Healthy Hearts Calculator and ModelHealth: CVD Technical Documentation

(Last updated December 6, 2018)

1 Introduction

The data used to generate the Healthy Hearts Calculator results were produced using an adapted version of the HealthPartners Institute ModelHealth™: Cardiovascular disease microsimulation model. ModelHealth: CVD is a collection of scientific evidence-based parameters, mathematical functions, and procedural logic—implemented using Visual Basic 6 and Microsoft Excel—designed to evaluate cardiovascular disease prevention policies at the population level. The primary unit of observation is a hypothetical person who takes on a variety of detailed attributes (such as age, sex, race/ethnicity, BMI, systolic blood pressure, disease status, etc.). The lifetime progression of these characteristics is simulated over time. Epidemiological data sourced from the Framingham Heart Study—a major cardiovascular disease surveillance study ongoing since 1948—plays an important role in this model's construction.

Although the mechanics of ModelHealth: CVD center on individuals—i.e., through microsimulation—policy relevance is achieved through aggregating a sufficient number of individuals to be representative of a policy-relevant group, such as the U.S. population. Policy interventions are evaluated by simulating the same population twice—once with the policy intervention of interest, such as a clinical preventive service, imposed, and once without it. In practice, this evaluation approach is comparable to a randomized controlled trial (RCT) design, with the treatment and placebo being applied to the same hypothetical research population.

The Healthy Hearts Calculator uses dynamically reweighted results from ModelHealth: CVD—aggregated amongst defined population strata (e.g., defined by age, sex, race/ethnicity, and CVD risk status)—to produce estimates of policy effects for specific geographical regions or custom-defined populations.

2 Model Overview

Initialization

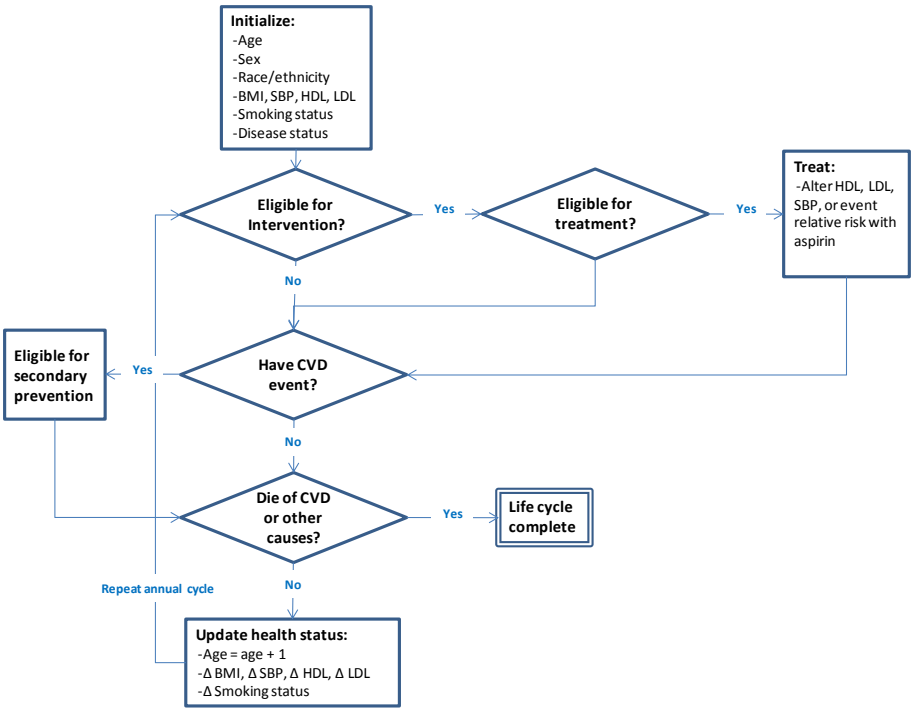
Figure 1 illustrates the process flow of ModelHealth: CVD. Each new simulation iteration first involves initializing a hypothetical person at a specific age (e.g., 18), with individual characteristics (such as sex and race/ethnicity) and initial health parameters (such as cholesterol and blood pressure levels and BMI) all drawn from U.S.-representative distributions. Thereafter, ModelHealth: CVD simulates the hypothetical person's lifespan and the natural history of cardiovascular disease in annual cycles.

Interventions and background preventive services

At the beginning of each annual cycle, the model determines whether the simulated individual receives a specified intervention of interest or a background preventive service. Background preventive services in ModelHealth: CVD—when they are not being evaluated directly—are screening for hypertension, screening for lipid disorders, and aspirin counseling, as recommended by the U.S. Preventive Services Task Force [1-3]. Eligibility for preventive services may be dictated by the parameters of a policy intervention—such as screening for lipid disorders in men aged 20-35 with elevated CVD risk in the treatment arm—or by contemporary adoption patterns of background preventive services (i.e., applied to both policy arms) observed in the population. Upon receiving a preventive service, the model determines whether the individual is eligible for treatment (e.g., taking statins for treating high cholesterol). Pharmacological

treatment criteria for dyslipidemia and hypertension are implemented to be consistent with the Adult Treatment Panel III 4] and the JNC-7 [5] guidelines, respectively.

Figure 1: ModelHealth: CVD Flow Diagram



Treatment

The effect of treatment for high cholesterol or high blood pressure is realized through its impact on high- and low-density lipoprotein cholesterol (HDL-C/LDL-C) or systolic blood pressure (SBP), respectively. For example, an individual with high cholesterol could be treated with a statin and see a 30 percent reduction in LDL and a 10 percent increase in HDL, but taking a statin does not translate to a direct reduction in the individual's risk of a myocardial infarction. Instead, these changes will translate to lowered risk of disease, as determined by the customized risk engine described in the following section. In contrast, taking aspirin on a daily basis directly alters the relative risk of having an event (such as a myocardial infarction or a gastrointestinal bleed).

Disease events

The next step in each annual cycle (following prevention/treatment) is to determine whether the individual experiences any non-fatal disease events during that year. Specifically, a person may: (a) have a myocardial infarction, (b) have an ischemic stroke, (c) have a hemorrhagic stroke, (d) experience angina pectoris, (e) develop congestive heart failure, (f) develop intermittent claudication, (g) develop diabetes, and/or (h) experience a gastrointestinal bleed. The annual risks of (a)-(g) are determined by equations derived specifically for this model using data from the Framingham Heart Study [6, 7]. If a person has a cardiovascular event—that is, one or more of (a)-(f)—and survives, that person becomes eligible for secondary prevention. Treatment for dyslipidemia and hypertension for secondary prevention are similarly based on ATP III and JNC-7 guidelines, respectively, and men and women who have a non-fatal myocardial infarction or ischemic

stroke are also eligible for aspirin chemoprophylaxis.

In each annual cycle, a person also faces a risk of dying from cardiovascular disease or from other causes. The annual risk of death from CVD-related causes also is based on a study-specific equation derived from the Framingham Heart Study. The probability of dying from a cause other than CVD is derived from U.S. life tables [8] and compressed mortality data in the CDC Wonder database [9]. A person who dies of any cause—or reaches the age of 100—exits the model, with the person's lifecycle complete.

Aging and progression of natural history

Finally, when a person survives a cycle, that individual's health status and parameters must be transitioned for the next cycle. Each cycle is annual, and therefore, the individual's age will simply increment by one. Biological cardiovascular risk factors—namely, HDL, LDL, SBP, and BMI—naturally progress over time, and annual transitions are modeled by a two-step process. First, it is determined whether the individual's risk factor increases, decreases, or stays the same. These probabilities are based on a multinomial logistic equation (which accounts for age, previous values, and other individual characteristics). Second, if a specific risk factor is determined to increase or decrease, a secondary set of equations determines the size of this change. The process repeats itself until the simulated person dies (or reaches age 100). Tobacco initiation and cessation probabilities are derived from National Health Interview Survey data [10] and published estimates from longitudinal studies [11, 12].

3 Model Data Sources and Parameters

A computational model with the degree of detail contained within ModelHealth: CVD requires a considerable amount of data and scientific evidence to specify all necessary parameters and inform the key transitional mechanisms. This lengthy section describes the many data sources (and in some cases, assumptions) required for the model to operate.

3.1 Parameter Initialization

Each iteration of ModelHealth: CVD begins with the initialization of a new representative individual to simulate. As a birth cohort study, the initial age for each agent is 18 years. Age sex and race/ethnicity assignment are derived from the American Community Survey three-year sample [13]. Lifetime education is derived from the combined 2009-2012 Current Population Surveys [14]. Initial CVD risk factors, including BMI, SBP, LDL, and HDL are derived from the combined 2001-2010 National Health and Nutrition Examination Survey (NHANES) surveys [15-19]. Diabetes and prior CVD status at model initialization also are derived from the combined NHANES surveys. Initial smoking status is derived from the 2009 National Health Interview Survey [20].

3.2 Progression of Biological Risk Factors

After each annual cycle in ModelHealth: CVD, an individual's time-dependent attributes must be transitioned to reflect the age progression and natural history of biological cardiovascular disease risk factors over one's lifetime. A person's age simply increments by one, but the remaining risk factors (BMI, HDL, LDL, and SBP) transition according to a two-step process. Change in smoking status is described in Section 3.3.

Step 1: Determine probability that a risk factor changes

In the first step of the process, a person faces a probability of increasing, decreasing, or staying the same in a

particular risk factor. For LDL, HDL, and BMI, staying the same is defined as a change of +/-1 percent per year. Due to the greater variability in measuring blood pressure, staying the same in SBP is classified as being within +/-3.5 percent per year. In all cases, these probabilities were estimated using multinomial logistic regression. HDL, LDL, and SBP were estimated using annualized Framingham Heart Study data adjusting for age, sex, and BMI [6, 7]. BMI was estimated from Behavioral Risk Factor Surveillance System (BRFSS) survey data (from current weight and previous year recall) adjusting for age, sex, and race/ethnicity [21].

For year-to-year BMI transitions, the increasing or decreasing cases were split in two additional sub-cases. Specifically, one allows for small changes or "drifting" (i.e., an increase or decrease of 1 to 5 percent), and the other accommodates larger changes (i.e., an increase or decrease of 5 percent or more). Our analysis of Framingham Heart Study and BRFSS data indicate that these weight-change modalities reflect what people typically experience in real life, and the probabilities of each modality shift as we age. For example, a typical male may be most at risk for significant weight gain in his 20s, be more likely to have his BMI drift up in his 30s and 40s, and then face a stronger tendency towards weight stabilization in his 50s and 60s.

Step 2: Determine size of risk factor change

Once a person's transition modality has been determined, the second step is to determine the size of the change. Age, sex, and (in the case of BMI) race/ethnicity-specific equations were estimated for each of these cases. Whereas the first step in the process is stochastically determined in each cycle (i.e., facing a probability of each scenario), the second step is deterministic, with the transition applied as a percentage change (or zero change, in the case that a risk factor remains stable from the previous year). **Table 2** summarizes the details of this two-step process of year-on-year transitions of risk factors.

Table 2: ModelHealth: CVD Annual Progression of Risk Factors

Step	Case	Source	Controlled Factors	Estimator
1	P(BMI Change)	BRFSS [21]	Age, sex, race/ethnicity, previous BMI	Multinominal Logit
1	P(HDL Change)	Framingham [6, 7]	Age, sex, BMI, previous HDL	Multinominal Logit
1	P(LDL Change)*	Framingham [6, 7]	Age, sex, BMI, previous LDL	Multinominal Logit
1	P(SBP Change)	Framingham [6, 7]	Age, sex, BMI, previous SBP	Multinominal Logit
2	Q(BMI Change)	BRFSS [21]	Age, sex, race/ethnicity, previous BMI	OLS
2	Q(HDL Change)	Framingham [6, 7]	Age, sex, BMI, previous HDL	Random Effects
2	Q(LDL Change)*	Framingham [6, 7]	Age, sex, BMI, previous LDL	Random Effects
2	Q(SBP Change)	Framingham [6, 7]	Age, sex, BMI, previous SBP	Random Effects

Notes: P() = probability. Q() = quantity. OLS = Ordinary least squares regression. BRFSS = Behavioral Risk Factor Surveillance System. *In practice, the progression of LDL is more complex than indicated in the table and text. LDL was not measured with the same regularity as HDL and total cholesterol in the Framingham Heart Study; therefore, transitions in LDL were modeled in additional two steps. First, the probability and quantity of change in total cholesterol was modeled as described above. Second, HDL and total cholesterol were used in a prediction equation—derived from NHANES with high explanatory power (i.e., $R^2 > 0.9$)—to estimate a corresponding LDL level. Although not included in the prediction equations, estimations related to changes in cholesterol and BP controlled for treatment.

3.3 Modeling smoking behavior

Overview

Individuals may be in one of four smoking states: never smoker, current smoker, recent quitter, or former smoker. Initial smoking status was derived from the 2014 National Health Interview Survey (NHIS) [20].

Lifetime smoking behavior

An individual's "risk" of changing smoking status (i.e., transitioning to another smoking state), is determined by current state, time in that state, and demographic characteristics. Individuals who have never smoked can either remain in the never smoker state or begin smoking and transition to the current smoker state. A

current smoker who is in the current smoker state can remain or quit and transition to the recent quitter state. A recent quitter either remains in the recent quitter state, relapses into the current smoker state, or moves to the former smoker state once four years have passed. A former smoker either relapses into the current smoker state or remains in the former smoker state.

Logistic regression equations determine the risk of smoking initiation or the probability of cessation from NHIS data [10]. We identified quitters as those indicating they had ceased cigarette use within the last 12 months with no indication of relapse. **Table 3** contains the results of these estimations.

Relapse after quitting tobacco use is time-sensitive. The longer a person has successfully quit smoking, the less likely he or she is to relapse. The cross-sectional design of NHIS made estimation of relapse rates that account for time since cessation difficult. Instead, we used published estimates based on longitudinal studies. These values were adjusted during calibration to provide reasonable values of age-, sex-, and race/ethnicity-specific tobacco use rates. **Table 4** contains these rates.

Table 3: Results of Logistic Regressions Predicting Adult Smoking Status

	Tobacco Initiation	Tobacco Cessation
Ref. Category	-27.7099	-1.772
Female	3.5358	-0.046
24-44	9.814	-0.1545
xFemale	-10.0481	-0.00165
45-64	10.441	-0.1181
xFemale	-5.817	0.2346
White	-6.3501	0.2966
xFemale	-3.8882	Not Significant
Black	3.4254	-0.0603
xFemale	-3.4627	Not Significant
Hispanic	5.0037	0.0776
xFemale	-0.0798	Not Significant
No High School	6.5959	-0.00755
xFemale	-3.8882	Not Significant
High School	9.2186	0.0191
xFemale	-3.4627	Not Significant
Post-Secondary	4.5348	0.3067
xFemale	-0.0798	Not Significant

Source: National Health Interview Survey [10]. Note: Table values represent coefficients in a multinomial logistic regression equation.

Table 4: Baseline Smoking Tobacco Relapse Rates

Years Since Successful Quit	Probability of Relapse	Source
1	0.37	[11]
2	0.08	[12]
3	0.08	[12]
4	0.08	[12]
5	0.08	[12]
6	0.038	[12]
7	0.038	[12]
8	0.021	[12]
9	0.021	[12]
10	0.021	[12]
11	0.005	[12]

Calibration of smoking behaviors to CBO model

Tobacco prevalence was calibrated to reflect baseline tobacco use projections of the Congressional Budget Office (CBO) prior to final analysis [22]. These calibrated initiation and cessation rates are used for all estimates. We were unable to obtain details regarding how the CBO parameterizes specific population groups. Instead, we worked with estimates derived from the 2012 CBO report (Figure 1-1, page 3) [22]. Using this

figure and the general description of the CBO's approach as a guide, we tested a reasonable set of parameter modifications to adjust the smoking prevalence rates produced by our model over the next 10 years to better reflect CBO's baseline.

Three key sources of deviation from the CBO model were identified and adjusted for within the model. The first source was the estimated initiation patterns from NHIS age-based categories that created a stepped function and subsequent "jagged" initiation patterns. The resolution was to smooth initiation rates using a moving average process across ages that held constant prevalence within each age group. This adjustment removed "jumps" in prevalence among birth cohorts, but initiation remained relatively high. The second source of deviation was that NHIS-based estimates suggest stable or increasing smoking prevalence among young adults and adolescents. Thus, prevalence in the original model differed from the CBO model, which shows a secular trend toward decreasing prevalence over time. The resolution to this issue was to decrease initiation rates across lower age ranges by lowering implied prevalence to 24-year-old prevalence and smoothing using a 10-year moving average process. The effect of this was a lowered prevalence among new birth cohorts that was a closer approximation to initial cohort and a prevalence pattern that approximated those of current 10- to 24-year-olds. This results in a new "steady-state" population prevalence of approximately 13-14%, which is lower than the current population-wide prevalence. Finally, the third source of deviation was that former smokers exhibited high relapse rates among older age groups (ages 50 or older), causing higher prevalence relative to the CBO model. The approach to resolve this issue was to utilize an exponential distribution, which decreased likelihood of relapse among former smokers, and relapse was eliminated for former smokers older than age 50.

3.4 Risk of Cardiovascular Disease Events

Published risk calculators for cardiovascular disease—such as PROCAM [23], SCORE [24], QRisk [25], or those derived from the Framingham Heart Study [26]—generally estimate an individual's 10-year risk of disease. These are difficult to translate to a microsimulation model with annual cycles. In addition, existing risk profiles commonly combine outcomes (such as chronic heart disease or cardiovascular disease, generally, compared to myocardial infarction or ischemic stroke, specifically—for example, see [27]). The distinction is particularly important for accurately estimating costs associated with disease. They may also exclude potentially policy-relevant risk factors (such as differentiating current smokers from recent quitters or former smokers), and/or include clinical risk factors that may not be salient to population-level policy evaluation (such as left ventricular hypertrophy in the risk of stroke—for example, see [28]). For these reasons, we used primary data from the Framingham Heart Study to derive and develop customized 1-year risk equations for use in ModelHealth: CVD.

We developed risk equations for eight outcomes: myocardial infarction (MI), ischemic stroke, hemorrhagic stroke, angina pectoris, congestive heart failure, intermittent claudication, non-specific cardiovascular disease-related death, and diabetes. The risk analysis uses the Original Cohort (beginning in 1948 with 5,209 attendees) and the Offspring (beginning in 1971 with 5,124 attendees) arms of the Framingham Heart Study. Data were sourced from the National Heart, Lung, and Blood Institute's (NHLBI's) Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC), with approval and human subjects oversight from the HealthPartners Institute for Education and Research's Institutional Review Board [6, 7]. Statistical survival analysis was performed using Stata, Version 11 (Statacorp, College Station, TX).

To use as much of this rich data source as possible, allow for time-varying covariates, and provide for a direct estimate of annual risk, we adopted a parametric over the more common semi-parametric Cox proportional hazard approach in our analysis. Similar parametric methods have been previously explored and validated by Framingham Heart Study researchers [29]. Age, BMI, HDL, LDL, SBP, and one's disease history are all included as potential time-varying covariates in the analyses.

Because age accounts for time within a single person's life and because we do not have strong evidence with respect to the impact of secular time trends, we estimated an individual's risk using the exponential proportional hazards model (which has a time independent or "memoryless" property). Specifically, estimation was conducted using the *streg* command in Stata. Time independence is particularly important when estimating annual risk (i.e., t = 1), because the additional information in the shape parameter (i.e., embodied in the so-called accelerated failure time metric) is never appropriately used and may otherwise systematically over-or under-estimate risk in a one year context. The resulting exponential model is estimated with a person j likelihood function of the risk of an event $\left(d_j \in \{0,1\}\right)$ between t_{0j} and t_j is

$$L_j = \left[\frac{e^{\left(-e^{\beta_0 + x_j\beta}\right)t_j}}{e^{\left(-e^{\beta_0 + x_j\beta}\right)t_{0j}}}\right]\left(e^{-e^{\beta_0 + x_j\beta}}\right)^{d_j}$$

with an individual's probability of an event in the next year equal to $F(1) = 1 - e^{\left(-e^{\beta_0 + x_j\beta}\right)}$.

Table 5: Summary of Risk Equations Derived from Framingham Heart Study Data

Risk of First Myocardial Infarction (MI)

	Hazard Ratio	Z-Score
Age	1.046	18.15
Sex	0.411	-14.25
HDL	0.985	-6.64
LDL	1.005	9.99
SBP	1.013	11.17
Smoke	1.701	8.84
Diabetes	2.029	9.46
Previous CVD	2.798	16.28

Risk of First Ischemic Stroke (IS)

	Hazard Ratio	Z-Score
Age	1.076	20.94
HDL	0.988	-4.39
SBP	1.022	15.63
Smoke	1.724	6.27
Diabetes	1.918	6.90
Previous CVD	2.243	10.09

Risk of First Hemorrhagic Stroke (HS)

	Hazard Ratio	Z-Score
Age	1.049	6.64
SBP	1.020	5.94
BMI	0.904	-4.75
Smoke	1.497	2.15
Previous CVD	1.568	2.35

Risk of Intermittent Claudication (IC)

	Hazard Ratio	Z-Score
Age	1.039	10.39
Sex	0.619	-5.32
HDL	0.993	-2.01
LDL	1.007	8.35
SBP	1.015	8.65
Smoke	2.871	12.05
Diabetes	2.237	7.20
Previous CVD	2.529	9.93

Risk of Angina Pectoris (AP)

	Hazard Ratio	Z-Score
Age	1.024	9.88
Sex	0.587	-8.42
HDL	0.989	-4.62
LDL	1.006	11.95
SBP	1.011	8.90
Previous CVD	2.750	13.84

Risk of First Congestive Heart Failure (CHF)

	Hazard Ratio	Z-Score
Age	1.074	22.35
HDL	0.986	-5.49
SBP	1.015	10.65
BMI	1.024	3.43
Smoke	1.401	4.15
Diabetes	2.176	9.92
Previous MI	3.885	17.76
Previous Other CVD	1.838	8.22

Risk of Diabetes

	Hazard Ratio	Z-Score
Age	1.064	30.67
BMI	1.108	20.90
SBP	1.004	2.91
HDL	0.968	-13.72

Risk of CVD-related Death

	Hazard Ratio	Z-Score
Age	1.068	26.50
Sex	0.569	-10.36
LDL	1.004	6.04
SBP	1.009	8.95
Smoke	1.676	8.83
Diabetes	1.403	5.27
Previous MI	2.875	17.48
Previous IS	3.546	19.93
Previous CHF	6.565	30.41
Previous Other CVD	1.747	9.87

Source: Author's analysis of data from the Framingham Heart Study [26]. Notes: Estimations are based on the exponential proportional hazards model. All continuous variables used in ModelHealth: CVD are natural log transformed; however, hazard ratios of non-log variables are presented here instead for easier interpretation.

3.5 Baseline Risk of GI Bleeding Events

We estimate the baseline risk of gastrointestinal (GI) bleeding events among persons not taking aspirin using an analysis of Italian observational data [30], with adjustments made for the U.S. age and sex distribution. Generally speaking, evidence suggests that men face higher risk of GI bleeds than women, and risk for both sexes increases with age. The derivation of and final probabilities for GI bleeding events without aspirin in the model are summarized in **Table 6** below.

Table 6: Summary of Risk for GI Bleeding Events without Aspirin in ModelHealth: CVD

Age	Major Bleeding without Aspirin Per 1000 Persons	Major GI Bleeds without Aspirin Per 1000 Persons	U.S. % Men	U.S. % Women	GI Bleeding Incidence Rate Ratio (Men to Women)	GI Bleeds per 1000 U.S. Men without Aspirin	GI Bleeds per 1000 U.S. Women without Aspirin
<50	0.6	0.4	51%	50%	1.69	0.5	0.3
50-59	1.4	0.9	49%	51%	1.69	1.2	0.7
60-69	2.6	1.7	48%	52%	1.69	2.1	1.3
70-79	4.6	3.0	45%	55%	1.69	3.9	2.3
80+	6.9	4.5	36%	64%	1.69	6.1	3.6
Source	[30]	[30]	[13]	[13]	[30]	Calculated	Calculated

Notes: GI = gastrointestinal; U.S. = United States. The first two columns present major bleeding and major GI bleeding rates from an Italian cohort study [30]. Major bleeding is defined in that study as major GI bleeding or cerebral hemorrhage corresponding with ICD-9-CM codes 531-535, 578.9, and 430-432. Major GI bleeding is defined as corresponding with ICD-9-CM codes 531-535 and 578.9. Major GI bleeding by age group is derived by adjusting the reported major GI bleeding rates by the reported ratio of major GI bleeding to cerebral hemorrhage (~65%). GI bleeds per 1000 men and women in the United States were estimated algebraically using the baseline rates reported in the Italian cohort study and the incidence rate ratio of major GI bleeding for men to women and adjusting for the proportion of women to men in the U.S. population by age group.

3.6 Risk of Death from Other Causes

The probability of dying from a cause other than CVD is derived from U.S. life tables [31] with deaths from CVD out using compressed mortality data in the CDC Wonder database [9]. These probabilities are summarized in **Table 7** below.

Table 7: Summary of Mortality Risk from Causes other than CVD

Age	Men	Women
	Average Annual Probability of Non-CVD	
30-39	0.14%	0.07%
40-49	0.23%	0.17%
50-59	0.50%	0.33%
60-69	0.92%	0.66%
70-79	1.98%	1.45%
80-89	4.74%	2.91%
90-100	16.85%	12.97%

Source: [9, 31]. Notes: CVD = cardiovascular disease. Mortality risk is based on annual probabilities by age and sex in the U.S. life tables [31] with CVD mortality subtracted out using underlying cause-of-death mortality data in the CDC Wonder database [9]. Causes for CVD mortality included ICD-10 codes I10-I25, I30-I51, and I60-I69.

3.7 Costs of Disease

Costs of cardiovascular disease and diabetes in ModelHealth: CVD were estimated through analysis of individual-level Medical Expenditure Panel Survey (MEPS) data. To improve estimates—particularly, among less common events such as hemorrhagic stroke—data from the 2001-2012 surveys [32] were combined and appropriately weighted, with costs deflated to 2012 dollars. We differentiated costs associated with an incident event (and those subsequently accrued during the year of the incident event) from ongoing costs from a previous event. Incident and ongoing costs due to diabetes could not be distinguished in the MEPS

survey, and we assumed these costs could be reasonably averaged across the duration of a diabetes diagnosis. In all cases, costs were derived from estimated actual expenditures (rather than recorded charges). We limited our analysis of costs to those of age 35 and older. Disease costs used in the model are summarized in the **Table 8** below.

Incident (first-year) costs

To identify all costs associated with the first-year of an incident cardiovascular event, we first combined total person-level expenditures across several major categories tracked by MEPS, including: inpatient hospital stays, outpatient visits, office-based medical provider visits, emergency room visits, prescribed medicines, home health expenses, and other medical expenses. Costs associated with dental visits were represented the only expenditure category tracked by MEPS which was not included in our analysis. Expenditures associated with lipid or blood pressure therapy were excluded (because our analysis includes these costs separately).

To identify incidence of a new event, we assumed that inpatient hospital stays indicated a significant event had occurred during that year. We used ICD9 coding to identify incident events associated with myocardial infarction (ICD9 410), ischemic (ICD9 434) or hemorrhagic stroke (ICD9 430, 421, or 432), angina pectoris (ICD9 413), congestive heart failure (ICD9 428), and intermittent claudication (ICD9 440). Diabetes status of individuals was determined by the combination of self-report, clinical encounters (either inpatient, outpatient, emergency, or office-based) with a primary coding of diabetes (ICD9 250), and prescription claims for diabetic medications.

Due to issues common to the analysis of healthcare costs—in particular, rare but extremely high cost events and heteroscedastic errors—we fit these data to a generalized linear model (GLM) with a log link function and gamma distributed variance. Specifically, adding controls for age, sex, and diabetes status, we fit the following model:

$$\text{Total Expenditure} = \beta_0 + (\text{age})\,\beta_{\text{age}} + (\text{sex})\,\beta_{\text{sex}} + (\text{diabetes})\,\beta_{\text{diabetes}} + (\text{MI})\,\beta_{\text{MI}} + (\text{IS})\,\beta_{\text{IS}} + (\text{HS})\,\beta_{\text{HS}} + (\text{AP})\,\beta_{\text{AP}} + (\text{CHF})\,\beta_{\text{CHF}} + (\text{IC})\,\beta_{\text{IC}}$$

where incident disease events, such as myocardial infarction (MI), are coded as dummy variables corresponding to observed inpatient stays (as described above). Marginal disease expenditures were estimated by estimating the difference in population average costs with and without that disease (i.e., the marginal value at population means).

Ongoing costs

To identify all ongoing costs associated with a previous cardiovascular event, we first combined total person-level expenditures across several major categories tracked by MEPS, including: inpatient hospital stays, outpatient visits, office-based medical provider visits, emergency room visits, prescribed medicines, home health expenses, and other medical expenses. As with the case of incident events, costs associated with dental visits were excluded. Expenditures associated with lipid or blood pressure therapy were also excluded (because our analysis includes these costs separately).

To identify previous events, we used a combination of self-reported status (e.g., "Have you ever been told by a medical provider that you had a heart attack or myocardial infarction?") and coding of office-based medical encounters. We used ICD9 coding to identify ongoing care associated with myocardial infarction (ICD9 410), ischemic or hemorrhagic stroke (ICD9 434, 430, 421, or 432), angina pectoris (ICD9 413), congestive heart failure (ICD9 428), and intermittent claudication (ICD9 440). So as not to double-count costs included in our analysis of incident events, those with an inpatient encounter during the survey year were not included among those deemed to have had a previous event. As with the case of incident event costs, diabetes

status of individuals was determined by the combination of self-report, clinical encounters (either inpatient, outpatient, emergency, or office-based) with a primary coding of diabetes (ICD9 250), and prescription claims for diabetic medications.

As with our analysis of incident event costs, we fit these data to a generalized linear model (GLM) with a log link function and gamma distributed variance. Specifically, adding controls for age, sex, and diabetes status, we fit the following model:

$$\text{Total Expenditure} = \beta_0 + (\text{age})\,\beta_{\text{age}} + (\text{sex})\,\beta_{\text{sex}} + (\text{diabetes})\,\beta_{\text{diabetes}} + (\text{MI})\,\beta_{\text{MI}} + (\text{IS})\,\beta_{\text{IS}} + (\text{HS})\,\beta_{\text{HS}} + (\text{AP})\,\beta_{\text{AP}} + (\text{CHF})\,\beta_{\text{CHF}} + (\text{IC})\,\beta_{\text{IC}}$$

where previous disease events, such as myocardial infarction (MI), are coded as dummy variables as described above. Marginal disease expenditures were estimated by estimating the difference in population average costs with and without that disease (i.e., the marginal value at population means).

Diabetes

In our analysis of costs associated with diabetes, we do not distinguish expenditures that are incident to diagnosis or ongoing, and we assume these costs may be reasonably averaged across the duration of disease. As with our cost analyses of CVD events, we determined an individual's diabetes status by the combination of self-report, clinical encounters (either inpatient, outpatient, emergency, or office-based) with a primary coding of diabetes (ICD9 250), and prescription claims for diabetic medications.

We combined total person-level expenditures across several major categories tracked by MEPS, including: inpatient hospital stays, outpatient visits, office-based medical provider visits, emergency room visits, prescribed medicines, home health expenses, and other medical expenses. Costs associated with dental visits and expenditures associated with lipid or blood pressure therapy were excluded. Cardiovascular disease status was identified as either having had an incident or previous event (as described above).

As with our cost analyses of CVD events, we fit these data to a generalized linear model (GLM) with a log link function and gamma distributed variance. Specifically, adding controls for age, sex, and diabetes status, we fit the following model:

$$Total\ Expenditure = \beta_0 + (age)\beta_{age} + (sex)\beta_{sex} + (diabetes)\beta_{diabetes} + (MI)\beta_{MI} + (IS)\beta_{IS} + (HS)\beta_{HS} + (AP)\beta_{AP} + (CHF)\beta_{CHF} + (IC)\beta_{IC}$$

where current or previous disease events, such as myocardial infarction (MI), are coded as dummy variables as described above. Marginal disease expenditures were estimated by estimating the difference in population average costs with and without that disease (i.e., the marginal value at population means).

GI Bleeding

Costs of GI bleeding episodes are included in the model as a harm associated with long-term aspirin use. Due to the relative rare occurrence of GI bleeding, we could not reliably estimate these costs using MEPS data and methods similar to those described above. Instead, we borrow a cost estimate, based on analysis of Agency for Healthcare Research and Quality (AHRQ) Health Care Utilization Project (HCUP) data, from a published cost-utility analysis which also evaluates aspirin for primary prevention of cardiovascular disease [33]. Specifically, we assume the average acute (first-year) costs associated with a GI bleed are $9,677 (2012 dollars), and that there are generally no substantial ongoing costs associated with these events.

Estimating costs using the methods above and stratifying by insurer type is not viable due to the small sizes observed among the rarer disease conditions within the MEPS surveys. Therefore, we adjusted the costs for all insurance types, as described above, by using a multiplier calculated as the cost per case ratio for an insurance type divided by the cost per case ratio across all insurance types for CVD events, incident and ongoing. These multipliers for incident CVD costs are 1.26 for private insurance, 0.88 for Medicare, 0.66 for Medicaid, 0.62 for the uninsured, and 0.90 for other or multiple types of insurance. These multipliers for ongoing CVD costs are 1.21 for private insurance, 0.78 for Medicare, 0.88 for Medicaid, 0.51 for the uninsured, and 0.77 for other or multiple types of insurance. Similarly, these multipliers for diabetes costs are 0.73 for private insurance, 0.75 for Medicare, 1.00 for Medicaid, 0.61 for the uninsured, and 1.07 for other or multiple types of insurance. For disease cases with large cell sizes, this multiplier approach yielded very similar results to those estimated directly. A summary of the final costs by disease and insurance-type can be found in the **Table 8** below.

Table 8: Summary of Disease Costs in ModelHealth: CVD

	Incident Costs					Ongoing Costs				
	Private	Medicare	Medicaid	Uninsured	Other	Private	Medicare	Medicaid	Uninsured	Other
MI	$46,689	$32,598	$24,585	$22,878	$33,333	$3,004	$1,952	$2,186	$1,277	$1,927
Stroke	$22,896	$15,986	$12,057	$11,220	$16,347	$6,501	$4,225	$4,730	$2,762	$4,170
AP	$30,572	$21,346	$16,098	$14,981	$21,826	$5,142	$3,342	$3,741	$2,185	$3,298
CHF	$37,844	$26,423	$19,928	$18,545	$27,019	$13,974	$9,082	$10,167	$5,938	$8,964
IC	$24,109	$16,833	$12,695	$11,814	$17,212	$7,908	$5,140	$5,754	$3,360	$5,073
Diabetes	$3,976	$4,069	$5,450	$3,293	$5,833	$3,976	$4,069	$5,450	$3,293	$5,833

Notes: Ongoing costs are exclusive of drug therapy costs for high cholesterol or hypertension; these costs are accounted for separately in the ModelHealth: CVD.

3.8 Impact of Disease on Morbidity (QALYs)

Quality of life weights for specific diseases and health conditions in the published literature vary considerably in elicitation methods and in their ability to generalize across conditions and population characteristics. We adopt the standard rules for quality-adjusted life year (QALY) weights established for all NCPP evaluations [34]. Specifically, perfect health is assigned a QALY weight of 1.0. We assume chronic diseases—i.e., angina pectoris, congestive heart failure, diabetes, intermittent claudication, or sequela resulting from ischemic or hemorrhagic stroke—reduce quality of life by 0.2.

For acute events and conditions, we make assumptions regarding the intensity and duration of burden. For myocardial infarction, we assume a QALY reduction of 0.3 for 3 months. For ischemic and hemorrhagic stroke, we assume an average QALY reduction of 0.4 over the course of a full year. For incident congestive heart failure, intermittent claudication, angina pectoris, and diabetes, we assume the same average QALY reduction in the first year as in subsequent chronic years (0.2). For major GI bleeding events, we assume a QALY reduction of 0.3 for 3 months. We assume the maximum average cumulative QALY reduction in any year is 0.5. The burden of disease assumptions are summarized in **Table 9**.

Table 9: Summary of Burden of Disease (QALY reductions) in ModelHealth: CVD

Disease/Condition	QALY Reduction	Duration	Total Annual Reduction
First-year burden			
Angina pectoris	0.1	12 months	0.1
Congestive heart failure	0.2	12 months	0.2
Diabetes	0.2	12 months	0.2
GI bleeding	0.3	3 months	0.025
Intermittent claudication	0.2	12 months	0.2
Myocardial infarction	0.3	3 months	0.025
Stroke, Hemorrhagic	0.4	12 months	0.4
Stroke, Ischemic	0.4	12 months	0.4
Ongoing burden			
Angina pectoris	0.1	12 months	0.2
Congestive heart failure	0.2	12 months	0.1
Diabetes	0.2	12 months	0.2
GI bleeding	0	N/A	0
Intermittent claudication	0.2	12 months	0.2
Myocardial infarction	0	N/A	0
Stroke, Hemorrhagic	0.4	12 months	0.4
Stroke, Ischemic	0.4	12 months	0.4

Notes: QALY = quality-adjusted life year. Assumed QALY values are chosen to be consistent with cost-effectiveness estimates in current and previous NCPP evaluations [35].

4 Clinical Preventive Services

The U. S. Preventive Services Task Force (USPSTF) makes several recommendations for the primary prevention of cardiovascular disease. Task Force recommendations are based on comprehensive reviews of the scientific evidence in order to weigh the balance of potential health benefits versus potential harms of a preventive service—and to assess the scientific confidence of any perceived net health benefits. According to the USPSTF, a preventive service receives an 'A' recommendation when the scientific evidence indicates that the magnitude of net health benefits is "substantial," and the certainty (i.e., strength, quality, etc. of evidence) to this degree of magnitude is "high" [36]. A preventive service receives a 'B' recommendation when the scientific evidence indicates that the magnitude of net health benefits is "moderate" with "high" certainty or that net health benefits are "substantial" or "moderate" with "moderate" certainty.

ModelHealth: CVD has been designed to assess three of the USPSTF grade 'A' and 'B' clinical preventive service recommendations related to cardiovascular disease: (1) aspirin chemoprevention counseling (a draft 'B' recommendation, for adults aged 50-59 with elevated risk), (2) screening for lipid disorders (a split 'A' and 'B' recommendation, according to target population), and (3) screening for hypertension (an 'A' recommendation) (**Table 10**). Whereas the USPSTF evaluates the expected net health impact of upon individuals in the preventive service target population, ModelHealth: CVD evaluates net health benefits and the cost-effectiveness of prevention policy at the population level.

Table 10: Summary of USPSTF Recommendations Included in ModelHealth: CVD

Recommendation	Year	Target Population	Grade
Aspirin for the Prevention of CVD and CRC [37]	2016	Men (Age 50-59) , ↑Risk	B
Aspirin for the Prevention of CVD and CRC [37]	2016	Women (Age 50-59) , ↑Risk	B
Screening for Lipid Disorders in Adults [2]	2008	Men (Age 20-35), ↑Risk	B
Screening for Lipid Disorders in Adults [2]	2008	Men (Age 35+)	A
Screening for Lipid Disorders in Adults [2]	2008	Women (Age 20-45), ↑Risk	B
Screening for Lipid Disorders in Adults [2]	2008	Women (Age 45+), ↑Risk	A
Screening for High Blood Pressure [1]	2007	Adults (Age 18+)	A

Note: The 2015 recommendation for aspirin is a draft recommendation.

4.1 Aspirin Counseling for Primary Prevention

Risk Assessment and Treatment Criteria

We follow the USPSTF's use of the 2013 ACC/AHA pooled cohort equations to calculate CVD risk [38, 39]. Men and women aged 50-59 with 10-year CVD risk of 10 percent are eligible for aspirin counseling. We assume that 90 percent of persons will accept aspirin counseling. We assume that all persons that accept aspirin counseling and do not have any contraindications (i.e., prior GI bleeding or hemorrhagic stroke) will initiate aspirin use. Aspirin use in the model is permanently discontinued if a person experiences an adverse event (i.e., a GI bleed or hemorrhagic stroke).

Screening Frequency

The USPSTF states that the optimal timing and frequency of aspirin counseling is unknown [38]. We follow the USPSTF's suggestion that a reasonable screening schedule be periodic after age 50 or when a change in CVD risk factors is detected. Specifically, we implement this approach by allowing counseling opportunities every 5 years or when, as a result of routine screening and management, any of the following changes are observed: a 10 mm Hg or greater increase in SBP, a 10 mg/dL or greater increase in LDL, a 2 kg/m^2 or greater increase in BMI, smoking initiation, a new diabetes diagnosis, or drug therapy changes for treating lipids or blood pressure.

Medication Use

We derived use rates of aspirin for primary and secondary prevention from 2014 NHIS data [20]. Specifically, aspirin use rates for primary prevention were estimated by the weighted proportion of the sample of those with no self-reported history of CVD (i.e., not told of prior CHD, MI, angina pectoris, or stroke) who report having been told to use aspirin by a medical care provider and are currently following that advice. Likewise, aspirin use rates for secondary prevention were estimated by the weighted proportion of the sample of those with self-reported history of CVD (i.e., previously told of prior CHD, MI, angina pectoris, or stroke) who report having been told to use aspirin by a medical care provider and are currently following that advice. The medication use rates for aspirin are presented in **Table 11**.

Table 11: Summary of Long-term Aspirin Use Rates Model Health: CVD

Parameter	Medication use rate
Aspirin use for primary prevention	77%
Aspirin use for secondary prevention	86%

Note: National Health Interview Survey [20].

Treatment Effects

CVD and bleeding relative risks were derived from eight low-dose (defined as 100mg per day or less) primary prevention trials identified by the USPSTF systematic evidence review [40-48]. Due to the limited number of low-dose aspirin trials reporting ischemic stroke events as an independent outcome [40], we use a combined stroke measure that includes hemorrhagic stroke events to approximate the effect of aspirin on ischemic stroke. This results in a conservative estimate of ischemic stroke benefits. All CVD benefits and harms are assumed to take effect immediately after initiating aspirin use, and all relative risks are assumed to return to 1.00 after discontinuing use of aspirin. The trials informing aspirin's primary prevention effects are summarized in **Table 12** and the relative risk parameters are summarized in **Table 13**.

Table 12: Summary of Aspirin Trials Informing Primary Prevention Treatment Effect Parameters

Study Name	Year Published	N	Dose, schedule	Age Range	Mean Age	Median follow-up	Model parameters informed
				(Years)	(Years)	(Years)	
AAA [41]	2010	3,350	100 mg, daily	50-75	62.0	*8.2	CVD death, GIB, HS, IS, MI
HOT [42]	1998	18,790	75 mg, daily	50-80	61.5	*3.8	CVD death, GIB, HS, MI
JPAD [43]	2008	2,539	100 mg, daily	30-85	64.5	4.4	CVD death, GIB, HS, IS, MI
JPPP [48]	2014	14,658	100 mg, daily	60-85	70.5	5	CVD death, HS, IS, MI
POPADAD [44]	2008	1,276	100 mg, daily	≥40	60.3	6.7	CVD death, IS, MI
PPP [45]	2001	4,495	100 mg, daily	≥50	64.4	*3.6	CVD death, HS, IS, MI
TPT [46]	1998	2,540	75 mg, daily	45-69	57.5	6.8	CVD death, GIB, HS, IS, MI
WHS [47]	2005	39,876	100 mg, QOD	≥45	54.6	*10.1	CVD death, GIB, HS, IS, MI

Notes: N = study population size at randomization; AAA = Aspirin for Asymptomatic Atherosclerosis Study; BMD = British Medical Doctors Study; HOT = Hypertension Optimal Treatment Study; JPAD = Japanese Primary Prevention of Atherosclerosis with Aspirin for Diabetes Study; JPPP = Japanese Primary Prevention Project Study; POPADAD = Prevention of Progression of Arterial Disease and Diabetes Study; PPP = Primary Prevention Project Study; TPT = Thrombosis Prevention Trial; UK-TIA = UK Transient Ischaemic Attack Aspirin Trial; WHS = Women's Health Study; QOD = every other day; CVD = cardiovascular disease; GIB = relative risk for gastrointestinal bleeding; HS = relative risk for hemorrhagic stroke; IS = relative risk for ischemic stroke; MI = relative risk for myocardial infarction. The mean age is at study enrollment. All studies included in this table are CVD primary prevention trials.

Table 13: Summary of Aspirin Treatment Effects (RR) for Primary Prevention of CVD

Condition	Base Case	Worst Case	Best Case	Other values
Relative Risk of Myocardial Infarction	0.83	0.94	0.74	
Relative Risk of Ischemic Stroke	0.86	0.98	0.76	
Relative Risk of Hemorrhagic Stroke	1.27	1.68	1.00	
Relative Risk of CVD-related Death	1.00	1.00	0.85	0.97
Relative Risk of GI Bleed	1.58	1.95	1.29	

Sources: [40-51]. Notes: For informing trial details, see **Table 12**. Best and worst cases are based on 95% confidence intervals. The "other value" for CVD-related death is based on the mean (but not statistically significant) found among primary prevention trials.

Aspirin also may be initiated following a non-fatal CVD event for the purposes of reducing the risk of subsequent events (secondary prevention). A meta-analysis of 16 secondary prevention aspirin trials indicates a 31 percent reduction in MI risk (95% Rate Ratio [RR] CI: 0.60-0.80) and a 22 percent reduction in ischemic stroke risk (95% RR CI: 0.61-0.99) [52]. Due to the relative rarity of hemorrhagic stroke and major GI bleeding and the smaller sample sizes of participants in secondary trials and insufficient evidence to distinguish clear differences between men and women in risk for hemorrhagic stroke and major GI bleeding, we calculated a combined unadjusted odds ratio from primary prevention trials to estimate the risk of these adverse events associated with aspirin use [53, 54]. We draw an individual-specific effect size from a triangle distribution based on the 95 percent confidence intervals. As with aspirin for primary prevention, treatment effects are adjusted (multiplied) by a treatment effectiveness parameter, which is 70% in the base case. A summary of the aspirin treatment effects when used for secondary prevention of CVD is given in **Table 14**.

Table 14: Summary of Aspirin Treatment Effects for Secondary Prevention of Cardiovascular Disease

Condition	Sex	Base Case	Worst Case	Best Case
Relative Risk of Myocardial Infarction	Men	0.69	0.80	0.60
Relative Risk of Myocardial Infarction	Women	0.69	0.80	0.60
Relative Risk of Ischemic Stroke	Men	0.78	0.99	0.61
Relative Risk of Ischemic Stroke	Women	0.78	0.99	0.61
Relative Risk of Hemorrhagic Stroke	Men	1.42	1.93	1.05
Relative Risk of Hemorrhagic Stroke	Women	1.42	1.93	1.05
Relative Risk of CVD-related Death	Men	0.98	0.87	0.78
Relative Risk of CVD-related Death	Women	0.98	0.87	0.78
Relative Risk of GI Bleed	Men	1.63	1.93	1.38
Relative Risk of GI Bleed	Women	1.63	1.93	1.38

Source: [52, 53]. Best and worst cases are based on 95% confidence intervals.

4.2 Screening for Lipid Disorders

Risk Assessment and Treatment Criteria

We follow the USPSTF's suggestion to use a 10-year CHD risk calculator to assess heart disease risk in men age 20-35 and women age 20 and older [2, 27]. We assume treatment will follow the recommended guidelines for drug therapy of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III) [4]. Specifically, we assume all individuals with LDL cholesterol levels greater than 160 mg/dL will initiate drug therapy. We assume those with lower LDL cholesterol levels will be treated based on heart disease risk. Specifically, drug therapy will be initiated at LDL levels up to 130 mg/dL in those with at least 10 percent risk of developing CHD in the next ten years and at LDL levels up to 100 md/dL in those with 10-year CHD risk exceeding 20 percent.

Screening Frequency

The Task Force did not find good evidence on the optimal screening interval, but we follow their suggestion of screening every 5 years as appropriate for most individuals [2].

Medication Use

We derived use rates of statins, together with use of antihypertensives, for primary and secondary prevention from 2001-2010 NHANES data [15-19]. Specifically, statin/antihypertensive use rates for primary prevention were estimated by the weighted proportion of the sample of those with no self-reported history of CVD (i.e., not told of prior MI, congestive heart failure, angina pectoris, or stroke) who report having been told to use a statin/antihypertensive by a medical care provider and are currently following that advice. Likewise, statin/antihypertensive use rates for secondary prevention were estimated by the weighted proportion of the sample of those with self-reported history of CVD (i.e., previously told of prior MI, congestive heart failure, angina pectoris, or stroke) who report having been told to use statin/antihypertensive by a medical care provider and are currently following that advice. The medication use rates for aspirin are presented in **Table 15**.

Table 15: Summary of Long-term Statin Use Rates ModelHealth: CVD

Parameter	Medication use rate
Statin use for primary prevention	
Age 18-39	62%
Age 40-64	84%
Age 65+	94%
Statin use for secondary prevention	
Age 18-39	77%
Age 40-64	89%
Age 65+	97%

Note: Estimated together with use of antihypertensive medications using National Health and Nutrition Examination Survey [15-19] data.

Treatment Effects

Due to the overwhelming use of statins (i.e., HMG-CoA reductase inhibitors) in the treatment of high cholesterol—recent estimates suggest rates in excess of 90 percent among Americans seeking pharmacological treatment [55]—we simplified treatment of dyslipidemia in ModelHealth: CVD to this drug class. We used several recent (and/or otherwise relevant) meta-analyses/reviews of statins to identify major

(of 1,000 or more persons) randomized controlled trials comparing lipid reduction associated with statins to a placebo [56-61]. Included trials—accounting for a total of 67,815 subjects—had a follow-up period of at least 52 weeks, involved subjects for primary or secondary prevention, were subject-blinded (at a minimum), and reported changes in LDL or HDL cholesterol as an outcome. Trials were excluded if additional (open label) lipid-lowering drugs were allowed for use in the placebo group (unless observed at rates lower than 10 percent). The trials included in our analysis are summarized in **Table 16**.

Table 16: Summary of Statin Trials Included in Estimation of Treatment Effects

Trial	Subjects	Ages	Baseline LDL	Baseline HDL	Mean ↓LDL	Mean ↑ HDL
4S	4,444	30 – 70	188.3	45.8	47.1	3.7
AFCAPS/TEXCAPS	6,605	45 – 73	150.4	36.3	41.8	1.9
ALERT	2,102	30 – 75	158.5	52.2	36.7	0
ASCOT-LLA	10,305	40 – 79	133	50.7	46.4	0.8
ASPEN	2,410	40 – 75	113.5	47	33.1	0.9
HPS	20,536	40 – 80	131.5	42.5	50.3	0.8
LIPID	9,014	31 – 75	150	36	37.5	1.8
PROSPER	5,804	70 – 82	146.9	50.3	39.7	2.5
WOSCOPS	6,595	45 – 64	192	44	49.9	2.2

Sources: 4S 62]; AFCAPS/TEXCAPS [63]; ALERT [64]; ASCOT-LLA [65]; ASPEN [66]; HPS [67];[68]; PROSPER [69]; WOSCOPS [70]. Notes: LDL and HDL unit measures are in mg/dL.

To accommodate differential drug response according to baseline (only one included trial included stepped treatment in its experimental protocol [62]), we estimated treatment effects on cholesterol levels using a simple weighted ordinary least squares regression, with baseline LDL or HDL levels (respectively) as the only predictor:

$$Effect_{Chol} = \beta_0 + (BaselineChol)\beta_{BaselineChol}$$

The average effect size of statins on LDL was estimated to be a 42.9 mg/dL reduction, with an additional marginal impact of 0.014 mg/dL reduction per mg/dL of baseline LDL. The average effect size of statins on HDL was estimated to be a 2.2 mg/dL increase, with a marginal impact of 0.017 mg/dL reduced effect per mg/dL of baseline HDL. These results indicate that the typical lipid modifying response to statin therapy is not highly sensitive to baseline lipid levels.

To accommodate interpersonal differences in the impact of drug therapy on LDL cholesterol in ModelHealth: CVD, we constructed a triangle distribution centered on the mean effect size described above, with upper and lower limits defined by the standard deviation in effect size observed in statin trials, to draw person-specific effect sizes. We estimated the standard deviation in LDL cholesterol reduction using a meta-analysis of (generally smaller/shorter) placebo controlled trials rather than the major trials summarized in **Table 16**, because the primary endpoints in these trials were cardiovascular disease outcomes (and as a result, standard deviations in cholesterol changes were not typically reported). We did find not good evidence on the interpersonal variability of treatment effects from statins on HDL, and we incorporate only mean treatment effects in this case.

Finally, all trials—with exception of WOSCOPS [70]—reported results solely based upon intention-to-treat analyses. The average weighted adherence to the treatment across study arms among included trials reporting this measure was 89.4 percent. To account for diminished average treatment effects attributable to non-adherence to prescribed therapy, we estimate an appropriate adjustment by dividing lipid impact by 0.9 in the base case. Finally, to account for real-world effectiveness (e.g., treatment plan fidelity), treatment effects are adjusted (multiplied) by a treatment effectiveness parameter. In the base case, this treatment effectiveness adjustment is 70% of the treatment efficacy derived from the statin trials. This adjustment is based on model calibration with reference to outcomes among persons using lipid medications in NHANES data [15-19]. Statin treatment effects in ModelHealth: CVD are summarized in **Table 17**.

Table 17: Summary of Statin Treatment Effects

	β0	β*BaselineChol*	Std. Dev.	Adherence Adjustment	Treatment Effectiveness
Statin Effect on LDL	42.881	0.014	24.382	90%	70%
Statin Effect on HDL	2.176	-0.017	N/A	90%	70%

Source: Analysis of clinical trials described in **Table 16**.

4.3 Screening for Hypertension

Risk Assessment and Treatment Criteria

The Task Force recommendations are consistent with the JNC 7 guidelines, and as such, the model assumes providers will initiate drug therapy when blood pressure when systolic blood pressure exceeds 140 mm Hg and will treat to the goal of reaching levels below that threshold [1, 5].

Screening Frequency

The Task Force did not find good evidence on the optimal screening interval, but we follow their suggestion to adopt the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) recommended guideline of screening every two years in persons with blood pressure less than 120/80 mm Hg and every year in persons with systolic blood pressure in excess of 120 mm Hg or diastolic blood pressure in excess of 80 mm Hg [1, 5].

Medication Use

We derived use rates of antihypertensives, together with use of statins, for primary and secondary prevention from 2001-2010 NHANES data [15-19]. Specifically, antihypertensive/statin use rates for primary prevention were estimated by the weighted proportion of the sample of those with no self-reported history of CVD (i.e., not told of prior MI, congestive heart failure, angina pectoris, or stroke) who report having been told to use a antihypertensive/statin by a medical care provider and are currently following that advice. Likewise, antihypertensive/statin use rates for secondary prevention were estimated by the weighted proportion of the sample of those with self-reported history of CVD (i.e., previously told of prior MI, congestive heart failure, angina pectoris, or stroke) who report having been told to use antihypertensive/statin by a medical care provider and are currently following that advice. The medication use rates for aspirin are presented in **Table 18**.

Table 18: Summary of Long-term Antihypertensive Medication Use Rates Model Health: CVD

Parameter	Medication use rate
Antihypertensive medication use for primary prevention	
Age 18-39	62%
Age 40-64	84%
Age 65+	94%
Antihypertensive medication use for secondary prevention	
Age 18-39	77%
Age 40-64	89%
Age 65+	97%

Note: Estimated together with use of statins using National Health and Nutrition Examination Survey [15-19] data.

Treatment Effects

We used recent meta-analyses/reviews of antihypertensive therapy to identify major (of 1,000 or more persons) randomized controlled trials comparing blood pressure reduction associated with drug therapy to a

placebo [71-79]. Included trials—accounting for a total of 54,863 subjects—had a follow-up period of at least 52 weeks, involved subjects for primary or secondary prevention, were subject-blinded (at a minimum), and reported changes in SBP as an outcome. In addition, due to the considerable heterogeneity in observed blood pressure lowering drug therapy strategies—including differences in first-line drugs, doses, and combinations [80]—we required treatment arm protocol to include stepped therapy (and preferably matched stepped therapy of a placebo in the control arm). Trials were excluded if additional (open label) blood pressure lowering drugs were allowed for use in the placebo group (unless observed at rates lower than 10 percent). The trials included in our analysis are summarized in **Table 19**.

Table 19: Summary of Antihypertensive Drug Trials Included in Estimation of Treatment Effects

Trial	Subjects	Ages	Baseline SBP	Mean ↓ SBP
FEVER	9,711	50 – 79	154.3	4.5
HYVET	3,845	80+	173.0	13.0
MRC-1	17,354	35 – 64	161.5	10.5
MRC-2	4,396	65 – 74	173.0	15.5
PROGRESS	6,105	30 – 90	147.0	9.0
SHEP	4,736	60+	170.3	14.0
STOP	1,627	70 – 84	195.0	22.0
Syst-China	2,394	60+	170.5	9.1
Syst-Eur	4,695	60+	174.0	13.0

Sources: FEVER [81]; HYVET [82]; MRC-1[83], MRC-2[84]; PROGRESS[85]; SHEP[86]; STOP [87]; Syst-China[88]; Sys-Eur [89].

To accommodate diverse treatment strategies (i.e., stepped and combination) with respect to baseline blood pressure relative to goal, we estimated treatment effects on blood pressure levels using a simple weighted ordinary least squares regression, with baseline SBP levels (respectively) as the only predictor:

$$Effect_{SBP} = \beta_0 + (BaselineSBP)\beta_{BaselineSBP}$$

The average effect size of antihypertensive drugs on SBP was estimated to be a 40.1 mmHg increase, counterintuitively, but this is offset by an additional marginal impact of 0.31 mmHg reduction per mmHg of baseline SBP (**Table 19**). Hence, the intercept on the treatment effect is negative, implying that antihypertensives begin to raise blood pressure around SBP baseline levels of 108 mmHg or lower. In practice, this threshold is well-below standard SBP goals (140 mmHg for most patients, 135 mmHg for diabetics), and such blood pressure raising effects (a statistical anomaly) are not invoked by the model.

To accommodate interpersonal differences in the impact of drug therapy on SBP in ModelHealth: CVD, we constructed a triangle distribution centered on the mean effect size described above, with upper and lower limits defined by the standard deviation in effect size observed in the antihypertensive trials, to draw person-specific effect sizes. The standard deviation of drug treatment on SBP was estimated from the subset of trials from **Table 19** that reported this measure [82, 88, 89].

Finally, all trials reported results solely based upon intention-to-treat analyses. The average weighted adherence to the treatment across study arms among included trials reporting this measure was 81.9 percent. To account for diminished average treatment effects attributable to non-adherence to prescribed therapy, we estimate an appropriate adjustment by dividing lipid impact by 0.8 in the base case. Finally, to account for real-world effectiveness (e.g., treatment plan fidelity), treatment effects are adjusted (multiplied) by a treatment effectiveness parameter. In the base case, this treatment effectiveness adjustment is 70% of the treatment efficacy derived from the antihypertensive drug trials. This adjustment is based on model calibration with reference to outcomes among persons using blood pressure medications in NHANES data [15-19]. Average blood pressure lowering effects of antihypertensive drugs used in ModelHealth: CVD are summarized in **Table 20**.

Table 20: Summary of Antihypertensive Drug Treatment Effects

	$\beta 0$	$\beta BaselineSBP$	Std. Dev.	Adherence Adjustment	Treatment Effectiveness
Antihypertensive Drug Effect on SBP	-40.101	0.310	16.90	80%	70%

Source: Analysis of clinical trials described in **Table 19**.

4.4 Background Utilization of Clinical Preventive Services

Whenever a specific USPSTF-recommended clinical preventive service is not being directly assessed, it operates as a background service in the model and is available to agents in both analysis arms with utilization at contemporary rates. Background rates of screening for lipids and aspirin use in the model are every 5 years in accordance with clinical guidelines [3, 4]. We assume that adults have a blood pressure measurement opportunity at least once per year. Good evidence is lacking for the percentage of individuals who would accept prevention screening—in accordance with USPSTF recommendations—when offered. We assume 90 percent of individuals will accept any of the USPSTF-recommended clinical preventive services [1-3]. This is implemented as a person-level parameter, such that a person who accepts screening will always do so and one who does not accept, will never do so.

5 Healthy Hearts Calculator Interventions

5.1 Pharmacist-involved Team-based Care for Hypertension

Eligibility

Eligibility for the modeled pharmacist-involved team-based care program for hypertension is based on the following criteria: age 18 or older and persistent hypertension, defined by a systolic blood pressure ≥140 mm Hg, for at least one year.

Intervention Effect

To inform the effectiveness and design of the intervention modeled, we consulted two evidence reviews conducted by the Community Guide [90, 91], as well as several additional systematic reviews and meta-analyses on team-based hypertension care interventions [92-96]. Combined with relevant studies published beyond the most recent search period of these reviews, we identified a total of 62 study arms that include a pharmacist in the "team" and were potentially pertinent to the modeled intervention. Among these study arms, 48 were conducted in the United States and 46 were randomized controlled trials (RCTs). Among the 34 RCT study arms conducted in the United States, 20 include programs with medication management as an intervention component, either made independently by a pharmacist or in coordination with a physician [97-116]. Table 21 below summarizes this evidence.

We assumed that the average benefit of participating in a pharmacist-involved team-based hypertension management is a reduction of systolic blood pressure (SBP) of 8.5 mm Hg. We also assume that hypertensive patients who are also taking lipid medications will see a benefit in their lipid management. Drawing from 5 randomized trials [105, 109, 117-119], we assume that the intervention leads to an average reduction in low-density lipoprotein (LDL) cholesterol of 8.1 mg/dL and will have no significant effect on high-density lipoprotein (HDL) cholesterol. Following Dehmer and colleagues [120], we assumed the following: the long-term effectiveness of the program declines at rate of 20 percent per year and patients are eligible to re-enroll in the program every 5 years, if their blood pressure subsequently slips out of control (SBP ≥ 140 mm Hg).

Table 21: Evidence summary of pharmacist hypertension interventions with medication management in U.S. RCTs

First author	Year	Location	Setting	N	Follow-up	Mean SBP Δ	
Bodgen [97]	1998	Honolulu, HI	Clinic	95	6m	-12	p<0.01
Borenstein [98]	2003	California	Clinic	197	12m	-11	p<0.01
Carter [99]	2008	Iowa	Clinic	179	9m	-8.7	p<0.001
Carter [100]	2009	Iowa	Clinic	402	6m	-12	p=0.05
Carter [101]	2015	15 US states	Clinic	539	9m	-6.1	p<0.002
Chisholm [102]	2002	Augusta, GA	Tertiary care clin.	23	12m	-27.5	p<0.01
Edelman [107]	2010	United States	VA Clinic	239	12.8m	-7.3	p=0.011
Green [108]	2008	Washington	Clinic	519	12m	-8.9	p<0.001
Hirsch [109]	2014	California	University clinic	160	9m	-3.5	p=0.22
Hunt [110]	2008	Oregon	Clinic	460	12m	-6	p=0.007
Magid [111]	2011	Denver, CO	Clinic	283	6m	-6	p=0.006
Magid [112]	2013	Colorado	Clinic	348	6m	-12.4	p<0.05
Margolis [113]	2013	Minnesota	Clinic	388	12m	-9.7	p<0.001
Mehos [103]	2000	Colorado	Clinic	36	6m	-10.1	p=0.069
Planas [104]	2009	Tulsa, OK	Comm. pharmacy	40	9m	-20.1	p=0.003
Rothman [114]	2005	North Carolina	University clinic	217	12m	-9	p=0.008
Scott [105]	2006	Sioux City, IA	Comm. health cent.	149	9m	-5.5	p<0.05
Solomon [115]	1998	United States	Clinic	133	6m	-6.9	p<0.05
Vivian [116]	2002	Philadelphia, PA	Clinic	53	6m	-14.1	p<0.05
Zillich [106]	2005	Iowa	Comm. Pharmacy	117	3m	-4.5	p=0.12
			Person-month weighted average treatment effect			**-8.5**	

Notes: U.S. = United States; RCT = randomized controlled trial; N = study sample size; SBP = systolic blood pressure in mm Hg; VA = Veteran's Administration; clin. = clinic; comm. = community; N/R = not reported.

5.2 Sodium Reduction

Eligibility

Healthy People 2020 [121] and the 2015-2020 Dietary Guidelines for Americans [122] set a goal to reduce daily sodium consumption to 2,300 mg or less among U.S. adults. The policy be modeled achieves this goal (population average sodium consumption reduced to 2,300 mg/day) over 10 years, with one-third of the reduction achieved in the first two years and the remaining two-thirds reduction achieved over the remaining eight years. All adults aged 18 and older are eligible for this intervention.

Intervention Effect

What We Eat in America [123] reports current daily sodium consumption by age and sex, which are the two most important demographic dimensions upon which sodium consumption varies, based on data from the 2011-2012 National Health and Nutrition Examination Survey (NHANES). Using these data with the age-sex population distribution reported in the 2012 U.S. Census data [124], we solved for the proportional reduction in sodium everyone would need to achieve to lower the population average sodium consumption to 2300 mg per day (35.9%, Table 22).

A recent Cochrane review [125] found high quality evidence that a 75 mmol per day reduction in sodium reduces systolic blood pressure by 5.39 mm Hg among persons with hypertension (based on 21 randomized controlled trials) and by 2.42 mm Hg among persons with normal blood pressure (based on 12 randomized controlled trials). This is the equivalent of a reduction of 0.31 mm Hg in systolic blood pressure for each 100 mg of sodium per day for hypertensives and 0.14 mm Hg for normotensives [126]. Blood pressure reduction benefits are realized through the reduction of risk for myocardial infarction, ischemic stroke, hemorrhagic stroke, angina, congestive heart failure, intermittent claudication, diabetes, and CVD-related death. Potential relationships between baseline sodium consumption and systolic blood pressure and hypertension treatment status were explored using 2001-2010 NHANES data [15-19], but such associations were not found to be evident for explicit inclusion within the model. Combined, Tables 23 and 24 show the policy effect on sodium consumption and systolic blood pressure for population groups defined by their age, sex, and hypertension status.

Table 22: Derivation of Sodium Reductions to Achieve Policy Goal

	18-19 y	20-29 y	30-39 y	40-49 y	50-59 y	60-69 y	70+ y	18+ y	Source
Current sodium consumption									
Men, mg/d	4220	4477	4559	4646	3996	3824	3328	*4219*	[123]
Women, mg/d	2949	3294	3179	3089	2972	2769	2526	*2996*	[123]
Men and Women, mg/d	*3598*	*3886*	*3859*	*3855*	*3469*	*3269*	*2867*	*3587*	[123, 124]
Proportion of Age 1+ U.S. population									
Men	1.8%	9.1%	8.3%	8.9%	8.8%	6.3%	5.1%	48.3%	[124]
Women	1.8%	9.1%	8.5%	9.2%	9.4%	7.0%	6.8%	51.7%	[124]
Reduction to achieve 2300 mg/day average									
Men, mg/d	1514	1606	1636	1667	1434	1372	1194	1514	Calculated, 35.9% ↓
Women, mg/d	1058	1182	1141	1108	1066	994	906	1075	Calculated, 35.9% ↓
Sodium consumption after 10 years with policy									
Men, mg/d	2706	2871	2923	2979	2562	2452	2134	*2705*	
Women, mg/d	1891	2112	2038	1981	1906	1775	1620	*1921*	
Men and Women, mg/d	*2307*	*2492*	*2475*	*2472*	*2224*	*2096*	*1838*	*2300*	

Notes: y, year; mg, milligram; d, day. Italic figures were calculated between sources [123, 124].

Table 23: Intervention Effect Sizes for Men by Age and Hypertension Status

	18-19 y	20-29 y	30-39 y	40-49 y	50-59 y	60-69 y	70+ y	Source
Baseline								
Sodium, mg/d	4220	4477	4559	4646	3996	3824	3328	[123]
Year 1								
Marginal Δ Sodium, mg/d	-252	-268	-273	-278	-239	-229	-199	
Total Δ SBP, Hypertensive, mm Hg	-0.78	-0.83	-0.85	-0.86	-0.74	-0.71	-0.62	[125]
Total Δ SBP, Normotensive, mm Hg	-0.35	-0.37	-0.38	-0.39	-0.33	-0.32	-0.28	[125]
Sodium, mg/d	3968	4209	4286	4368	3757	3595	3129	
Year 2								
Marginal Δ Sodium, mg/d	-252	-268	-273	-278	-239	-229	-199	
Total Δ SBP, Hypertensive, mm Hg	-1.56	-1.66	-1.69	-1.72	-1.48	-1.42	-1.23	[125]
Total Δ SBP, Normotensive, mm Hg	-0.71	-0.75	-0.76	-0.78	-0.67	-0.64	-0.56	[125]
Sodium, mg/d	3715	3942	4014	4090	3518	3367	2930	
Year 3								
Marginal Δ Sodium, mg/d	-126	-134	-136	-139	-119	-114	-100	
Total Δ SBP, Hypertensive, mm Hg	-1.96	-2.07	-2.11	-2.15	-1.85	-1.77	-1.54	[125]
Total Δ SBP, Normotensive, mm Hg	-0.88	-0.94	-0.95	-0.97	-0.84	-0.80	-0.70	[125]
Sodium, mg/d	3589	3808	3877	3951	3399	3252	2830	
Year 4								
Marginal Δ Sodium, mg/d	-126	-134	-136	-139	-119	-114	-100	
Total Δ SBP, Hypertensive, mm Hg	-2.35	-2.49	-2.54	-2.58	-2.22	-2.13	-1.85	[125]
Total Δ SBP, Normotensive, mm Hg	-1.06	-1.12	-1.15	-1.17	-1.00	-0.96	-0.84	[125]
Sodium, mg/d	3463	3674	3741	3813	3279	3138	2731	
Year 5								
Marginal Δ Sodium, mg/d	-126	-134	-136	-139	-119	-114	-100	
Total Δ SBP, Hypertensive, mm Hg	-2.74	-2.90	-2.96	-3.01	-2.59	-2.48	-2.16	[125]
Total Δ SBP, Normotensive, mm Hg	-1.24	-1.31	-1.34	-1.36	-1.17	-1.12	-0.98	[125]
Sodium, mg/d	3337	3540	3605	3674	3160	3024	2631	
Year 6								
Marginal Δ Sodium, mg/d	-126	-134	-136	-139	-119	-114	-100	
Total Δ SBP, Hypertensive, mm Hg	-3.13	-3.32	-3.38	-3.45	-2.96	-2.84	-2.47	[125]
Total Δ SBP, Normotensive, mm Hg	-1.41	-1.50	-1.53	-1.56	-1.34	-1.28	-1.11	[125]
Sodium, mg/d	3211	3406	3468	3535	3040	2909	2532	
Year 7								
Marginal Δ Sodium, mg/d	-126	-134	-136	-139	-119	-114	-100	
Total Δ SBP, Hypertensive, mm Hg	-3.52	-3.73	-3.80	-3.88	-3.33	-3.19	-2.78	[125]
Total Δ SBP, Normotensive, mm Hg	-1.59	-1.69	-1.72	-1.75	-1.51	-1.44	-1.25	[125]
Sodium, mg/d	3084	3272	3332	3396	2921	2795	2432	
Year 8								
Marginal Δ Sodium, mg/d	-126	-134	-136	-139	-119	-114	-100	
Total Δ SBP, Hypertensive, mm Hg	-3.91	-4.15	-4.23	-4.31	-3.70	-3.54	-3.08	[125]
Total Δ SBP, Normotensive, mm Hg	-1.77	-1.87	-1.91	-1.94	-1.67	-1.60	-1.39	[125]
Sodium, mg/d	2958	3138	3196	3257	2801	2681	2333	
Year 9								
Current Δ Sodium, mg/d	-126	-134	-136	-139	-119	-114	-100	
Total Δ SBP, Hypertensive, mm Hg	-4.30	-4.56	-4.65	-4.74	-4.07	-3.90	-3.39	[125]
Total Δ SBP, Normotensive, mm Hg	-1.94	-2.06	-2.10	-2.14	-1.84	-1.76	-1.53	[125]
Sodium, mg/d	2832	3005	3060	3118	2682	2566	2233	
Year 10								
Marginal Δ Sodium, mg/d	-126	-134	-136	-139	-119	-114	-100	
Total Δ SBP, Hypertensive, mm Hg	-4.69	-4.98	-5.07	-5.17	-4.44	-4.25	-3.70	[125]
Total Δ SBP, Normotensive, mm Hg	-2.12	-2.25	-2.29	-2.33	-2.01	-1.92	-1.67	[125]
Sodium, mg/d	2706	2871	2923	2979	2562	2452	2134	

Notes: y, year; SBP, systolic; mg, milligram; d, day; Δ, change in; mm, millimeter; Hg, mercury. Hypertensive indicates persons treated for hypertension or with systolic blood pressure ≥ 140 mm Hg. Normotensive indicates persons not treated for hypertension and with systolic blood pressure < 140 mm Hg.

Table 24: Intervention Effect Sizes for Women by Age and Hypertension Status

	18-19 y	20-29 y	30-39 y	40-49 y	50-59 y	60-69 y	70+ y	Source
Baseline								
Sodium, mg/d	2949	3294	3179	3089	2972	2769	2526	[123]
Year 1								
Marginal Δ Sodium, mg/d	-176	-197	-190	-185	-178	-166	-151	
Total Δ SBP, Hypertensive, mm Hg	-0.55	-0.61	-0.59	-0.57	-0.55	-0.51	-0.47	[125]
Total Δ SBP, Normotensive, mm Hg	-0.25	-0.28	-0.27	-0.26	-0.25	-0.23	-0.21	[125]
Sodium, mg/d	2773	3097	2989	2904	2794	2603	2375	
Year 2								
Marginal Δ Sodium, mg/d	-176	-197	-190	-185	-178	-166	-151	
Total Δ SBP, Hypertensive, mm Hg	-1.09	-1.22	-1.18	-1.15	-1.10	-1.03	-0.94	[125]
Total Δ SBP, Normotensive, mm Hg	-0.49	-0.55	-0.53	-0.52	-0.50	-0.46	-0.42	[125]
Sodium, mg/d	2596	2900	2799	2720	2617	2438	2224	
Year 3								
Marginal Δ Sodium, mg/d	-88	-98	-95	-92	-89	-83	-76	
Total Δ SBP, Hypertensive, mm Hg	-1.37	-1.53	-1.47	-1.43	-1.38	-1.28	-1.17	[125]
Total Δ SBP, Normotensive, mm Hg	-0.62	-0.69	-0.67	-0.65	-0.62	-0.58	-0.53	[125]
Sodium, mg/d	2508	2802	2704	2627	2528	2355	2148	
Year 4								
Marginal Δ Sodium, mg/d	-88	-98	-95	-92	-89	-83	-76	
Total Δ SBP, Hypertensive, mm Hg	-1.64	-1.83	-1.77	-1.72	-1.65	-1.54	-1.40	[125]
Total Δ SBP, Normotensive, mm Hg	-0.74	-0.83	-0.80	-0.78	-0.75	-0.70	-0.63	[125]
Sodium, mg/d	2420	2703	2609	2535	2439	2272	2073	
Year 5								
Marginal Δ Sodium, mg/d	-88	-98	-95	-92	-89	-83	-76	
Total Δ SBP, Hypertensive, mm Hg	-1.91	-2.14	-2.06	-2.00	-1.93	-1.80	-1.64	[125]
Total Δ SBP, Normotensive, mm Hg	-0.86	-0.97	-0.93	-0.91	-0.87	-0.81	-0.74	[125]
Sodium, mg/d	2332	2605	2514	2442	2350	2189	1997	
Year 6								
Marginal Δ Sodium, mg/d	-88	-98	-95	-92	-89	-83	-76	
Total Δ SBP, Hypertensive, mm Hg	-2.19	-2.44	-2.36	-2.29	-2.20	-2.05	-1.87	[125]
Total Δ SBP, Normotensive, mm Hg	-0.99	-1.10	-1.06	-1.03	-1.00	-0.93	-0.85	[125]
Sodium, mg/d	2244	2506	2419	2350	2261	2107	1922	
Year 7								
Marginal Δ Sodium, mg/d	-88	-98	-95	-92	-89	-83	-76	
Total Δ SBP, Hypertensive, mm Hg	-2.46	-2.75	-2.65	-2.58	-2.48	-2.31	-2.11	[125]
Total Δ SBP, Normotensive, mm Hg	-1.11	-1.24	-1.20	-1.16	-1.12	-1.04	-0.95	[125]
Sodium, mg/d	2155	2408	2324	2258	2172	2024	1846	
Year 8								
Marginal Δ Sodium, mg/d	-88	-98	-95	-92	-89	-83	-76	
Total Δ SBP, Hypertensive, mm Hg	-2.73	-3.05	-2.95	-2.86	-2.75	-2.57	-2.34	[125]
Total Δ SBP, Normotensive, mm Hg	-1.23	-1.38	-1.33	-1.29	-1.24	-1.16	-1.06	[125]
Sodium, mg/d	2067	2309	2228	2165	2083	1941	1771	
Year 9								
Current Δ Sodium, mg/d	-88	-98	-95	-92	-89	-83	-76	
Total Δ SBP, Hypertensive, mm Hg	-3.01	-3.36	-3.24	-3.15	-3.03	-2.82	-2.58	[125]
Total Δ SBP, Normotensive, mm Hg	-1.36	-1.52	-1.46	-1.42	-1.37	-1.28	-1.16	[125]
Sodium, mg/d	1979	2211	2133	2073	1995	1858	1695	
Year 10								
Marginal Δ Sodium, mg/d	-88	-98	-95	-92	-89	-83	-76	
Total Δ SBP, Hypertensive, mm Hg	-3.28	-3.66	-3.54	-3.44	-3.31	-3.08	-2.81	[125]
Total Δ SBP, Normotensive, mm Hg	-1.48	-1.65	-1.60	-1.55	-1.49	-1.39	-1.27	[125]
Sodium, mg/d	1891	2112	2038	1981	1906	1775	1620	

Notes: y, year; SBP, systolic; mg, milligram; d, day; Δ, change in; mm, millimeter; Hg, mercury. Hypertensive indicates persons treated for hypertension or with systolic blood pressure ≥ 140 mm Hg. Normotensive indicates persons not treated for hypertension and with systolic blood pressure < 140 mm Hg.

6 Model Validation

Baseline rates of CVD events are generated by the combination of population characteristics at model initiation, the model's estimation of the natural progression of CVD risk factors as individuals age, and the

model's risk equations for disease. **Table 25** below presents lifetime age-adjusted prevalence rates for hypertension, elevated lipids, coronary heart disease, and stroke generated by the model for a birth cohort starting at age 18 and compares these values to corresponding rates observed national data sources as a benchmark for the external validity of the ModelHealth: CVD natural history engine.

Table 25: Validation of baseline model CVD risk factors and event prevalence

	Total	Men	Women	Non-Hispanic white	Non-Hispanic black	Hispanic
Hypertension (SBP≥140 or DBP ≥90 or taking hypertension medication)						
ModelHealth: CVD	29.2%	30.0%	28.4%	26.1%	45.0%	27.5%
NHANES (2007-2010)[127]	29.6%	30.5%	28.6%	28.6%	41.3%	27.7%
Elevated lipids (LDL≥130)						
ModelHealth: CVD	29.8%	27.8%	31.6%	29.6%	29.9%	30.2%
NHANES (2009-2012)[128]	31.7%	31.0%	32.0%	30.7%	32.2%	35.3%
Coronary heart disease						
ModelHealth: CVD	6.5%	8.6%	4.7%	6.3%	7.2%	6.7%
BRFSS (2010)[129]	6.0%	7.8%	4.6%	5.8%	6.5%	6.1%
Stroke						
ModelHealth: CVD	2.5%	2.6%	2.4%	2.3%	4.1%	2.3%
BRFSS (2010)[130]	2.6%	2.7%	2.6%	2.4%	3.9%	2.5%

Notes: CVD = cardiovascular disease; SBP = systolic blood pressure; DBP = diastolic blood pressure; NHANES = National Health and Nutrition Examination Survey; LDL = low-density lipoprotein; BRFSS = Behavioral Risk Factor Surveillance System. Risk factor and event prevalence rates are age-adjusted. ModelHealth: CVD data are generated from a US-representative birth cohort starting at age 18.

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