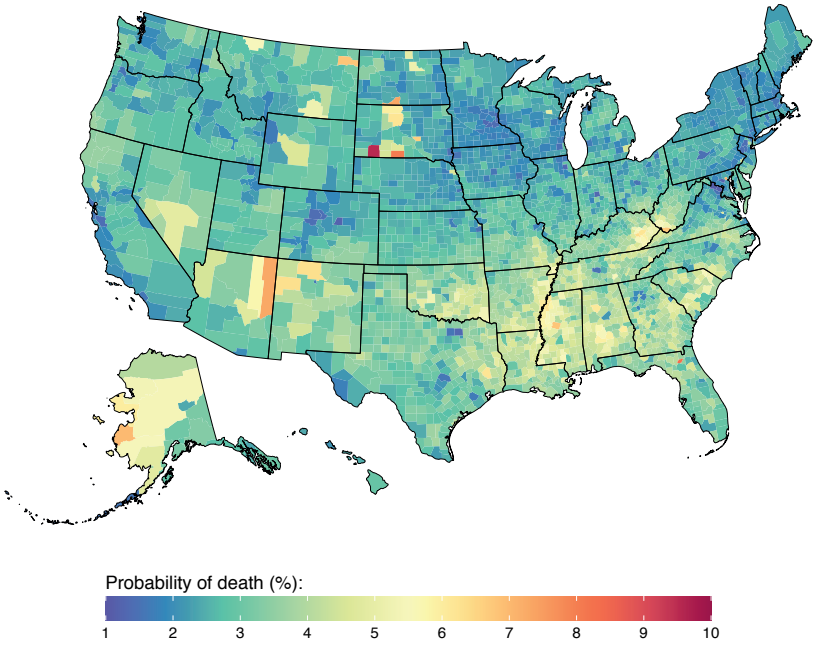
eFigure 1. Correlation matrix for variables included in the regression analysis of variation in life expectancy.



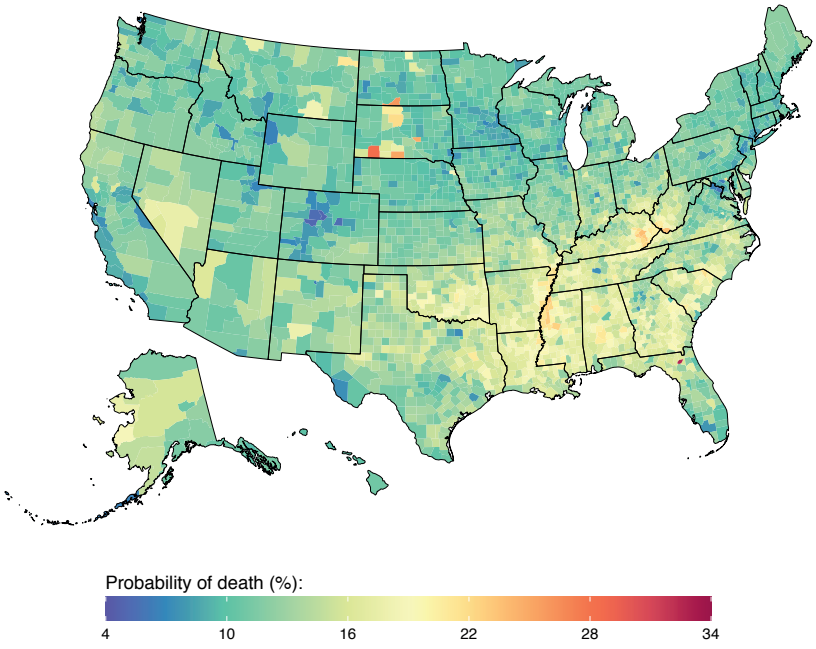
eFigure 2. Probability of death between age 0 and 5 ($_5q_0$) by county, 2014.



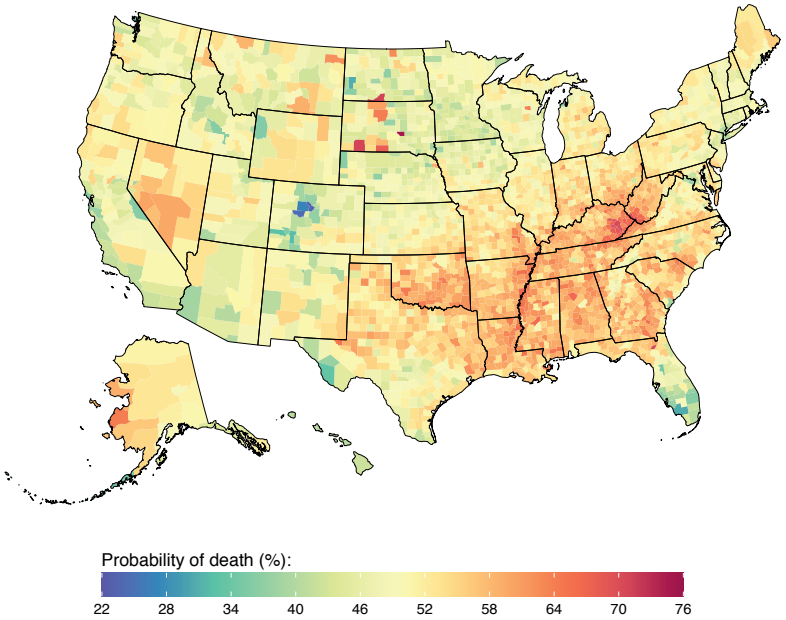
eFigure 3. Probability of death between age 5 and 25 ($_{20}q_5$) by county, 2014.



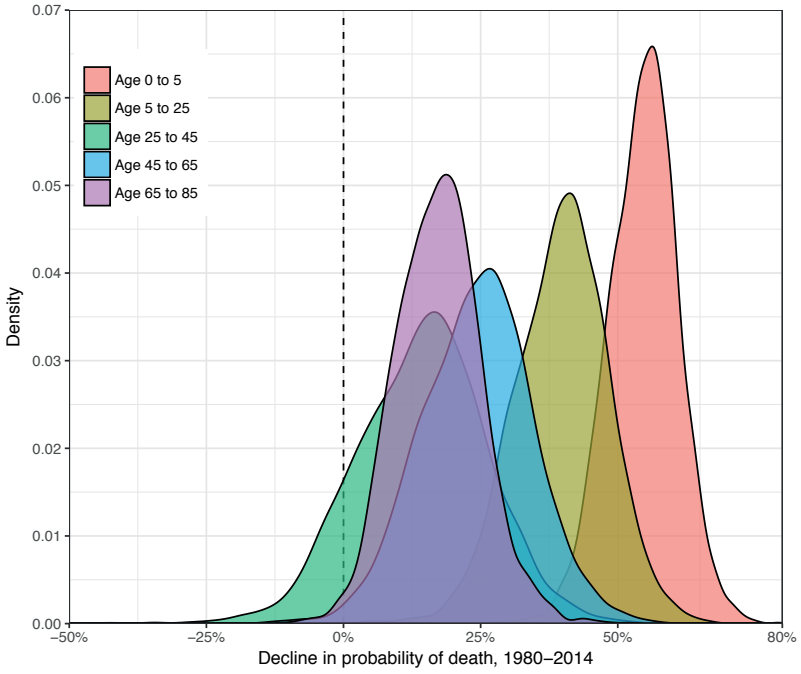
eFigure 4. Probability of death between age 25 and 45 ($_{20}q_{25}$) by county, 2014.



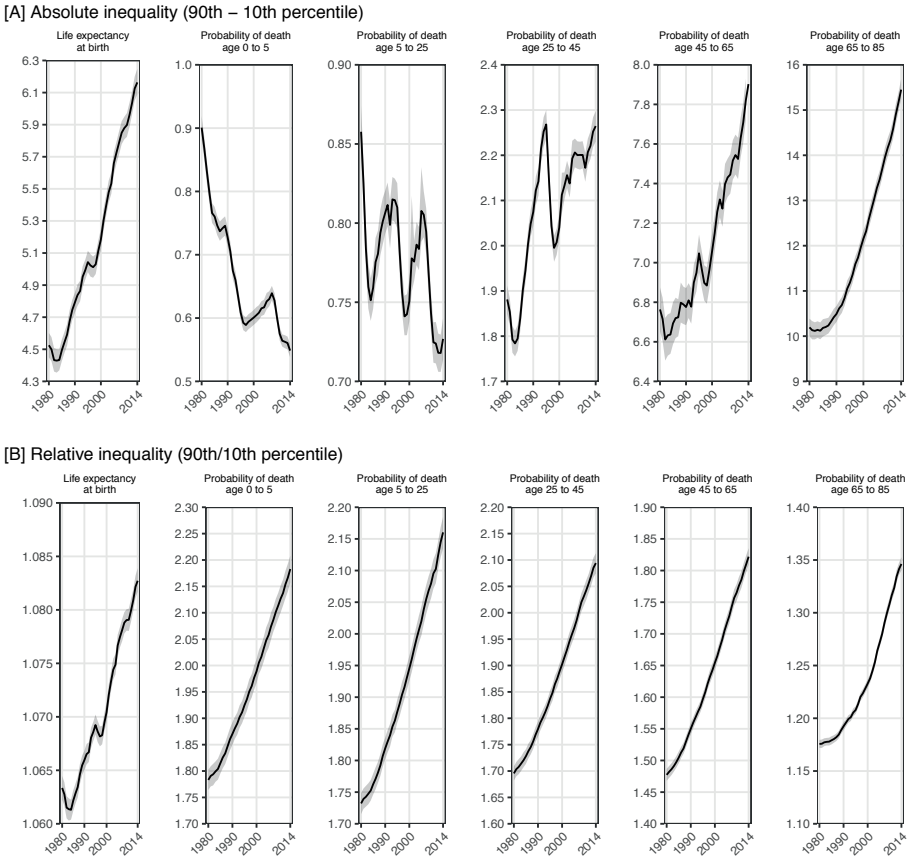
eFigure 5. Probability of death between age 45 and 65 ($_{20}q_{45}$) by county, 2014.



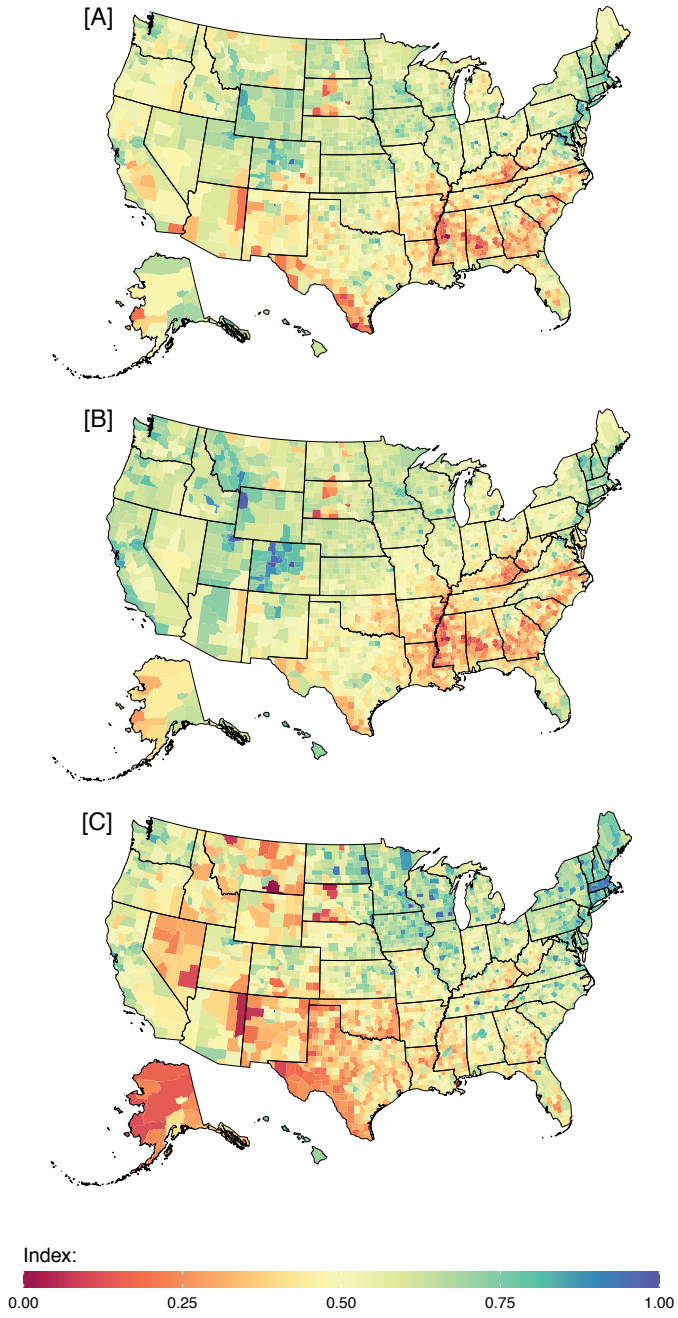
eFigure 6. Probability of death between age 65 and 85 ($_{20}q_{65}$) by county, 2014.



eFigure 7. Distribution of county-level declines in age-specific mortality risks, 1980–2014. Density plot (smoothed histogram) of the percent decline in age-specific mortality risks between 1980 and 2014 for 3,110 counties. Colors indicate age group, as described in the plot key.



eFigure 8. Absolute and relative inequality among counties in life expectancy and age-specific mortality risks, 1980–2014.



eFigure 9. Index of socioeconomic and race/ethnicity factors, behavioral and metabolic risk factors, and health care factors by county, 2009.
A, Socioeconomic and race/ethnicity factors index. B, Behavioral and metabolic risk factors index. C, Health care factors index.

eTable 1. Counties combined to ensure historically stable units of analysis.

State	Group	Areas
Alaska	1	Kusilvak Census Area (2158), Wade Hampton Census Area (2270)[a]
	2	Kobuk Census Area (2140),[a] Northwest Arctic Borough (2188)
	3	Aleutian Islands Census Area (2010),[a] Aleutians East Borough (2013), Aleutians West Census Area (2016)
	4	Dillingham Census Area (2070), Lake and Peninsula Borough (2164)
	5	Denali Borough (2068), Yukon-Koyukuk Census Area (2290)
	6	Hoonah-Angoon Census Area (2105), Skagway Municipality (2230), Skagway-Yakutat-Angoon Census Area (2231),[a] Skagway-Hoonah-Angoon Census Area (2232),[a] Yakutat City and Borough (2282)
	7	Ketchikan Gateway Borough (2130), Petersburg Borough (2195), Prince of Wales-Hyder Census Area (2198), Prince of Wales-Outer Ketchikan Census Area (2201),[a] Wrangell City and Borough (2275), Wrangell-Petersburg Census Area (2280)[a]
Arizona	1	La Paz County (4012), Yuma County (4027)
Colorado	1	Adams County (8001), Arapahoe County (8005), Boulder County (8013), Broomfield County (8014), Denver County (8031), Jefferson County (8059), Weld County (8123)
Florida	1	Dade County (12025),[a] Miami-Dade County (12086)
Hawaii	1	Kalawao County (15005), Maui County (15009)
Maryland	1	Montgomery County (24031), Prince George's County (24033)
Montana	1	Park County (30067), Yellowstone National Park (30113)[a]
New Mexico	1	Cibola County (35006), Valencia County (35061)
South Dakota	1	Oglala Lakota County (46102), Shannon County (46113)[a]
	2	Jackson County (46071), Washabaugh County (46131)[a]
Virginia	1	Fairfax County (51059), Fairfax City (51600)
	2	Rockingham County (51165), Harrisonburg City (51660)
	3	James City County (51095), Williamsburg City (51830)
	4	Prince William County (51153), Manassas City (51683), Manassas Park City (51685)
	5	Rockbridge County (51163), Buena Vista City (51530)
	6	Spotsylvania County (51177), Fredericksburg City (51630)
	7	Augusta County (51015), Staunton City (51790), Waynesboro City (51820)
	8	Pittsylvania County (51143), Danville City (51590)
	9	Greensville County (51081), Emporia City (51595)
	10	Albemarle County (51003), Charlottesville City (51540)
	11	Bedford County (51019), Bedford City (51515)[a]
	12	Halifax County (51083), South Boston City (51780)[a]
	13	Southampton County (51175), Franklin City (51620)
	14	Alleghany County (51005), Clifton Forge City (51560)[a]
	15	York County (51199), Newport News City (51700)

[a]County no longer exists due to boundary or name change.

eTable 2. Data sources used for covariates in the small area models.

Variable	Data sources	Data processing
Percent of the population age 25 and older who have completed high school	1980 census;[a] 1990 census;[b] 2000 census;[c] 2009–2014 ACS[d]	Linear interpolation was used fill in intermediate years between data sources. The rate of change calculated between 2007 and 2012 was applied to fill in estimates for 2013 and 2014.
Percent of the population who are Hispanic	1980 census;[e] 1990–2014 NCHS Bridged Race Files[f,g,h]	Linear interpolation was used to fill in intermediate years between data sources.
Percent of the population who are Black and some other race	1980–1989 Census Bureau Intercensal County Estimates by Age, Sex, and Race;[i] 1990–2014 NCHS Bridged Race Files[f,g,h]	Linear interpolation was used to fill in intermediate years between data sources.
Percent of land area in a Native American reservation	2013 Cartographic Boundary File, State-County for United States;[j] AIANNH Areas National Shapefile[k]	Geographic boundaries of AIANNH Areas were intersected with county boundaries using ArcGIS. The area of the intersection and the area of the county were calculated using an Albers Equal Area Conic projection. The proportion of the land area that is in a reservation was generated by dividing the area of the reservation by the total area in each county.
Household median income	1980 census;[l] 1989, 1993, 1995–2014 Small Area Income and Poverty Estimates;[m] 1980–2014 Bureau of Labor Statistics, Consumer Price Index[n]	Data were adjusted for inflation using the consumer price index, and linear interpolation was used to generate values between observed data points. Income was then log-transformed.
Population density	1980–1989 Census Bureau Intercensal County Estimates by Age, Sex, and Race;[i] 1990–2014 NCHS Bridged Race Files;[f,g,h] 2013 Cartographic Boundary File, State-County for United States[j]	The area of each county was calculated using an Albers Equal Area Conic projection. The total population of each county was divided by the total area of the county, and was then log-transformed.

[a]Missouri Census Data Center. 1980 Census Summary Tape File 3, Table NT48A. MCDC Data Archive (Uexplore/Dexter). http://mcdc2.missouri.edu/applications/uexplore.shtml. Accessed April 22, 2013.

[b]Minnesota Population Center. 1990 Census Summary Tape File 3, Table P057. National Historical Geographic Information System: Version 2.0. Minneapolis, MN: University of Minnesota 2011. http://www.nhgis.org. Accessed July 18, 2013.

[c]US Census Bureau. 2000 Census Summary Tape File 3, Table DP2; using American FactFinder; http://factfinder2.census.gov. Accessed April 18, 2013.

[d]US Census Bureau. American Community Survey, 2009–2014 American Community Survey 5-Year Estimates, Table S1501; using American FactFinder; http://factfinder2.census.gov. Accessed December 8, 2015.

[e]Minnesota Population Center. 1980 Census Summary Tape File 1, Table NT8. National Historical Geographic Information System: Version 2.0. Minneapolis, MN: University of Minnesota 2011. http://www.nhgis.org. Accessed January 13, 2016.

[f]National Center for Health Statistics, Centers for Disease Control and Prevention, US Census Bureau. United States Bridged-Race Intercensal Population Estimates 1990–1999. Hyattsville, United States: National Center for Health Statistics, Centers for Disease Control and Prevention, 2004. Accessed November 21, 2011.

[g]National Center for Health Statistics, Centers for Disease Control and Prevention, US Census Bureau. United States Bridged-Race Intercensal Population Estimates 2000–2009. Hyattsville, United States: National Center for Health Statistics, Centers for Disease Control and Prevention, 2012. Accessed October 30, 2012.

[h]National Center for Health Statistics, Centers for Disease Control and Prevention, United States Census Bureau. United States Vintage 2014 Bridged-Race Postcensal Population Estimates 2010–2014. Hyattsville, United States: National Center for Health Statistics, Centers for Disease Control and Prevention, 2015. Accessed December 18, 2015.

[i]US Census Bureau. Intercensal County Estimates by Age, Sex, Race: 1980–1989. http://www.census.gov/popest/data/counties/asrh/1980s/PE-02.html. Accessed January 8, 2015.

[j]US Census Bureau. TIGER/Line Shapefile, 2013 Cartographic Boundary File, State-County for United States, 1:20,000,000. https://catalog.data.gov/dataset/2013-cartographic-boundary-file-state-county-for-united-states-1-20000000. Accessed February 2, 2015.

[k]US Census Bureau. TIGER/Line Shapefile, 2012, Series Information File for the Nation, Current American Indian/Alaska Native/Native Hawaiian Areas (AIANNH) National Shapefile. http://catalog.data.gov/dataset/tiger-line-shapefile-2012-series-information-file-for-the-nation-current-american-indian-alaska. Accessed February 10, 2015.

[l]Minnesota Population Center. 1980 Census Summary Tape File 3, Table NT69. National Historical Geographic Information System: Version 2.0. Minneapolis, MN: University of Minnesota 2011. http://www.nhgis.org. Accessed November 12, 2015.

[m]US Census Bureau. Small Area Income and Poverty Estimates. https://www.census.gov/did/www/saipe/data/statecounty/data/index.html. Accessed December 28, 2015.

[n]US Bureau of Labor Statistics. Consumer Price Index: All Urban Consumers History, All Items 1913–2015. http://www.bls.gov/data/. Accessed March 24, 2015.

eTable 3. Data sources used for the regression analysis of variation in life expectancy.

Variable	Data sources
Population living in households below the federal poverty line based on household income and size (%)	Small Area Income and Poverty Estimates.[a]
Median household income ($)	Small Area Income and Poverty Estimates.[a]
High school graduates, age 25+ (%)	American Community Survey.[b]
College graduates, age 25+ (%)	American Community Survey.[b]
Unemployment rate, age 16+ (%)	BLS Local Area Unemployment Statistics.[c]
Black population (%)	NCHS Bridged Race File.[d]
American Indian, Native Alaskan, and Native Hawaiian population (%)	NCHS Bridged Race File.[d]
Hispanic population (%)	NCHS Bridged Race File.[d]
Obesity prevalence, ages 20+ (%)	Dwyer-Lindgren et al.,[e] based on the Behavioral Risk Factor Surveillance System.[f]
No leisure-time physical activity prevalence, age 20+ (%)	Dwyer-Lindgren et al.,[e] based on the Behavioral Risk Factor Surveillance System.[f]
Cigarette smoking prevalence, age 18+ (%)	Dwyer-Lindgren et al.,[g] based on the Behavioral Risk Factor Surveillance System.[f]
Hypertension prevalence, age 30+ (%)	Olives et al.,[h] based on the Behavioral Risk Factor Surveillance System[f] and National Health and Nutrition Examination Survey.[i]
Diabetes prevalence, age 20+ (%)	Dwyer-Lindgren et al.,[j] based on the Behavioral Risk Factor Surveillance System[f] and National Health and Nutrition Examination Survey.[i]
Insured population, age <65 (%)	Small Area Health Insurance Estimates.[k]
Quality index	Dartmouth Atlas Project.[l] Following Chetty et al.,[m] the quality index was constructed by taking the mean of the z-scores for six variables related to primary care access and quality among Medicare enrollees: the percent of enrollees who had an ambulatory care visit to a primary care clinician; the percent of diabetic enrollees who had an A1C test; the percent of diabetic enrollees who had an eye exam; the percent of diabetic enrollees who had an LDL-C test; the percent of female enrollees who had a mammogram; and the discharge rate for ambulatory care sensitive conditions.
Doctors per 1,000 population	Area Health Resource File.[n]

[a]US Census Bureau. 2009 Small Area Income and Poverty Estimates. https://www.census.gov/did/www/saipe/data/statecounty/data/index.html. Accessed October 31, 2012.

[b]US Census Bureau. American Community Survey, 2011 American Community Survey 5-Year Estimates, Table S1501; using American FactFinder; http://factfinder2.census.gov. Accessed April 17, 2013.

[c]US Bureau of Labor Statistics. Local Area Unemployment Statistics: Labor Force Data by County, 2009 Annual Averages. http://download.bls.gov/pub/time.series/la/. Accessed December 14, 2015.

[d]National Center for Health Statistics, Centers for Disease Control and Prevention, US Census Bureau. United States Bridged-Race Intercensal Population Estimates 2000–2009. Hyattsville, United States: National Center for Health Statistics, Centers for Disease Control and Prevention, 2012. Accessed October 30, 2012.

[e]Dwyer-Lindgren L, Freedman G, Engell RE, et al. Prevalence of physical activity and obesity in US counties, 2001–2011: A road map for action. Population Health Metrics. 2013;11(1):7.

[f]Centers for Disease Control and Prevention. Behavioral Risk Factor Surveillance System. http://www.cdc.gov/brfss/. Accessed July 24, 2013.

[g]Dwyer-Lindgren L, Mokdad AH, Srebotnjak T, Flaxman AD, Hansen GM, Murray CJ. Cigarette smoking prevalence in US counties: 1996–2012. Population Health Metrics. 2014;12(1):5.
[h]Olives C, Myerson R, Mokdad AH, Murray CJL, Lim SS. Prevalence, awareness, treatment, and control of hypertension in United States counties, 2001–2009. PLoS ONE. 2013;8(4):e60308.
[i]Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey. http://www.cdc.gov/nchs/nhanes.htm. Accessed September 30, 2013.
[j]Dwyer-Lindgren L, Mackenbach JP, van Lenthe FJ, Flaxman AD, Mokdad AH. Diagnosed and undiagnosed diabetes prevalence by county in the U.S., 1999–2012. Diabetes Care. 2016;39(9):1556–62.
[k]US Census Bureau. 2009 Small Area Health Insurance Estimates. https://www.census.gov/did/www/sahie/data/20082014/index.html. Accessed June 8, 2016.
[l]The Dartmouth Atlas of Health Care. 2009 Selected measures of primary care access and quality. http://www.dartmouthatlas.org/tools/downloads.aspx#primary. Accessed June 16, 2016.
[m]Chetty R, Stepner M, Abraham S, et al. The association between income and life expectancy in the United States, 2001–2014. JAMA. 2016;315(16).
[n]Health Resources and Services Administration. 2014–2015 Area Health Resource Files: Total active non-federal MDs. http://ahrf.hrsa.gov/download.htm. Accessed October 12, 2015.

eTable 4. Principal component analysis of socioeconomic and race/ethnicity factors.[a]

	Component							
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Poverty	-0.485	0.041	-0.080	0.256	-0.179	0.434	0.078	-0.681
Income	0.475	-0.028	0.174	0.146	0.311	-0.419	0.237	-0.627
High school	0.464	-0.207	-0.238	0.024	-0.026	0.298	-0.746	-0.195
College	0.397	-0.072	0.161	0.561	0.024	0.529	0.372	0.278
Unemployment	-0.298	-0.345	0.036	-0.044	0.862	0.193	-0.072	0.060
Black	-0.260	-0.476	0.295	0.568	-0.204	-0.404	-0.286	0.099
Native	-0.064	0.322	-0.731	0.485	0.209	-0.255	-0.019	0.114
Hispanic	-0.068	0.707	0.507	0.195	0.205	0.038	-0.394	0.030
Standard deviation	1.837	1.096	1.052	0.945	0.850	0.641	0.462	0.278
Proportion of variance	0.422	0.150	0.138	0.112	0.090	0.051	0.027	0.010

[a]A principal component analysis was carried out on the following socioeconomic and race/ethnicity factors: the percent of the population below the poverty line (Poverty); the logged median household income (Income); the percent of the population that has graduated high school (High school); the percent of the population that has graduated college (College); the unemployment rate (Unemployment); the percent of the population that is black (Black); the percent of the population that is American Indian, Native Alaska, or Native Hawaiian (Native); and the percent of the population that is Hispanic (Hispanic). The top portion of the table shows the variable loadings for each component while the bottom portion shows the standard deviation and the proportion of variance explained by each component.

eTable 5. Principal component analysis of behavioral and metabolic risk factors.[a]

	Component				
	1	**2**	**3**	**4**	**5**
Obesity	-0.468	0.141	0.321	-0.756	-0.293
Inactivity	-0.468	-0.085	0.586	0.295	0.586
Smoking	-0.385	-0.850	-0.202	0.102	-0.280
Hypertension	-0.459	0.208	-0.715	-0.157	0.458
Diabetes	-0.451	0.455	-0.040	0.553	-0.532
Standard deviation	1.987	0.740	0.468	0.397	0.359
Proportion of variance	0.789	0.109	0.044	0.032	0.026

[a]A principal component analysis was carried out on the following behavioral and metabolic risk factors: obesity prevalence (Obesity); no leisure-time physical activity prevalence (Inactivity); cigarette smoking prevalence (Smoking); hypertension prevalence (Hypertension); and diabetes prevalence (Diabetes). The top portion of the table shows the variable loadings for each component while the bottom portion shows the standard deviation and the proportion of variance explained by each component.

eTable 6. Principal component analysis of health care factors.[a]

	Component		
	1	**2**	**3**
Insurance	0.627	-0.262	0.734
Quality	0.606	-0.429	-0.670
MDs	0.491	0.864	-0.110
Standard deviation	1.291	0.890	0.735
Proportion of variance	0.556	0.264	0.180

[a]A principal component analysis was carried out on the following health care factors: insurance prevalence under age 65 (Insured); health care quality index (Quality); doctors per 1,000 population (MDs). The top portion of the table shows the variable loadings for each component while the bottom portion shows the standard deviation and the proportion of variance explained by each component.

eTable 7. Multivariate regression models.[a]

Variable	Model 1	Model 2	Model 3	Model 4
Intercept	69.264 (2.613)[b]	92.546 (0.258)[b]	66.167 (0.497)[b]	85.935 (2.164)[b]
Poverty	-0.077 (0.009)[b]			0.022 (0.008)[b]
Income	0.006 (0.231)			0.489 (0.185)[b]
High school	0.104 (0.006)[b]			-0.027 (0.007)[b]
College	0.061 (0.004)[b]			-0.011 (0.005)[b]
Unemployment	-0.037 (0.008)[b]			-0.031 (0.006)[b]
Black	-0.036 (0.002)[b]			0.002 (0.003)
Native	-0.049 (0.003)[b]			-0.017 (0.003)[b]
Hispanic	0.038 (0.002)[b]			0.011 (0.003)[b]
Obesity		0.065 (0.010)[b]		-0.002 (0.010)
Inactivity		-0.070 (0.008)[b]		-0.092 (0.011)[b]
Smoking		-0.206 (0.007)[b]		-0.154 (0.009)[b]
Hypertension		-0.148 (0.011)[b]		-0.174 (0.019)[b]
Diabetes		-0.334 (0.017)[b]		-0.235 (0.028)[b]
Insurance			0.062 (0.007)[b]	0.037 (0.005)[b]
Quality			0.086 (0.003)[b]	0.034 (0.002)[b]
MDs			0.199 (0.035)[b]	-0.301 (0.026)[b]
R^2	0.69	0.77	0.31	0.82
Adjusted R^2	0.69	0.77	0.31	0.82

[a]Regression results from multivariate ordinary least squares regressions with life expectancy at birth as the outcome variable. Three sets of variables were considered: socioeconomic and race/ethnicity factors (the percent of the population below the poverty line [Poverty]; the logged median household income [Income]; the percent of the population that has graduated high school [High school]; the percent of the population that has graduated college [College]; the unemployment rate [Unemployment]; the percent of the population that is black [Black]; the percent of the population that is American Indian, Native Alaska, or Native Hawaiian [Native]; and the percent of the population that is Hispanic [Hispanic]), behavioral and metabolic risk factors (obesity prevalence [Obesity]; no leisure-time physical activity prevalence [Inactivity]; cigarette smoking prevalence [Smoking]; hypertension prevalence [Hypertension]; and diabetes prevalence [Diabetes]), and health care factors (insurance prevalence under age 65 [Insured]; health care quality index [Quality]; doctors per 1,000 population [MDs]). The numbers in parentheses are the standard errors for the estimated coefficients.

[b]$P < 0.05$

Chapter 7

Self-reported general health, physical distress, mental distress, and activity limitation by US county, 1995–2012

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ABSTRACT

Background

Metrics based on self-reports of health status have been proposed for tracking population health and making comparisons among different populations. While these metrics have been used in the US to explore disparities by sex, race/ethnicity, and socioeconomic position, less is known about how self-reported health varies geographically. This study aimed to describe county-level trends in the prevalence of poor self-reported health and to assess the face validity of these estimates.

Methods

We applied validated small area estimation methods to Behavioral Risk Factor Surveillance System data to estimate annual county-level prevalence of four measures of poor self-reported health (low general health, frequent physical distress, frequent mental distress, and frequent activity limitation) from 1995 and 2012. We compared these measures of poor self-reported health to other population health indicators, including risk factor prevalence (smoking, physical inactivity, and obesity), chronic condition prevalence (hypertension and diabetes), and life expectancy.

Results

We found substantial geographic disparities in poor self-reported health. Counties in parts of South Dakota, eastern Kentucky and western West Virginia, along the Texas-Mexico border, along the southern half of the Mississippi river, and in southern Alabama generally experienced the highest levels of poor self-reported health. At the county level, there was a strong positive correlation among the four measures of poor self-reported health and between the prevalence of poor self-reported health and the prevalence of risk factors and chronic conditions. There was a strong negative correlation between prevalence of poor self-reported health and life expectancy. Nonetheless, counties with similar levels of poor self-reported health experienced life expectancies that varied by several years. Changes over time in life expectancy were only weakly correlated with changes in the prevalence of poor self-reported health.

Conclusions

This analysis adds to the growing body of literature documenting large geographic disparities in health outcomes in the United States. Health metrics based on self-reports of health status can and should be used to complement other measures of population health, such as life expectancy, to identify high need areas, efficiently allocate resources, and monitor geographic disparities.

BACKGROUND

Measures of survival, such as life expectancy, have long been used to compare the health status of different populations and to track changes in health status over time.[1,2] While objective, and relatively easily measured, these metrics fail to capture differences in health due to non-fatal (or not yet fatal) conditions.[3] Moreover, they fail to take into account individuals' own assessment of and satisfaction with their health and functioning. In response to these limitations, metrics based on self-reported health status have been proposed as a complement to objective measures for use in tracking levels of population health over time and for evaluating disparities in health.[4,5]

The Behavioral Risk Factor Surveillance System (BRFSS) is an annual telephone survey conducted in all states and supported by the Centers for Disease Control and Prevention.[6,7] Since 1993, the BRFSS has included four core "Healthy Days" questions in which respondents are asked to rate their overall health and to report the number of days in the past month that they experienced poor physical health, poor mental and emotional health, or were unable to participate in their usual activities. These questions are designed to elicit respondents' self-assessment of and satisfaction with their health generally and with their recent physical health, mental and emotional health, and functional limitations.[4] Health metrics based on these and similar questions have been shown to be highly correlated with metrics based on lengthier survey instruments[8,9] health behaviors and risk factors,[10–12] chronic health conditions,[13] health care utilization,[14] and mortality risk.[15]

Healthy days questions from the BRFSS have been used to track national- and state-level trends in poor self-reported health[16] and to explore disparities by gender,[17] race/ethnicity,[18] socioeconomic status,[16] and employment status.[19] However, these data have only been used in a limited way to explore local-level variations in poor self-reported health. Jia et al.[20] and others[21] considered county-level measures of poor self-reported health based on the healthy days questions, but focused on county-level correlates of poor self-reported health rather than on spatial patterns and disparities. The County Health Rankings & Roadmaps Program includes three county-level measures of poor self-reported health based on BRFSS healthy days questions, but recent methodological changes make it difficult to track trends over time.[22]

In this analysis, we used validated small area estimation methods to estimate the prevalence of four measures of poor self-reported health—low general health, frequent physical distress, frequent mental distress, and frequent activity limitation—by county from 1995 to 2012. We used these estimates to explore spatial patterns in poor self-reported health and to quantify county-level geographic disparities.

We performed two additional analyses combining these estimates of poor self-reported health with other estimates of health risk factors and outcomes at the county level. First, we compared the prevalence of poor self-reported health to the prevalence of behavioral and metabolic risk factors (i.e., obesity, smoking, and physical inactivity) and chronic conditions (i.e., hypertension and diabetes) to assess the face validity of self-reported health as a proxy for a county's population health. We expected the prevalence of poor self-reported health to be higher in places with higher prevalence of risk factors and chronic conditions known to result in considerable health burden.

Second, we compared the prevalence of poor self-reported health to estimates of life expectancy at the county-level, in order to assess whether geographic county-level disparities in life expectancy and self-reported health follow the same pattern. We expected the prevalence of poor self-reported health to be strongly and negatively correlated with life expectancy, albeit not perfectly as life expectancy and self-reported health may reflect somewhat different aspects of a county's health burden.

METHODS

Data

We analyzed data from the BRFSS surveys conducted from 1995, the first year in which all 50 states participated in the BRFSS, through 2012, the most recent year in which county identifiers were publicly available. The BRFSS included four "healthy days" questions:

1. Would you say in general that your health is—excellent, very good, good, fair, or poor?
2. Now thinking about your physical health, which includes physical illness and injury, for how many days during the past 30 days was your physical health not good?
3. Now thinking about your mental health, which includes stress, depression, and problems with emotions, for how many days during the past 30 days was your mental health not good?
4. During the past 30 days, for about how many days did poor physical or mental health keep you from doing your usual activities, such as self-care, work, or recreation?

Only the first question was asked by all states in 2002; consequently we excluded data on the remaining questions for this year only.

We created four binary variables from these questions: low general health (responding "fair" or "poor" to question 1); frequent physical distress (reporting 14 or more days in response to question 2); frequent mental distress (reporting 14 or more days in response to question 3); and frequent activity limitation (reporting 14 or more days in response to question 4). The

14 day cut-off used for frequent physical distress, mental distress, and activity limitation is in line with previous research utilizing these questions, and is intended to identify individuals who experienced significant health burden in the previous month.[10–12, 17–19] In addition, we extracted county of residence, age, gender, race/ethnicity (white non-Hispanic, black non-Hispanic, native non-Hispanic, or Hispanic), education status (less than high school, high school graduate, some college, or college graduate), marital status (never married, currently married, or formerly married), and, starting in 2011, phone type (landline only, cell phone only, or dual) from the survey. Respondents with missing values on any of these variables were excluded from the analysis. There were 5,239,833 respondents in the study period. Of these, 2.2% were missing some demographic information, 3.8% were missing one or more outcome variables, and 5.1% were missing the county variable, primarily due to CDC data suppression rules. In total, 4,698,203 (89.7%) had no missing values and were included in the analysis. The survey response rate in the BRFSS varied by year and by state; in 2012, the response rate ranged from 27.7 to 60.4% among states.[23]

Small area estimation model

We used previously described and validated small area models to estimate county-level prevalence of low general health, frequent physical distress, frequent mental distress, and frequent activity limitation.[24] These models are designed to "borrow strength" across time, space, and from external data sources (i.e., covariates) in order to increase the effective amount of information available for each county. Briefly, these models were specified as:

$$Y_{j,t,a,r,m,e} \sim \text{Binomial}(p_{j,t,a,r,m,e},\ N_{j,t,a,r,m,e})$$
$$\text{logit}(p_{j,t,a,r,m,e}) = \beta_0 + \beta_{1,a} + \beta_{2,r} + \beta_{3,m} + \beta_{4,e} + \boldsymbol{\beta_5}\cdot\boldsymbol{X_{j,t}} + u_j + w_t + d_{j,t}$$

where $N_{j,t,a,r,m,e}$, $Y_{j,t,a,r,m,e}$, and $p_{j,t,a,r,m,e}$ are the total number of respondents; the number of respondents with low general health, frequent physical distress, frequent mental distress, or frequent activity limitation, depending on the model; and true prevalence, respectively, in county j, year t, age group a, race/ethnicity group r, marital status group m, and education group e. The β terms are fixed effects: β_0 is the intercept; $\beta_{1,a}$ are age group effects and are included to account for differences in self-reported health among age groups; $\beta_{2,r}$, $\beta_{3,m}$, and $\beta_{4,e}$ are race/ethnicity, marital status, and education effects, respectively, and are included to account for differences in self-reported health among each of these groups; $\boldsymbol{\beta_5}$ is a vector of coefficients on three county-level covariates that are expected to be predictive of poor self-reported health (percent of the population living in poverty, the unemployment rate, and the percent of households which are rural). The remaining terms are random effects. u_j and w_t are county- and year-level random effects, respectively, each of which is assumed to follow a conditional autoregressive distribution that allows for spatial (u_j) and temporal (w_t) smoothing (specifically, the distribution described by Leroux et al.[25]). $d_{j,t}$ is a county-year-level random

effect with a non-separable "Type IV" interaction between space and time as described by Knorr-Held,[26] but using the conditional autoregressive distribution described by Leroux et al.[25] for both the spatial and temporal dimensions. Gamma(1, 1,000) priors were assigned for the precision parameters of each random effect. Normal(0, 1.5) priors were assigned for the logit-transformed autocorrelation parameter of each random effect.

Models were fit using the TMB package[27] in R version 3.2.4[28] and 1,000 draws of $p_{j,t,a,r,m,e}$ were simulated from the posterior distribution. These draws were post-stratified by race, marital status, and education using population counts from the census and American Community Survey to ensure that prevalence estimates represent the demographic composition of a county even where response rates vary among different demographic groups. Draws were then age-standardized using the 2010 census population as the standard. Point estimates were calculated from the mean of the 1,000 draws and 95% uncertainty intervals (UIs) were calculated from the 2.5th and 97.5th percentiles. State- and national-level estimates were generated by population-weighting the county-level estimates.

Separate models were fit for males and females for each of the four measures, for eight total models. Prior to 2011, the BRFSS sample did not include cell phones, raising the possibility of non-coverage bias; the correction method described by Dwyer-Lindgren et al. was applied to address this issue.[29]

Comparison to risk factors, chronic conditions, and life expectancy

After modeling county-level prevalence of low general health, frequent physical distress, frequent mental distress, and frequent activity limitation, we compared these measures to existing estimates of county-level prevalence of behavioral and metabolic risk factors (smoking, obesity, and physical inactivity), and chronic conditions (hypertension and diabetes), also derived from BRFSS data.[24, 29–31] For each of these variables, we calculated the Pearson correlation coefficient with each of the four measures of poor self-reported health in the most recent year of data available (ranging from 2009 for hypertension to 2012 for diabetes).

We also compared the prevalence of low general health, frequent physical distress, frequent mental distress, and frequent activity limitation with life expectancy in 2012 (Laura Dwyer-Lindgren, Amelia Bertozzi-Villa, Rebecca W Stubbs, Chloe Morozoff, Johan P Mackenbach, Frank J van Lenthe, Ali H Mokdad, and Christopher JL Murray: Inequalities in life expectancy among US counties, 1980 to 2014: Temporal trends and key drivers., forthcoming). We used loess regression—a non-parametric smoothing technique[32]—to characterize the relationship between each of these four variables and life expectancy. We also examined the correlation between change in prevalence of low general health, frequent physical distress, frequent mental distress, and frequent activity limitation, and change in life expectancy between 1995 and 2012.

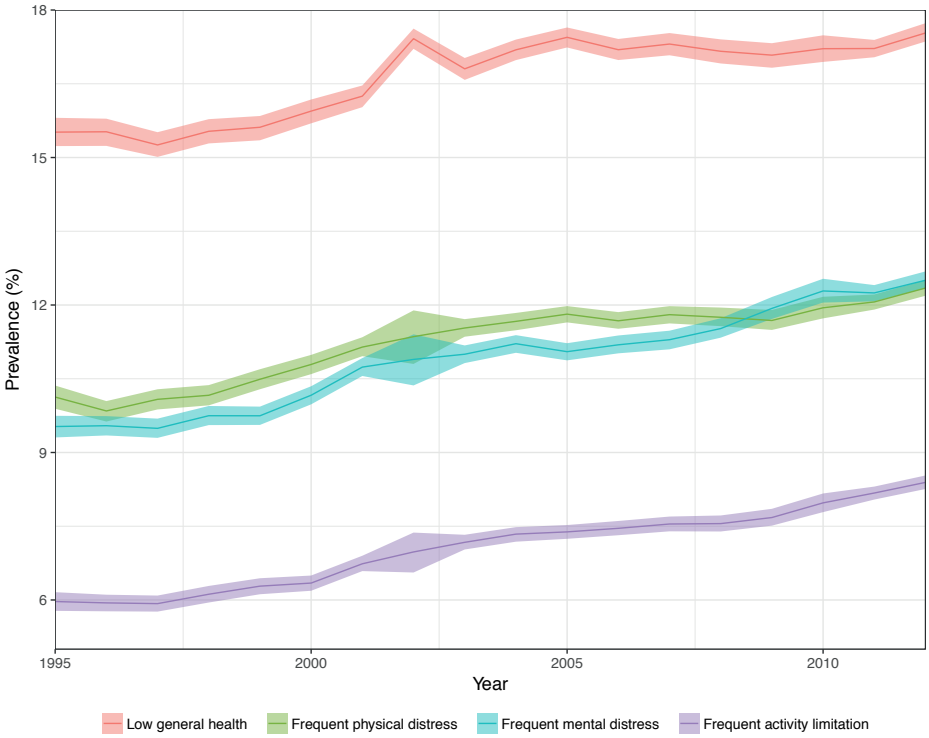

Figure 1. National trends in low general health, frequent physical distress, frequent mental distress, and frequent activity limitation, 1995–2012.

RESULTS

Nationally, the prevalence of all four measures of poor self-reported health increased between 1995 and 2012: from 15.5% (95% UI: 15.2–15.8%) to 17.5% (17.4–17.7%) for low general health; from 10.1% (9.9–10.4%) to 12.3% (12.2–12.5%) for frequent physical distress; from 9.5% (9.3–9.7%) to 12.5% (12.3–12.7%) for frequent mental distress; and from 6.0% (5.8–6.2%) to 8.4% (8.3–8.5%) for frequent activity limitation (Figure 1). The prevalence was higher among women than among men in all years. In 2012, the prevalence among women exceeded that among men by 7.6% (18.2% [18.0–18.4%] vs. 16.9% [16.6–17.1%]) for low general health; 23.2% (13.6% [13.4–13.8%] vs. 11.0% [10.9–11.2%]) for frequent physical distress; 38.6% (14.5% [14.3–14.6%] vs. 10.4% [10.2–10.7%]) for frequent mental distress; and 20.8% (9.2% [9.0–9.3%] vs. 7.6% [7.4–7.8%]) for frequent activity limitation.

There was significant variation in all four outcomes at the county level in all years. The standard deviation of county-level prevalence of low general health decreased somewhat between 1995 (5.4 percentage points) and 2012 (5.1 percentage points). The standard

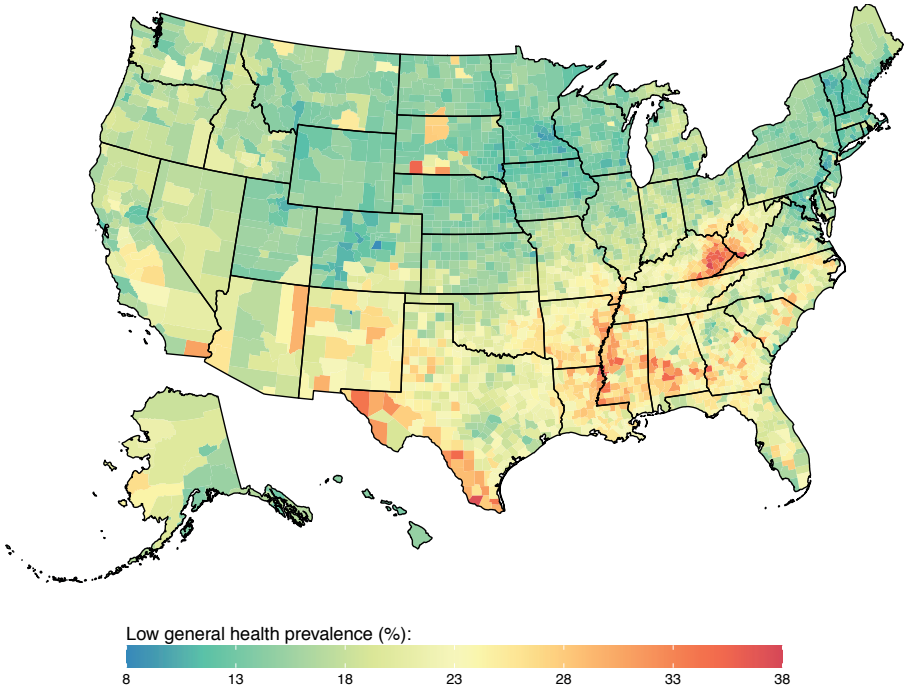

Figure 2. Low general health prevalence, 2012.

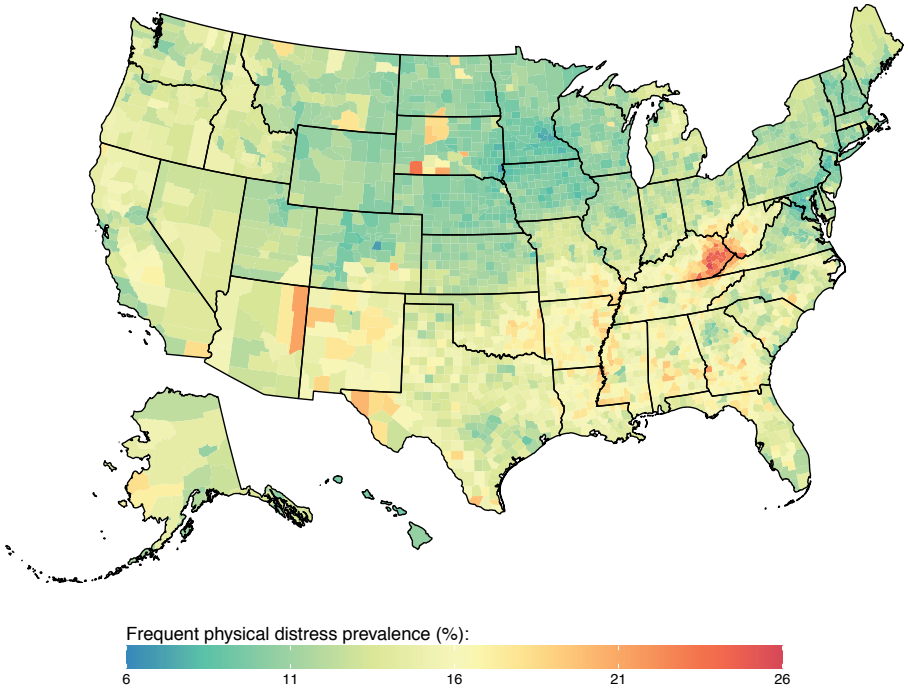

Figure 3. Frequent physical distress prevalence, 2012.

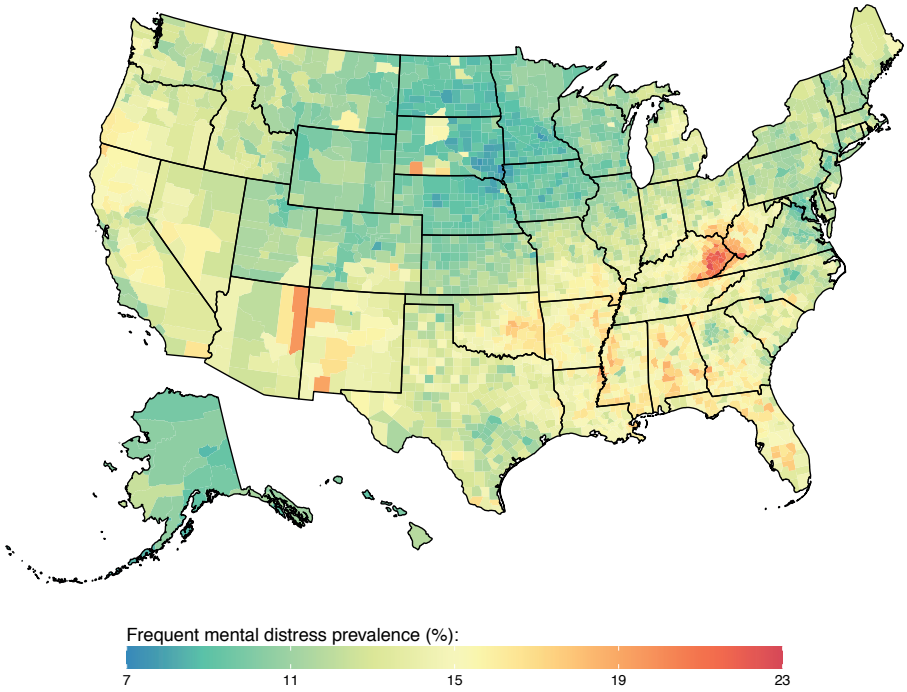

Figure 4. Frequent mental distress prevalence, 2012.

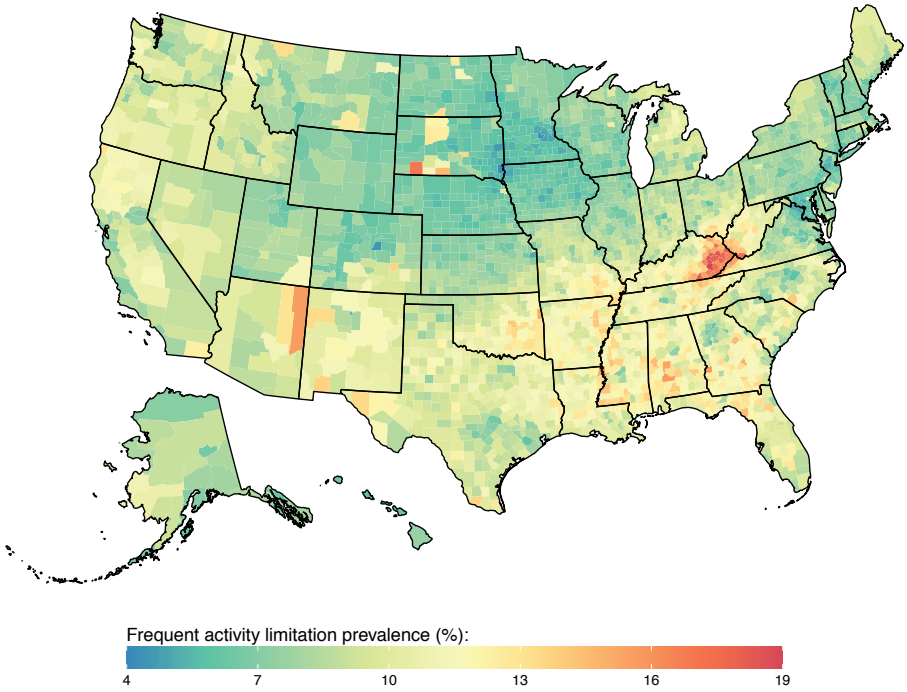

Figure 5. Frequent activity limitation prevalence, 2012.

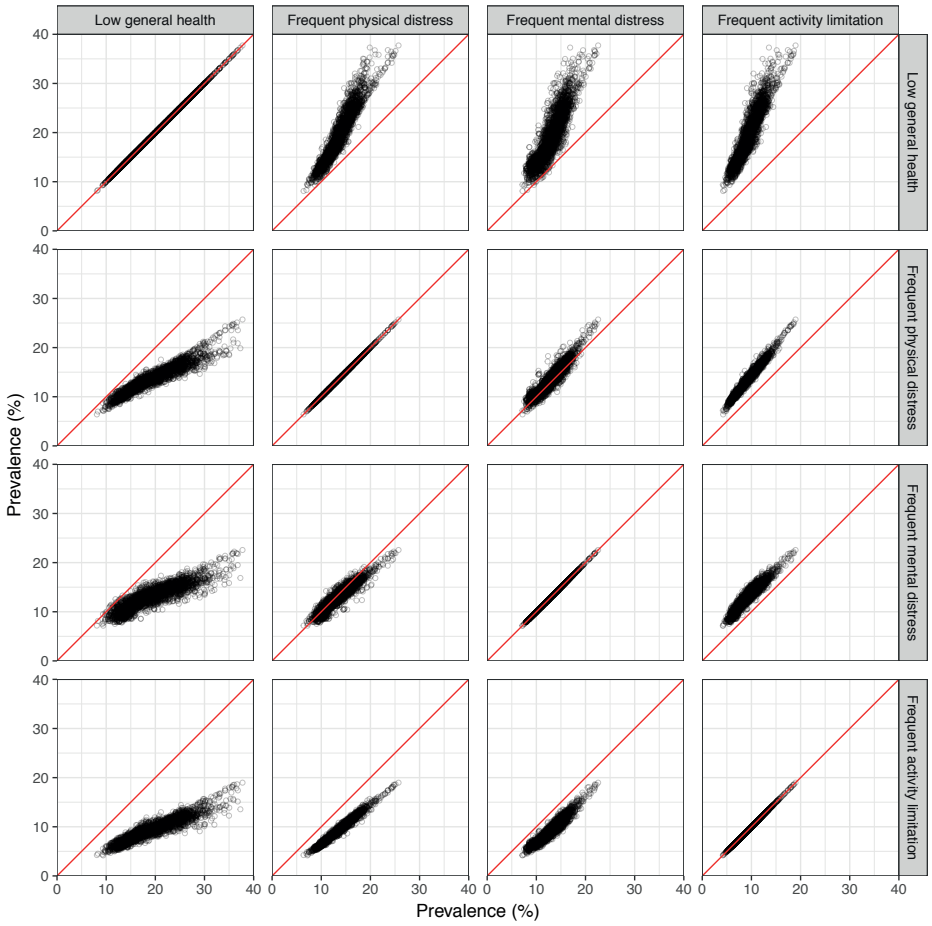

Figure 6. Comparison among self-reported health measures, 2012.

deviation of county-level prevalence of frequent physical distress, frequent mental distress, and frequent activity limitation increased over this same period (from 2.2 to 2.7, 2.0 to 2.4, and 1.9 to 2.2 percentage points, respectively). Counties with the lowest prevalence of low general health (Figure 2) were located primarily in New England and north-western states stretching from Utah to Wisconsin. In contrast, counties with the highest prevalence of low general health were found in parts of South Dakota, eastern Kentucky and western West Virginia, along the Texas-Mexico border, along the southern half of the Mississippi river, and in southern Alabama. Spatial patterns were similar for frequent physical distress, frequent mental distress, and frequent activity limitation (Figures 3, 4 and 5). Results for all counties and all years are reported in Additional file 1.

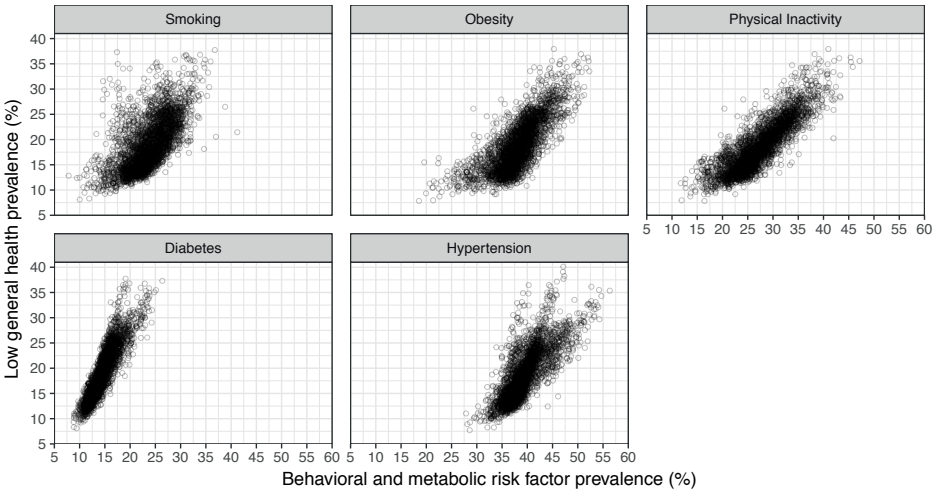

Figure 7. Relationship between low general health prevalence and prevalence of smoking, obesity, physical inactivity, diabetes, and hypertension.

Pairwise correlation coefficients between all four measures in 2012 were very high (Figure 6), ranging from 0.88 (low general health and frequent mental distress) to 0.99 (frequent physical distress and frequent activity limitation). At the national level, the prevalence of low general health (17.5% [17.4–17.7%]) was highest and the prevalence of frequent activity limitation (8.4% [8.3–8.5%]) was lowest among the four measures, while prevalence of frequent mental distress (12.5% [12.3–12.7%]) and frequent physical distress (12.3% [12.2–12.5%]) were intermediate. This pattern was also observed at the county level, where the prevalence of low general health was nearly always the highest among the four measures, while the prevalence of frequent activity limitation was always the lowest. Levels of frequent physical and mental distress were generally similar within counties, except at the high end of the distribution: counties with very high prevalence of both typically had a slightly higher prevalence of frequent physical distress than frequent mental distress.

Low general health prevalence was positively correlated with the prevalence of behavioral and metabolic risk factors—0.63 for smoking, 0.76 for obesity, and 0.85 for physical inactivity—and with the prevalence of diabetes (0.90) and hypertension (0.78) (Figure 7). Generally similar correlations were found between these variables and frequent physical distress, frequent mental distress, and frequent activity limitation (data not shown).

Life expectancy was negatively correlated with all four measures (Figure 8). The relationship between life expectancy and low general health was somewhat curvilinear, with a steeper decline in life expectancy as low general health prevalence moved from very low values to

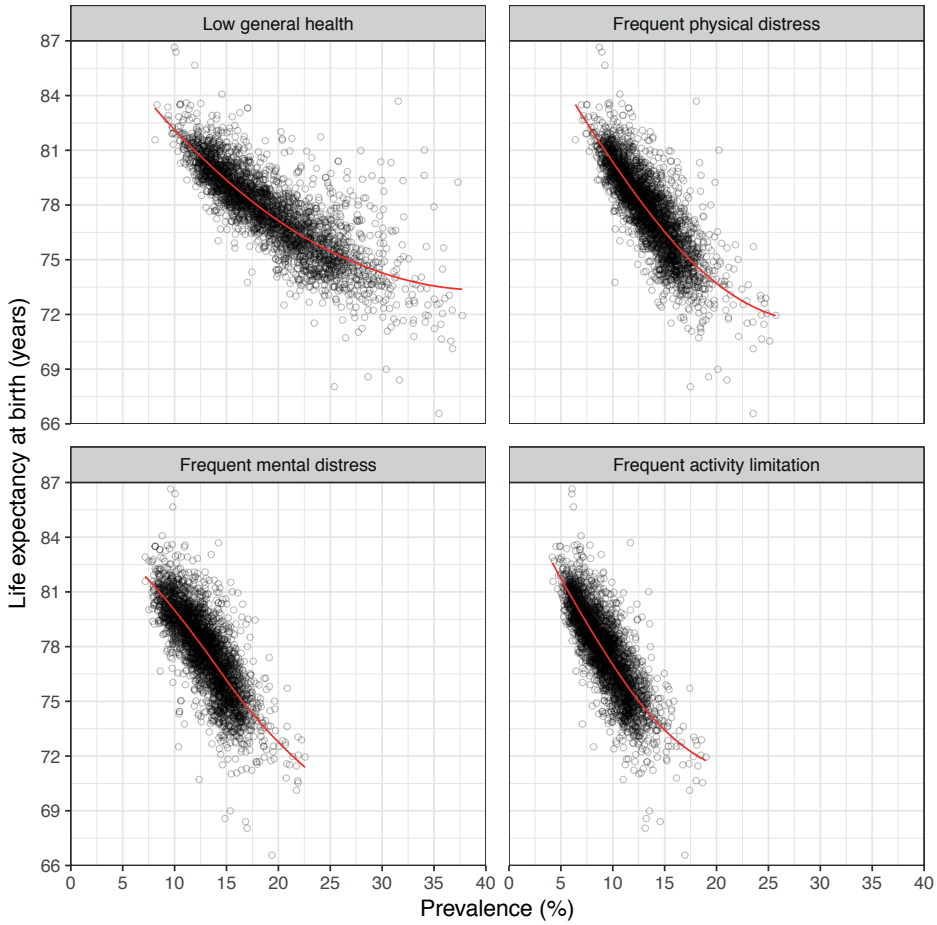

Figure 8. Relationship between life expectancy and self-reported health measures, 2012.

more moderate values, and a more moderate decline in life expectancy as low general health prevalence increased from moderate to high values. The relationship between life expectancy and the other three measures was closer to linear, but flattened somewhat among counties with very high prevalence of frequent physical distress, frequent mental distress, and frequent activity limitation.

Figure 9 shows the difference between observed life expectancy and life expectancy predicted based on low general health prevalence, frequent physical distress, frequent mental distress, and frequent activity limitation. The spatial patterns are generally similar across these four measures. Counties in Western and Southwestern states (excluding Nevada) and in southern Florida tended to have higher life expectancy than average given their prevalence of poor self-reported health. In contrast, counties in Alaska, the Deep South (excluding Florida) and

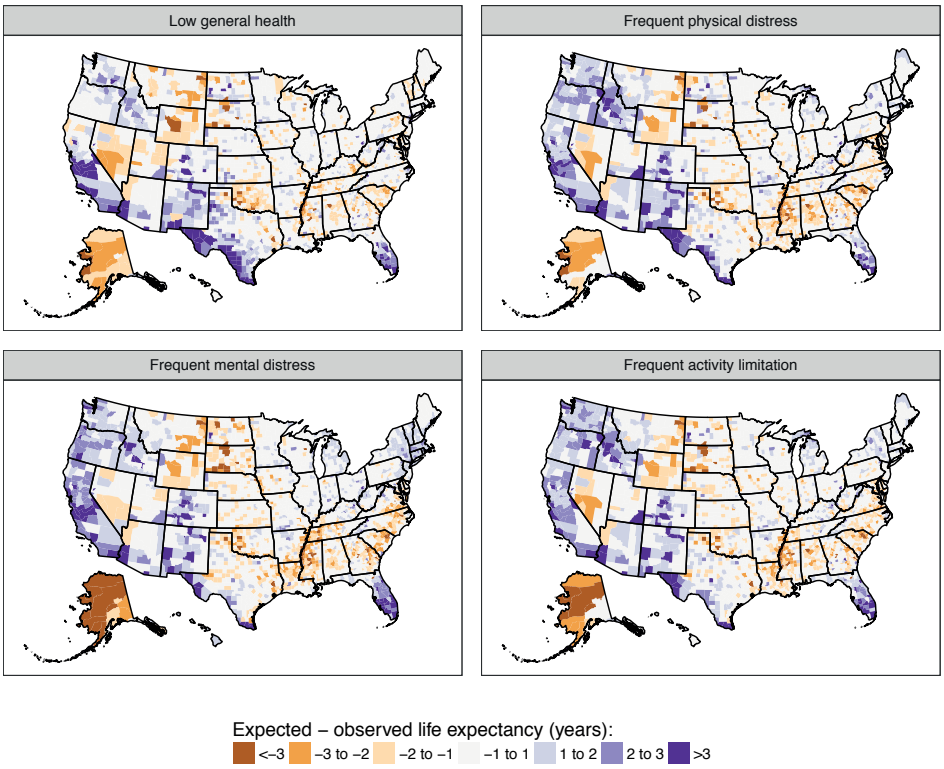

Figure 9. Gap between observed life expectancy and predicted life expectancy based on poor self-reported health prevalence, 2012.

parts of Nevada and the upper Midwest and Great Plains regions tended to have lower life expectancy then average, given their prevalence of poor self-reported health.

Between 1995 and 2012, life expectancy increased in most counties (99.7%), while the prevalence of low general health, frequent physical distress, frequent mental distress, and frequent activity limitation also increased in most counties (88.1, 99.3, 98.3, and 99.2% of counties, respectively). There was a small negative correlation between change in life expectancy and change in the prevalence of frequent physical distress, frequent mental distress, and frequent activity limitation (Pearson correlation coefficients: −0.27, −0.23, and −0.22, respectively). When examined separately by sex, the correlations were again negative, but were generally larger among women (−0.25 to −0.35) than among men (−0.08 to −0.15). There was a weak positive correlation between changes in low general health prevalence and changes in life expectancy (0.09 overall; 0.12 for men and 0.06 for women).

DISCUSSION

This analysis found increasing rates and considerable geographic disparities in poor self-reported health within the US. These findings underscore the utility of local measurements of population health status and highlight the need for closer attention paid to geographic disparities in health outcomes.

The four measures considered—low general health, frequent physical distress, frequent mental distress, and frequent activity limitation—were highly correlated, though with important differences in some counties. Each of these measures were intended to capture a distinct facet of health: general health status (low general health), recent physical health (frequent physical distress), recent mental and emotional health (frequent mental distress), and recent day-to-day functioning (frequent activity limitation). The high correlations among these measures is likely a reflection of the close connections between different domains of health, though it may also indicate some overlap in the way each of the four healthy days questions were understood by respondents. Moreover, the close relationship between these four measures may also reflect shared determinants among different health domains, for example, socioeconomic factors.

Consistent with previous research at the individual level,[10–12] we found that population-level prevalence of poor self-reported health (all four measures) was positively correlated with the prevalence of behavioral and metabolic risk factors. This may reflect a direct pathway from these risk factors to poorer health outcomes (e.g., smoking causing respiratory disease), but may also reflect individuals' expectation of future health based on what they know about their own behaviors.[5] We also found a positive population-level relationship between poor self-reported health and chronic conditions such as diabetes and hypertension. These findings serve as an important external check on the validity of the self-reported health measures: all else equal, we expect poorer overall health when the prevalence of behavioral and metabolic risk factors or chronic conditions is high. However, the correlation among these variables may also reflect some common underlying determinants.

All four measures of poor self-reported health were strongly and negatively correlated with life expectancy at the county level. Nonetheless, life expectancy among counties with comparable levels of poor self-reported health often varied by multiple years, while the prevalence of poor self-reported health varied considerably among counties with similar life expectancy. This may reflect differences in non-fatal health outcomes: life expectancy captures only differences in survival, but not differences in health due to disabling but non-fatal conditions. However, this may also reflect differences in how respondents understand and respond to the healthy days questions, e.g., different understanding of what constitutes "good" health or

a "healthy" day.[33, 34] Further research is required in the US to disentangle the extent to which geographic (or other) disparities in self-rated health reflect true disparities in health status.

Consistent with other studies utilizing BRFSS data, our analysis found that rates of poor self-reported health have increased at the national level as well as in most counties between 1995 and 2012.[16] Over this same period, however, life expectancy has also increased nationally and in most counties (Laura Dwyer-Lindgren, Amelia Bertozzi-Villa, Rebecca W Stubbs, Chloe Morozoff, Johan P Mackenbach, Frank J van Lenthe, Ali H Mokdad, and Christopher JL Murray: Inequalities in life expectancy among US counties, 1980 to 2014: Temporal trends and key drivers., forthcoming). While changes in life expectancy were negatively correlated with changes in most of the self-reported health measures considered (i.e., the counties with smaller increases in life expectancy tended to have larger increases in poor self-reported health), this relationship is relatively weak. Additionally, comparative studies have highlighted differential trends in poor self-reported health among various US surveys.[35] Further research is needed to identify what is driving changes in poor self-reported health in the US and to identify to what extent these trends reflect true changes in underlying health status.

This study has a number of limitations. Survey response rates to the BRFSS are low and item non-response is also a concern. In both cases, missingness is not at random. Although we use post-stratification to explicitly account for factors such as education that are known to be related to both the likelihood of responding and the likelihood of reporting poor self-reported health, it is still possible that differential non-response biases our results. Moreover, the BRFSS, a telephone survey, excludes individuals with no phone and, prior to 2011, excluded individuals with only a cell phone. We have attempted to correct the latter issue, but some non-coverage bias may remain. The data sources we used for populations counts for post-stratification and for covariates for the small area models may also be subject to error. The small area model smooths both spatially and temporally; while this allows us to produce more precise estimates than otherwise possible, the model may in some cases over-smooth and thus underestimate variation in self-reported health. Finally, the BRFSS data used in this analysis were also used for generating the estimates of smoking, obesity, physical inactivity, diabetes, and hypertension prevalence and the correlation between the self-reported health measures and these risk factors may be somewhat higher in this analysis than they would be if these measures were based on independent data sources.

CONCLUSIONS

Our findings revealed large disparities in the prevalence of poor self-reported health among counties in the US. Poor self-reported health was positively correlated with risk factor

prevalence and prevalence of chronic health conditions and negatively correlated with life expectancy at the county level. Local information on health outcomes should be used by policymakers and health professionals to identify communities that are lagging behind, to evaluate the impact of policies and programs, and to monitor geographic inequalities.

DECLARATIONS

Funding

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Availability of data and materials

BRFSS data are available from http://www.cdc.gov/brfss/. The datasets generated for this analysis are included as a supplemental file as part of this publication.

Authors' contributions

AHM and LDL conceived of the study. LDL carried out the statistical analyses and wrote the initial draft of the manuscript. All authors contributed to interpreting results. All authors contributed to revising the manuscript and read and approved the final version of the manuscript.

Competing interests

The authors declare that they have no competing interests.

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ADDITIONAL FILE 1

Prevalence of low general health, frequent physical distress, frequent mental distress, and frequent activity limitation by county, year, and sex. Available at: https://static-content.springer.com/esm/art%3A10.1186%2Fs12963-017-0133-5/MediaObjects/12963_2017_133_MOESM1_ESM.xlsx

Chapter 8

Discussion

This thesis has described the development of a methodology for estimating risk factor prevalence and health outcomes at the county level in the United States (US). Using this methodology, estimates of smoking prevalence, alcohol use prevalence, diabetes prevalence, cause-specific mortality rates, life expectancy, and self-reported health status were constructed for each county. These estimates were then used to describe spatial patterns, quantify geographic disparities and track changes in disparities over time, and explore drivers of disparities in life expectancy among counties. This final chapter summarizes the main findings of this thesis, discusses relevant methodological limitations, considers the findings of this thesis in the context of previous research, and discusses the implications of these findings for policy and for future research.

SUMMARY OF FINDINGS

First research question

Can methods be developed that both address small numbers issues and also account for known biases in available data, allowing for sufficiently precise estimates of health-related risk factors and mortality for US counties?

In chapters 2–5, this thesis employed an empirical validation strategy based on simulating data for small areas from observed data in relatively large areas to assess the performance of the proposed small area models. With respect to the models for risk factor prevalence based on survey data, the validation results demonstrate that the typical error associated with the modeled county-level prevalence estimates is small compared to both typical levels of prevalence and the magnitude of variation among counties (Table 1). With respect to the models used to estimate mortality rates, the validation points to minimal bias and a mean absolute relative error around 6.5% for populations of at least 1,000 (which includes more than 99% of all county-years). In both cases, estimates are considerably more precise when

Table 1. Validation results compared to county-level estimates for smoking, alcohol use, and diagnosed diabetes.

Risk factor	RMSE (percentage points)[a]	Estimated county prevalence, all years (%)		
		Minimum	Median	Maximum
Smoking – males	2.7	8.9	28.2	50.5
Smoking – females	2.8	5.4	23.7	42.8
Alcohol use – males	3.3	11.4	59.1	84.4
Alcohol use – females	3.4	6.2	41.5	79.4
Diagnosed diabetes	1.2	2.7	8.6	20.4

[a]Root mean squared error for a county with ten respondents per year.

larger sample sizes or larger populations (still well within the range observed at the county level) are available. Moreover, chapter 5 compared the final small area model for mortality rates to two previously published models and found substantial gains in model performance not only in terms of precision, but also in terms of bias and uncertainty interval coverage.

Chapters 2–5 also described methods for correcting various biases in the underlying data used to generate county-level estimates, specifically: non-coverage bias due to omission of cell phones from the BRFSS sample frame prior to 2011 (chapter 2); discontinuities due to changes in item wording between survey rounds (chapter 3); self-report bias related to undiagnosed health conditions (chapter 4); and bias introduced by the presence of garbage codes in death registration data (chapter 5). These methodological developments are considerably more difficult to formerly validate as appropriate 'gold standard' data are not available. Nonetheless, chapters 2–5 demonstrate that corrections for these biases can be operationalized in the context of small area analyses. Furthermore, while formal validation is impractical, implementing these corrections improves the face-validity of the resulting estimates, particularly with regards to temporal trends and comparisons with alternate data sources at the national level.

Second research question

To what extent does the prevalence of health-related risk factors and health outcomes vary among counties in the US, and are inequalities increasing or decreasing over time?

This thesis considered three sets of risk factors—smoking, alcohol use, and diabetes—as well as three sets of health outcomes—cause-specific mortality rates, life expectancy, and self-reported health status. In all cases, there was considerable inequality among counties in all years examined. This was true both when considering absolute measures of inequality as well as when considering relative measures. Furthermore, there were large disparities in terms of temporal trends; for most risk factors and health outcomes, both counties with increases and counties with decreases were identified.

Figure 1 depicts the change in geographic inequality between 2002 and 2012 for many of the risk factors and health outcomes measured in this thesis, considering two measures of absolute inequality (the standard deviation and the difference between the 90th and 10th percentile) and two corresponding measures of relative inequality (the coefficient of variation and the ratio of the 90th to the 10th percentile). For all three risk factors, absolute geographic inequality increased, while relative geographic inequality increased for smoking, declined for binge drinking, and was relatively unchanged for diabetes. Absolute geographic inequality increased for all health outcomes except self-reported low general health and mortality from cardiovascular diseases and transport injuries, while relative geographic inequality increased

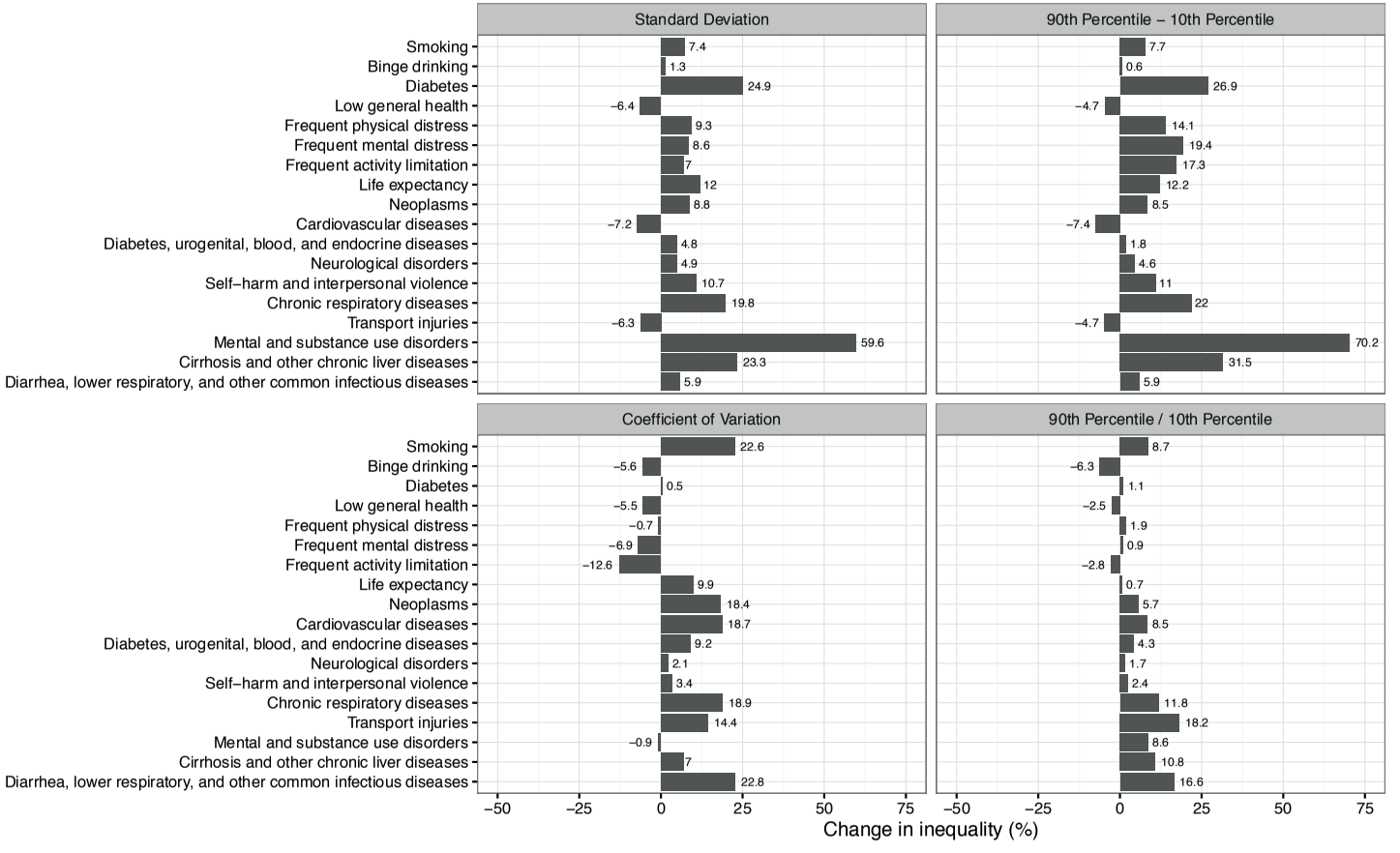

Figure 1. Change in geographic inequality between 2002 and 2012.

for most health outcomes apart from self-reported health status. The magnitude of the changes in geographic inequality varied widely among the different risk factors and health outcomes, and in some cases among different inequality measures.

Third research question

What proportion of the variation observed in life expectancy at the county level can be explained by variation in socioeconomic factors, behavioral and metabolic risk factors, and access to and quality of health care?

Chapter 6 explored the extent to which variation in socioeconomic factors, behavioral and metabolic risk factors, and health care factors can explain variation in life expectancy at the county level. Taken separately, socioeconomic factors (poverty, income, unemployment, education, and race/ethnicity) explained 60% of the variation in life expectancy while behavioral and metabolic risk factors (obesity, physical inactivity, smoking, hypertension, and diabetes) and health care factors (insurance rates, quality of care, and medical doctors per capita) explained 74% and 27%, respectively.

When considered simultaneously, all three sets of variables explained 74% of the variation, but the effect of socioeconomic factors was non-significant and the effect of health care factors was substantially reduced. This indicates that a substantial portion of the variation in life expectancy at the county level can be explained by variation in risk factors, and that much of the relationship between socioeconomic factors and risk factors at the county level is mediated via risk factors.

METHODOLOGICAL LIMITATIONS

Validation of the small area methodology

The first research question in this thesis focused on developing methods for generating county-level estimates of risk factors and health outcomes. Validating this methodology was essential to answering the first research question, nonetheless there are several important limitations related to this validation. First, although considerable emphasis was placed on validation of the methodology, it was only possible to rigorously validate the small area models. Methods related to bias corrections—e.g., garbage code redistribution when examining cause-specific mortality rates—were not validated beyond examining the face-validity of the resulting spatial and temporal trends. Second, the strategy employed to validate the small area models assumes that the counties included in the validation set differ from other counties in ways that are relevant for small area estimation only in terms of population size. This is a difficult assumption to validate and it's easy to imagine violations of this assump-

tion: for example, the degree of spatial relatedness among counties may differ between the often more densely population counties included in the validation set and more sparsely populated counties not included in the validation set. Third, the validation framework utilized is computationally expensive, so in some cases, the fact that the model performed well in one setting was taken as evidence of sufficient performance in other, similar settings: for example, with respect to mortality rates, the model was only validated for all-cause mortality, not for each individual cause considered. While this is likely often the case, there is always the possibility that the models will perform sub-optimally due to an idiosyncrasy in the data or the particular outcome considered.

Quantification of geographic inequalities

The second research question focused on quantifying geographic inequalities and evaluating whether geographic inequalities are increasing or decreasing with time. The most important limitation relevant to this portion of the analysis is related to those just discussed with respect to the first research question: the quality of an estimate of geographic inequalities is constrained by the quality of the underlying county-level estimates of risk factors and health outcomes. Moreover, small area models such as those employed in this thesis are 'shrinkage' models which work by smoothing observed data. This allows for more precise estimates overall but likely results in some under-estimation of the true variance. The extent to which this expected under-estimation may vary among different estimated quantities or over time is not clear, but to the extent that it does vary this may compromise comparisons made across indicators or conclusions drawn about temporal trends.

An additional limitation is inherent in any attempt to summarize geographic inequalities using a single metric: conclusions drawn about the relative rankings of different risk factors or health outcomes in terms of magnitude of geographic inequalities or about temporal trends in geographic inequalities are sensitive to how inequality is operationalized. Earlier in this chapter, four different inequality metrics, including two absolute and two relative measures, were used to compare temporal changes in geographic inequality among different risk factors and health outcomes. Displaying results in terms of multiple measures partially addresses this challenge, however it precludes unqualified answers to questions such as "are inequalities increasing or decreasing over time?" Moreover, it will never be feasible to consider all possible formulations of geographic inequality.

Finally, interpretation of temporal trends in geographic disparities is potentially complicated by migration. This thesis did not formerly consider the extent to which changes in the magnitude of geographic disparities are due to changes in the health of otherwise stable populations as compared to selective migration resulting in greater (or less) segregation of healthy and unhealthy individuals. Individual-level migration data linkable to the data sources used

in this thesis would be ideal for assessing the extent to which selective migration of healthier or less healthy individuals is driving changes in geographic differences in health, however these type of data are unavailable. Counts of migrants to and from each pairing of counties are available, however, and could be used to simulate the potential impact of migration under varying assumptions of the relative health status of migrants compared to non-migrants.[1,2]

Analysis of drivers of county-level inequalities in life expectancy

The third research question in this thesis focused on drivers of county-level inequalities in life expectancy. A major limitation with respect to this research question (as with the second), is the quality of the inputs to this analysis, particularly life expectancy and the risk factors included as potential drivers, all of which were estimated using a similar methodology. Moreover, the small area models used to generate estimates of both risk factors and life expectancy included several of the same or very similar covariates (e.g., education, poverty), which were in turn also used as socioeconomic variables in the analysis of drivers of county-level inequalities in life expectancy. The strength of the relationship between these socioeconomic variables and the outcome variables in the small area models (i.e., life expectancy or risk factor prevalence) was estimated as part of the model fitting process, so it's unlikely that this process itself induces correlations that do not otherwise exist. Nonetheless, there is still some possibility that the reuse of these socioeconomic variables at multiple stages of this analysis lead to an overestimation of the strength of the relationship between life expectancy and these socioeconomic variables as well as life expectancy and risk factor prevalence.

In addition to limitations related to the inputs to this part of the analysis, there are also limitations related to the model utilized to assess the contribution of different drivers to inequalities in life expectancy. A relatively small number of variables were used to represent the socioeconomic characteristics, mix of behavioral and metabolic risk factors, and health care access and quality within each county, and it is likely that not all relevant factors in each of these domains were captured. Similarly, other potentially influential domains like environmental risk factors[3,4] were not included. Furthermore, a cross-sectional design was used in order to maximize the number of factors which could be included in the analysis. This design does not allow for parsing the extent to which changes in variation in life expectancy are related to changes in variation in socioeconomic factors, behavioral and metabolic risk factors, and health care factors. Additionally, assuming these factors are causally related to life expectancy, a cross-sectional model does not allow for potential lags between 'exposure' and 'outcome', nor does it account for potential migration in the interim. Finally, the nature of this model makes it difficult to assess the extent to which the relationship between the various 'drivers' and life expectancy is due to contextual effects as compared to the composition of the individuals in a given county.

INTERPRETATION OF FINDINGS

Small area methodology

A large number of potential small area models have been proposed for estimating health-related indicators for small areas such as counties in the US and similar administrative areas in other countries.[5–11] Performance of these models has generally been assessed in one of three ways: internal validity checks, such as comparing aggregated small area estimates to direct estimates from the same data source for larger geographies (e.g., states in the US), or comparing small area estimates to direct estimates only in areas with a large sample size or population;[5–8] external validity checks comparing small area estimates to direct estimates from an alternate data source (typically a census or much larger survey);[6,9] and using simulated data so that small area estimates can be compared to a known true value.[10,11] These studies have consistently found that small area models outperform direct estimates and earlier approaches such as synthetic estimation. However, while these approaches to assessing model performance are useful, there are important limitations. Internal validity checks only assess performance at more aggregate geographies or for larger areas and provide little information about the reliability of the estimates for smaller areas. External validity checks are only possible in the limited circumstance where data for the indicator of interest are available in a census or similar data source—it is not clear that results for these indicators generalize to other risks or health outcomes. Similarly, results based on simulated data are potentially sensitive to the assumptions underlying how the simulated data were constructed and it is not clear that model performance will be the same in 'real world' applications.

This thesis used an empirical validation approach pioneered by Srebotnjak et al.[12] and previously applied to evaluating the performance of county-level small area models for diagnosed diabetes prevalence,[12] hypertension prevalence,[13] and life expectancy[14] in the US. This method avoids the limitations inherent in the previously described approaches by simulating based on the observed county-level data to be modeled, ensuring that results are applicable to the case at hand while allowing for assessment of performance for areas (in this case, counties) across a wide range of population sizes. Previous studies using this assessment methodology have reported that the small area models tested produced sufficiently precise estimates even for relatively small sample sizes (when considering survey data) or small populations (when considering life expectancy). This thesis confirms this finding for small area models applied to diabetes and life expectancy and demonstrates that this finding also holds for small area models applied to smoking, alcohol use, cause-specific mortality rates, and self-reported health. These consistent findings across a fairly wide range of outcomes and using multiple validation strategies strongly suggests that small area estimation methods are likely to be useful for many different estimation problems at the county level in the US and equivalent sub-national divisions in other countries.

In addition to confirming these earlier findings, this thesis expands upon existing knowledge in two important ways. First, chapter 5 demonstrates that there is utility in continued development of small area estimation methodologies. The model developed in this thesis for estimating mortality rates takes advantage of recent technological improvements that make fitting more complex models possible. Compared to previously described models, these developments resulted in substantially more precise, less biased estimates and more accurate quantification of uncertainty. Second, chapters 2–5 demonstrate the potential for incorporating various bias corrections into the overall estimation strategy alongside the small area models. 'Perfect' data sources are rarely available, particularly at the county level, so the ability to correct for known biases as part of an overall small area estimation strategy dramatically expands the scope of potential data sources, and therefore outcomes, that could potentially be examined.

Spatial patterns of risk factor prevalence and health outcomes in the US

Numerous previous studies have considered county-level spatial patterns in some risk factor or health outcome in the US using an assortment of methodologies.[2,5,7,12–21] Where these studies overlap with the risks and outcomes considered in this thesis, the spatial patterns described are broadly similar. For example, chapter 5 identifies areas in central Appalachia, Oklahoma, and the Southwest with elevated mortality rates from mental and substance use disorders that are comparable to the areas identified by Rossen et al.[17] as having elevated mortality rates from drug poisoning. Similarly, the results for cardiovascular disease mortality from chapter 5 are consistent with earlier reports[18] of elevated mortality from heart disease in the southeastern US.

These similarities notwithstanding, this thesis expands upon previous research on spatial patterns in risk factor prevalence and health outcomes in the US in two significant ways. First, in contrast to many earlier analyses, this thesis considered annual estimates over an extended period of time, which is the basis for two insights: in most cases, spatial patterns evolve significantly over time, and counties vary not only in their current level but also in their trajectory. Second, with respect to previous analyses of mortality, most studies have focused on a single cause of death, whereas this thesis considered a comprehensive set of 21 causes of death. Considering all causes simultaneously improves comparability and prevents double counting. Furthermore, previous analyses of mortality rates at the county level have focused on a relatively small set of causes of death (e.g., heart disease,[18,22] stroke,[21,23] breast cancer,[20] and drug use[17,24]) but little attention has been paid to other causes that account for substantial burden such as neurological disorders, infectious diseases including diarrhea and lower respiratory infections, and transport injuries. This thesis finds that spatial patterns in both the level and rate of change in mortality vary substantially by cause, highlighting the

need to consider not just spatial patterns in all-cause mortality or selected causes, but spatial patterns across a range of high-burden causes.

Increasing geographic disparities in life expectancy in the US

Studies by Ezzati et al.[2] and Wang et al.[15] both found evidence of increasing geographic disparities in life expectancy among counties in the US in recent decades. Other researchers, also using county-level data, have identified increasing disparities in life expectancy with reference to county urbanicity[25] and socioeconomic status.[26,27] Chapter 6 of this thesis confirms the earlier finding of increasing geographic disparities in life expectancy in the US over the past few decades and adds evidence that inequality has continued to increase in recent years. Moreover, the magnitude of this increase is large: the absolute gap in life expectancy between the 90th and 10th percentiles increased by 39% (1.7 years) between 1980 and 2014, with more than half the increase occurring from 2000 onwards.

Recently, Currie and Schwandt[28] used county-level data to analyze trends in all-cause mortality by poverty status, revealing different trends by age group, with inequality (with reference to county poverty) increasing among older age groups but declining among children and young adults. Chapter 6 reveals similar patterns with respect to absolute geographic disparities in risk of death from all causes, with disparities declining substantially under age 25, increasing moderately between ages 25 and 45, and increasing substantially above age 45.

Taken together, this research strongly suggests that disparities in longevity, particularly but not exclusively with reference to location, have been increasing in the US for decades primarily due to increasing disparities in mortality for middle and older ages. While this thesis did not formerly consider the extent to which these changes may be driven by selective migration (e.g., exodus of healthier individuals from less healthy locations), simulations carried out by Ezzati et al.[2] suggest that increases in county-level geographic inequality in life expectancy are unlikely to be due solely to migration patterns.

A small number of studies have considered trends in geographic disparities in life expectancy or some measure of all-cause mortality in other countries, though generally at a less granular level as compared to counties in the US. Consistent with the findings in this thesis regarding increasing geographic disparities in life expectancy at the county level in the US from 1980 to 2014, increasing geographic disparities have also been described in Canada at the provincial level from 1986 to 1997 (after earlier periods of decline),[29] in the United Kingdom at the local authority level from the 1969 to 2007 (also after earlier periods of decline),[30] and in Eastern Europe (for men only) at the region level from 1991 to 2008.[31] At the same time, decreases in geographic disparities have been identified in Austria at the commune level from 1969 to 2004,[32] in Spain at the provincial level from 1981 to 1995,[33] and in the Netherlands (for

men only) at the region level from 1988 to 2009,[34] and relatively stable levels of geographic disparities have been found at the region level in Western Europe from 1991 to 2008.[31] This variation in experience across countries highlights that increasing geographic disparities in mortality and life expectancy are neither inevitable nor irreversible.

The increase in geographic inequalities in life expectancy in the US observed between 1980 and 2014 was accompanied by an increase in geographic inequality in cause-specific mortality rates for a number of causes, particularly: mental and substance use disorders; cirrhosis and other common liver diseases; chronic respiratory diseases; self-harm and interpersonal violence; and neoplasms. This thesis did not explicitly consider the driving forces behind the observed increases in geographic inequality for these specific causes of death or for life expectancy more generally, but there are likely multiple factors at play, and these factors may have evolved over the time period considered. Describing these mechanisms will be an important area for future research and could help inform efforts to reverse these trends.

Drivers of geographic disparities in life expectancy in the US

Correlations between longevity and summary measures of socioeconomic status, racial and ethnic composition, risk factor prevalence, and health care quality and availability have previously been documented at the county level.[35–38] Cullen et al.[35] and Davids et al.[37] considered a number of these different factors simultaneously at the county level and found that collectively they can explain much of the variation in longevity among counties. This thesis again confirms these earlier outcomes, finding both that these relationships exist independently at the county level and that collectively these factors can explain the majority of the variation in life expectancy among counties in the US.

This thesis goes beyond earlier research at the county level and considers the potential for mediation of the relationship between socioeconomic factors, behavioral and metabolic risk factors, health care access and quality factors, and life expectancy. The results of this analysis suggest that essentially all of the relationship between socioeconomic factors and life expectancy at the county-level is mediated via differences in the prevalence of behavioral and metabolic risk factors.

Individual-level analysis of prospective cohort studies in both the US[39–42] and other high income countries[42–45] have consistently found that differences in behavioral and metabolic risk factors mediate the relationship between socioeconomic factors and risk of death to a substantial degree. Results vary depending on study design, socioeconomic factors considered, behavioral and metabolic risks considered, and setting, but the proportion of the relationship between socioeconomic factors and mortality risk mediated by behavioral and metabolic risk factor is typically found to be between one- and three-quarters in these

studies. Findings from individual-level analyses are thus partially consistent with the findings of this thesis: both identify a role for behavioral and metabolic risk factors in mediating the relationship between socioeconomic factors and mortality, however the magnitude of this effect is smaller in the analyses of individual-level data compared to county-level data. There are a number of potential causes for this discrepancy. The relationship between socioeconomic factors, behavioral and metabolic risk factors, and mortality may be different at the ecological level as compared to the individual level. The choice of outcome—life expectancy, accounting for deaths at all ages, compared to mortality risk, typically among middle aged or older adults only—may also matter. Furthermore, both types of analyses are potentially sensitive to unmeasured confounding.

There are important limitations to the analysis in this thesis, as previously discussed, so it is not possible to definitely characterize these county-level relationships as causal or, consequently, to assert that modifying one or more of these factors would change inequalities in life expectancy among counties. Nonetheless, the findings regarding the importance of both socioeconomic factors and behavioral and metabolic risk factors in explaining county-level variation in longevity are suggestive, and are supported by a large body of literature documenting socio-economic gradients in mortality risk among individuals and demonstrating the importance of behavioral and metabolic risk factors in explaining these socio-economic gradients.

POLICY IMPLICATIONS AND RECOMMENDATIONS

County-level estimates of risk factor prevalence and health outcomes should be used for policy development and public health practice in the US

This thesis demonstrated the practicality of reliably estimating risk factor prevalence and health outcomes at the county level using existing national data sources. There are a number of different ways that these types of data can and should be used to inform policy and public health practice, particularly regarding program development and resource allocation. First, with respect to national- and state-level policies and programs designed to target particular risk factors or health outcomes, county-level estimates should be used to identify areas most in need of intervention and with the greatest potential to benefit. As illustrated in earlier chapters, these areas vary somewhat depending on the particular outcome considered: e.g., nationally, the counties most impacted by cardiovascular diseases are located primarily in the South, while counties most impacted by cirrhosis and other chronic liver diseases are located primarily in the Western US. Second, with respect to local health departments, most of which serve a single county or small group of counties,[46] county-level estimates of risk factor prevalence and health outcomes should be used to identify the most pressing local

needs and guide resource allocation. Moreover, local estimates can be used by local health departments as evidence when advocating for additional funds from local taxpayers or state, federal, and private sources for particular programs. In both cases, using local estimates to more efficiently deploy resources is particularly important given increasingly constrained public health budgets in the US.[46]

County-level estimates of risk factor prevalence and health outcomes should be used for monitoring disparities as part of tracking progress towards national health targets

In the US, overarching national health objectives are established and tracked in decennial cycles as part of the *Healthy People* Program. The most recent iteration, *Healthy People 2020,* includes "achieve health equity, eliminate disparities, and improve the health of all groups" among its four overarching goals, and specifically identifies disparities by race, ethnicity, gender, sexual identity and orientation, disability status, and geographic location.[47] Nonetheless, tracking geographic disparities in the indicators identified in *Healthy People* targets remains largely limited to comparing the census regions (Northeast, Midwest, South, and West), metropolitan and non-metropolitan areas, or, less commonly, states. The results of this thesis clearly demonstrate important differences in both exposure to risk factors and health outcomes among counties within states and regions and in similarly urban (or rural) locations. County-level estimates of risk factor prevalence and health outcomes should be used in place of or in addition to these more aggregate measures for tracking trends in geographic disparities.

Behavioral and metabolic risk factors are an important target for improving health outcomes overall and reducing inequalities

The relationship between behavioral and metabolic risk factors such as smoking, obesity, physical inactivity, hypertension, and diabetes and increased risk of mortality is well-established at the individual level.[48] This thesis additionally provided evidence that variation in the prevalence of behavioral and metabolic risk factors at the county level is related to disparities in county-level life expectancy.

A wide range of evidence-based and cost-effective intervention strategies targeting these risk factors are available.[49] For example, increasing tobacco prices through taxes and implementing indoor smoking bans have both been shown to reduce smoking prevalence,[50,51] but many counties and states have not fully implemented these policies.[52] Mixed-use development, improved connectivity, and access to green space have been shown to increase physical activity and can be promoted through zoning regulations but are similarly variable across counties.[53–55]

Addressing behavioral and metabolic risk factors, including smoking, obesity, physical inactivity, hypertension, and diabetes, should be a priority not just for improving population health overall in the US, but also for attempting to reduce geographic disparities in longevity and other health outcomes. County-level estimates of these risk factors can be used by local and state health officials and policymakers to pinpoint targets for future interventions in particular counties or regions. National action aimed at reducing the impact of these risk factors is also warranted.

DIRECTIONS FOR FUTURE RESEARCH

There are at least five avenues for future research building on this thesis: further development and improvement of the underlying methods for estimating county-level trends; expansion beyond fatal to non-fatal health outcomes; analysis at even more local levels; analyses in other countries; and further explanatory work focused on drivers of geographic inequalities.

Methodological improvements

Among the large number of opportunities for improving the methodologies described in this thesis, there are two areas with particular potential. First: joint modeling of outcomes. Each risk factor and health outcome considered in this thesis was modeled independently and for each indicator separate models were fit for men and women. Risk factor exposures and health outcomes are often similar among men and women living in the same county; likewise, spatial and temporal patterns in health outcomes with similar underlying risk factors (e.g., lung cancer and chronic obstructive pulmonary disease, both of which are closely linked with smoking) are also likely to be similar. Thus joint modeling of related indicators and/or joint modeling for males and females may improve the precision of the resulting predictions by introducing another dimension for "borrowing strength." Second: more fully accounting for uncertainty from all stages of analysis. This thesis used simulation methods to account for parameter uncertainty from the small area models, however there are other sources of uncertainty that were not fully accounted for, most importantly the uncertainty introduced by the garbage redistribution algorithms utilized for cause-specific mortality rates, which is likely non-negligible. Developing methods to more accurately reflect uncertainty at each stage of analysis and propagate this uncertainty through to the final estimates would allow for more accurate assessments of the precision of county-level estimates.

Non-fatal health outcomes

This thesis considered primarily fatal health outcomes, examining county-level trends in cause-specific mortality rates as well as overall longevity as measured by life expectancy at birth. Self-reported health status is intended to capture information on morbidity and be

sensitive to non-fatal health problems, but is relatively non-specific. The methods developed in this thesis could be adapted for measuring non-fatal health outcomes. This will require identifying additional data sources with county-level resolution and appropriate information about non-fatal health outcomes: cancer registries, disease surveillance systems, hospital and pharmacy records, and insurance claims data are all potential data sources, though each with its own set of strengths and limitations.

More local levels of analysis

Most public health activities and many other government functions are organized by county in the US.[46] County is also the finest geographic level typically available in national data sources for health-related indicators. Consequently, counties are an important level of analysis in the US, but even more local level analyses may be useful in some settings, particularly in large and diverse counties where there is likely to be significant within-county variation in risk factor exposure and health outcomes. Where data with the necessary geographic resolution are available (possibly for a particular region, state, or county), it should be possible to adapt the methods presented in this thesis for analyses by census tract, ZIP (postal) code, or other smaller geographies.

Analyses in other countries

This thesis has focused exclusively on describing trends at the county-level in the US. The methods developed in this thesis are likely to be more broadly useful, however. Many countries have similar survey and deaths registration data with appropriate geographic identifiers for subnational analyses and the small area models described in this thesis could be applied to these type of data in other countries with minimal modification. In many cases, the validation framework used in this thesis to assess the performance of the small area models with reference to county-level trends in the US could also be repurposed in order to assess performance for various subnational units in other countries.

Further explanatory analysis

This thesis explored potential drivers of variation in life expectancy among counties, however there are at least two directions in which this analysis should be further developed. First, there is room for improvement methodologically. Ordinary least squares regression on a cross-sectional dataset was used for exploring drivers of variation in life expectancy in this thesis. More sophisticated methods would allow for a more detailed and nuanced accounting of geographic variation. In particular, using time-series methods and data would allow for exploration of what is driving changes in geographic inequalities over time. Similarly, multilevel analyses would allow for exploration of compositional versus contextual effects of the different factors considered in this thesis. Future research could also explore the sensitivity of the findings of such analyses to the inclusion of certain variables (e.g., education) in both

the small area models used to generate life expectancy and risk factor prevalence as well the final analysis of drivers of variation in life expectancy. Second, this thesis considered a relatively small set of potential drivers of inequalities in life expectancy, but a much larger pool of potential explanatory factors could be explored within a similar framework. This could include additional factors not considered here—for example, differences in features of the natural and built environment, or differences in policy or in program implementation—or could further delve into the root causes of variation in some of the factors identified in this thesis (e.g., root causes of variation in physical activity).

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Chapter 9

Summary & Samenvatting

SUMMARY

Risk exposures, health outcomes, and longevity are known to vary regionally within the United States of America (US). Relatively little, however, is known about how these health indicators vary on a smaller geographic scale. Below the state level, the US is administratively divided into approximately 3,100 counties. County-level measurements of risk exposures, health outcomes, and longevity are important for at least three reasons: local information is valuable to public health practitioners and policy-makers; geographic differences in health outcomes can facilitate identifying and addressing avoidable health differences; and understanding how health outcomes vary on a fine-scale geographically can lead to new or deeper insights into the underlying drivers of ill health.

This thesis addresses three related questions. First, can methods be developed that both address small numbers issues and also account for known biases in available data, allowing for sufficiently precise estimates of health-related risk factors and mortality for US counties? Second, to what extent does the prevalence of health-related risk factors and health outcomes vary among counties in the US, and are inequalities increasing or decreasing over time? And third, what proportion of the variation observed in life expectancy at the county level can be explained by variation in socioeconomic factors, behavioral and metabolic risk factors, and access to and quality of health care?

In this thesis, small area models are proposed for estimating smoking prevalence, excessive alcohol use prevalence, diabetes prevalence, the prevalence of poor self-reported health, cause-specific mortality rates, and life expectancy at the county level. Data from the Behavioral Risk Factor Surveillance System (BRFSS), an annual telephone survey conducted by the Centers for Disease Control and Prevention, are used for estimating county-level prevalence of smoking, alcohol use, diabetes, and poor self-reported health. For estimating cause-specific mortality rates for 21 mutually exclusive and exhaustive causes of death and life expectancy at the county level, death registration data from the National Vital Statistics System (NVSS) are used. In addition, corrections for various known biases in these data sources are implemented alongside these small area models. Finally, the estimates derived from these models are used to explore spatial patterns, quantify geographic disparities, describe changes in the magnitude of geographic disparities over time, and explore the drivers of variation in health outcomes among counties.

Chapters 2–5 describe the proposed small area models for estimating risk factor and low self-reported health prevalence based on BRFSS data and mortality rates based on NVSS data. An empirical validation strategy, based on simulating data for small areas from observed data in relatively large areas is employed to assess the performance of these models in counties of

varying population sizes. For models based on BRFSS data, this validation strategy demonstrates that the expected error associated with modeled county-level prevalence estimates is small compared to both typical levels of prevalence and the magnitude of variation among counties. For models based on NVSS data, this validation strategy demonstrates that estimates have minimal bias, relatively high precision, and well-calibrated 95% uncertainty intervals. In both cases, the models produce more precise results for counties with larger sample sizes or populations, but perform well even for very small counties. Similar small area modeling strategies are likely to be useful for estimating a wide variety of health indicators at the county level in the US and for equivalent subnational areas in other countries.

These chapters also describe methods for correcting various biases in the underlying data used to generate county-level estimates, specifically non-coverage bias due to omission of cell phones prior to 2011 in the BRFSS, discontinuities due to changes in item wording between BRFSS survey rounds, self-report bias related to undiagnosed health conditions, and bias introduced by the presence of 'garbage codes' (implausible or imprecise underlying cause of death codes) in death registration data. These corrections are difficult to formerly validate as appropriate 'gold standard' data sources do not exist, particularly at the county level. However, this thesis demonstrates that these bias corrections can be operationalized in the context of small area analyses, and noticeably improve the face-validity of the resulting estimates, particularly with regards to temporal trends and comparisons with alternate data sources at the national level.

Chapters 2–7 use the generated county-level estimates of smoking prevalence, excessive alcohol use prevalence, diabetes prevalence, cause-specific mortality rates, life expectancy, and self-reported health status to describe spatial patterns and quantify county-level geographic disparities in levels and trends. For all health indicators considered, there was considerable inequality among counties in all years examined. This was true both when considering absolute and relative measures of inequality. Moreover, there were large disparities in temporal trends in addition to levels: for most indicators, both counties with increases and counties with decreases were identified. For cause-specific mortality rates specifically, spatial patterns differed by cause, in some cases substantially, underscoring the utility of examining individual causes in addition to summary measures of health such as life expectancy.

Chapter 6 specifically focused on trends in geographic disparities in life expectancy. Between 1980 and 2014, absolute geographic inequalities in mortality risk declined for children (ages 0 to 5) and adolescents (ages 5 to 25), but increased for adults, particularly adults over age 65. This resulted in an increase in geographic inequalities in life expectancy over this period, such that by 2014 life expectancy ranged by two decades among counties. Chapter 8 compared changes in geographic inequalities for all health indicators considered in this thesis over the

decade from 2002 to 2012. Absolute geographic inequalities increased for all health indicators considered except self-reported low general health, mortality from cardiovascular diseases, and mortality from transport injuries. Relative geographic inequalities also increased for most health indicators considered, but declined for self-reported measures of poor health and binge drinking. These increasing trends in geographic inequalities across a wide range of health indicators are cause for concern as they may indicate increasing individual-level health disparities.

Finally, chapter 6 considered the extent to which variation in socioeconomic factors, behavioral and metabolic risk factors, and health care factors can explain variation in life expectancy at the county level. Taken separately, socioeconomic factors (poverty, income, unemployment, education, and race/ethnicity) explained 60% of the variation in life expectancy while behavioral and metabolic risk factors (obesity, physical inactivity, smoking, hypertension, and diabetes) and health care factors (insurance rates, quality of care, and medical doctors per capita) explained 74% and 27%, respectively. When considered simultaneously, all three sets of variables explained 74% of the variation, but the effect of socioeconomic factors was non-significant and the effect of health care factors was substantially reduced. This indicates that a substantial portion of the variation in life expectancy at the county level can be explained by variation in risk factors, and that much of the relationship between socioeconomic factors and risk factors at the county level is mediated via risk factors. Policy action to reduce geographic disparities in socioeconomic factors, exposure to behavioral and metabolic risk factors, and access to and quality of health care may all be useful for improving health overall and reducing geographic inequalities. Targeting behavioral and metabolic risk factors may be particularly profitable given the strength of the relationship between variation in these risk factors and variation in life expectancy and the evidence that the relationship between socioeconomic factors and life expectancy is mediated largely via these risk factors.

SAMENVATTING

Het is bekend dat er regionale verschillen bestaan in risicofactoren van de gezondheid, in gezondheidsuitkomsten en in sterftepatronen in de Verenigde Staten (VS). Er is echter nog weinig bekend hoe deze gezondheidsindicatoren verschillen tussen kleine geografische eenheden. Staten in de VS zijn administratief onderverdeeld in ongeveer 3100 "counties". Metingen van (risicofactoren van de) gezondheid en sterfte op het niveau van deze counties is belangrijk om tenminste drie redenen: het is van belang voor professionals in de volksgezondheid en voor lokale beleidsmakers; geografische verschillen in gezondheidsindicatoren kunnen helpen bij het identificeren en reduceren van vermijdbare gezondheidsverschillen; en begrip van de variatie in gezondheid tussen kleine geografische eenheden kan leiden tot beter inzicht in de onderliggende oorzaken van gezondheidsproblemen.

Dit proefschrift beantwoordt deze onderling aan elkaar gerelateerde vragen. Ten eerste wordt onderzocht of methoden kunnen worden ontwikkeld die problemen met kleine aantallen aankunnen, tegelijkertijd rekening houden met bias in beschikbare data, en zo tot voldoende nauwkeurige schattingen kunnen leiden van (risicofactoren van) de gezondheid en sterfte in counties in de VS. Ten tweede wordt onderzocht in hoeverre de prevalentie van (risicofactoren van) gezondheid en sterfte tussen counties in de VS varieert, en of de ongelijkheid tussen counties in deze uitkomsten toe- of afgenomen is in de afgelopen jaren. Ten derde wordt bestudeerd welk deel van de variatie in de levensverwachting tussen counties kan worden verklaard door variatie in sociaaleconomische factoren, ongezond gedrag en metabole risicofactoren, en door toegang tot en kwaliteit van de gezondheidszorg.

In dit proefschrift zijn eerst "small area" modellen ontwikkeld voor het schatten van de prevalentie van roken, excessief alcoholgebruik, diabetes, een slecht ervaren gezondheid, en van doodsoorzaakspecifieke sterfte en de levensverwachting in counties. Gegevens van het Behavioral Risk Factor Surveillance System (BRFSS), een jaarlijks afgenomen telefonische enquête uitgevoerd door het Centers for Disease Control and Prevention, werden gebruikt voor het schatten van de prevalentie in roken, alcoholgebruik, diabetes en een slecht ervaren gezondheid. Voor het schatten van de doodsoorzaakspecifieke sterfte van 21 elkaar uitsluitende doodsoorzaken en de levensverwachting in counties, is gebruik gemaakt van data van de sterfteregistraties van het National Vital Statistics System (NVSS). Verder zijn correcties voor verschillende vormen van bias in deze databronnen geïmplementeerd in de modellen. Tenslotte zijn de schattingen die met de modellen werden verkregen gebruikt om ruimtelijk patronen te beschrijven, geografische ongelijkheid te kwantificeren, veranderingen in de omvang van deze ongelijkheden over de tijd te bestuderen, en de oorzaken van de variatie tussen counties te verkennen.

Hoofdstukken 2-5 beschrijven de ontwikkelde small-area modellen voor het schatten van de prevalentie van risicofactoren en diabetes gebaseerd op de BRFSS data, en sterftecijfers uit de NVSS database. Een empirische strategie voor de validatie, gebaseerd op gesimuleerde data voor kleine geografische gebieden die waren afgeleid van geobserveerde data in relatief grote gebieden, is gebruikt om te testen hoe goed de modellen presteerden in counties met een verschillende bevolkingsgrootte. Voor modellen gebaseerd op de BRFSS data werd gevonden dat de verwachte fout voor de gemodelleerde prevalenties in counties klein was, ten opzichte van gangbare prevalenties en de omvang van de variatie in prevalenties tussen counties. Voor modellen gebaseerd op de NVSS data werd gevonden dat schattingen een minimale bias hadden, een relatief hoge nauwkeurigheid en goed gecalibreerde 95% "onzekerheidsintervallen" hadden. In beide gevallen produceerden de modellen nauwkeuriger resultaten voor counties met grotere steekproeven of populaties, maar werkten zij ook goed voor counties met een kleine populatie. Vergelijkbare small-area modellen zijn vermoedelijk nuttig voor het schatten van een variëteit van gezondheidsuitkomsten op het niveau van counties in de VS en voor vergelijkbare regionale gebieden in andere landen.

Deze hoofdstukken beschrijven ook methoden voor het corrigeren van verschillende vormen van bias in de data, die werden gebruikt voor het genereren van de schattingen. Het gaat hierbij in het bijzonder om de bias die wordt veroorzaakt doordat een deel van de potentiële BRFSS deelnemers niet telefonisch kon worden bereikt omdat ze geen mobiele telefoon hadden (voor 2011), om bias door veranderingen in de formulering van items tussen verschillende ronden van dataverzameling in de BRFSS, bias die wordt veroorzaakt door zelfrapportage van niet-gediagnosticeerde gezondheidsproblemen, en de bias die wordt veroorzaakt door niet plausibele of onduidelijke doodsoorzaken in de doodsoorzakenregistratie. Deze correcties zijn vaak moeilijk formeel te valideren omdat databases met een gouden standaard niet bestaan, vooral niet op het niveau van counties. Het proefschrift laat echter zien dat correcties voor deze vormen van bias kunnen worden uitgewerkt en toegepast in de context van small area analyses, en daarmee de indruksvaliditeit van de schattingen duidelijk verbeteren vooral ten aanzien van trends over de tijd en vergelijkingen met databronnen op landelijk niveau.

Hoofdstukken 2-7 gebruiken de schattingen van de prevalentie van roken, excessief alcoholgebruik, diabetes, de doodsoorzaakspecifieke sterftecijfers, levensverwachting en ervaren gezondheid om ruimtelijke patronen te beschrijven, en om de omvang van en trends in geografische ongelijkheid te kwantificeren. Voor alle gezondheidsindicatoren die werden bestudeerd bestond aanzienlijke variatie tussen counties in de bestudeerde tijdsperiode. Dit was zowel het geval voor maten van de absolute als de relatieve ongelijkheid. Er was ook grote variatie in trends over de tijd. Voor de meeste gezondheidsindicatoren konden zowel counties worden geïdentificeerd met een toename als met een afname in de prevalentie.

Vooral voor doodsoorzaakspecifieke sterfte varieerde de patronen naar doodsoorzaak soms zelf substantieel, waarmee wordt benadrukt dat het zinnig is zowel afzonderlijke doodsoorzaken als samengestelde maten van de volksgezondheid (zoals de levensverwachting) te bestuderen.

Hoofdstuk 6 richtte zich specifiek op trends in geografische ongelijkheid in de levensverwachting. Tussen 1980 en 2014 daalde de absolute ongelijkheid tussen counties in sterfte voor kinderen (van 0 tot 5 jaar) en van kinderen, adolescenten en jong volwassenen (van 5 tot 25 jaar), maar nam de ongelijkheid onder volwassenen van 65 jaar en ouder toe. Dit resulteerde in een toename van geografische ongelijkheid in de levensverwachting over deze periode; in 2014 varieerde de levensverwachting meer dan twintig jaar tussen counties. Hoofdstuk 8 vergeleek de veranderingen in geografische ongelijkheid voor alle andere gezondheidsindicatoren die in dit proefschrift werden bestudeerd tussen 2002 en 2012. De absolute geografische ongelijkheid nam toe voor alle gezondheidsindicatoren, maar daalde voor een slecht ervaren gezondheid en voor "binge drinken". Deze toename in geografische ongelijkheid voor diverse gezondheidsindicatoren vormt een bron van zorg, omdat ze een indicatie kunnen zijn van toenemende ongelijkheid op het individuele niveau.

Hoofdstuk 6 bestudeerde tenslotte ook de mate waarin variatie in sociaaleconomische factoren, ongezond gedrag, metabole risicofactoren en gezondheidszorggerelateerde factoren de variatie in levensverwachting tussen counties kan verklaren. Afzonderlijk bestudeerd verklaarden sociaaleconomische factoren (armoede, inkomen, werkloosheid, opleidingsniveau en ras/etniciteit) 60% van de variatie in de levensverwachting. Obesitas, ongezond gedrag (lichamelijke inactiviteit, roken) en metabole risicofactoren (hypertensie en diabetes) verklaarden 74% en gezondheidszorggerelateerde factoren (percentages verzekerden, de kwaliteit van de zorg en het aantal artsen per hoofd van de bevolking) verklaarden 27% van de variatie in de levensverwachting. Alle drie groepen samen verklaarden 74% van de variatie, maar de bijdrage van sociaaleconomische factoren was in dit model niet statistisch significant en de bijdrage van gezondheidszorggerelateerde factoren werd in dit model aanzienlijk verkleind. Dit impliceert dat een aanzienlijk deel van de variatie in levensverwachting tussen counties kan worden verklaard door variatie in ongezond gedrag en metabole risicofactoren, en dat veel van het verband tussen sociaaleconomische factoren en de levensverwachting wordt verklaard door deze risicofactoren. Beleidsmaatregelen gericht op de verkleining van geografische ongelijkheid in sociaaleconomische factoren, blootstelling aan ongezond gedrag en metabole risicofactoren, en toegang tot en kwaliteit van de gezondheidszorg kunnen bijdragen aan het verbeteren van de volksgezondheid en het terugbrengen van de geografische ongelijkheid. Maatregelen gericht op gezond gedrag en metabole risicofactoren kunnen hierbij van bijzondere waarde zijn, vanwege de sterkte van het verband tussen variatie in deze risicofactoren en variatie in levensverwachting, en

het bewijs dat het verband tussen sociaaleconomische factoren en levensverwachting wordt verklaard door deze risicofactoren.

Appendix

Curriculum vitae

List of publications

PhD portfolio

Acknowledgments

CURRICULUM VITAE

Laura Dwyer-Lindgren was born on August 26th, 1986 in Hinsdale, Illinois in the United States. She obtained a bachelor's degree in biology and chemistry from Greenville College in Greenville, Illinois in 2008 and a master of public health degree from the University of Washington in Seattle, Washington in 2012. From 2009 to 2012, Laura was a post-bachelor fellow at the Institute for Health Metrics and Evaluation (IHME) at the University of Washington where she contributed to the Global Burden of Diseases, Injuries, and Risk Factors 2010 (GBD2010) Study and the Malaria Control Policy Assessment (MCPA) Project. From 2012 to 2017, Laura was a researcher at IHME where she contributed to research on county-level trends in risk factors and mortality rates in the US and to the Gavi Full Country Evaluation in Bangladesh, Mozambique, Uganda, and Zambia. From 2014 to 2017, Laura worked on a PhD in the Department of Public Health at Erasmus MC, Rotterdam.

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Roth GA, **Dwyer-Lindgren L**, Bertozzi-Villa A, Stubbs RW, Morozoff C, Naghavi M, et al. Trends and patterns of geographic variation in cardiovascular mortality among US counties, 1980–2014. *JAMA*. 2017;317(19):1976–92.

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**This thesis

PHD PORTFOLIO

Name: Laura Dwyer-Lindgren	PhD period: 2013–2017
Erasmus MC Department: Public Health	Promotor: Prof.dr. Johan P Mackenbach
Research School: NIHES	Promotor: Prof.dr. Frank J van Lenthe

1. PhD training	Year	Workload	
		Hours	ECTS
General courses			
Strategic Leadership Program	2015	28	
Integrity in Science	2016		0.3
Project Management Essentials	2016	14	
Specific courses			
Environmental and Occupational Health	2011		3
Bayesian Statistics for the Social Sciences	2011		4
Intro to Epidemiology	2011		4
Spatial Epidemiology	2012		3
Society and Health	2012		3
Social Epidemiology	2015		0.7
Policy Development and Advocacy for Global Health	2016		3
Causal Mediation Analysis	2016		0.7
Seminars and workshops			
Researcher Journal Club	2013–2015	80	
IHME Seminar	2013–2015	70	
Methods & Metrics Seminar	2016	15	
Presentations			
IHME Internal Research Seminar *('Small Area Estimation of Smoking Prevalence in the US')*	2013		1
CDC Seminar *('Salt, Sugar, and Smoke: Mapping Health Risks in the US')*	2014		1
National Tobacco Control Program Technical Assistance Webinar *('Cigarette Smoking Prevalence in US Counties')*	2014		1
Conferences			
PAA Annual Meeting	2013		1
IUSSP	2013		1
APHA Annual Meeting	2013		1
PAA Annual Meeting	2015		1
Spatial Statistics Conference (poster presentation)	2015		1
NACCHO Annual Meeting	2015		1
APHA Annual Meeting	2016		1
2. Teaching			
Supervising post-bachelor fellows	2014–2017	200	
Supervising masters theses	2015–2016	20	
'Introduction to R' course (2 days)	2015	24	
'Introduction to R' course (4 days)	2016	48	
Total		**499**	**31.7**

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