## **Circulation**

## **AHA PRESIDENTIAL ADVISORY**

Forecasting the Burden of Cardiovascular Disease and Stroke in the United States Through 2050–Prevalence of Risk Factors and Disease: A Presidential Advisory From the American Heart Association

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**BACKGROUND:** Cardiovascular disease and stroke are common and costly, and their prevalence is rising. Forecasts on the prevalence of risk factors and clinical events are crucial.

**METHODS:** Using the 2015 to March 2020 National Health and Nutrition Examination Survey and 2015 to 2019 Medical Expenditure Panel Survey, we estimated trends in prevalence for cardiovascular risk factors based on adverse levels of Life's Essential 8 and clinical cardiovascular disease and stroke. We projected through 2050, overall and by age and race and ethnicity, accounting for changes in disease prevalence and demographics.

**RESULTS:** We estimate that among adults, prevalence of hypertension will increase from 51.2% in 2020 to 61.0% in 2050. Diabetes (16.3% to 26.8%) and obesity (43.1% to 60.6%) will increase, whereas hypercholesterolemia will decline (45.8% to 24.0%). The prevalences of poor diet, inadequate physical activity, and smoking are estimated to improve over time, whereas inadequate sleep will worsen. Prevalences of coronary disease (7.8% to 9.2%), heart failure (2.7% to 3.8%), stroke (3.9% to 6.4%), atrial fibrillation (1.7% to 2.4%), and total cardiovascular disease (11.3% to 15.0%) will rise. Clinical CVD will affect 45 million adults, and CVD including hypertension will affect more than 184 million adults by 2050 (>61%). Similar trends are projected in children. Most adverse trends are projected to be worse among people identifying as American Indian/Alaska Native or multiracial, Black, or Hispanic.

**CONCLUSIONS**: The prevalence of many cardiovascular risk factors and most established diseases will increase over the next 30 years. Clinical and public health interventions are needed to effectively manage, stem, and even reverse these adverse trends.

Key Words: AHA Scientific Statements = cardiovascular diseases = forecasting = heart disease risk factors = population forecast = stroke

n the United States in 2020, cardiovascular disease (CVD)—including coronary heart disease (CHD), heart failure (HF), and atrial fibrillation (AF)—and stroke affected an estimated 9.9% of all adults >20 years of age, or roughly 28.6 million individuals.<sup>1</sup> CVD and stroke

are the most common causes of death in the United States, and they are associated with substantial morbidity, impaired quality of life, and high cost.<sup>1</sup> Unfortunately, after decades of progress in reducing CVD- and strokeassociated morbidity and mortality, these trends have

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reversed in recent years.<sup>2</sup> There is also emerging evidence of worsening trends in adverse levels of the health factors and health behaviors contained in the American Heart Association's (AHA's) Life's Essential 8,3 including maintaining a healthy blood pressure, body weight, blood sugar, and blood cholesterol; getting adequate sleep and physical activity; refraining from smoking; and eating a healthy diet, which underlie CVD and stroke outcomes.<sup>4,5</sup>

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In addition to worsening cardiovascular outcomes overall, deep inequities remain. Individuals from specific racial or ethnic groups, particularly Black populations, Hispanic people, and American Indian/Alaska Native (AI/AN) populations,<sup>6-9</sup> as well as particular subgroups of the Asian American population, experience markedly higher rates of adverse cardiovascular risk factors.<sup>10</sup> These populations also have higher rates of both incident and prevalent CVD and stroke and higher cardiovascular mortality as a result.<sup>11</sup> Individuals living in poverty, those who lack insurance coverage, and those living in rural areas<sup>12</sup> also experience higher rates of CVD and stroke and worse outcomes.13

Two major demographic shifts taking place in the United States will affect CVD and stroke trends in the coming decades: the aging of the population and its racial and ethnic diversification.<sup>14</sup> First, the year 2030 marks the initial year that all baby boomers (the generation born between 1945 and 1965) will be >65 years of age;  $\approx 1$  in 5 US residents will be >65 years of age by the mid-2030s, outnumbering children for the first time in US history. The number of people ≥85 years of age is projected to nearly double from 2016 to 2035 (from 6.5 million to 11.8 million) and nearly triple by 2060 (to 19 million). Second, over this same time frame, the non-Hispanic White population in the United States is expected to shrink from 197 million in 2016 to 179 million people in 2060, whereas the Asian population (18.3 million to 36.8 million), Hispanic population (57.4 million to 111.2 million), and multiracial population (8.5 million to 25.3 million) are each expected to more than double. The Black population (43 million to 60.7 million) and AI/ AN population (4 million to 5.6 million) are also projected to grow significantly by 2060. Projected demographic shifts are particularly evident in children: in 2016, just over half of all US children identified as non-Hispanic Black, Hispanic, AI/AN, multiracial, or Asian, and this is expected to grow to two-thirds by 2060.

Given population aging and diversification and adverse trends in the prevalence of CVD and stroke, new, innovative strategic approaches are clearly needed. As clinical leaders and policymakers plan interventions and project future needs for workforce and health care infrastructure, detailed data on trends and future projections of the prevalence of CVD and stroke risk factors and of clinical CVD and stroke are crucial. Knowledge about the absolute numbers of individuals with these adverse risk factors and conditions

may also be valuable for health care resource planning. Building on prior work by the AHA projecting the future prevalence of disease,15-18 we set out to estimate, using national survey and epidemiological data, the prevalence and number of people with adverse CVD and stroke risk factors and behaviors and overt CVD and stroke from 2020 to 2050, for both adults and children overall and across a range of sociodemographic subgroups.

#### METHODS

#### **Baseline Prevalence**

We estimated prevalence of an adverse level of each of the elements of AHA's Life's Essential 8,3 including the clinical manifestations of the 4 health factors (hypertension, diabetes, hypercholesterolemia, and obesity) and suboptimal levels of the 4 health behaviors (sleep, physical activity, smoking, and diet; Figure 1). We also estimated the prevalence of 4 distinct diseases- CHD, HF, stroke, and AF-as well as a composite outcome henceforth referred to as total CVD and stroke that included any of these 4 conditions. We estimated the baseline prevalence of each outcome (except for AF) using data from the 2015 to March 2020 prepandemic NHANES (National Health and Nutrition Examination Survey). NHANES is a survey of a nationally representative sample administered by the National Center for Health Statistics, which is part of the Centers for Disease Control and Prevention. The survey includes interview and physical examination components; the interview includes demographic, socioeconomic, dietary, and health-related questions; and the examination component consists of medical, dental, and physiological measurements, as well as laboratory tests administered by trained medical personnel.<sup>19</sup> Lists of qualifying measures and questions used to define each outcome for adults and children are presented in Supplemental Tables 1a and 1b; sample sizes by race and ethnicity are shown in Supplemental Table 2.

We estimated prevalence of AF using the 2015 to 2019 MEPS (Medical Expenditure Panel Survey).<sup>20</sup> MEPS is a nationally representative survey of the civilian noninstitutionalized population administered by the Agency for Healthcare Research and Quality. MEPS provides data on participants' use of medical services and the corresponding medical costs. Medical conditions are identified in MEPS Medical Condition files on the basis of self-reports of conditions leading to medical visits or treatment within the interview year. Medical conditions are classified with the International Classification of Diseases, 9th or 10th Revision, Clinical Modifications codes according to selfreported conditions that were transcribed by professional coders. There may be differences in prevalence estimates between NHANES and MEPS because of methodological differences in ascertainment. Prevalence in NHANES

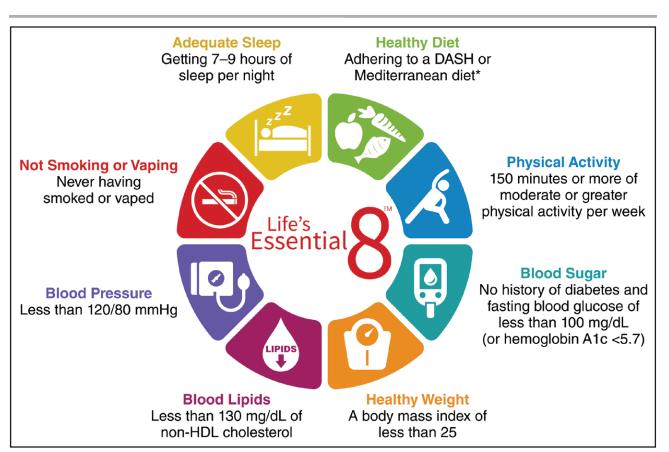
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#### Figure 1. Life's Essential 8.

Life's Essential 8 are the key measures for improving and maintaining cardiovascular health as defined by the American Heart Association. They consist of 4 health behaviors (physical activity, healthy diet, adequate sleep, not smoking or vaping) and 4 health factors (blood pressure, blood lipids, healthy weight, and blood sugar). DASH indicates Dietary Approaches to Stop Hypertension. \*Healthy Eating Index score <50.

is based on stated lifetime prevalence of the condition because it is assessed with "Have you ever been told that you have been diagnosed with..." questions. Prevalence from MEPS is based on treated prevalence because individuals are identified to have a condition if they sought medical care for that condition within the year.

We estimated the prevalence of each outcome using logit regression models adjusting for demographics (age, sex, and race and ethnicity). We used stepwise regression models to determine the significant interactions of demographics to be included in the models. We predicted the prevalence of each outcome in each age/sex/race and ethnicity cell using coefficients from the logit regressions for the 2017 to March 2020 NHANES cycle (or the 2019 MEPS for AF). Age groups for adults were 20 to 44, 45 to 64, 65 to 79, and  $\geq$ 80 years. Age groups for children were 2 to 5, 6 to 11, and 12 to 19 years. Race and ethnicity categories were Hispanic, non-Hispanic Black, non-Hispanic White, non-Hispanic Asian, and AI/AN or multiracial based on NHANES categories because of small sample size for the AI/AN and multiracial groups. We generated bootstrapped SEs for the estimates of total CVD and stroke prevalence. We repeated the analyses of logit regression models, replacing the race and ethnicity stratifications with sex and age categories.

Because NHANES and MEPS do not include people in long-term care, which represents ≈3% of the US adult population, we adjusted the NHANES and MEPS prevalence estimates to account for prevalence of disease in the long-term care population. Specifically, we adjusted the prevalence from NHANES and MEPS by a scaling factor estimated from the prevalence of hypertension, CVD and stroke, and diabetes in nursing homes from the 2017 to 2018 National Study of Long-Term Care Providers.<sup>21</sup> The overall CVD and stroke scaling factor was applied to total CVD and stroke, CHD, HF, stroke, and AF. We were unable to adjust the prevalence of other risk factors because of a lack of available data on their prevalence in the nursing home population. For total CVD and stroke, we also multiplied the bootstrapped SEs by the long-term care scaling factor.

#### **Prevalence Projections**

We considered the baseline prevalence of each outcome from NHANES to represent prevalence for 2018. We examined NHANES data from 2000 to 2020 and chose to use 2010 to 2020 for our trends calculations because of meaningful changes in trends around 2010, which have been shown in other datasets as well, and changes in disease definitions over the past 2 decades. LWW Art:CIR001256 May 31, 2024 2:25 PM 4 Color Fig(s): F1-11

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Specifically, we used NHANES data from 2010 to 2020 to estimate growth or decline rates in age-adjusted prevalence of the risk factors and clinical CVD, and we applied that growth or decline factor to age/sex/race and ethnicity-specific prevalence for the years 2020 to 2050. Growth and decline factors were estimated separately for adults and children given differences in variable definitions and cutoffs between the 2 populations. For adults, we did not estimate a growth or decline factor for inadequate sleep or poor diet because sufficient historical data were not available for these outcomes. For AF, the baseline prevalence represented prevalence (from MEPS) for 2019. We rescaled the hypertension growth factor to AF baseline prevalence given the relationship between these 2 clinical conditions and applied that to project age/sex/race and ethnicity-specific prevalence of AF in 2020 to 2050. For children, we did not estimate a growth or decline factor for hypertension, inadequate physical activity, tobacco use, or poor diet because of changes in definitions and limitations in data availability.

We combined estimates of prevalence by age/sex/ race and ethnicity with the 2010 Census projections of population counts for 2020 through 2050 to generate the projected number of people with each condition for 2020 through 2050. Projected population counts for 2020 through 2050 were obtained from the 2017 Population Projections of the US resident population by age, sex, race, and Hispanic origin generated by the US Census Bureau. The 2017 population projections incorporated differences in the fertility and mortality of native and foreign-born US residents, thus better accounting for the effect of international migration on the population of the United States. The series used the cohortcomponent method and historical trends in births, deaths, and international migration to project the future size and composition of the national population.

We multiplied the predicted prevalence of each outcome in each age/sex/race and ethnicity cell by the projected population counts in the corresponding cells for 2020 through 2050 to project the number of people with each outcome in each cell in each of the years. We then aggregated the number of people with the outcome by age, by sex, and by race and ethnicity and calculated the projected prevalence of each outcome overall and by each demographic characteristic.

We estimated uncertainty around the prevalence and counts estimates using a bootstrapping approach. We ran 1000 iterations estimating the number of people with each condition by subgroup in each year of the forecast. This analysis accounted for uncertainty in condition prevalence and prevalence growth/decline rates. To account for variation in prevalence estimates, in each bootstrap iteration, we redrew logit coefficients used to predict the prevalence of the condition in each subgroup from a multivariate normal distribution with the estimated coefficients as the mean and the estimated variance-

covariance matrix as the variance. For each iteration, we used redrawn coefficients to estimate prevalence for all subgroups, thus accounting for interdependency across subgroups. We also redrew linear regression coefficients that were used to calculate prevalence growth and decline rates using normal distributions defined by the estimated coefficients and SEs. For outcomes for which a growth or decline rate was not estimated, we redrew the rate using a normal distribution with a zero mean and a 95% CI, the bounds of which were calculated from the growth rate for obesity rescaled to the baseline prevalence of the outcome of interest. The lower bound of uncertainty intervals around estimated prevalence and count estimates is the 5th percentile, and the upper bound is the 95th percentile of the bootstrapped results. Using these bounds, we generated 90% credible ranges for the results.

#### Scenario Analyses

To illustrate the potential of prevention efforts to improve health outcomes, we used the Prevention Impacts Simulation Model (PRISM) simulation tool of the Centers for Disease Control and Prevention to explore 2 potential intervention scenarios. PRISM is a population-level, system dynamics model that synthesizes effect estimates from the literature and prevalence estimates from surveillance data, including NHANES, to simulate health, mortality, and economic outcomes for the US population.<sup>22</sup> It was developed in 2005 and most recently updated in 2019 to analyze the potential impacts of strategies to address CVD and stroke risk factors. PRISM simulates the flow into and out of populations of people as they develop chronic conditions and risk factors and die and has been validated in prior work.<sup>22</sup> The first scenario assumed that the published targets for Healthy People 2030 would be achieved, including reducing the prevalence of hypertension, hypercholesterolemia, diabetes, and obesity by  $\approx 10\%$  and improving the proportion of people with hypertension, hypercholesterolemia, and diabetes who have their conditions controlled by ≈20%.23 The second scenario assumed a more aggressive approach to a few key factors in addition to the changes in scenario 1, in particular reducing the prevalence of obesity by half and doubling risk factor control; details for the scenarios are shown in Supplemental Table 3. Both scenarios assumed that interventions began in 2025 and took 5 years to reach full implementation.

Analyses were conducted by Research Triangle Institute International under a contract from the AHA. Funding for the analyses was provided by the AHA, and the AHA convened a Steering Committee and Writing Group from among experienced volunteers with diverse expertise in cardiovascular and stroke epidemiology and predictive modeling. The study was exempt from Institutional Review Board review because it did not constitute human subjects research due to the deidentified

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nature of the data.<sup>24</sup> We conducted our statistical analysis using Stata version 17.0 (StataCorp LLC, 2021).

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### RESULTS

### Prevalence and Number of Adults With Adverse Cardiovascular Health Factors, Health Behaviors, and Clinical CVD and Stroke

We first estimated the burden of adverse levels of Life's Essential 8 among adults  $\geq$ 20 years of age overall. Figure 2, top demonstrates the projected prevalence of adverse levels of the health factors over time. For example, we estimate that the prevalence of hypertension will increase from 51.2% in 2020 to 61.0% in 2050. Larger increases were projected for diabetes (16.3% to 26.8%) and obesity (43.1% to 60.6%). However, there was a continued projected decline in hypercholesterolemia (45.8% to 24.0%).

Figure 2, middle shows the projected prevalence of adverse levels of the health behaviors over time. The prevalences of poor diet (52.5% to 51.1%), inadequate physical inactivity (33.5% to 24.2%), and current smoking status (15.8% to 8.4%) were estimated to improve over time, whereas the prevalence of inadequate sleep (40.3% to 42.1%) was projected to worsen.

The prevalence of adults with clinical diagnoses of CVD or stroke is lower than the prevalence of risk factors but is also generally projected to rise over time, particularly for stroke. Figure 2, bottom shows estimates for overall rates of CVD and stroke, with CHD projected to rise from 7.8% to 9.2%, HF from 2.7% to 3.8%, stroke from 3.9% to 6.4%, and total CVD and stroke from 11.3% to 15.0%. Combining clinical CVD and hypertension, prevalence is projected to reach more than 61%. Full results for each factor and condition, along with uncertainty intervals, are available in Supplemental Table 4.

Figure 3 demonstrates these trends by the projected number of adults with each adverse level of a health factor, health behavior, or clinical condition. In 2050, the overall size of the adult US population is projected to reach nearly 302000000. We estimate that hypertension and obesity will each affect >180000000 adults by 2050, whereas the prevalence of diabetes will climb to >80000000. Poor diet, rising to >15000000, and inadequate sleep, climbing to >125000000 adults affected, are also on highly adverse trends in terms of absolute numbers. Overall CVD and stroke are projected to increase from 28000000 to 45000000 adults, with the steepest increase among individual conditions seen in stroke (10000000 to nearly 20000000). Combining clinical CVD and hypertension, the number of affected individuals is projected to reach >184000000. Full results for each factor and condition, along with uncertainty intervals, are available in Supplemental Table 5.

### Prevalence and Number of Adults With Adverse Levels of Cardiovascular Health Factors, Health Behaviors, and Clinical CVD and Stroke, by Age Group

When these trends were disaggregated by age group, a number of additional findings became evident. Figure 4 shows the projected percent prevalence and number of people for the adverse health factors by age group. Although hypertension was most prevalent in individuals ≥80 years of age, the number of people with hypertension was highest-and rising-in younger and middleaged adults. For diabetes and hypercholesterolemia, the highest prevalence was seen in the 65- to 79-year-old age bracket, but for obesity, which often presages these other health factors, the highest prevalence and highest growth were in the 20- to 44- and 45- to 64-year-old age brackets. Figure 4 also shows levels of adverse health behaviors by subgroup. Individuals ≥80 years of age had the highest percent prevalence of poor sleep and inadequate physical activity, perhaps tied to the physiological effects of aging; younger age groups had higher rates of smoking and poor diet. Poor diet was the health behavior with the greatest number of individuals affected, with projections suggesting nearly 70000000 young adults with poor diet in 2050. Full results for each factor and condition are available in Supplemental Table 6 (prevalence) and Supplemental Table 7 (number).

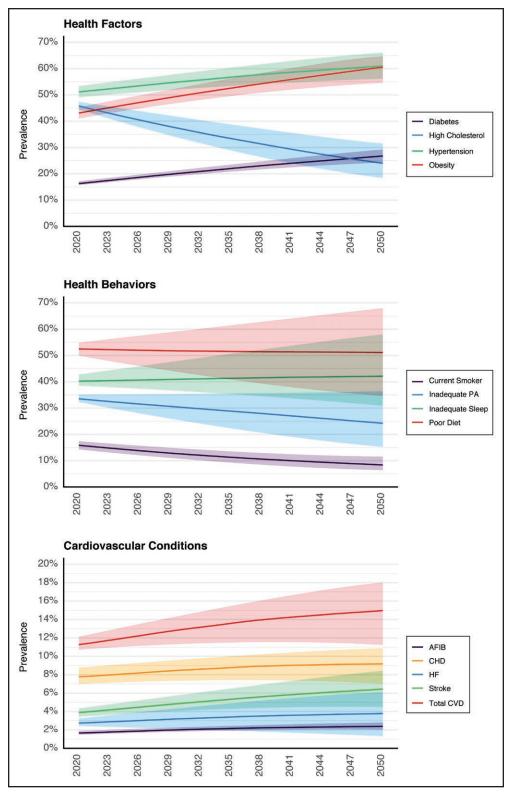
Figure 5 shows the projected percent prevalence and number of people for the clinical cardiovascular conditions. Overall, adults ≥80 years of age had the highest prevalence of CVD and stroke and a high projected growth, a result of longer life expectancy for individuals aging into this cohort in the next 30 years. However, given the overall distribution of age within the population, there was a higher absolute number of individuals projected to have CVD and stroke in the cohort <80 years of age: nearly 14000000 individuals 45 to 64 years of age and 15000000 people 65 to 79 years of age. Among the individual conditions, prevalence patterns were similar, with the oldest adults bearing the greatest burden by percent prevalence but the groups 45 to 64 and 65 to 79 years of age having an equal or higher total number of individuals affected.

### Percent and Number of Adults With Adverse Levels of Cardiovascular Health Factors, Health Behaviors, and Clinical CVD and Stroke, by Racial or Ethnic Category

Because of notable demographic shifts in the United States, with rapid growth projected among Asian populations and Hispanic populations in particular, the overall shifts in percent prevalence and the number of people affected by cardiovascular risk factors and clinical



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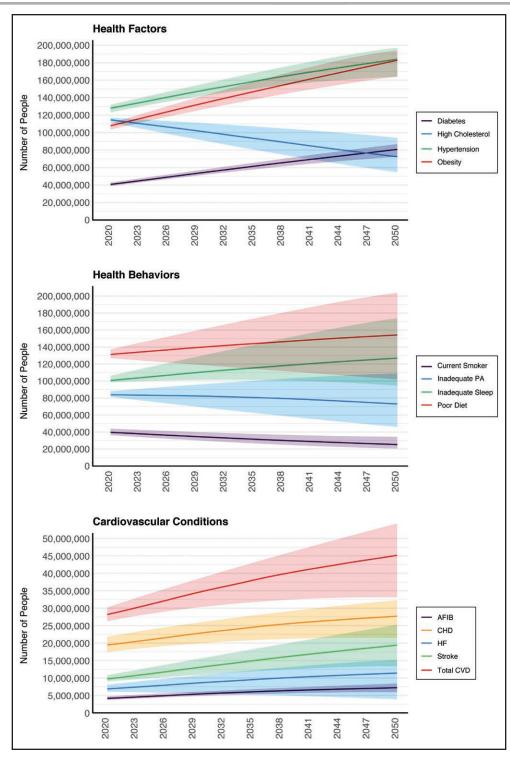


## Figure 2. Proportion of US adults with adverse levels of cardiovascular health factors and health behaviors and cardiovascular disease and stroke, 2020 to 2050.

For adults, we did not estimate a growth or decline factor for inadequate sleep or poor diet because sufficient historical data were not available for these outcomes; thus, changes in prevalence reflect population and demographic shifts alone. AFIB indicates atrial fibrillation; CHD, coronary heart disease; CVD, cardiovascular disease; HF, heart failure; and PA, physical activity.

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## Figure 3. Number of US adults with adverse levels of cardiovascular health factors, health behaviors, and cardiovascular disease and stroke, 2020 to 2050.

For adults, we did not estimate a growth or decline factor for inadequate sleep or poor diet because sufficient historical data were not available for these outcomes; thus, changes in prevalence reflect population and demographic shifts alone. AFIB indicates atrial fibrillation; CHD, coronary heart disease; CVD, cardiovascular disease; HF, heart failure; and PA, physical activity.

disease mask important differences by racial and ethnic subgroups.

Figure 6 shows the projected percent prevalence and number of adults for the adverse levels of health factors

by subgroup. Black adults had the highest prevalence of hypertension, diabetes, and obesity but the lowest prevalence of hypercholesterolemia. Absolute increases in prevalence were generally greatest in the Hispanic

80,000,000

70,000,000

60,000,000

50,000,000

40,000,000

30,000,000

20.000.000

10,000,000

80.000.000

70.000.000

60,000,000

50,000,000

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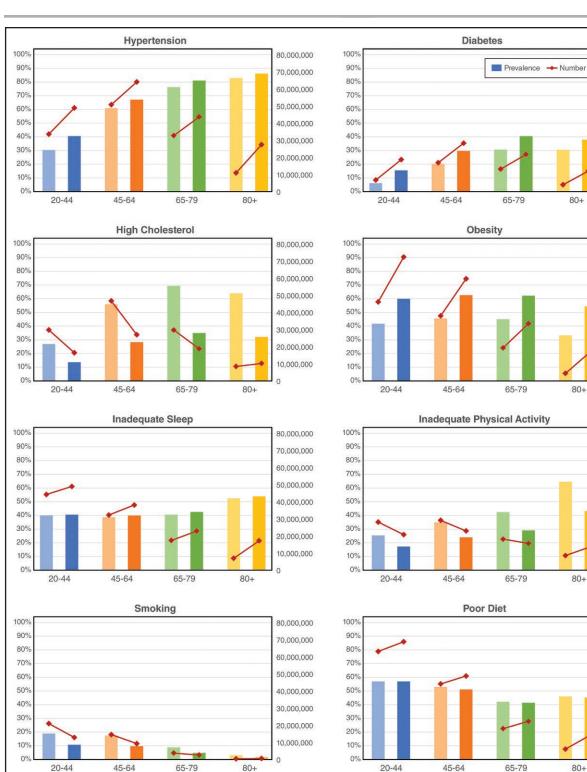
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80+

80+

80+



#### Figure 4. Prevalence and number of US adults with adverse levels of cardiovascular health behaviors and health factors in 2020 and 2050, by age group.

Bars represent estimated prevalence and number in 2020 and 2050. For adults, we did not estimate a growth or decline factor for inadequate sleep or poor diet because sufficient historical data were not available for these outcomes; thus, changes in prevalence reflect population and demographic shifts alone.

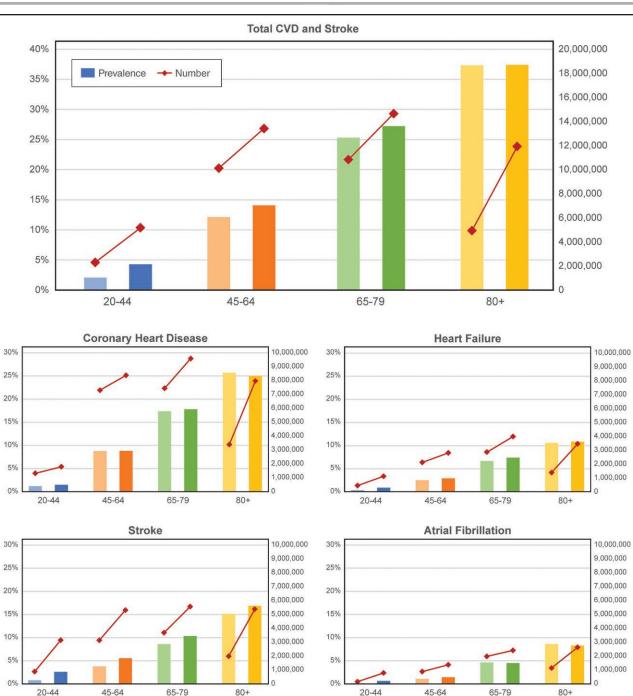
population, whereas relative growth was also high in the Asian population, reflecting demographic shifts. Figure 6 also shows adverse levels of health behaviors by subgroup. Black adults had the highest projected prevalence of inadequate sleep and poor diet; Asian adults had the highest projected prevalence of inadequate physical

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Figure 5. Prevalence and number of US adults with cardiovascular disease and stroke in 2020 and 2050, by age group. Bars represent estimated prevalence and number in 2020 and 2050. CVD indicates cardiovascular disease.

activity; and the aggregated group of AI/AN/multiracial adults had the highest projected prevalence of smoking. Again, growth was particularly notable in Hispanic populations for each of the adverse health behaviors. Full results for each factor and condition are available in Supplemental Table 8 (prevalence) and Supplemental Table 9 (number).

Figure 7 shows the projected percent prevalence and number of people for the clinical cardiovascular

conditions. Overall, AI/AN/multiracial adults and White adults had the highest prevalence of total CVD and stroke, driven in part by the generally older age of the White population. Hispanic adults again had the greatest projected population growth for total CVD and stroke. Among the individual conditions, prevalence patterns varied; Black adults had the highest rates of HF and stroke, whereas White adults had the highest rates of CHD and AE.

70%

60%

50%

40%

30%

20%

10%

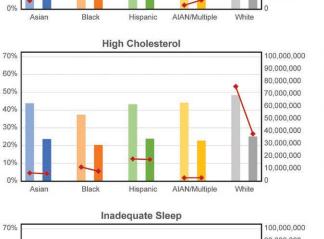
Hypertension Diabetes 70% 100,000,000 100.000.000 90,000,000 90,000,000 60% Prevalence - Number 80.000.000 80.000.000 50% 70,000,000 70,000,000 60,000,000 60,000,000 40% 50,000,000 50.000.000 30% 40,000,000 40.000.000 30,000,000 30,000,000 20% 20,000,000 20,000,000 10% 10,000,000 10,000,000 0% AIAN/Multiple AIAN/Multiple Black Hispanic White Asian Black Hispanic White **High Cholesterol** Obesity 100.000.000 70% 100.000.000 90.000.000 90,000,000 60% 80,000,000 80,000,000 50% 70,000,000 70,000,000 60,000,000 60.000.000 40% 50,000,000 50,000,000 30% 40 000 000 40 000 000 30,000,000 30.000.000 20% 20.000.000

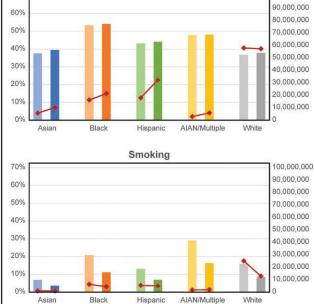
10%

0%

Asian

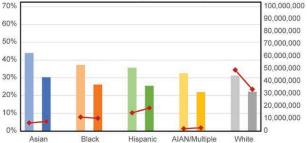
Black





Inadequate Physical Activity

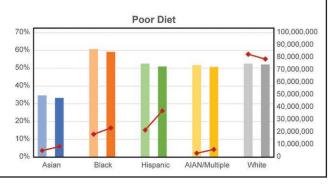
Hispanic



AIAN/Multiple

10,000,000

White



#### Figure 6. Prevalence and number of US adults with adverse levels of cardiovascular health factors and health behaviors in 2020 and 2050, by race and ethnicity.

Bars represent estimated prevalence and number in 2020 and 2050. For adults, we did not estimate a growth or decline factor for inadequate sleep or poor diet because sufficient historical data were not available for these outcomes; thus, changes in prevalence reflect population and demographic shifts alone. AIAN indicates American Indian/Alaska Native.

### Adverse Cardiovascular Risk Factors Among Children

Hispanic

Although the prevalence of some CVD and stroke risk factors in children 2 to 19 years of age is markedly lower than in adults, there were concerning trends among key risk factors that were also notable in the adult population. For example, although hypertension, hypercholesterolemia, and diabetes are rare among children (and diabetes in the pediatric population is still predominantly type 1), the prevalence of obesity in children is estimated to rise from 20.6% in 2020 to a striking 33.0% in 2050 (Figure 8A). The prevalences of inadequate physical activity and poor diet are each near 60%. Although tobacco

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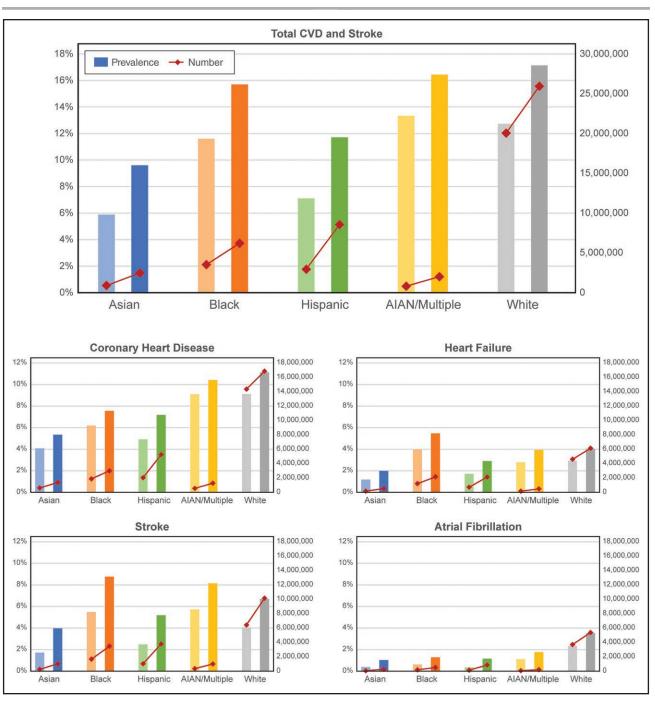


Figure 7. Prevalence and number of US adults with cardiovascular disease and stroke in 2020 and 2050, by race and ethnicity. Bars represent estimated prevalence and number in 2020 and 2050. AIAN indicates American Indian/Alaska Native; and CVD, cardiovascular disease.

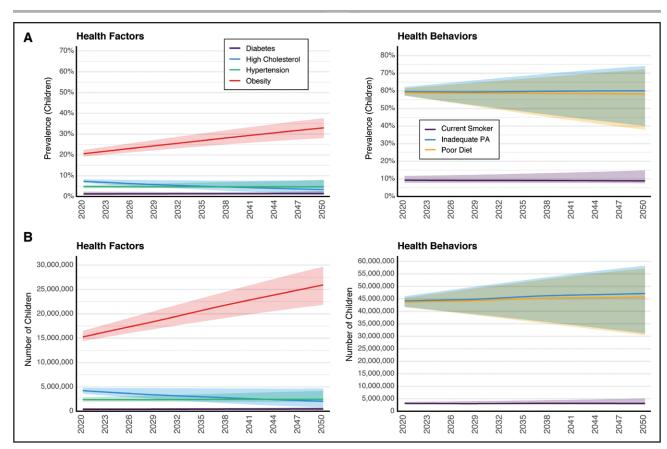
use rates are <10% and declining, these data should be interpreted with caution because of uncertainty about data on noncigarette tobacco products (Unlike adults, children are now asked about noncigarette tobacco products in national survey data, but the questions have only been recently introduced, so trends are uncertain). Of note, sleep was not estimated in children because of data limitations.

These changes in prevalence correspond to a projected rise in the number of children with obesity from just over

15 million in 2020 to nearly 26 million in 2050 (Figure 8B). The number of children with inadequate physical activity and poor diet is projected to rise more slowly but still exceed 45 million by 2050. Full results, along with uncertainty intervals, are provided in Supplemental Table 10 (prevalence) and Supplemental Table 11 (number).

As in the adult population, these projections differed by age group (Figure 9), although not all risk factors were estimable in the youngest children (2-5 and 6-11)years of age) because of the low prevalence and lack

Forecasting Cardiovascular Disease and Stroke Prevalence



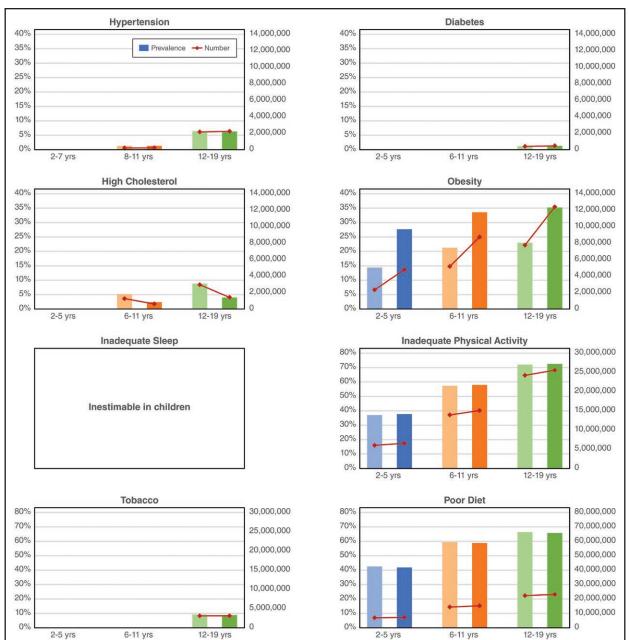
**Figure 8. Trends in US children with adverse levels of cardiovascular health factors and health behaviors, 2020 to 2050. A**, Trends in proportion of US children with adverse levels of cardiovascular health factors and health behaviors, 2020 to 2050. For children, we did not estimate a growth or decline factor for hypertension, inadequate PA, tobacco use, or poor diet because sufficient and consistent historical data were not available for these outcomes; thus, changes in prevalence reflect population and demographic shifts alone. Hypertension was estimated for children ages 12 to 19 years of age; and obesity, inadequate PA, and poor diet were estimated for children 2 to 19 years of age. **B**, Trends in number of US children with adverse levels of cardiovascular health factors and health behaviors, 2020 to 2050. Tobacco includes both cigarettes and noncigarette products. For children, we did not estimate a growth or decline factor for hypertension was estimated for children 8 to 19 years of age; high cholesterol data were not available for these outcomes; thus, changes in prevalence reflect population and demographic shifts alone. Hypertension was estimated a growth or decline factor for hypertension, inadequate PA, tobacco use, or poor diet because sufficient and consistent historical data were not available for these outcomes; thus, changes in prevalence reflect population and demographic shifts alone. Hypertension was estimated for children 8 to 19 years of age; high cholesterol was estimated for children 12 to 19 years of age; and obesity, inadequate PA, and poor diet were estimated for children 2 to 19 years of age. PA indicates physical activity.

of available data. However, obesity showed a steep projected growth in all age groups: from 14.4% to 27.7% in children 2 to 5 years of age, from 21.3% to 33.6% in children 6 to 11 years of age, and from 23% to 35.2% in individuals 12 to 19 years of age. The prevalences of inadequate physical activity and poor diet also increase with age, although longitudinal growth projections are similar across age groups.

Projections also differed by race and ethnicity (Figure 10). Black children had the highest prevalence of hypertension and diabetes, whereas Hispanic children had the highest prevalence of obesity and the greatest projected growth in hypertension, diabetes, and obesity. In terms of health behaviors, Asian children and Hispanic children had the highest prevalence of inadequate physical activity, AI/AN/2-or-more-races children had the highest prevalence of smoking, and Black children and White children had the highest prevalence of poor diet. The absolute increase in each risk factor was greatest for Hispanic children, reflecting broader trends in population growth.

### **Scenario Analyses**

When we used the PRISM simulation tool to explore the potential effect of reaching the Healthy People 2030 targets, including reducing the prevalence of hypertension, hypercholesterolemia, diabetes, and obesity by roughly 10% and improving the control of blood pressure, blood sugar, and cholesterol by roughly 20%, we estimated that these efforts would be associated with 17% to 23% reductions in incident CVD and stroke and cardiovascular mortality in 2050 compared with our base-case projections (Figure 11). We estimate that these reductions would equate to 1.2 million CVD and stroke events in 2050, including roughly 437 400 CHD events, 281 600 strokes, and 240000 CVD and stroke deaths. Further



## Figure 9. Prevalence and number of adverse levels of cardiovascular health factors and health behaviors in US children in 2020 and 2050, by age group.

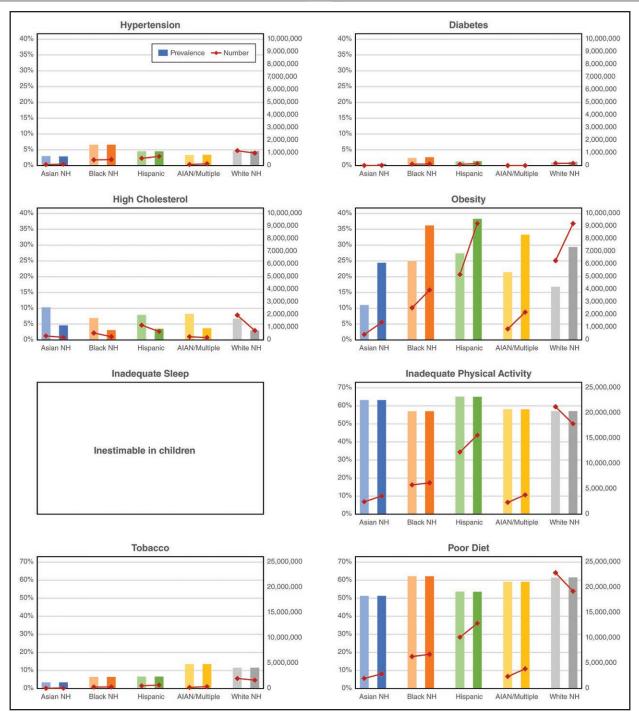
Tobacco includes both cigarettes and noncigarette products. Hypertension was not estimable in children 2 to 7 years of age; high cholesterol was not estimable in children 2 to 5 years of age; and diabetes and tobacco use were not estimable in children 2 to 5 and 6 to 11 years of age. Sleep estimates could not be produced for any individual pediatric age group. For children, we did not estimate a growth or decline factor for hypertension, inadequate physical activity, tobacco use, or poor diet because sufficient historical data were not available for these outcomes; thus, changes in prevalence reflect population and demographic shifts alone.

reductions in risk factors, in particular reducing obesity by half and doubling risk factor control, would be needed to achieve even greater reductions of up to 30% to 40% in event and mortality rates in 2050 (Figure 11).

## DISCUSSION

The forecast for cardiovascular health through 2050 is alarming in the absence of substantial interventions to alter prevailing trends, suggesting a need for significant and sustained action. Overall, we project that many key cardiovascular risk factors and adverse health behaviors, particularly obesity, are likely to increase markedly by 2050. The prevalence rates for hypertension and obesity will likely exceed 50% overall and >80% in some key subgroups such as Black adults and older adults. The growth in these risk factors will have a direct impact on CVD and stroke with an associated substantial increase in overt disease over time. Along with shifts in population demographics and aging, these changes suggest a marked growth in

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## Figure 10. Prevalence and number of adverse levels of cardiovascular health factors and health behaviors in US children in 2020 and 2050, by race and ethnicity.

Tobacco includes both cigarettes and noncigarette products. For children, we did not estimate a growth or decline factor for hypertension, inadequate physical activity, tobacco use, or poor diet because sufficient historical data were not available for these outcomes; thus, changes in prevalence reflect population and demographic shifts alone. Hypertension was estimated for children 8 to 19 years of age; high cholesterol was estimated for children 6 to 19 years of age; diabetes and tobacco use were estimated for children 12 to 19 years of age; and obesity, inadequate physical activity, and poor diet were estimated for children 2 to 19 years of age. AIAN indicates American Indian/Alaska Native; and NH, non-Hispanic.

the overall burden of CVD and stroke in the United States that will have an enormous adverse impact on the health of the nation. Although the declines in smoking and hypercholesterolemia are promising and may translate into cardiovascular health gains, these gains will likely be offset by increases in the prevalence of hypertension, diabetes, and obesity. A simulation of the potential effects of implementing existing national goals under Healthy

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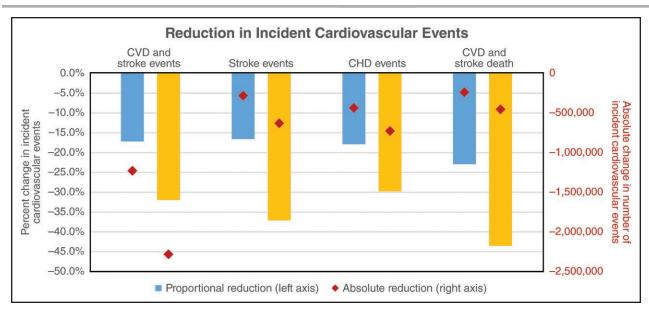


Figure 11. Projected impact of improvements in risk factor prevalence and control on incident cardiovascular disease events in the year 2050.

We used the Prevention Impacts Simulation Model simulation tool to explore 2 potential intervention scenarios. The estimates represent reductions compared with the counterfactual (current trends) in the year 2050. The first scenario (blue bars) assumed that the published targets for Healthy People 2030 would be achieved, including reducing the prevalence of hypertension, hypercholesterolemia, diabetes, and obesity by  $\approx$ 10% and improving the proportion of people with hypertension, hypercholesterolemia, and diabetes who have their conditions controlled by  $\approx$ 20%. The second scenario (yellow bars) assumed a more aggressive approach to a few key factors in addition to the changes in scenario 1, in particular reducing the prevalence of obesity by half and doubling risk factor control. Both scenarios assumed that interventions began in 2025 and took 5 years to reach full implementation. See text for additional details. Bars indicate proportional reduction (left axis); and diamonds, absolute reduction (right axis). CHD indicates coronary heart disease; and CVD, cardiovascular disease (including CHD and heart failure).

People 2030 suggests that meaningful improvements are achievable with concerted, focused efforts at improvement, although a substantial burden of disease will remain even under the most optimistic scenarios.

Among the most striking findings were the projected inequities in risk factors and outcomes, disparities that will be magnified as the population becomes more diverse. For instance, a doubling in the number of Hispanic American individuals and Asian American individuals by 2060 will translate to large increases in the number of CVD and stroke events occurring in these populations, even if the rate of CVD were to remain unchanged.<sup>25,26</sup> Ongoing high rates of adverse outcomes in Black adults and high levels of risk factors in children and people from AI/AN backgrounds or identifying with 2 or more races also warrant ongoing focused attention. The reasons for these inequities are complex but include the effects of individual, structural, and systemic racism, as well as socioeconomic factors and access to care.<sup>27-32</sup> Broader public policy and systems changes will be needed to address the root causes of these persistent inequities.<sup>33</sup> The AHA has advocated, for example, for health insurance access that is adequate, accessible, and affordable.<sup>34</sup> Further work should specifically address individual, structural, and systemic racism<sup>27-32</sup> as an important driver of health inequities.<sup>35</sup> Affecting these issues will also require tailored cardiovascular health education, community-based interventions, and culturally

appropriate efforts for improving cardiovascular prevention and treatment in these major population groups.<sup>36–38</sup>

We also projected a significant increase in the number of older adults with CVD and stroke by 2050, largely due to the aging of the population more broadly. As medications and procedures continue to delay individual cardiovascular mortality, the number of older adults living with clinically significant CVD and stroke will increase, and the distribution of the types of events they will experience will also shift. This also suggests that a greater understanding of the effects of medications and procedures in older adults is needed because these individuals have been historically underrepresented in clinical trials and mechanistic studies. Rising clinical needs of an aging population will also require appropriate expansion of the cardiovascular workforce, including physicians, pharmacists, nurses, dieticians, physical therapists, and other health care professionals. Resources and longterm care facilities for people with significant morbidity and disability related to stroke or other types of CVD will also be required.

At the other end of the spectrum, another of our key findings was the striking prevalence and predicted steep growth of cardiovascular risk factors in children, particularly obesity, inadequate physical activity, and poor diet, which has implications for how clinicians and public health leaders might focus their efforts to address these issues. Racial and ethnic inequities in risk factors were LWW Art:CIR001256 May 31, 2024 2:25 PM 4 Color Fig(s): F1-11

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alarming, suggesting that culturally appropriate, tailored interventions should be prioritized here as well. Further support of policies and programs in schools and communities for healthy eating and regular physical activity is also needed.<sup>39,40</sup> In addition, major initiatives to help children and adolescents understand the downstream impact of healthy habits are crucial to engendering lasting change. Broader interventions, whether family based or public health in nature such as the Supplemental Nutrition Assistance Program and the Women, Infants, and Children program, should incorporate pediatric expertise and input when feasible. Last, although our data did not allow us to examine individual noncigarette tobacco products such as vaping, addressing the growth in tobacco and nicotine use remains a critical area for preventing the development of CVD and stroke in children and young adults.41

Our findings have important implications for primary prevention in young and middle-aged adults,<sup>42-45</sup> particularly because the prevalences of hypertension, diabetes, and obesity continue to rise. Indeed, it is unlikely that we will make meaningful progress in reducing the epidemic of CVD without substantial investment in major efforts to reduce obesity. The recent approval of glucagon-like peptide 1 agonists and related drugs to treat diabetes and obesity may lead to a sea change in our medical approach to these conditions. Some estimates suggest that as many as a third of US adults could be eligible for glucagon-like peptide 1 treatment based on trial criteria; if drug efficacy is extrapolated to the US population, it implies a relative reduction of >40% in obesity prevalence and as much as a 17% relative reduction in cardiovascular events.<sup>46</sup> Our PRISM modeling exercise similarly suggested that reductions in obesity would translate into major improvements in cardiovascular events such as heart attacks and strokes, although they rely on assumptions about the relationship between obesity and event rates that predate these new therapies. These estimates obviously make assumptions about uptake and efficacy that may not be realized because of a number of barriers, including patient preference, clinician knowledge, and costs of these drugs, but this issue will be extremely important to monitor going forward and to take into account in future forecasting exercises.

Another important approach to addressing hypertension, diabetes, and obesity is the AHA's recently announced initiative on Cardiovascular-Kidney-Metabolic Health, which draws much-needed attention to the deleterious relationships among cardiometabolic disease, chronic kidney disease, and clinical cardiovascular events.47,48 The initiative focuses on the central role of adiposity as a mechanism behind the onset of hypertension, metabolic disease, and vascular disease and recognizes that CVD and stroke continue to be the main causes of mortality among patients with diabetes and obesity. The recognition that kidney disease acts

to increase CVD and stroke independently of diabetes is also crucial; this is an important area for future work. The recently developed Predicting Risk of Cardiovascular Disease Events equations complement this focus.49 These equations include risk prediction over a wider age span (30-79 years) and over a longer time horizon (30 years), creating new opportunities to focus primary prevention on a younger cohort.

On a positive note, the projected decline in hypercholesterolemia is notable. Declines in the prevalence of this condition in both children and adults were seen in the historical data (2010-2020) we used to calculate trends, Although perhaps unexpected, these patterns have been reported previously. For example, a prior report using NHANES data found that the prevalence of high cholesterol decreased from 59% in 1976 to 1980 to 42% in 1988 to 1994, 33% in 2001 to 2004, and 27% in 2007 to 2010.50 Because the NHANES variable reflects either elevated blood lipids or treatment for hypercholesterolemia, these declines do not reflect better treatment of disease but rather lower prevalence of disease. Furthermore, data from other sources such as the Behavioral Risk Factor Surveillance Survey have also reported steep declines in high cholesterol during the same time frame.<sup>51</sup> It is possible that diet and nutrition recommendations that have led to reductions in overall fats and *trans* fats in particular have led to these changes, albeit perhaps at the expense of a rise in dietary sugars, diabetes, and obesity. How these factors will balance out in their effect on clinically evident CVD or stroke in the future is unknown but bears close monitoring.

The AHA presidential advisory on food is medicine offers a synergistic road map to deploy the research, advocacy, and professional and public awareness that are needed for the widespread adoption and coverage of food is medicine interventions.<sup>52</sup> The approaches proposed in the advisory include medically tailored meals, medically tailored groceries, and produce prescriptions. Similar work around lifestyle and behavior changes, including physical activity, is critically important for young adults and children with cardiovascular risk factors. These interventions have also become an increasingly attractive approach for preventing and managing hypertension, diabetes, obesity, and their clinical consequences.52-55 Another key area of health for young adults is maternal health; the peripartum period can both unveil and exacerbate CVD and stroke risk factors and overt disease, and an increasing focus on this crucial moment in the life course could help reduce the burden of CVD and stroke among women, as well as transmission to their offspring, in years to come.56-58

Secondary prevention also has a critical role to play given the rising prevalence of CHD, HF, and stroke. The AHA has, since 2000, leveraged its implementation and quality improvement platforms, exemplified by the Get With The Guidelines programs, to conduct pioneering

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quality and health services research and to improve health outcomes for patients with CVD and stroke by improving adherence to the most updated recommendations for optimal care.59-62 Analyses of data from these programs provide evidence that management of patients according to the strongest (Class I) recommendations improves outcomes, including mortality.63,64 The Get With The Guidelines registries and related hospital certification and recognition programs provide participating hospitals with the tools to promote consistent adherence to the latest evidence-based clinical guidelines, to measure processes of care and outcomes, and to benchmark performance against national and regional standards.65-67 The Get With The Guidelines registries, which now consist of 5 core programs with data including >13 million patients, have led to measurable reductions in health disparities, although further work is needed.68,69 In the future, a focus on growth and sustainment of outpatient registries is crucial to achieving further improvement in secondary prevention metrics.

Another key area for intervention is brain health<sup>70</sup> given the striking projected increases in the prevalences of AF and stroke, as well as a growing understanding of the link between midlife cardiometabolic health and later-life cognitive decline.<sup>71</sup> The aging of the population will contribute to this increase because stroke and cognitive decline are most common in the elderly. The increasing prevalence may also reflect the fact that hypertension, which we project to increase, plays a relatively greater role in causing stroke,72 whereas hypercholesterolemia, which is projected to decrease, has a stronger relationship with coronary artery disease. Many analyses have recently demonstrated an increasing risk of stroke in younger adults,73-75 perhaps related to the increase in cardiometabolic disorders occurring at younger ages, as well as substance use disorders that may trigger stroke.76,77 Understanding the factors driving the increasing prevalence of stroke and implementing the best preventive and treatment strategies for stroke at both younger and older ages will be critical.<sup>59,62</sup> Beyond stroke, the growing prevalence of cardiometabolic risk factors threatens to increase the burden of aging-related cognitive decline and dementia. Recent research has suggested that vascular risk factors contribute to neurodegenerative diseases such as Alzheimer disease, leading to the broader concept of Alzheimer disease-related disorders, including vascular dementia and others.78-80 Accumulating evidence demonstrates the importance of physical activity in the prevention and treatment of several psychological and neurological conditions.<sup>81,82</sup> Our analyses did not include dementia as an outcome, but this is an important area for future study. In addition, although we could not measure psychological health in this effort because of data limitations, a large body of research supports the relationship between depression and other mental health conditions and the development

and prognosis of CVD and stroke.<sup>83</sup> The mind-heart-body connection remains an important area for future research and intervention.

Our findings also afford an opportunity to acknowledge the substantial progress made over the past 60 years in reducing the burden of CVD and stroke. In 1950, CVD and stroke were responsible for 425.6 deaths per 100000 people.<sup>84</sup> When we standardize mortality rates to the 2000 US population, we observe a 72.5% decline in the rate of death resulting from heart disease (from 588.8 deaths per 100000 people in 1950 to 161.5 deaths per 100 000 people in 2019) and a 79.5% decline in the rate of death from cerebrovascular diseases (from 180.7 deaths per 100 000 people in 1950 to 37.0 deaths per 100000 people in 2019).<sup>85</sup> These large declines are the result of greater understanding of the mechanisms underlying CVD and stroke, marked improvements in the control of cardiovascular risk factors and management of overt disease, and enormous strides in resuscitation science.<sup>86</sup> The AHA has played a major role in this progress through its large investments in basic, epidemiological, clinical, and implementation research; efforts to develop and disseminate clinical standards for prevention and treatment; public awareness campaigns; and advocacy. Yet, our findings highlight the continued need for highquality CVD and stroke data, research, and implementation in the coming decades.87

Our projections should be viewed in the context of previous similar efforts led by the AHA, as well as disease-specific projections completed by other groups. Prior projections as part of this series of work have proved accurate, assisting these planning and implementation efforts.<sup>17,18</sup> For example, the 2011 AHA publication forecasting the prevalence of CVD and stroke predicted a prevalence of CHD in 2020 of 8.6%; our estimate using the most recent NHANES data is 7.8%.<sup>18</sup> Estimates for HF (3.1% versus 2.7%) and stroke (3.6% versus 3.9%) are also reasonably accurate. Where the 2011 forecast differs most meaningfully is in hypertension; the previous prediction of the prevalence of hypertension reaching 35.7% in 2020 is lower than our finding of 51.2% in the observed data, largely because the definition of hypertension changed between the 2 analyses (The 2011 article used cutoffs of 140 mm Hg for systolic blood pressure and 90 mmHg for diastolic blood pressure; the current work uses 130 and 80 mm Hg, respectively). Other groups have also produced forecasting estimates, including recent work by Mohebi et al.<sup>88</sup> Our numbers are close to theirs in the nearer years (within a few percentage points, or 10% on a relative basis) but diverge to a greater degree by 2050 because we build disease-specific trends into our analyses rather than using only demographic changes in our projections. Collectively, these findings highlight the continued need for high-quality CVD and stroke data, research, and implementation in the coming decades.<sup>84</sup>

An important limitation is that these projections did not include estimates accounting for the COVID-19 pandemic. NHANES data collection efforts were paused during the early months of the COVID-19 pandemic (March-December 2020), resulting in a lack of comparable available data, and stable estimates from the later stages of the pandemic are not yet available. Other data sources that include postpandemic data such as the National Health Interview Survey generally report that 2021 and 2022 data appear relatively stable from before the pandemic,<sup>89</sup> which is reassuring, but differences in methodology preclude direct comparisons with our numbers. There is also substantial remaining uncertainty about the long-term effect of COVID-19 on cardiovascular risk factors and cardiovascular outcomes. During the pandemic, there was clear evidence of elevated mortality not only from COVID-19 itself but also from cardiovascular conditions, including heart attacks and strokes, particularly among Black individuals, Hispanic individuals, and Asian individuals.<sup>90</sup> However, the degree to which these elevations represent the effects of care disruption and stress related to COVID-19, which might diminish with time, compared with secondary inflammatory effects, which could have longer-term ramifications, remains uncertain. Data from the US Department of Veterans Affairs suggest that some of the cardiovascular effects of COVID-19 might be guite long-lasting, raising the possibility that our estimates would need to be revised even farther upward as new information becomes available.91 Given the broad uncertainty in this area, it will be important to revisit these projections with postpandemic data when feasible.

There are additional limitations to this study. First, we relied on 10 years of historical data to inform trends in risk factor and disease prevalence going forward; different choices on the duration of time used to calculate these trends could have yielded different estimates. We assumed no change in the diagnostic or therapeutic milieu for these conditions, and we did not model alternative scenarios that included major breakthrough therapies, although historical trends do include any such changes that occurred from 2010 to 2020. We have no way to separate out age, period, and birth cohort effects from therapeutic effects, but our use of condition-specific growth factors attempts to account for differences in therapeutic effects that could differ by condition. We assume that any future unanticipated advances would lead to lower-than-projected prevalence rates, making our estimates conservative in that sense. Major medical advances, for example, widespread use of newer agents such as glucagon-like peptide-1 agonists and other treatments for obesity, could have substantial effects on our projections but also could potentially exacerbate disparities if their distribution is not equitable.<sup>92</sup> Farther in the future, the potential for gene editing for both monoForecasting Cardiovascular Disease and Stroke Prevalence

genic and polygenic diseases presents similar opportunities and concerns.

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Second, we use race in this document as a proxy for individual, structural, and systemic racism and other differences in social determinants of health and lived experience among people in specific racial or ethnic groups, acknowledging that race is a social construct and an imperfect proxy for these factors. Smaller populations, including the combined category in NHANES data of AI/AN and multiracial people, are inadequately characterized in this work and should be a focus of data advancements, inclusion in CVD and stroke research. and therapeutic efforts in coming years. We were also unable to disaggregate Asian populations and Hispanic populations further, which masks potentially significant differences in access and outcomes among disparate Asian subgroups and Hispanic subgroups. There were populations with unique risk profiles for CVD and stroke that that we were unable to study at all, including LGBTQ+ (lesbian, gay, bisexual, transgender, gueer, and others) populations, because of a lack of available data, but this is another important area for advances in both data and tailored clinical interventions.<sup>93</sup> Similarly, although robust data suggest that people living in rural areas have a greater and more rapidly growing burden of CVD compared with those living in urban areas, publicly available NHANES data do not allow geographic stratification; thus, we were unable to make projections based on rurality or geography. Future forecast analyses could consider alternative data sources that allow geographic stratification and incorporate projected population shifts between urban and rural areas in the coming decades.

Third, our study did not include international data, which is an important area for future analysis. Fourth, because of historical limitations in data collection, we could not examine trends in noncigarette tobacco use, which is growing in prevalence, particularly in the pediatric and young adult population. Fifth, the PRISM analyses include risk estimates based on an explicit set of modeling assumptions that are described in detail elsewhere<sup>22</sup>; different choices, including different approaches to racespecific or race-agnostic prediction models, could yield different results. Sixth, we also did not include estimates of the prevalence or impact of mental health diagnoses, although we acknowledge that mental health is a key contributor to cardiovascular risk and health outcomes and an important area for future research. Last, we acknowledge that any set of predictions about the future must be interpreted with a great deal of caution because we are unable to anticipate major changes in diagnosis and treatment or even the advent of another global pandemic. Nonetheless, there is value in the exercise of making the best predictions possible with available data and being willing to course correct when new evidence becomes available.

## CONCLUSIONS

The prevalence of many cardiovascular risk factors and cardiovascular and cerebrovascular diseases will increase markedly over the next 30 years, absent interventions to change these trajectories. There are deep inequities among people who identify as Black, Hispanic, AI/AN, or multiracial in prevalence and in outcomes of disease that warrant targeted and sustained intervention. The aging of the population will require attention to workforce and to new approaches to care delivery to ensure adequate capacity to provide high-quality cardiovascular care. Clinical and public health interventions are urgently needed to effectively manage, stem, and even reverse these adverse trends in CVD and stroke and should be a priority on the national level.

### ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

#### Disclosures

#### Writing Group Disclosures

This advisory was approved by the American Heart Association Science Advisory and Coordinating Committee on April 16, 2024, and the American Heart Association Executive Committee on May 7, 2024. A copy of the document is available at https://professional.heart.org/statements by using either "Search for Guidelines & Statements" or the "Browse by Topic" area. To purchase additional reprints, call 215-356-2721 or email Meredith.Edelman@wolterskluwer.com

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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives \$5000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns \$5000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition. "Modest.

†Significant.

#### **Reviewer Disclosures**

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†Significant.

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