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Bending the Curve in Cardiovascular Disease Mortality: Bethesda + 40 and Beyond

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Abstract

More than 40 years after the 1978 Bethesda Conference on the Declining Mortality from Coronary Heart Disease (CHD) provided the scientific community with a blueprint for systematic analysis to understand declining rates of CHD, there are indications the decline has ended or even reversed despite advances in our knowledge about the condition and treatment. Recent data show a more complex situation, with mortality rates for overall cardiovascular disease (CVD), including CHD and stroke, decelerating while those for heart failure are increasing. To mark the 40th anniversary of the Bethesda Conference, the National Heart Lung and Blood Institute (NHLBI) and the American Heart Association (AHA) co-sponsored the “Bending the Curve in Cardiovascular Disease Mortality: Bethesda + 40” symposium. The objective was to examine the immediate and long-term outcomes of the 1978 conference and understand the current environment. Symposium themes included trends and future projections in CVD (in the US and internationally), the evolving obesity and diabetes epidemics, and harnessing emerging and innovative opportunities to preserve and promote cardiovascular health (CVH) and prevent CVD. In addition, participant-led discussion explored the challenges and barriers in promoting CVH across the lifespan and established a potential framework for observational research and interventions that would begin in early childhood (or ideally in utero). This report summarizes the relevant research, policy and practice opportunities discussed at the symposium.

Keywords

Cardiovascular Disease Prevention; Cardiovascular Health Promotion; Lifespan; Trends

Introduction

The 1978 Bethesda Conference on the Declining Mortality from Coronary Heart Disease¹ brought together a panel of international experts from a wide range of disciplines, including epidemiology, clinical cardiology, and public health. The panel called attention to the previously unappreciated and unexplained abatement of the epidemic of coronary heart disease (CHD). A report stemming from the 1978 conference served in many ways as a model for a systematic and careful analysis for understanding the decline in CHD mortality. The panel concluded that the decline was almost certainly real and likely due to multiple factors, including changes in risk factor profiles and improved clinical management. However, this phenomenon appeared to be confined to the United States (US) with only equivocal evidence that similar declines were occurring in other countries. In the ensuing years, age-adjusted cardiovascular death rates have continued to decline sharply in many countries though less so in the US (since about 2010).² Despite increased knowledge and advances in treatment made over the 40 years since the Bethesda Conference, several

questions remain about the decline, including whether it has halted or reversed in the US, why that may be happening, and why disparities have persisted.

In 2018, the National Heart, Lung, and Blood Institute (NHLBI) and the American Heart Association (AHA) co-sponsored a symposium held during the AHA's 2018 Scientific Sessions titled, "Bending the Curve in Cardiovascular Disease Mortality: Bethesda + 40." The intent was to review the short-term outcomes following the 1978 Bethesda Conference, contemporary trends in and the current burden of total cardiovascular disease (CVD) in the US in comparison with global CVD mortality trends, potential determinants of these trends, and emerging opportunities to preserve and promote cardiovascular health (CVH) and prevent CVD. This report summarizes the symposium and identifies relevant research, policy, and practice opportunities.

The Aftermath of the 1978 Bethesda Conference

The goals of the 1978 conference included determining whether the decline was real and, if so, the potential factors underlying it and to suggest new studies to monitor and understand trends. The panel's recommendations focused on improved surveillance systems, standardized data collection and endpoints, and opportunities for prevention and therapeutic trials. The NHLBI and the scientific community responded to those recommendations with a substantial investment in population studies, including cohort studies and surveillance projects (Supplemental Table). By substantially increasing the understanding of the causes of all common forms of CVD, the progression of subclinical disease, and the precipitators of clinical events, those cohort studies and surveillance projects provided insight into factors that underly recent trends.

The Current Pattern of CVD in the US

Vital Statistics for Patterns in CVD mortality

CVD—a broad category that includes CHD, stroke, heart failure (HF), and other heart diseases (HD) and CVD—has been the leading cause of mortality in the US since 1910, with the exception of the flu pandemic years 1918–1920. CHD mortality rates have decreased nearly 75% since 1968 (Figure 1). In recent years, from 1999 to 2011, the average annual percent change in the age-adjusted mortality rate was –3.8% for total CVD, –5.0%, for CHD, and –4.5% for cerebrovascular disease (Figure 2).³ However, the rate of decline slowed considerably thereafter beginning in 2011 to less than 1% annualized from 2011 to 2018 for total CVD with near stagnation of mortality rates from total CVD. However, there is some heterogeneity in trends by CVD subgroups. CHD mortality, which accounts for well over half of all HD deaths and is by far the most common underlying cause of cardiovascular death listed on death certificates, has continued to decline with a pattern similar to total CVD. In contrast, the age-adjusted mortality rate from other HD, in particular HF, which accounts for 12.4% of all HD deaths as ascertained by the underlying cause, increased by 20.0% from 2011 to 2016.^{4, 5}

Racial/ethnic disparities have been persistent in total CVD mortality and deaths due to leading subtypes of CVD, including CHD and stroke (Figure 3).⁶ For example, Black and

White individuals had similar HD rates in 1968 (1071.6 per 100,000 in Black individuals; 1032.2 per 100,000 in White individuals) but the rates began to diverge around 1975 when the rate of decline became faster for Whites.⁶ As a result, from 1968 to 2015, the Black-White disparity in HD death rates increased 16.3%. Black individuals continue to have the highest mortality for total CVD, CHD, and stroke compared with all other racial/ethnic groups.⁷ In particular, the largest Black-White disparities persist in cardiovascular deaths related to hypertension and heart failure (Supplemental Figure 1). In contrast, White individuals have a higher rate of cardiovascular deaths related to atrial fibrillation than Black individuals.⁸ Disparities are also prominent by urbanization status in the US with rural counties having greater age-adjusted mortality rates for CVD compared with more urban counties (Figure 4).⁹

In contrast with the continued declining rate of HD (including CHD and all other HD) mortality, the absolute number of deaths from HD has increased steadily from 2011 to 2016 by 6.2%, after declining 16.1% (from 710,760 to 596,577) from 2000 to 2011.¹⁰ The increase in absolute numbers is multifactorial and can be attributed, at least in part, to population growth and aging as well as increasing prevalence of obesity and diabetes. Specifically, the population of older adults (65 years and older), which accounts for approximately 80% of all HD deaths, grew by 19% from 2011 to 2016, a 5-fold greater increase than the overall population.¹⁰ By 2030, the population of older adults is projected to increase an additional 49% from 49.2 million to 73.1 million. Therefore, the number of HD deaths will continue to grow unless the rate of decline of the HD mortality rate accelerates to overcome the approximately 3% annual increase in the population of older adults. In particular, among HD deaths, the rate of growth of HF deaths is likely to be higher based on the relatively larger increases in HF deaths in older adults since 2011. The projected growth of HD deaths may be further amplified through direct and indirect sequelae of the novel coronavirus 2019 (COVID-19) pandemic based on preliminary reports identifying excess cardiovascular deaths in 2020 to-date.¹¹

Community Surveillance for Non-Fatal CVD Events

The Atherosclerosis Risk in Communities (ARIC) Study¹² initiated in 1985 as a response to opportunities identified in the 1978 Bethesda Conference, addressed a fundamental goal of the conference to further our understanding of secular trends in CHD mortality.^{13, 14} Community surveillance methods used in ARIC were developed in the Community Cardiovascular Surveillance Program (CCSP), which was conducted from 1981 to 1984 with funding from the National Institutes of Health (NIH) with aim of designing, planning, and conducting a feasibility study of a surveillance system for CVD. ARIC community surveillance conducted continuous, population-based retrospective surveillance of hospital discharges and out-of-hospital deaths from 1987 through 2014 in persons age 35–74 (extended to 84 in 2005) in four geographically defined communities (Forsyth County, NC; Jackson, MS; suburban Minneapolis, MN; and Washington County, MD). Deaths due to CHD as well as hospitalized myocardial infarction (MI) events were identified and validated through review of medical records for hospitalization events and interviews with witnesses and other informants for out-of-hospital deaths. A strength of the ARIC community surveillance study was its focus on evaluating and measuring the two main constituents of

trends in CHD mortality: trends in the incidence of MI and trends in survival after MI. In an analysis of event trends, simulation-based inference was used to estimate trends in rates of events per 10,000 persons per year in the four communities across age, race, and sex groups. The simulation-based approach allowed testing whether the absolute decrease in event rates per year from 2011 to 2014 was slower compared with 1987–2010. Although rates of validated CHD mortality have declined dramatically in the past 30 years, the models found a high probability that the decline in CHD mortality rates indeed slowed from 2011 to 2014, particularly among individuals older than 50 years of age. The evidence supported the conclusion that the flattening of trends for CHD mortality rates in these communities was a function of flattening of trends for both MI incidence and post-MI survival. These data from community-based surveillance are consistent with the national data described above, provide insight into some of the potential influences underlying those trends, and underscore the importance of revitalizing prevention approaches to reduce CHD burden in the community. They also underscore the ongoing need for active surveillance programs for chronic diseases of aging in the US, since national death data rely on death certification (with its inherent limitations) and there are no current national surveillance systems for incident non-fatal CVD events.

An International Perspective on CVD Morbidity and Mortality Trends

In 2017, CVD was the leading cause of death worldwide, accounting for nearly 32% of all deaths (Of the 55.9 million total deaths, 17.8 million were CVD deaths).¹⁵ Nearly 54% of CVD deaths were caused by CHD and 31% by stroke. CVD contributed to 15% of the global burden of disability-adjusted life years (DALY),¹⁶ and the onset of CVD tends to occur at significantly younger ages in low- and middle-income countries (LMICs) compared with high-income countries.¹⁷ LMICs have the highest prevalence of CVD, accounting for more than 75% of CVD events worldwide. While the absolute burden of CVD has increased globally and has shifted heavily toward LMICs (largely because of population growth and aging), age-adjusted CVD mortality rates have declined in some LMICs, albeit gradually compared with the steep declines observed in many high-income countries (Figure 5). Further, the largest causes of mortality in many of these countries continue to undergo an epidemiological transition from predominantly infectious diseases to non-communicable diseases in a compressed time frame, leading to a dual burden of disease, with substantial variation between countries. Addressing this significant burden of CVD in such a wide variety of rapidly developing and under-developed countries requires an understanding of the complex dynamics of CVD risk factors and their interactions. Particularly relevant are the inequities in access to health care — specifically, availability and distribution of evidence-based and high-quality care in LMICs. However, the capacity to deliver such care is limited, with many LMICs having less than optimal numbers of health care providers (who are also maldistributed between urban and rural locations), which worsens the inequities in cardiovascular care. Furthermore, little research has been conducted in LMICs, with more than 80% of research and research funding available from the high-income countries that bear only 20% of the world's disease burden.¹⁸ As a consequence, the applicability of research findings to LMIC settings is uncertain.

Likely Contributors to the Decline and Stagnation of US and Global CVD Mortality Rates

Application of IMPACT and CHD Policy Models in the US and Globally—The decline in CVD mortality is one of the most significant epidemiological phenomena of the 20th century, with massive reductions in CHD mortality of more than 60% in multiple western countries over four decades.¹⁹ In the Multinational Monitoring of Determinants and Trends in Cardiovascular Disease (MONICA) study populations, CHD mortality rates fell 4% per year. About two-thirds of the observed decline could be attributed to the fall in incident event rates, while one third was attributable to reductions in case fatality.²⁰ Modelling studies are also consistent in identifying the drivers of the CHD epidemic. Both the IMPACT and US CHD policy models suggested that in the US population between 1980 to 2000, risk factor changes and improvements in treatments accounted for roughly equal proportions of the mortality decline. Specifically, the IMPACT model aims to explain the changes in CHD mortality rates observed in the US population and other countries by quantifying the contributions from national trends in CHD risk factors and treatments for CHD. This model found that approximately 44% was attributable to changes in risk factors, including reductions in total cholesterol (24%), systolic blood pressure (20%), smoking prevalence (12%), and physical inactivity (5%) that were offset by increases in the prevalence of obesity and diabetes (–17%).²¹ These increases in obesity and diabetes continued to be a major concern in children and adults between 1999 to 2015, with an attributable burden for mortality and disability that was substantial.²² Currently, obesity and diabetes contribute to 14% of deaths and 11% of DALYs in the US, an increase of 45% for DALYs from 1990 to 2010.²³ Apart from trends in hypertension prevalence, other CHD risk factors in the US show a favorable direction, with declines in tobacco smoking and cholesterol levels and increases in physical activity. However, these risk factors still account for a substantial amount of years of life lost and DALYs in the US. Many of these risk factors are, in large part, determined by unhealthy diets, and 26% of deaths and 14% of DALYs are attributable to the independent contribution of dietary composition.²³

Across numerous countries, the IMPACT model has consistently found that 40%–72% of the decline in CHD deaths could be attributed to risk factor changes and 23%–55% to treatments. Particularly powerful drivers included population-wide declines in smoking, blood pressure and cholesterol levels, and improvements in acute care and secondary prevention interventions, including heart failure treatments. In regions where CHD rates were increasing, such as Beijing or Tunisia, adverse population-level trends in smoking, cholesterol and blood pressure drove mortality upwards.^{24,25} An interesting observation from IMPACT modelling is the halving of the CHD mortality rates in Poland following almost immediately after the massive socioeconomic changes during the 1990s. Risk factor changes at the population level explained about 54% of the decline and 37% was explained by the increased use of evidence-based treatments.²⁶ This is an example of how trends can change swiftly, driven by risk factor changes and social policy at the population-level.

Contribution of Obesity and Diabetes to CVD Trends—Obesity has reached epidemic levels in the present era—affecting 42.4% of the US population over age 20 years in 2017–2018²⁷ compared with 15% at the time of the 1978 Bethesda Conference.^{28, 29} Future projections based on state-level distributions of body mass index from 1993 to 2016

predict a 50% prevalence of obesity by 2030 with some states approaching 60% and no state below 35%. Obesity is associated with multiple cardiovascular and other adverse health outcomes,³⁰ including earlier onset of CVD and all-cause morbidity translating into a shorter health-span and overall life-span. Type 2 diabetes is often cited alongside obesity given their interrelated pathophysiology³¹ and parallel increases over time.³² Diabetes affects 12.3% of US adults older than 20, and nearly one in four (24.7%) older adults over 65 has diabetes.³³ With few exceptions, racial/ethnic minorities and adults and children with fewer socioeconomic resources experience the greatest burden of obesity and diabetes.³⁴ With rising rates of obesity among children and adolescents, and changing demographics of our society (e.g., aging, immigration, and diversification by race and ethnicity),³² populations at risk for obesity and diabetes will continue growing.

The modern obesity epidemic emerged as a result of multiple societal factors that influenced energy balance. With the growth of the workforce in the 1980s and 1990s and longer work hours, the consumption of energy-dense and nutritionally poor “convenience” or “fast” foods and beverages (e.g., processed foods, packaged foods) increased. At the same time, automation of occupational tasks by computers coupled with longer commute times, as families moved to suburban communities and away from cities, reduced physical activity at work and constrained leisure time available for physical activity. What had been societal changes in the 1980s have normalized in the contemporary era, and new threats, including mobile technologies, have emerged that promote sedentary behaviors and interrupt sleep. Despite the clear threat for increases in future obesity prevalence posed by these trends in behavioral factors, few interventions short of bariatric surgery have demonstrated success in sustained weight management.³⁵

A biologically plausible consequence of the obesity epidemic is a leveling—with an eventual increase— of the prevalence of CVD following decades of decline. A rigorous body of research across basic, clinical and population domains describes the action of adipose tissue secreting hormones that damage the vasculature and cause systemic low-grade inflammation.³⁶ Population studies that estimate the contribution of obesity to CVD based on attributable fractions (i.e., the theoretical proportion of disease that could be prevented if the exposure is completely eliminated in the population), report that between 7%–44% of CVD events are due to obesity.^{37, 38} Obesity and diabetes are two of the four metabolic risk factors (in addition to high blood pressure and dyslipidemia) that are estimated to account for 60% of CVD mortality worldwide.³⁹ These estimated fractions vary by demographic characteristics (e.g., sex, race/ethnicity, age), adjustments for covariates and outcome (e.g., fatal, incident, and type of CVD). Further, the disparate burden of obesity and diabetes experienced by racial/ethnic minorities may underlie the marked disparities in some CVD subtypes such as heart failure.^{40, 41}

Role of Social Determinants Towards CVD Morbidity and Mortality

Recent reports from the Institute of Medicine (IOM)⁴² and the AHA⁴³ have highlighted the critical role that social determinants of health (SDOH) may play in CVD health outcomes. The World Health Organization (WHO) defines SDOH as the “structural determinants and conditions in which people are born, grow, live, work, and age” that affect health,

functioning, and quality of life.⁴⁴ There are five key domains of SDOH: economic stability, neighborhood and built environment, education, social and community context, and health and health care.⁴⁵ These constructs cover a number of critical factors including socioeconomic status, adverse life course experiences, social support, family structure, access to care, neighborhood environment, and stress, including stress associated with perceived or actual discrimination.^{43, 46}

Economic stability and education have been linked with individual metrics of CVH and CVD outcomes in cross-sectional and longitudinal studies.^{43, 47} Those with low education tend to have poorer levels of CVH, including higher rates of smoking, obesity, high blood pressure, and high total cholesterol, compared with well-educated groups.⁴⁸ Additionally, racial/ethnic differences in modifiable CVH behaviors, such as smoking, physical activity, and diet, may be primarily explained by socioeconomic factors.⁴⁹ Low socioeconomic status throughout life, and especially starting in childhood, is also associated with poor levels of the CVH component metrics.⁵⁰ A recent meta-analysis⁵¹ found that almost all studies showed a relationship between childhood adversity and adult CVD risk, underscoring the critical role of these factors for primordial prevention of CVD. Several systematic reviews and meta-analyses have also shown that neighborhood disadvantage and features of neighborhood built environment (e.g., healthy food access, walkability/physical activity access) are associated with CVD risk factors, events, and mortality.^{52–54} Neighborhood and other social factors may explain the substantial geographic variation in CVD mortality even within cities across census-tract levels.⁸ For example, Figure 6 shows census tract-level heterogeneity in both age-adjusted prevalence of CHD and the Centers for Disease Control and Prevention's social vulnerability index (SVI) for three major metropolitan cities in the US⁵⁵ with the largest life expectancy gap (Chicago; Washington, DC; and New Orleans). The marked variation in the age-adjusted prevalence of CHD clearly mirrors that of the SVI at the neighborhood level. Clinical and public health attempts to improve CVH and reduce the burden of CVD are unlikely to be successful unless the background disparities in multi-level social determinants of health over the lifespan are also addressed.

Bending the Curve: Reigniting Progress and Achieving CVH Equity

The following sections highlight several strategies that might be employed more effectively to address the challenge of CVD prevention and CVH promotion. These approaches leverage efforts to understand better and intervene to reverse current adverse trends and promote favorable trends in health care delivery, health behaviors, and social conditions.

Million Hearts

Million Hearts is a national initiative in the US, co-led by the Centers for Disease Control and Prevention and the Centers for Medicare and Medicaid Services and executed by over 100 public and private partners.⁵⁶ The goal is to prevent one million heart attacks, strokes, and related events over a five-year period through ambitious but achievable targets on a small set of high-impact indicators of CVH. In its first five-year phase (2011–2016), Million Hearts reported no change in population-level measures of aspirin use for secondary

prevention, blood pressure control, statin use, or daily sodium consumption. Physical activity and tobacco prevalence improved modestly.⁵⁷

In total, 213 million opportunities to prevent CVD events were missed during 2011–2016: 9 million people with an indication for aspirin did not take it; 40 million had uncontrolled hypertension (based on a goal <140/<90 mmHg); 39 million were not on a statin despite an indication based on most current evidence; 54 million smoked; and 71 million did not get at least 150 minutes of physical activity a week.⁵⁷ Notably, middle-aged individuals (35–64 years old) are less likely than those older or younger to take a recommended daily aspirin or statin and they consume more sodium⁵⁷. A third of middle-aged individuals are physically active for less than ten minutes a week, an only about half of those with hypertension have it under control. Between 2010 to 2015, more than 50% of U.S. counties showed an increase in mortality from cardiac causes in middle-aged individuals.⁵⁸

Bright spots across the country shed light and hope on this situation. Over 100 “Million Hearts Hypertension Control Champions,” who represent individual practitioners, health systems and community health centers, have been recognized for achieving control rates of over 80%⁵⁶, and many clinicians are adopting out-of-office monitoring of blood pressure, in accordance with national guideline recommendations.⁵⁹ However, such success stories are not yet widespread. Even more challenging is how to implement complex policies aimed at obesity prevention and management, such as sugar-sweetened beverage taxation and changes within the built environment to promote physical activity and prevent food insecurity.
52–54, 60, 61

Without the systematic spread of preventive actions, over 16 million CVD events will occur between 2017 to 2022, including 2.2 million emergency department visits, 11.8 million hospitalizations, and 2.2 million deaths.⁶² Prevention, early detection, and control of a few common risk factors would reduce the prevalence of these events and the loss of family members, friends, and co-workers to a largely preventable disease. A sustained, national focus on implementing effective prevention strategies in communities, health care settings, and homes would help bend the curves of CVD rates down again, realizing the vision of the original Bethesda conferees.

Dissemination and Implementation Research

The limited successes to date observed in Million Hearts underscore the importance of research on effective implementation of evidence-based programs and policies in practices and communities. Active dissemination and implementation research in health (DIRH) provides a unique opportunity to reverse the stalled CHD mortality decline and drive progress in CVH. At its core, DIRH addresses the gap between the promise of proven, effective health interventions and their successful, sustained implementation in the real world.⁶³ DIRH provides a framework for accelerated adoption, adaptation, scale-up, and dissemination of effective strategies for the prevention, treatment, and control of diseases and risk factors. Embracing DIRH in CVD prevention and control in acute and chronic management of CVD could help galvanize reversal of the adverse CHD mortality trends. For example, although the hypertension control rate at the national level has stagnated over the past decade and currently is at 48.3%,⁶⁴ there is compelling evidence that control rates of

80%–90% are achievable in clinical practice, even in large, ethnically diverse populations.⁶⁵ If a successful national program of active dissemination, implementation, and scale-up of lessons learned from these DIRH studies could be put into practice, an enormous number of lives could be saved or prolonged without morbidity. A similar approach could address dyslipidemia, heart failure, and several other CVD conditions and risk factors for which knowledge exists on effective strategies, barriers, and facilitators of implementation success in clinical and public health practice. DIRH can also be invaluable in addressing CVH promotion and CVD prevention at the community level to help stimulate further CVD mortality decline. A report⁶⁶ showing declining ideal CVH in White individuals and persistently poor CVH in African Americans and Mexican Americans is an important call to action for all communities to raise awareness about CVD and risk factors, increase the number of people taking action to promote ideal CVH, and reduce related racial and ethnic health disparities.⁶⁷ DIRH provides successful models for active community engagement for promoting CVH, preventing CVD and risk factors, and addressing the social and environmental determinants of health across the lifespan.⁶⁸ Examples of all active DIRH grants funded by NHLBI and other NIH institutes can be reviewed using the NIH Research Portfolio Online Reporting Tools from the NIH RePORTER website (n=169 as of 5/6/20).⁶⁹

Precision Medicine and Public Health

Precision medicine uses information about genes, environment, and lifestyle to tailor and optimize prevention and medical treatment for each individual.⁷⁰ Researchers have conducted genome-wide association studies and whole-genome sequencing studies to search for genetic variants that can predict risk of disease or response to treatment, and significant variants have been identified on every chromosome.⁷¹ For example, a risk score that incorporates information about 27 gene variants may have utility to identify individuals who will benefit more (that is, have lower risk of CHD) from taking a statin drug to lower low density lipoprotein (LDL) cholesterol.⁷² Precision public health extends the ideas of precision medicine to populations. Whereas precision medicine aims to identify the best treatment for an individual patient, precision public health seeks to identify the best means to promote health in particular communities or strata of the population. For example, a precision public health program might identify (through genetic testing or other means) a segment of the population prone to have high cholesterol or that metabolizes nicotine more quickly and is more susceptible to addiction; once identified, targeted prevention strategies could be delivered to the high-risk group. Those seeking to develop precision medicine and public health interventions face a number of challenges.⁷³ Such measures must prove to be superior (in terms of efficacy and cost-effectiveness) to existing methods. For example, a test that incorporates genetic information must predict risk or treatment response above and beyond well-documented environmental exposures or easily measured physiologic factors linked to CVD. Until precision medicine and public health interventions have been sufficiently vetted, medical and public health professionals continue to rely on traditional, evidence-based measures to reduce CVD risk in the clinic and community.^{74, 75}

Big Data, Mobile Devices, and the Internet of Things

Despite the progress in CVD diagnosis and treatment, the burden of CVD persists or is rising in many communities in the US and around the world, due, in large part, to the low

percentage of adults and children who meet ideal levels for all metrics of the AHA characterization of CVH.^{22, 76, 77} This reality has called attention to the fact that “health” takes place in the real world—outside the healthcare system—and involves daily decisions (e.g., physical activity, dietary intake) that currently go largely unmeasured. Recent advances in technology, particularly the broad consumer availability of mobile, wearable, and connected devices (i.e., Internet of Things), have made real-world, continuous monitoring and promotion of health possible. The accompanying explosion of health-related “big data” —from devices to images to electronic health records (EHR)—has coincided with advances in artificial intelligence (e.g., machine learning) to enable enhanced research, diagnostic, and predictive capabilities at the individual and population level.

A prime example of the opportunity for mobile/wearable devices to advance CVH broadly is helping people achieve recommended levels of physical activity, one of the pillars of AHA’s Life’s Simple 7.^{76, 78} Mobile devices, including the mobile phones used by the majority of the world’s population, can readily capture quantitative real-world measures of physical activity in individuals and across geographies.⁷⁹ Recent national guidelines, systematic reviews, and scientific statements document the evidence that mobile phones and wearable devices can increase physical activity^{80, 81}, particularly when partnered with evidence-based behavioral interventions, such as coaching, leveraging social networks, or using behavioral economic nudges.^{80, 82} These efforts would benefit from better integration into healthcare settings.⁸³ Beyond the utility for integration into healthcare delivery, mobile devices and apps can provide community-level assessment of mobility and the built environment, as well as links to community resources that promote active transportation (e.g., bike share programs) and leisure activity (e.g., parks and hiking trails).^{84, 85}

A vexing issue with the health applications of these novel technologies is the “digital divide” —that they are often more available initially to an already advantaged subset of the population, or based on non-diverse datasets, contributing to health inequity.⁸³ Promoting greater access and equity of health technologies has to be a priority to achieve greater CVH for all. Indeed, the rapid proliferation of mobile and connected devices globally has already had a dramatic impact on technology access for a large majority of the world’s population. Promisingly, we are now in a world where a fitness assessment can be implemented through a smartphone, mobile/wearable devices can detect atrial fibrillation and heart attacks, real and virtual health coaches can “chat” with patients to help them self-manage hypertension and diabetes, and retinal images can be analyzed automatically to provide expert-level diagnosis anywhere and reveal changes predictive of cardiovascular risk.^{79, 86, 87}

A multitude of large-scale research studies are now underway that incorporate mobile/connected device data with clinical and -omics data, to gain a greater understanding of how these real-world data can translate into further evidence to improve disease detection, health promotion, and ultimately health outcomes. The NIH *All of Us* Research Program incorporates mobile health (mHealth) technology and EHR in its intended recruitment and follow up of at least 1 million diverse participants across the US.⁸⁸ The new NIH RURAL study⁸⁹ will also include real-world data from mobile phones and wearables with the intent of understanding why many communities in the southeast U.S. have not seen as much improvements in CVD as other regions. In fact, the AHA has just funded a strategically

focused research network (SFRN) aimed at health technology solutions for CVH and brain health.⁹⁰ Finally, the current COVID-19 pandemic has also forced many health systems to develop and optimize telehealth capacities to deliver care remotely, which may improve both access and quality of cardiovascular care.

Consumers, researchers, and healthcare providers appropriately want transparency about the accuracy, data privacy, and health benefits of these new technologies, with many organizations working on “digital health” guidelines, standards, and regulation.⁹¹ Further work is also needed in ensuring equitable access, stronger links to scientific guidelines, and integration into clinical care. There is a shared mission among CVH societies, government funding agencies, technology companies, public health groups, and regulatory bodies to accelerate the translation of these promising technologies to advance equitable CVH for all to achieve a world free of CVD.

New Surveillance Approaches for Monitoring Impact

Disease prevention and health promotion programs are often deployed at the county or city level. Novel approaches to community surveillance open new avenues to monitor the impact of such community interventions, programs, and policies. Limited access to standardized information on local disease occurrence and outcomes hinders the ability of programs like these to evaluate the impact of policy and programmatic changes. This gap defines an opportunity to integrate surveillance into local disease prevention and health promotion efforts to assist stakeholders in establishing priorities and guiding program planning, implementation, and evaluation.⁹²

Digital technology, including mHealth and EHR, offers opportunities to enhance surveillance feasibility and impact. Opportunities and limitations relevant to the application of mHealth to surveillance have been delineated,⁹³ including the challenge of the digital divide, as reflected by disparities in access to technology related to age, race/ethnicity, and social determinants of health.⁹⁴ While mHealth offers the potential to enable integration of personal sensor and environmental data to other surveillance data sources, privacy concerns could limit the utility of mHealth to surveillance, and its role remains to be defined.

EHRs provide access to dense longitudinal clinical datasets that combined with data science techniques such as machine learning can greatly expand the reach of surveillance while generating new challenges. Phenotypes must be standardized to optimize reliability, and data generated from heterogeneous sources must be integrated. Examples of the utilization of EHRs for surveillance have been published.^{95, 96} Within the EHR environment, methodological rigor, attention to new sources of bias (e.g., digital divide, differential internet access by geography, populations, socioeconomic status), and medical records shortcomings (e.g., missing data, variations in care-seeking behaviors, data quality) are critically important. To this end, EHR are collected in clinical environments and are influenced by the patient’s health status and care seeking behavior and the clinician’s care and documentation practices. Hence, patients and clinicians, not researchers, determine the time of observation, which affects inferences that can be drawn from the results. Large-scale collection of data as enabled by digital technology and EHR share the limitations and biases inherent to all data generated in the course of care, regardless of sample size. Far from

reducing uncertainty, reliance on EHRs can, in fact, amplify it as large numbers will yield tighter confidence intervals without lessening bias or minimizing confounding by indication and other factors. Many large-scale networks, such as the CDC-funded multi-state EHR-based network for disease surveillance (MENDS),⁹⁷ and the Patient-Centered Outcomes Research Institute (PCORI)-funded PCORNet, developed methods to consolidate EHR data from various healthcare systems and patient populations into a standardized format. Investigators from these EHR “networks of networks” are developing methodology to use these extensive EHR data sources for public health surveillance. Widespread adoption of Fast Healthcare Interoperability Resources (FHIR) and Substitutable Medical Applications, Reusable Technologies (SMART) on FHIR standards may increase the utility of EHR data for research and surveillance purposes.

Future efforts could build on a foundation of new surveillance approaches that integrate data from EHRs, mobile devices, and internet of things, to improve healthcare quality through programs like Million Hearts and to identify opportunities to leverage precision medicine and precision public health (e.g., environmental change). These efforts should leverage knowledge gained from current dissemination and implementation research and identify topics for new research projects. All of these strategies will likely be needed to improve population CVH in ways that will dramatically reduce CVD mortality rates.

A Bold New Goal: 50by50by50

When the AHA defined “ideal CVH” (defined by 7 metrics: non-smoking; ideal healthy diet, physical activity levels, and body weight; and ideal blood pressure, cholesterol, and glucose levels) in its 2020 Strategic Impact Goal, it reframed thinking about CVD.⁷⁶ From this new perspective, popularized as “Life’s Simple 7”, strategies of prevention became anchored positively in health and not only disease. Prior evidence that ideal CVH at age 50 predicts decades of CVD-free survival and other significant health benefits pointed to a goal of promoting and preserving ideal CVH, through the strategy of primordial prevention. First articulated by Strasser in 1978⁹⁸, his vision of “preserving entire risk-factor-free societies from the penetration of risk factor epidemics” awaits full realization until this strategy is implemented continuously throughout the life course beginning from the earliest years of life.

The rapidly growing body of research on CVH has documented its low prevalence at age 50, due to a decline in prevalence beginning in childhood. Data are presently very limited at pre-adolescent ages but show a loss of ideal CVH from about 50% at age 10 to 10% at age 50. This is highly inconsistent with AHA’s goal “to improve the cardiovascular health of all Americans by 20% by 2020” and even more so with preservation of ideal CVH to age 50.⁷⁶

A major impetus to mobilizing primordial prevention to promote and preserve ideal CVH was AHA’s One Brave Idea initiative launched in January 2016 that called for proposals for a “moon shot” project to end CHD and its consequences.⁹⁹ AHA’s call, though lacking a specific target or timeline, raised new possibilities, coming in the context of AHA’s and others’ commitments to improve population CVH, a growing momentum behind community-focused efforts to address the CVD problem, and national and international

health organizations setting quantitative time-specific targets to reduce CVD or noncommunicable disease mortality.¹⁰⁰

These developments converged to result in a proposed CVD endgame, anchored in ideal CVH for all. If the prevalence of ideal CVH in early life were increased and its loss from childhood were averted, then reaching age 50 in ideal CVH might, in time, become the norm. In the corresponding absence of risk factors, as ample data show, their consequences would no longer occur. This, then, is a potential strategy of the CVD endgame: Promote and preserve ideal CVH for all throughout life, beginning in early life, to sustain a 50% or greater prevalence of ideal CVH at ages 50 years and younger by 2050 or sooner, or “50by50by50”. This could be an interim target of the endgame to be played out beyond 2050, thereby achieving, as nearly as possible, the true end of CVD.

Participant Convergence on Opportunities

After formal presentations by the invited speakers covering the topics above, the audience participated in breakout groups to provide further input. They listed additional challenges and barriers against achieving ideal CVH, such as overall low public awareness of the concept of ideal CVH including the AHA Life’s Simple 7, the typically long lag time in translating scientific findings into actionable policies, insufficient time and compensation for preventive efforts in clinical encounters, and unique challenges faced by communities such as grocery gaps, crime, and unhealthful environmental exposures. The audience recognized and supported concerted efforts to tackle these challenges and overcome barriers in promoting CVH across the lifespan, particularly at the community level, such as the NHLBI’s Disparities Elimination through Coordinated Interventions to Prevent and Control Heart and Lung Disease Risk (DECIPHeR) initiative.¹⁰¹

Participants converged on the idea that the starting age for both additional observational research and interventions should begin in early childhood, ideally *in utero* or even before conception. For school-aged children, school-based interventions could be explored, including developing simple messages that can readily be remembered for a life-time—an example outside of the cardiovascular arena was the successful “Stop, Drop, and Roll” campaign that taught children simple safety techniques for when clothing catches fire. But beyond schools, other opportunities exist at the community-level that could potentially reach people of all ages.

Conclusions

As reviewed above, the large societal, public health, behavioral, and environmental forces that contributed to the CVD epidemic of the 20th century, as well as the subsequent and dramatic decades-long reductions in CVD mortality, have been well described as a result of initiatives stemming from the initial 1978 Bethesda Conference. The major causal risk factors for CVD that account for the vast majority of CVD cases and mortality, as well as their upstream determinants and downstream consequences, have been delineated, and proven public health and healthcare interventions exist. Nonetheless, we now find ourselves in a period of flattening or stagnated CVD mortality rates, with real concerns that ongoing epidemics of obesity and diabetes (among other factors) are driving an increase in CVD

burden (particularly in heart failure and hypertension) among a growing and aging population. Given that so much information was gleaned as a result of the 1978 Bethesda Conference, it is hoped that the Bethesda + 40 Conference agenda and findings, summarized above, can create a roadmap for similar innovations in research, policy, and health care to re-energize CVH promotion and CVD prevention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Nonstandard Abbreviations and Acronyms

AHA	American Heart Association
ARIC	The Atherosclerosis Risk in Communities Study
CCSP	Community Cardiovascular Surveillance Program
CHD	Coronary Heart Disease
CVH	Cardiovascular Health
CVD	Cardiovascular Disease
DALY	Disability-Adjusted Life Year
DECIPHeR	Disparities Elimination through Coordinated Interventions to Prevent and Control Heart and Lung Disease Risk
DIRH	Dissemination and Implementation Research in Health
EHR	Electronic Health Records
FHIR	Fast Healthcare Interoperability Resources
HF	Heart Failure
HD	Heart Diseases

IOM	Institute of Medicine
LDL	Low-density lipoprotein
LMIC	Low and Middle Income Countries
MENDS	Multi-state EHR-based Network for Disease Surveillance
MI	Myocardial Infarction
MONICA	Multinational Monitoring of Determinants and Trends in Cardiovascular Disease
NHLBI	National Heart, Lung, and Blood Institute
NIH	National Institutes of Health
PCORI	Patient-Centered Outcomes Research Institute
SDOH	Social Determinants of Health
SFRN	Strategically Focused Research Networks
SMART	Substitutable Medical Applications, Reusable Technologies
SVI	Societal Vulnerability Index
WHO	World Health Organization

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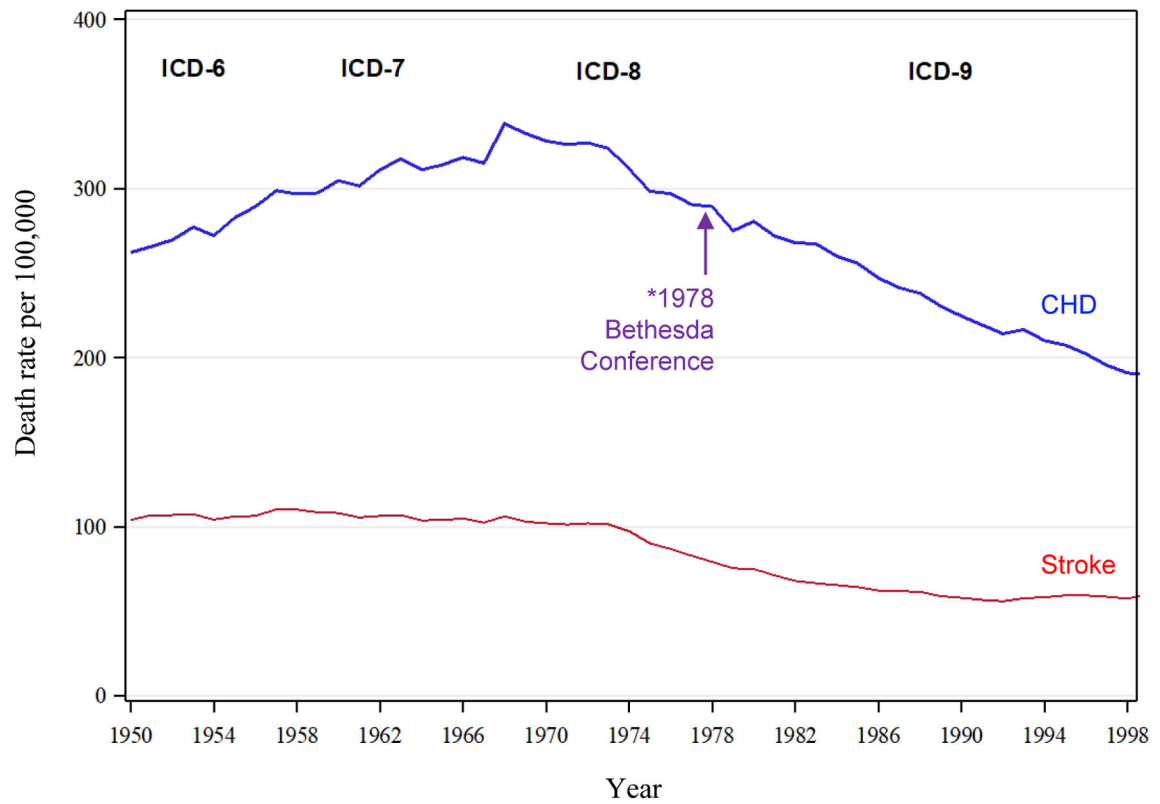


Figure 1. Trends in unadjusted death rates per 100,000 population attributable to coronary heart disease and stroke as underlying causes of death in the United States, 1950–1998.

Declines in crude death rates per 100,00 population of coronary heart disease and stroke between 1950 to 1998.

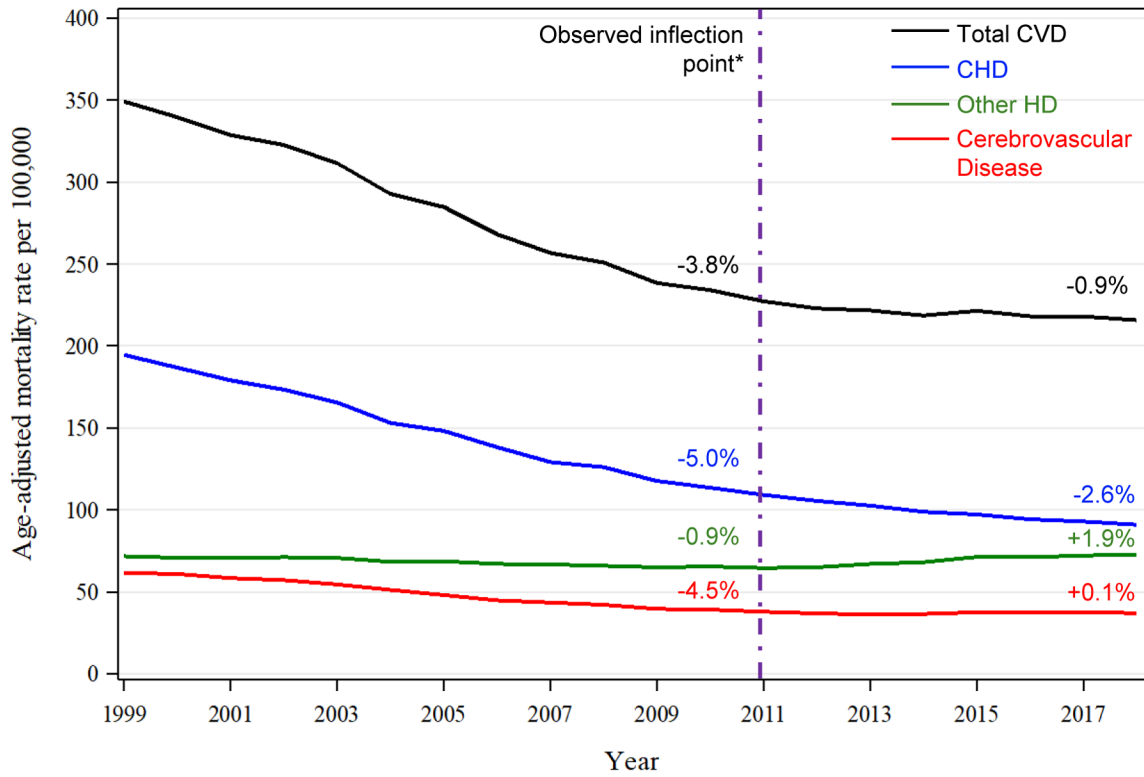


Figure 2. Trends in age-adjusted mortality rates per 100,000 population attributable to total cardiovascular disease and to leading subtypes of cardiovascular disease as underlying causes of death in the United States with average annual percentage change before and after the inflection point* between 1999 to 2011 and 2011 to 2018.

Declines in age-adjusted mortality rates per 100,000 population attributable to total cardiovascular disease and to leading subtypes of cardiovascular disease as underlying causes of death in the United States with average annual percentage change before and after the inflection point* between 1999 to 2011 and 2011 to 2018.

CVD = Cardiovascular Disease
 CHD = Coronary Heart Disease
 HD = Heart Disease

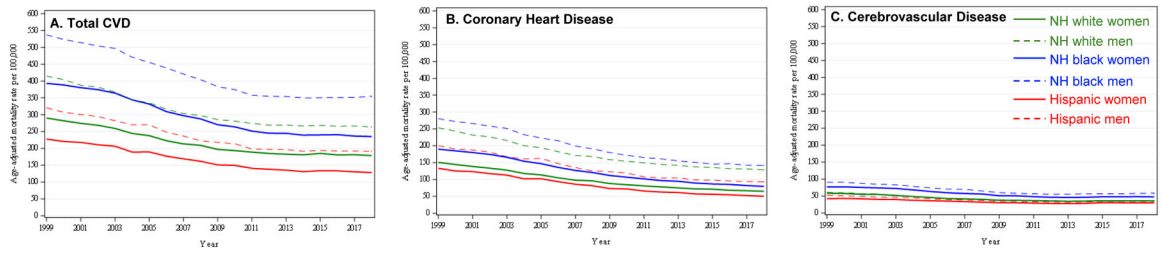


Figure 3. Trends in race-sex stratified age-adjusted mortality rates per 100,000 population attributable to total cardiovascular disease and by leading subtypes, coronary heart disease and cerebrovascular disease as underlying causes of death in the United States, 1999–2018.

Declines in total cardiovascular disease, coronary heart disease, and cerebrovascular disease mortality rates between 1999–2018

CVD = Cardiovascular Disease

NH = non-Hispanic

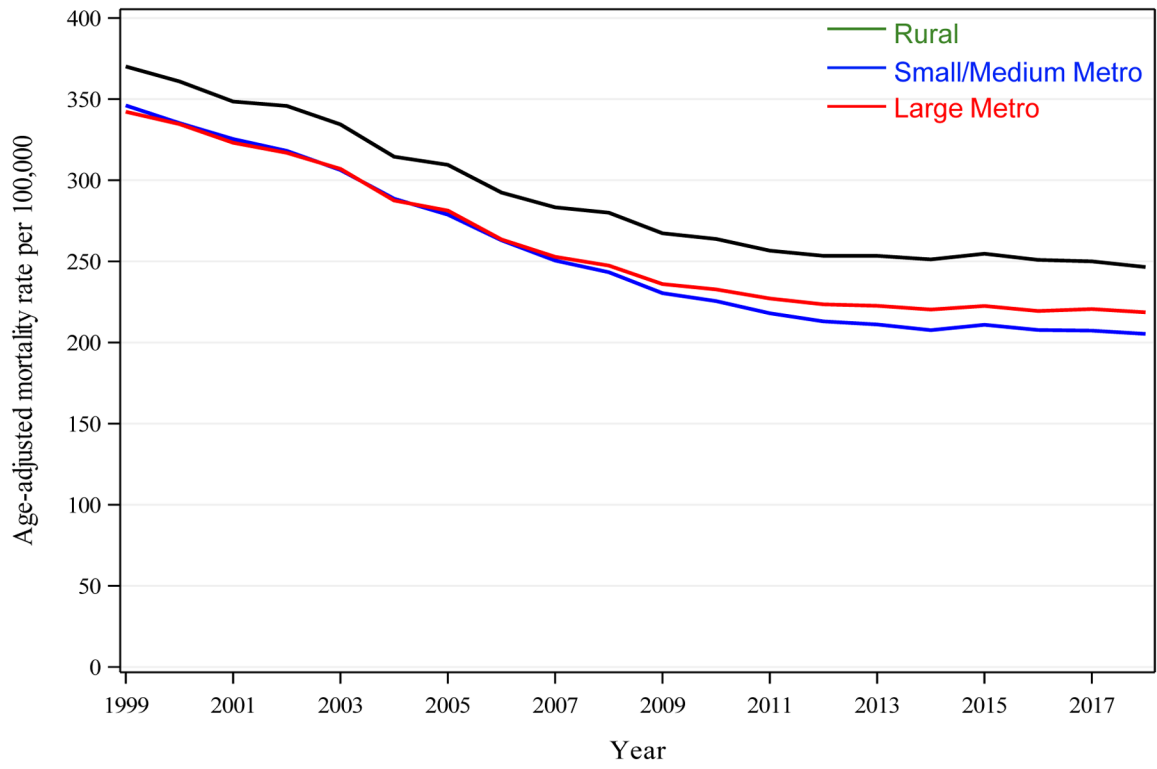


Figure 4. Trends in age-adjusted mortality rates per 100,000 population from total cardiovascular disease for both sexes stratified by urbanization status in the United States, 1999–2018.

Declines in cardiovascular mortality rate per 100,000 stratified by county-level urbanization between 1999–2018

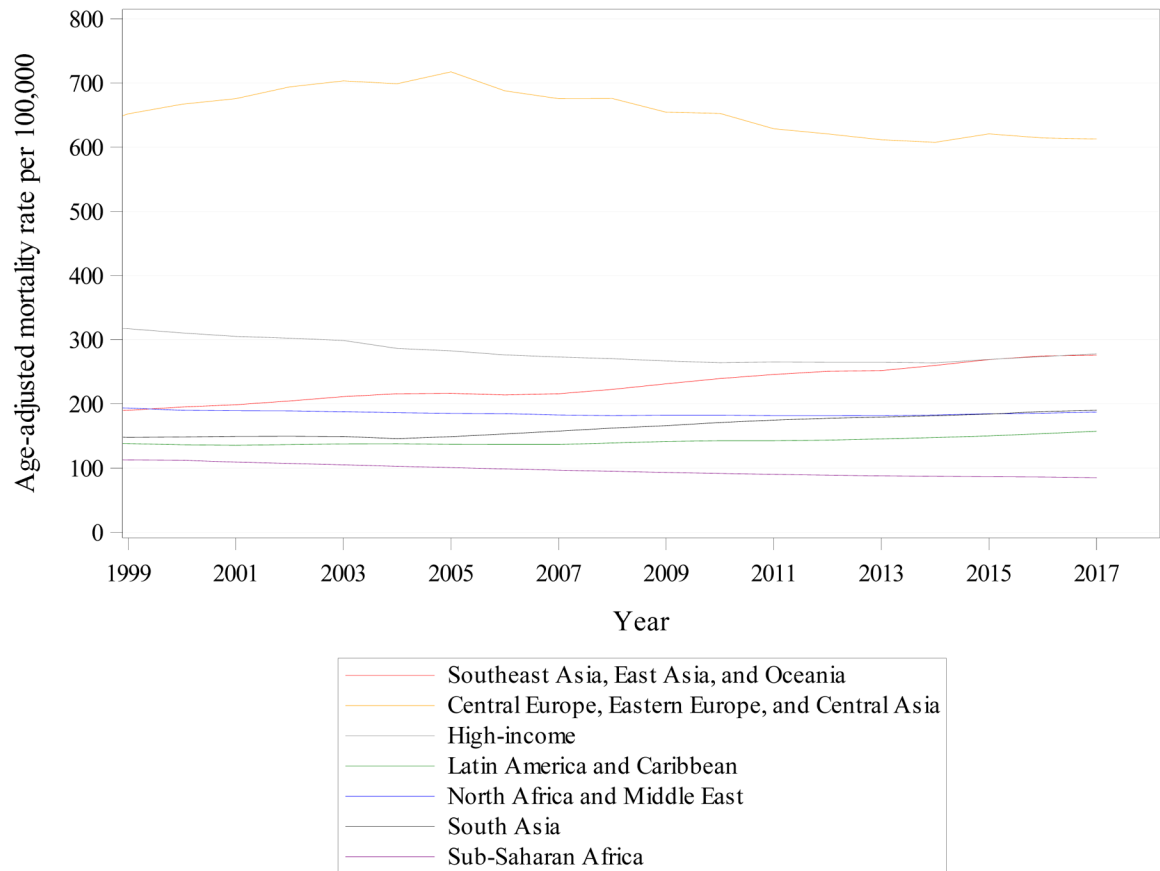


Figure 5. Trends in age-adjusted mortality rates per 100,000 population attributable to cardiovascular disease stratified by Global Burden of Disease Super Regions, 1999–2017.
 Age-adjusted mortality rates per 100,000 population across Global Burden of Disease Super Regions, 1999–2017

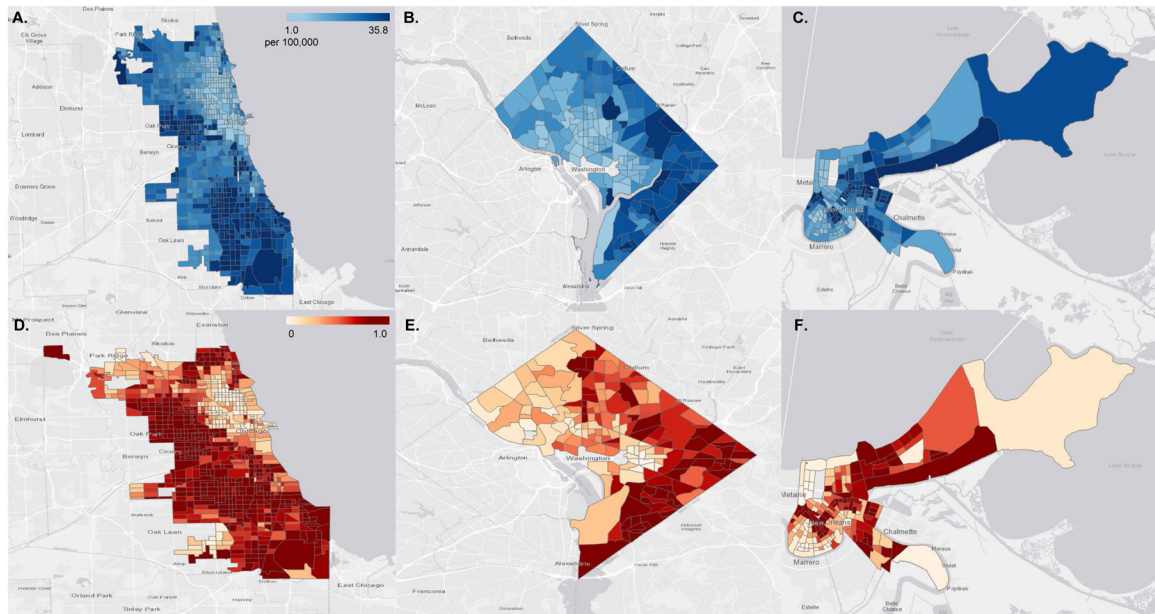


Figure 6. Small-area geographic scale distribution of age-adjusted prevalence of coronary heart disease (per 100,000) and the Centers for Disease Control and Prevention's Social Vulnerability Index at the census tract level in 3 major metropolitan areas in the United States, both sexes, 2017.

Neighborhood-level differences in age-adjusted prevalence of coronary heart disease and the social vulnerability index in Chicago (A, D), Washington D.C. (B, E), and New Orleans (C, F).