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Forecasting the Economic Burden of Cardiovascular Disease and Stroke in the United States through 2050: A Presidential Advisory From the American Heart Association

Supplemental Materials

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I. ADDITIONAL METHODS

A. Identification of cardiovascular risk factors and cardiovascular disease and stroke (CVDS) conditions in the Medical Expenditure Panel Survey data

Supplemental Table 1 lists the codes/questions used to identify cardiovascular risk factors in the Medical Expenditure Panel Survey (MEPS) data, while **Supplemental Table 2** lists the codes/questions used to identify CVDS conditions of interest in the MEPS data. For this analysis we used the 2015 through 2019 cycles of the MEPS data.

Supplemental Table 1. Questions/Codes Used to Define Cardiovascular Risk Factors in the 2015 through 2019 cycles of the Medical Expenditure Panel Survey data

Condition/Risk Factor	Qualifying Measures from MEPS
Hypertension	ICD-9: 401, 403 ICD-10: I10-I15
Hypercholesterolemia	ICD-9: 272 ICD-10: E78
Diabetes	ICD-9: 250 ICD-10: E10-E14

MEPS = Medical Expenditure Panel Survey

Supplemental Table 2. Questions/Codes Used to Define Cardiovascular Disease and Stroke Conditions of Interest in the 2015 through 2019 cycles of the Medical Expenditure Panel Survey data

Condition/Risk Factor	Qualifying Measures from MEPS
Coronary Heart Disease	ICD-9: 410, 411, 412, 413, 414 ICD-10: I20 - I25
Heart Failure	ICD-9: 428 ICD-10: I50, I42, I43
Stroke	ICD-9: 430, 431, 433, 434, 436, 438 ICD-10: I60-I69
Atrial Fibrillation	ICD-9: 427 ICD-10: I48
Other Cardiovascular Disease	ICD-9: 390, 391, 393–400, 402, 404, 405, 415-426, 429, 432, 435, 437, 440–448, 450–459, 745–747 ICD-10: I00, I01, I02, I04, I05, I06, I07, I08, I09, I11, I13, I26, I27, I28, I30, I31, I32, I33, I34, I35, I36, I37, I38, I39, I40, I41, I44, I45, I46, I47, I49, I51, I52, I70-I79, I80-83, I85-89, I95-99

MEPS Medical Expenditure Panel Survey

B. Additional Methodological Details for Calculation of Health Care Costs

We estimated projections of the health care costs (also known as "direct costs") of cardiovascular risk factors and CVDS conditions using the following four steps.

First, we estimated per person health care costs as a function of a health condition or risk factor using a two-part regression model. In the first part of the two-part model, we used a logistic regression model to predict the probability of any expenditures. For the second part of the model, we used a generalized linear model with a gamma distribution and a log link to estimate total annual health care expenditures for people with any expenditures.

When developing the model used to estimate costs of hypertension, diabetes, and hypercholesterolemia, we included these 3 risk factors, potentially costly or prevalent non-cardiovascular health care conditions (human immunodeficiency virus infection, cancer, injuries, pneumonia, chronic obstructive pulmonary disease, asthma, depression, mental health/substance abuse, arthritis, pregnancy, back pain, and skin conditions), and sociodemographic characteristics (age, sex, race andethnicity, education, income, insurance type, and region). Our models estimating costs of coronary heart disease, heart failure, stroke, atrial fibrillation, and other cardiovascular disease included these CVDS conditions, other health care conditions as in the risk factor models above, and sociodemographic characteristics.

Second, we calculated expenditures attributable to each CVDS condition or risk factor as the difference in predicted expenditures for a person with the specified condition and predicted expenditures for a similar person without the condition. We estimated the per person cost attributable to each condition or risk factor for each age group X sex category based on coefficients from the national, pooled model.

Typically, to calculate disease-attributable expenditures, first, expenditures are predicted using observed diseases. Second, expenditures are predicted setting the disease of interest (e.g., coronary heart disease) to zero and leaving all other covariates as they are in the data. Finally, the difference between the two sets of predicted expenditures is the disease-attributable expenditure. However, in previous work, we have shown that, in nonlinear models, such as the model used here, this approach will lead to double counting of expenditures for co-occurring diseases, regardless of whether one disease causes the other.[1] Double counting of expenditures is a particular problem in cases where more than one condition is treated during a single office visit or hospitalization. We used a technique, termed "complete classification" and described in an earlier study, to ensure that no double counting occurs.[1] Using the parameters of the econometric model, we specifically treated each disease and combination of diseases observed in the data as a separate entity when calculating the attributable costs. For example, coronary heart disease alone and coronary heart disease with stroke would be treated as two different diseases in the attributable expenditure calculation described above. We then divided the total expenditures attributable to the combinations of diseases back to the constituent diseases using the parameters from the model to construct shares for each constituent disease within a combination (i.e., a share of all coronary heart disease with stroke disease costs that are attributable to coronary heart disease). The shares attribute a greater share of the joint expenditures to the disease with the larger coefficient in the main effect. The formula to construct the shares is based on the seminal publication by Trogdon, Finkelstein, and Hoerger.[1]

Our third step in calculating projections of direct health care costs was to adjust the per person cost estimates from MEPS to account for nursing home spending. We used an approach developed by Neuwahl et al to estimate nursing home costs of CVDS, hypertension, and diabetes.[2] Data on nursing home costs associated with other risk factors were not available. We started with the 2021 National Health Expenditure Accounts data from the "Nursing Care Facilities and Continuing Care Retirement

Communities" category and adjusted it to represent costs for nursing care facilities only. Specifically, the 2021 Census Service Annual Survey reported that 76.5% of costs from that category were for nursing care facilities. We then calculated total nursing home costs of each condition by applying the attributable fraction of nursing home costs of hypertension, heart disease, and diabetes to the total nursing home costs. We calculated the atrial fibrillation as the difference in prevalence of these conditions in the nursing homes and in the community using data from the 2017-2018 National Study of Long-Term Care Providers.[3] Finally, we divided total nursing home costs of each condition by the total number of people (in nursing homes and community) with the condition to calculate nursing home costs of each condition per person with the condition. We added per person nursing home costs to the per person costs from MEPS to estimate health care costs of each condition accounting for nursing home costs.

Fourth, to estimate projected costs, we first followed recommendations from AHRQ to inflate dollar values to 2022 dollars using Personal Consumer Expenditures Health Component.[4,5]

Fifth, the coefficient of variation in unit cost for each condition of interest was estimated from the generalized linear model described above. This coefficient of variation was then multiplied by the point estimate of health care costs of each condition (after accounting for nursing home costs) to compute the standard deviation of unit costs.

We then multiplied the per-person cost of each CVDS condition or risk factor in each age/sex cell by the projected number of people with the condition or risk factor in the corresponding age/sex/race-ethnicity cell for years 2020 to 2050. We followed the same approach multiplying the per person costs in each age/sex cell by the projected number of people in each age/sex/education, age/sex/income, and age/sex/insurance category.

We calculated the projected number of people with each condition and risk factor using similar methodology as described elsewhere.[6] However, instead of the NHANES data, we used 2015–2019 MEPS to predict prevalence of each condition and risk factor. In MEPS, conditions are identified if a respondent had health care visits or received care for the condition during the interview year, thus in our calculation of costs for the conditions, only those patients who receive treatment incur health care costs within a given year. We applied the historical rates of increase or decline in age-/sex-specific prevalence using the 2009-March 2020 NHANES data developed for the prevalence projections to the baseline prevalence from MEPS.[6]

Finally, we used Congressional Budget Office assumptions for future health care cost growth above and beyond growth due to population growth and aging.[7] We assumed that the costs of CVDS conditions and risk factors would increase at the same rate as overall health care expenditures between 2020 and 2050: an average annual rate of 1.91%.

C. Additional Methodological Details for Calculation of Productivity Losses

We estimated two types of "indirect" costs: lost productivity from morbidity and lost productivity from premature mortality. We estimated these indirect costs among adults aged 20-79 years old.

Morbidity Costs of Cardiovascular Risk Factors and Conditions

Morbidity costs represent the value of foregone earnings from lost productivity due to CVDS conditions or risk factors. The morbidity costs included two components: work loss among currently employed individuals and work loss among individuals too sick to work.[8] We estimated per capita work loss days due to CVDS conditions or risk factors by age and sex using 2015–2019 MEPS. We estimated negative binomial models for annual days of work missed due to illness or injury and used the same specifications for each CVDS condition and risk factor as in the health care cost regressions with an additional control for occupation type. Per capita work days lost attributable to CVDS conditions or risk factors for each age/sex cell were based on coefficients from the national, pooled model. We avoided double-counting of costs resulting from individuals with multiple conditions by employing the method described by Trogdon and colleagues.[1] We generated total work loss costs by multiplying per capita work days lost due to CVDS conditions and risk factors (by age and sex) by (a) prevalence of the condition or risk factor (by age, race and ethnicity, and sex) from MEPS, (b) the probability of employment given the condition or risk factor (by age, race and ethnicity, and sex) from MEPS, (c) mean per capita daily earnings (by age and sex) from the 2022 Current Population Survey, and (d) Census population projections counts (by age, race and ethnicity, and sex). We repeated these calculations of total work loss costs for education, income, and insurance subgroups.

To estimate work loss among individuals too sick to work due to CVDS conditions and risk factors, we first estimated the number of people too sick to work who would have been employed except for their condition. For the community-living population, we multiplied the number of people not in the labor force due to illness/disability by age from the 2022 Current Population Survey by the percentage of all work loss attributable to the condition based on the MEPS regression analysis for work loss days described above. The assumption was that the percentage of workdays missed due to the condition was the same for days missed by being out of the labor force and days missed conditional on working. For the nursing home population, we multiplied the number of nursing home residents with hypertension, heart disease, or diabetes from the 2017-2018 National Study of Long-Term Care Providers (as percentage of total population) by Census population counts and the probability of employment among people with CVDSS conditions or risk factors from MEPS. The last component accounts for individuals with these conditions who might not work even if they had not been in nursing homes. Finally, we multiplied the sum of the number of people living in nursing homes and the community too sick to work due to each condition or risk factor by 250 work days per year and mean annual earnings from the 2022 Current Population Survey.

Mortality Costs of CVDS Conditions

Mortality costs represent the value of foregone earnings and household productivity losses from premature mortality due to CVDS conditions (coronary heart disease, stroke, atrial fibrillation, and other cardiovascular disease). We estimated mortality costs using the human capital approach, which values premature death from a disease as future foregone productivity losses .[8-10] We used the number of deaths with each condition by age group, sex, race andethnicity, education, income, and insurance and multiplied them by estimates of the present value of lifetime earnings and household productivity costs to calculate total mortality costs.

We obtained death rates for each CVDS condition by age, race and ethnicity, and sex from the 2021 CDC Wide-ranging Online Data for Epidemiologic Research (CDC WONDER) mortality data.[11] CDC WONDER is a public-use online database for epidemiologic research that contains information about mortality (deaths) and Census data. We pulled the rates of deaths with each CVDS condition as the underlying cause of death.

Assuming the death rates remain constant within each age, race and ethnicity, and sex cell, we multiplied the death rates by Census population projections to project the number of CVDS and diabetes deaths by age, race and ethnicity, sex, and year through 2050. We applied age group- and sex-specific death rates across all education, income, and insurance categories to Census population projections by education, income, and insurance subgroups because CDC WONDER does not provide mortality data by these characteristics.

For the baseline year of projections, we estimated the present value of future earnings using national estimates of annual earnings from the 2022 Current Population Survey (inflated to 2022 dollars). We estimated the present value of household production using the dollar value of household production from the Expectancy Data Economic Demographers' "Dollar Value of a Day, 2020" publication (inflated it to 2022 dollars).[12] For each year of age at which the expected production occurs, we multiplied future costs by the probability of surviving to that year. We used 2021 U.S. life tables from the National Vital Statistics Report to calculate compounded survival rates for each age group.[13] To ensure that losses were applied only to the populations expected to incur the losses, we multiplied the age group- and sex-specific labor costs by age group- and sex-specific employment rates, and we multiplied age group- and sex-specific percentages of people living in households by household production losses by age and sex.[9] We also adjusted future earnings for expected future growth in productivity using a 1% annual growth rate and discounted the costs using a 3% annual discount rate.[9]

To generate projections of indirect costs, we assumed that the real value of indirect costs will grow through 2050 at the average annual growth rate of real earnings (0.8%) estimated by the Congressional Budget Office.[7]

D. Subgroup Analyses

We examined health care costs, productivity losses due to morbidity, productivity losses due to mortality, and total cost of CVDS by age group (20-44 years, 45-64 years, 65-79 years, 80 years or older), sex (men, women), racial or ethnic population groups (White non-Hispanic, Black non-Hispanic, Asian non-Hispanic, Hispanic, or American Indian/Alaska Native or multiracial); educational attainment (less than high school; completed high school/GED diploma; some college/associate's degree; bachelor's degree or higher); income (very low, low, middle, high); and insurance status (Medicare, Medicaid, no insurance private/commercial/other). For the insurance status analysis, the four subgroups were mutually exclusive – i.e., an individual could only contribute data to one subgroup. Any patient enrolled in Medicare was assigned to the Medicare group regardless of the presence of other forms of insurance (including Medicaid), since Medicare is typically the primary payor.

E. Uncertainty Intervals

We estimated uncertainty around the cost estimates using a bootstrapping approach with 1,000 iterations.

For health care costs, we accounted for uncertainty in condition prevalence, rate of growth/decline in prevalence, and per-person medical costs. First, for each bootstrap iteration, we estimated the number of people with each condition by subgroup. To account for variation in prevalence estimates, in each bootstrap iteration, we redrew logit coefficients used to predict 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 growth and decline rates using normal distributions defined by the estimated coefficients and standard errors. Second, we applied subgroup-specific per-person medical costs to the estimated number of people with the condition in each subgroup and aggregated costs across groups. Third, we defined a gamma distribution for per-person costs at the aggregate level using the mean and standard deviation (calculated as mean multiplied by the coefficient of variation, which was derived from the condition coefficient and its standard error from the cost regression model). Fourth, we took a draw from a standard uniform distribution (range: 0-1), and then for each year, we assigned the value of the cumulative distribution function of the gamma distribution described above corresponding to the standard uniform draw.

For productivity losses related to morbidity, we accounted for uncertainty in condition prevalence, prevalence growth/decline rates, and per-person workdays lost. We estimated uncertainty around work loss costs among employed individuals using the same approach as for medical costs but using variation around per-person workdays lost instead of medical costs. We estimated uncertainty around work loss costs among those who are too sick to work using variation around counts of people with the condition.

For productivity losses due to premature mortality, we accounted for uncertainty around mortality rates using standard errors available from the CDC WONDER. For each bootstrap iteration, we drew from a standard uniform distribution and assigned the value of the cumulative distribution function of the gamma distribution defined based on the mortality rate and standard errors corresponding to the standard uniform draw.

For each iteration, we summed estimated health care costs and productivity losses due to morbidity and premature mortality to compute the total cost for each condition. We also summed each iteration’s costs for coronary heart disease, stroke, heart failure, atrial fibrillation, and other cardiovascular disease to calculate the total cost of all CVDS conditions combined.

The 5th and 95th percentile values constituted the lower and upper bound respectively of the 90% uncertainty interval.

II. ADDITIONAL RESULTS

Supplemental Table 3. Annual Per-Capita Health Care Costs of Cardiovascular Risk Factors and Conditions in Key Subgroups. The table shows the annual health care cost ("direct cost") attributable to key cardiovascular risk factors or CVD, among individuals who received health care for a given condition. All costs are inflated to 2022 US Dollars and rounded to two significant figures.

	Annual incremental health care cost of living with a cardiovascular risk factor or condition among those who sought care, *2022 USD*							
	Cardiovascular Risk Factors			CVDS Conditions				
	Hypertension	Diabetes	Hypercholesterolemia	Coronary Heart Disease	Stroke	Heart Failure	Atrial Fibrillation	Other Cardiovascular Disease
Sex								
Men	2,500	6,900	1,200	12,000	35,000	17,000	12,000	10,000
Women	2,600	7,700	1,300	15,000	34,000	18,000	15,000	11,000
Age Group								
20-44 years	1,700	4,200	870	6,700	16,000	4,700	5,500	4,800
45-64 years	2,200	6,200	1,100	9,800	30,000	14,000	8,500	7,700
65-79 years	2,900	8,600	1,400	14,000	36,000	19,000	13,000	11,000
80 years or older	3,200	10,000	1,400	18,000	47,000	21,000	18,000	15,000

CVDS = Cardiovascular Disease and Stroke

Supplemental Table 4. Trends in Population-Level Economic Burden of Cardiovascular Risk Factors in U.S. Adults, 2020-2050. All costs are in 2022 USD billions. Numbers in parentheses represent percentage change from 2020.

	2020	**2030**	**2040**	**2050**
	Costs in USD *billions* (90% uncertainty interval) [percentage change from 2020]			
Hypertension	160.1 (133.0 – 189.6) [ref]	254.0 (206.6 – 304.9) [59%]	370.5 (292.0 – 456.1) [131%]	512.7 (393.5 – 637.4) [220%]
Diabetes	186.4 (172.2 – 201.8) [ref]	329.5 (299.4 – 362.9) [77%]	519.0 (461.5 – 579.6) [178%]	765.2 (670.3 – 863.1) [311%]
Hypercholesterolemia	54.0 (36.1 – 74.0) [ref]	61.2 (40.2 – 84.6) [13%]	64.6 (41.5 – 92.6) [20%]	65.8 (40.0 – 97.5) [22%]

Supplemental Table 5. Trends in Population-Level Economic Burden of Cardiovascular Disease and Stroke (CVDS) in U.S. Adults, Overall and by Condition, 2020-2050. All costs are in 2022 USD billions. Numbers in parentheses represent percentage change from 2020.

	2020	2030	2040	2050
	Costs in USD *billions* (90% uncertainty interval) [percentage change from 2020]			
All CVDS Combined				
Total Cost	627.2 (601.3 – 658.9) [ref]	951.0 (872.7 – 1051.4) [52%]	1364.9 (1182.9 – 1591.5) [118%]	1850.9 (1517.3 – 2,265.5) [195%]
Health Care Costs	393.2 (368.0 – 424.2) [ref]	679.6 (604.6 – 775.1) [73%]	1051.9 (879.7 – 1265.7) [168%]	1489.8 (1177.1 – 1883.3) [279%]
Productivity Losses – Premature Mortality	217.4 (214.1 – 220.4) [ref]	245.2 (241.4 – 248.9) [13%]	276.5 (272.0 – 280.8) [27%]	311.8 (306.5 – 316.8) [43%]
Productivity Losses – Morbidity	16.6 (15.0 – 18.6) [ref]	26.2 (20.6 – 33.6) [58%]	36.5 (25.1 – 51.7) [120%]	49.3 (30.6 – 73.9) [197%]
Coronary Heart Disease				
Total Cost	260.4 (245.5 – 277.4) [ref]	354.8 (326.4 – 385.4) [36%]	465.8 (411.3 – 517.6) [79%]	583.6 (491.0 – 666.1) [124%]
Health Care Costs	144.7 (130.0 – 161.5) [ref]	224.4 (196.9 – 253.6) [55%]	318.4 (265.2 – 367.8) [120%]	417.3 (323.8 – 495.5) [188%]
Productivity Losses – Premature Mortality	108.7 (106.7 – 110.9) [ref]	121.9 (119.6 – 124.5) [12%]	137.8 (135.0 – 140.8) [27%]	155.4 (152.1 – 158.9) [43%]
Productivity Losses – Morbidity	7.0 (6.1 – 7.9) [ref]	8.5 (7.2 – 10.1) [22%]	9.6 (7.6 – 12.3) [37%]	10.9 (8.0 – 15.1) [57%]
Heart Failure				
Total Cost	46.6 (40.2 – 54.9) [ref]	72.1 (50.1 – 110.5) [55%]	104.9 (54.7 – 196.2) [125%]	142.4 (55.9 – 311.2) [206%]
Health Care Costs	32.2 (25.9 – 40.3)	55.2 (34.0 – 92.7)	85.6 (36.9 – 173.9)	120.5 (35.6 – 283.8)

	[ref]	[72%]	[166%]	[274%]
Productivity Losses – Premature Mortality	13.7 (13.0 – 14.5) [ref]	15.8 (15.0 – 16.8) [15%]	17.7 (16.7 – 18.8) [29%]	19.9 (18.8 – 21.2) [45%]
Productivity Losses – Morbidity	0.7 (0.4 – 1.2) [ref]	1.1 (0.4 – 2.8) [54%]	1.5 (0.4 – 5.1) [117%]	2.0 (0.3 – 7.8) [196%]
Atrial Fibrillation				
Total Cost	59.4 (48.0 – 72.2) [ref]	93.6 (75.2 – 114.5) [58%]	133.6 (105.7 – 165.3) [125%]	174.8 (137.1 – 219.3) [194%]
Health Care Costs	54.8 (43.3 – 67.5) [ref]	88.0 (69.4 – 108.4) [61%]	127.2 (99.9 – 158.8) [132%]	167.3 (130.2 – 211.5) [205%]
Productivity Losses – Premature Mortality	2.9 (2.7 – 3.2) [ref]	3.4 (3.2 – 3.7) [16%]	3.7 (3.4 – 4.0) [27%]	4.1 (3.7 – 4.5) [39%]
Productivity Losses – Morbidity	1.6 (1.0 – 2.4) [ref]	2.2 (1.3 – 3.3) [34%]	2.7 (1.6 – 4.2) [68%]	3.4 (1.9 – 5.4) [112%]
Stroke				
Total Cost	66.6 (57.7 – 78.7) [ref]	145.9 (81.4 – 219.4) [119%]	263.2 (105.4 – 436.1) [295%]	423.2 (130.9 – 736.8) [535%]
Health Care Costs	30.5 (21.9 – 42.3) [ref]	99.2 (39.5 – 166.5) [225%]	204.6 (57.6 – 367.0) [570%]	350.6 (75.7 – 650.5) [1049%]
Productivity Losses – Premature Mortality	34.5 (33.1 – 35.7) [ref]	40.0 (38.4 – 41.6) [16%]	45.6 (43.7 – 47.4) [32%]	51.9 (49.7 – 54.1) [51%]
Productivity Losses – Morbidity	1.6 (1.0 – 2.4) [ref]	6.8 (1.5 – 13.1) [316%]	13.0 (1.6 – 26.2) [699%]	20.7 (1.8 – 42.3) [1170%]

Supplemental Table 6. Trends in Population-Level Economic Burden of Cardiovascular Disease and Stroke in U.S. Adults, By Key Subgroups, 2020-2050. Total costs – including direct costs related to health care spending and indirect costs related to productivity losses from morbidity and premature mortality – are shown in 2022 USD billions. Numbers in parentheses represent percentage change from 2020.

	2020	2030	2040	2050
	Costs in USD *billions* (percentage change from 2020)			
Sex				
Women	272.8 (ref)	433.7 (59%)	641.6 (135%)	885.0 (224%)
Men	354.4 (ref)	517.3 (46%)	723.3 (104%)	966.0 (173%)
Age Group				
20-44 years	52.7 (ref)	86.9 (65%)	129.6 (146%)	190.4 (261%)
45-64 years	210.7 (ref)	257.6 (22%)	360.9 (71%)	493.1 (134%)
65-79 years	236.6 (ref)	367.5 (55%)	448.3 (89%)	569.1 (140%)
80 years or older	127.1 (ref)	238.9 (88%)	426.1 (235%)	598.5 (371%)
Race and Ethnicity				

Asian Non-Hispanic	17.3	34.7	62.7	103.4
	(ref)	(100%)	(262%)	(497%)
Black Non-Hispanic	83.3	124.7	184.1	257.7
	(ref)	(50%)	(121%)	(209%)
Hispanic	52.2	103.2	185.3	307.5
	(ref)	(98%)	(255%)	(489%)
White Non-Hispanic	462.2	667.1	896.8	1123.2
	(ref)	(44%)	(94%)	(143%)
American Indian/Alaska Native or multiracial	12.1	21.3	36.0	59.2
	(ref)	(75%)	(197%)	(387%)
Insurance Type				
Medicare	384.2	625.4	901.1	1205.4
	(ref)	(63%)	(135%)	(214%)
Medicaid	33.6	44.4	62.6	86.5
	(ref)	(32%)	(86%)	(157%)
Private and Other Insurance	182.3	243.8	347.2	483.1
	(ref)	(34%)	(91%)	(165%)
No insurance	27.0	37.4	54.0	76.0
	(ref)	(39%)	(100%)	(181%)
Educational Attainment				
Less than High School	89.7	113.9	155.6	189.2
	(ref)	(27%)	(74%)	(111%)
High School/GED Degree	199.0	275.8	387.8	486.0
	(ref)	(39%)	(95%)	(144%)
Some College/Associate's Degree	167.3	279.5	408.5	577.8

	(ref)	(67%)	(144%)	(245%)
Bachelor's Degree or Higher	171.2	281.8	413.0	597.9
	(ref)	(65%)	(141%)	(249%)
Income				
Very Low	95.2	143.5	206.5	279.8
	(ref)	(51%)	(117%)	(194%)
Low	81.8	127.7	186.8	253.4
	(ref)	(56%)	(128%)	(210%)
Middle	183.5	281.7	407.0	552.6
	(ref)	(54%)	(122%)	(201%)
High	266.7	398.1	564.6	765.1
	(ref)	(49%)	(112%)	(187%)

Supplemental Table 7. Deterministic Sensitivity Analyses. Varying the annual rate of growth in medical costs (base case = 1.91%, range 1.31% to 2.51%) produced a -13.1% to +15.5% change in the projected total cost related to cardiovascular disease and stroke (CVDS) in 2050, with higher growth rates producing higher projections of health care costs and hence of total cost. Varying the annual change in real (i.e., inflation-adjusted) earnings (base-case value = 0.8%, range 0.3% to 1.3%) produced a -2.% to +3.1% change in the projected total cost of CVDS in 2050.

	Annual change in medical costs, %	Annual change in real earnings, %	Health care costs for CVDS in 2050 $, *billions* (% change from base-case estimate for 2050)	Productivity losses from CVDS in 2050 $, *billions* (% change from base-case estimate for 2050)	Total cost of CVDS in 2050 $, *billions* (% change from base-case estimate for 2050)
Base-Case Analysis					
	1.91	0.80	1489.8 (ref)	361.1 (ref)	1850.9 (ref)
Sensitivity Analyses					
	1.31	0.80	1248.0 (-16.2%)	361.1 (0.0%)	1609.1 (-13.1%)
	2.51	0.80	1776.7 (+19.2%)	361.1 (0.0%)	2137.84 (+15.5%)
	1.91	0.30	1489.8 (0.0%)	311.1 (-13.9%)	1800.9 (-2.7%)
	1.91	1.30	1489.8 (0.0%)	418.9 (+16.0%)	1908.7 (+3.1%)

Supplemental Table 8. Limitations. The results of a model such as ours are dependent on a series of assumptions about inputs and trends, each of which is subject to error.

Input Parameter or Model Characteristic	Limitation or Source of Uncertainty
Race and ethnicity taxonomy and sample size	• Analysis adopted the race and ethnicity taxonomy used in the source data, which may mask substantial within-group differences. • Small sample size precluded separate evaluation of American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and multiracial populations, which have a disproportionately high burden of cardiovascular risk factors and CVDS conditions.
Population	• Restricted to U.S. adults ages 20 years or older. Unable to assess the cost of cardiovascular risk factors and CVDS conditions in children using our cross-sectional approach since the costs of these conditions typically manifest many decades into the future. • Did not include health care costs for active-duty armed forces and the National Guard/Reserves who are insured by TRICARE. • Did not include incarcerated populations, which are known to have a higher prevalence of cardiovascular risk factors than the general population. • Restricted to the U.S. population, but similar increases in health care and societal costs of cardiovascular risk factors and CVDS conditions are expected in other countries, particularly in lower- and middle- income countries that face a high burden of CVDS conditions and limited access to resources for prevention and treatment.
Cardiovascular Risk Factors	• Among the cardiovascular risk factors identified by the AHA's key health markers for primordial prevention, Life's Essential 8™, we only quantified the incremental cost of living with hypertension, diabetes, and hypercholesterolemia. • We did not quantify the incremental cost of living with obesity since its short-term cardiovascular risk is primarily mediated through increased risk of hypertension, diabetes, and hypercholesterolemia. • We did not quantify the incremental costs of tobacco use because CVDS represents only one of many conditions caused by tobacco use (including malignancies and lung diseases); focusing on costs related to CVDS substantially underestimates the health economic burden of tobacco use. • We did not quantify the incremental costs of physical inactivity because costs estimated from observational data represent a combination of a lack of leisure-time physical activity among those who can perform it, and an

	inability to perform physical activity where social, environmental, or clinical factors constrain physical activity levels. People with underlying medical conditions that have led to inactivity would likely have higher costs than inactive people without such underlying conditions, but we could not clearly classify people in these two groups and could not accurately quantify costs attributable to physical inactivity. • Available datasets precluded independently examining the incremental cost of poor diet or sleep since these are inconsistently captured.
Baseline prevalence	• Relied on patient self-report of seeking care for risk factors and conditions, which can be challenging for some risk factors such as hypercholesterolemia or hypertension. • Clinical and cost inputs were derived using pre-pandemic data given the substantial disruption to cardiovascular care delivery in the early years of the COVID-19 pandemic. The pandemic produced short-term increases in adverse cardiovascular and all-cause mortality,[14,15] but whether it will lead to long-term changes in burden of cardiovascular risk factors or CVDS conditions remains uncertain.
Mortality estimates	• Mortality estimates relied on 2021 lifetables and age-/sex-specific cause of death, which could change over time. • Age-/sex-specific mortality rates were used in education, income, and insurance subgroups as differences by these categories are not available in the source data (CDC WONDER). • Productivity losses due to premature death relied on correct capture of underlying cause of death, which may underestimate the burden of certain cardiovascular conditions, particularly heart failure.[16]
Baseline utilization	• Per-person cost estimates were not stratified by race, ethnicity, or socioeconomic characteristics, because barriers to accessing care can falsely decrease costs among groups that have historically been marginalized or excluded from care, and thus give the false impression that CVDS-related costs are lower in these groups; applying the same average costs across these groups may potentially mask both over- and under-use among individual groups. • Preliminary data suggest changes in health care-seeking behavior due to the COVID-19 pandemic, which may affect intermediate- to long-term CVDS outcomes.
Baseline costs	• Cost projections were based on nationally representative mean costs. However, patient-level health care costs are positively skewed, and some individuals will accrue much higher costs. • Health care costs may be altered by newer models of care delivery, such as telemedicine. • Estimates of morbidity-related productivity losses did not include household production losses.

	• Estimates did not include costs associated with informal or unpaid caregiving. Prior studies have estimated that costs of informal caregiving for patients with CVDS represent an additional 11% of health care and productivity costs attributable to CVD, costing an estimated $64.3 billion dollars in 2022 U.S. dollars.[17] Informal caregiving costs are particularly substantial among patients with a prior stroke and among individuals 80 years or older.
Trends over time	• Historic trends derived from pre-pandemic data and would need to be updated if future studies demonstrate persistent changes in risk factor burden or outcomes related to the pandemic. • Future estimates of the size and composition of the U.S. population were based on data from the U.S. Census, which account for births, deaths, and net international migrations.[18] Major change is social or immigration policy may alter long-term demographic trends. • Major advances in prevention may lower the future prevalence of cardiovascular risk factors and CVDS conditions and reduce associated costs in the future. For instance, widespread adoption of disruptive therapies like glucagon-like peptide-1 agonists may lower the prevalence of obesity and related metabolic conditions and associated health care costs, but, at least in the short-term, markedly increase pharmaceutical spending. • Inequitable adoption of new technologies, often driven by cost-related barriers to access, may exacerbate the disparities between major groups described here. • Simplifying assumption that health care costs of cardiovascular risk factors and CVDS conditions will grow at a similar rate, but this may not be true. Some evidence to suggest that over the past three decades, costs for cardiovascular risk factors may have increased faster than costs related to CVDS conditions.[19,20] • Projections may be underestimates if economic productivity continues to increase, particularly among older individuals.
Other	• We did not analyze overall health care costs, but focused on cardiovascular risk factors and conditions, since CVDS are leading causes of death in the U.S.

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