Special Report

The Impact of Prevention on Reducing the Burden of Cardiovascular Disease

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Objective—Cardiovascular disease (CVD) is prevalent and expensive. While many interventions are recommended to prevent CVD, the potential effects of a comprehensive set of prevention activities on CVD morbidity, mortality, and costs have never been evaluated. We therefore determined the effects of 11 nationally recommended prevention activities on CVD-related morbidity, mortality, and costs in the United States.

Research Design and Methods—We used person-specific data from a representative sample of the US population (National Health and Nutrition Education Survey IV) to determine the number and characteristics of adults aged 20-80 years in the United States today who are candidates for different prevention activities related to CVD. We used the Archimedes model to create a simulated population that matched the real US population, person by person. We then used the model to simulate a series of clinical trials that examined the effects over the next 30 years of applying each prevention activity one by one, or altogether, to those who are candidates for the various activities and compared the health outcomes, quality of life, and direct medical costs to current levels of prevention and care. We did this under two sets of assumptions about performance and compliance: 100% success for each activity and lower levels of success considered aggressive but still feasible.

Results—Approximately 78% of adults aged 20-80 years alive today in the United States are candidates for at least one prevention activity. If everyone received the activities for which they are eligible, myocardial infarctions and strokes would be reduced by 63% and 31%, respectively. If more feasible levels of performance are assumed, myocardial infarctions and strokes would be reduced 36% and 20%, respectively. Implementation of all prevention activities would add ≈221 million life-years and 244 million quality-adjusted life-years to the US adult population over the coming 30 years, or an average of 1.3 years of life expectancy for all adults. Of the specific prevention activities, the greatest benefits to the US population come from providing aspirin to high-risk individuals, controlling pre-diabetes, weight reduction in obese individuals, lowering blood pressure in people with diabetes, and lowering LDL cholesterol in people with existing coronary artery disease (CAD). As currently delivered and at current prices, most prevention activities are expensive when considering direct medical costs; smoking cessation is the only prevention strategy that is cost-saving over 30 years.

Conclusions—Aggressive application of nationally recommended prevention activities could prevent a high proportion of the CAD events and strokes that are otherwise expected to occur in adults in the United States today. However, as they are currently delivered, most of the prevention activities will substantially increase costs. If preventive strategies are to achieve their full potential, ways must be found to reduce the costs and deliver prevention activities more efficiently. **(*Circulation*. 2008;118:576-585.)**

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Three chronic diseases—cancer, cardiovascular disease (CVD), and diabetes—are responsible for a majority of the morbidity, mortality, and health care costs in the United States.[1–8] To help reduce the toll of these diseases, the American Cancer Society, American Diabetes Association, and American Heart Association have recommended a variety of prevention activities.[8] Each is supported by good evidence of effectiveness[8–16] and widely accepted. However, despite this support, there are large gaps in how well they are applied, and a high proportion of the US population is not receiving prevention activities from which they would benefit.[17–21]

To stimulate greater attention to prevention and to help physicians and health care delivery organizations implement prevention activities, it is important to know the answers to several questions. First, how many people alive today are candidates for at least one prevention activity? Second, how much of the morbidity, mortality, and cost of these diseases is potentially preventable? Stated another way, by how much could the burden of chronic diseases be reduced if prevention activities were applied with 100% performance, compliance, and effectiveness? Third, what could realistically be accomplished if patients, physicians, and health plans throughout the country pursued prevention at levels of performance and compliance achieved by the most successful organizations? Fourth, how do the various prevention activities compare? Which are the most important in terms of their potential effects on health outcomes, costs, and cost-effectiveness? Fifth, what does prevention cost? If pursued at maximum feasibility levels, would the costs be offset by the savings? Finally, what are the main factors that determine the cost-effectiveness of a prevention activity, and what are the best ways to make prevention more attractive financially? This report offers answers to these questions for the prevention of CVD.

Research Design and Methods

Overview

Ideally, the answers to the above questions would be obtained by examining the results of clinical trials. While there are studies that document that each of the prevention activities is effective, none of the existing studies addresses a representative sample of the US population, addresses specific treatment goals that are being recommended, or includes representative US costs. Furthermore, it is not possible to conduct the needed trials because of the large number of activities, long time horizons, large numbers of subjects required, and high cost of such research.

Lacking clinical trials, the only alternative is to use a mathematical model. For this analysis, we selected the Archimedes model from other available mathematical models because of its ability to simulate the US population at a person-specific level, its ability to simulate current patterns of care, its inclusion of all the relevant diseases and prevention activities in a single integrated model, its ability to analyze the prevention activities precisely as they are recommended, its ability to address all the questions of interest using a consistent methodology, and its demonstrated accuracy in reproducing the trials that document the effectiveness of each of the recommended interventions.

Archimedes Model

The Archimedes model is a person-by-person, object-by-object, large-scale simulation model of physiology, disease, and health care systems written at a high level of detail using object-oriented programming and run on a distributed computing network.[22–26] The core of the model is a set of ordinary and differential equations that represent the physiological pathways pertinent to diseases and their complications. Currently, the model includes coronary artery disease (CAD), stroke, diabetes and its complications, congestive heart failure, obesity, smoking, asthma, and the metabolic syndrome in a single integrated model. The model also includes aspects of diseases and health care systems needed to analyze downstream clinical events, utilization, and costs including signs and symptoms; patient encounters with the health care system (eg, emergency room visits, office visits, and admissions); protocols and guidelines; tests and treatments; patient adherence to treatment recommendations; and clinical events that affect logistics, utilization, and financial costs.

Physiological variables that are continuous in reality are continuous in the model (eg, blood pressure and glucose levels), time is continuous, symptoms are driven by underlying variables, tests measure underlying variables, treatments affect underlying variables, and outcomes are determined by the progression of the variables.

Costs related to the conditions that are in the model are calculated by tracking all the pertinent cost-generating events using micro-costing methods.[32] Costs of other conditions that are not currently calculated in the model, such as cancer or osteoporosis ("unrelated costs"),[32] are added separately as a function of variables that are in the model (eg, age, sex, weight, and disease states).

The model uses person-specific data from real populations (eg, the National Health and Nutrition Education Survey [NHANES]) to create simulated populations that match the real populations, person by person. Each individual can be matched to variables such as demographics, risk factors, biological variables, current and past medical histories, and current treatments. The methods for creating the copies of real people preserve the distributions and correlations of all the important risk factors and biological variables.

The model's accuracy is checked by using it to simulate clinical trials that have been conducted in the real world and comparing the predicted results with the real results. This has been done successfully for several hundred treatments and outcomes in 48 randomized controlled trials thus far. Methods and results for the first 74 validation exercises involving 18 trials have been published.[24] More than half of those (10 of 18 trials) were independent validations[33] in which no results in the trial were used to build or modify the model. More information about the Archimedes model, including additional details about the equations and sources, is available elsewhere.[26]

The Current Study

For this study, we analyzed 11 prevention activities relating to CVD and combinations of these activities (Table 1). We

Table 1. Interventions Studied

Intervention	Total Eligible Population ×1000, %	Treatment Goals	Feasible Performance, % Achieved*
Baseline (without interventions)	200 000 (100)	...	...
Provide aspirin if 10-year MI risk ≥10%	12 315 (6.2)†	81 mg aspirin/day	50
Lower LDL cholesterol to <160 mg/dL in low-risk individuals‡	15 445 (7.7)	<160 mg/dL	75
Lower LDL cholesterol to <130 mg/dL in high-risk individuals§	17 857 (8.9)	<130 mg/dL	70
Lower LDL cholesterol to <100 mg/dL in people with CAD	3212 (1.8)	<100 mg/dL	70
Lower blood pressure to 140/90 mm Hg in nondiabetic individuals	30 820 (15.4)	<140/90 mm Hg	75
Lower A1C to <7.0% in diabetic individuals	5739 (2.9)	<7.0%	60
Lower blood pressure to 130/80 mm Hg in diabetic individuals	11 498 (5.8)	<130/80 mm Hg	60
Lower LDL cholesterol to <100 mg/dL in diabetic individuals	13 000 (6.5)	<100 mg/dL	65
Reduce FPG to <110 mg/dL	16 392 (8.2)	FPG <110 mg/dL	60
Smoking cessation	49 265 (24.6)	Stop immediately	30
Reduce weight to BMI <30 kg/m^2	60 257 (30.1)	BMI <30 kg/m^2	20

Treatment goals were obtained from published guidelines.[8,27–31] FPG, fasting plasma glucose.

*Derived from refs. 37–43 and defined as a performance level by health plans or in large health care systems that has been achieved in a clinical setting.

†Assumes that 70% of the population at risk is already taking aspirin,[36] leaving 12 315 million (6.2%) still eligible.

‡Low risk defined as having 0 or 1 of the following risk factors: blood pressure >140/90 mm Hg, HDL cholesterol <40 mg/dL, family history of MI before age 55 years, male >45 or female >55 years of age.

§High risk defined as having two or more of the risk factors defined in the above footnote.

conducted the analysis in three steps. First, we used person-specific data from the most current NHANES (1998–2004) to determine the characteristics (including sex and ethnicity), risk factors, and current levels of prevention in the US population.[34] We also used the NHANES data to create simulated populations that matched the real US population.

Second, we created a care delivery setting that could serve as a representation of how health care is currently delivered in the United States. We modified different aspects of the care setting through sensitivity analysis. For the representative setting, we based the use of prevention activities and degree of control of risk factors on the practices and success rates in the NHANES population. We based the treatment of symptoms and complications (eg, management of diabetes and CVD) on national guidelines. We based the costs of drugs on information provided by drugstore.com and the cost of general medical care (eg, emergency visits, office visits and admissions, and procedures) on costs experienced by Kaiser Permanente Southern California or from the literature.[35] The costs of the prevention activities assumed for the reference case are given in Table 2. For the reference case, the costs of unrelated care and extra costs for the last year of life (beyond the costs related to the diseases calculated explicitly in the model) were set to zero. Different assumptions about the costs of prevention activities, general medical costs, and unrelated medical costs were all studied through sensitivity analysis.

The third step was to use the simulated populations and simulated care delivery setting to conduct 13 simulated clinical trials. Eleven of the trials addressed prevention activities, one by one (Table 1). The other two trials addressed the combination of all 11 activities, given either with 100% performance and success in reaching the treatment targets or at more feasible levels. To the extent possible, the reference assumptions about feasible levels of performance (Table 1) were based on the levels of success that have been achieved in various clinical settings.[36–42] Uncertainty about feasible performance levels was studied through sensitivity analysis. Additional simulated trials were conducted to study the sensitivity of the results to bundling of prevention services.

Analogous to the treatment arms of a clinical trial, the simulated population created for each trial was subjected to two management protocols. One management protocol represented "current care": for each individual, we determined that person's current level of adoption of prevention (eg, smoking habits, weight, and blood pressure) and assumed that the level of care responsible for that level of prevention would continue. Behaviors and physiological variables would be allowed to progress naturally as occurs with age but with no changes in any aspects of their care relevant to the prevention activities listed in Table 1. In these current care treatment arms, individuals were given additional treatments (beyond their current levels of prevention care) only if they developed symptoms, in which case the model assumed they sought care, or if clinical events such as heart attacks occurred.

Each of the first 11 "one-by-one" trials also had a "prevention" arm in which people who were candidates for the applicable prevention activity were identified and treated to a level slightly (≈2%–3%) below whatever target was specified for the applicable prevention activity. For these treatment arms, each individual in the simulated population was examined at the initiation of the trial and annually thereafter to determine whether he or she was a candidate for treatment according to whatever prevention activity was the subject of the trial. If a person met the criteria for the applicable

Table 2. Cost of Interventions

Intervention	Annual Visits, n	Medications/Year	Lab Tests/Year	Total Cost/Year
Aspirin to high-risk patients	1 @ $74	$17	NA	$91
Lower LDL cholesterol to <160 mg/dL in low-risk individuals	1 @ $74	Branded statin at $1082	Creatinine, ALT, lipid panel @ $125	$1281
Lower LDL cholesterol to <130 mg/dL in high-risk individuals	2 @ $74	Branded statin at $1543	Creatinine, ALT, lipid panel @ $125	$1816
Lower LDL cholesterol to <100 mg/dL in people with CAD	3 @ $74	Branded statin at $1543	Creatinine, ALT, lipid panel @ $125 × 3	$2140
Lower blood pressure in nondiabetic individuals	4 @ $74	Angiotensin inhibitor @ $1238	K^+, creatinine, BUN @ $48	$1582
A1C control in diabetic individuals	4 @ $74	Generic and branded glucose lowering agents @ $3150	A1C @ $59 × 2	$3564
Lower blood pressure in diabetic individuals	4 @ $74	Angiotensin inhibitor and generic thiazide @ $1238	K^+, creatinine, BUN @ $48	$1582
Lower LDL in diabetic individuals	3 @ $74	Branded statin @ $1543	Creatinine, ALT, lipid panel @ $125 × 3	$2140
Reduce fasting glucose <110 mg/dL	2 @ $74	Generic glucose-lowering agent @ $524	Creatinine, ALT, BUN @ $60	$732
Smoking cessation	1 @ $80	Patch and a drug @ $270	NA	$350
Weight reduction (cost derived from ref. 44)	$1356 in year 1, $672 annually thereafter	NA	NA	$1356 year 1, $672 year 2+

BUN, blood urea nitrogen.

prevention activity, then he or she would be treated to slightly below the corresponding target of that prevention activity. For example, if the trial was to estimate the effect of controlling A1C in people with currently uncontrolled diabetes, then each individual in the simulated population was given a simulated examination at the start of the trial to determine whether he or she had a diagnosis of diabetes and an A1C level >7%. If so, that person was treated to reduce their A1C level to 6.8%. Everyone with a condition was then reexamined at annual intervals to determine whether their A1C levels had increased to >7% and treated as needed to maintain A1C levels <7%. People who were not candidates for the applicable prevention activity at the start of the simulation were followed annually (screened) to see if they developed the condition in the interval following the previous examination, and if so, they were treated accordingly. The cost of screening (ie, office visits and tests) was not considered.

For each of these simulated trials, we calculated the outcomes under two sets of assumptions about performance and compliance. In the first case, we analyzed the outcomes that would occur if 100% performance and compliance levels were achieved. This trial was done to estimate the maximum potential of prevention achievable by the recommended activities. In the second case, we applied more realistic, albeit aggressive, assumptions about what might constitute levels of performance that were feasible.

In addition to the one-by-one trials, we created two simulated trials to estimate the overall proportion of US adults who are candidates for any intervention and the overall effect of providing all of the prevention activities to anyone who was a candidate for them. In one of these trials, all people who were candidates for any of the prevention activities were treated with 100% performance and effectiveness. In the other, treatments were delivered at the more feasible levels of performance.

The sample size for each simulated trial was 50 000. The results were then scaled to the US adult population, which in 2005 was ≈200 million individuals. Each trial was run for 30 years. All outcomes were calculated continuously and reported at annual intervals. For each trial, we calculated a wide range of health and economic outcomes. Here we report the total number of myocardial infarctions (MIs) (including repeat MIs), deaths from coronary heart disease (CHD), stroke, life-years, quality-adjusted life-years (QALYs), cost of prevention activities, cost of care other than the prevention activities, total medical costs, and cost per QALY. Quality-of-life weights for the various clinical states and outcomes were based on a survey by Sullivan and Ghushchyan[43] and varied in the sensitivity analysis. For calculating cost per QALY, both costs and QALYs were discounted 3%, with different discount rates studied through sensitivity analysis.

Results

Of the 200 million people in the United States today between the ages of 20 and 80 years, ≈156 million (78%) meet the indications for at least one of the prevention activities listed in Table 1. Table 1 shows the numbers of people who are candidates for each particular activity; they vary widely from ≈3.2 million individuals with CAD and LDL cholesterol >100 mg/dL (1.8% of adults) to ≈60 million who have BMI >30 kg/m^2 (30.1% of adults).

Table 3 shows the outcomes that can be expected to occur in today's adults (independent of sex or ethnicity) over the next 30 years in the reference health care setting if the use of

Table 3. Effect of Interventions Over 30 Years on Outcomes and Costs (Thousands) in the US Population, Assuming 100% Performance

	MI Total	Stroke Total	Life-Years Total	QALYs	Cost of Prevention Interventions	Cost of All Medical Activities Except Prevention Interventions	Cost of Total Medical	Cost/QALY
Baseline (without interventions)	43 208±736	33 138±665	4 870 695	4 459 603	—	$9 504 964 366	$9 504 964 366	NA
Difference caused by prevention activities (thousands)								
Do everything, 100% performance	−27 429 (−63%)	−10 212 (−31%)	220 710 (5%)	243 926 (5%)	8 530 159 750	−904 118 726 (−10%)	7 626 041 025 (80%)	$36 380
Aspirin to high-risk individuals	−3409 (−8%)	331 (1%)	17 417 (0%)	17 005 (0%)	50 094 774	604 823 (0%)	50 699 597 (1%)	$2779
BMI <30 kg/m^2	−7133 (−17%)	−1083 (−3%)	55 200 (1%)	65 779 (1%)	1 204 091 934	−192 856 223 (−2%)	1 011 235 711 (11%)	$18 941
Blood pressure <140/90 mm Hg in nondiabetic individuals	−2851 (−7%)	−4574 (−14%)	39 124 (1%)	38 737 (1%)	1 973 968 837	−185 029 283 (−2%)	1 788 939 554 (19%)	$52 983
CAD: LDL cholesterol <100 mg/dL	−2246 (−5%)	−176 (−1%)	14 052 (0%)	10 985 (0%)	367 637 668	22 827 810 (0%)	390 465 478 (4%)	$39 130
Diabetes: blood pressure <130/80 mm Hg	−3355 (−8%)	−2337 (−7%)	30 984 (1%)	32 626 (1%)	824 447 730	−100 554 813 (−1%)	723 892 917 (8%)	$25 317
Diabetes: A1C <7%	−1086 (−3%)	263 (1%)	25 282 (1%)	38 389 (1%)	1 780 231 248	−231 969 165 (−2%)	1 548 262 083 (16%)	$48 759
Diabetes: LDL cholesterol <100 mg/dL	−4434 (−10%)	−760 (−2%)	18 036 (0%)	18 350 (0%)	1 077 255 101	−24 148 005 (0%)	1 053 107 096 (11%)	$67 199
High-risk CAD: LDL cholesterol <130 mg/dL	−3094 (−7%)	−1636 (−5%)	21 525 (0%)	21 222 (0%)	1 549 184 577	−17 874 128 (0%)	1 531 310 449 (16%)	$83 327
Low-risk CAD: LDL cholesterol <160 mg/dL	−924 (−2%)	−553 (−2%)	3707 (0%)	3990 (0%)	736 032 166	−53 235 769 (−1%)	682 796 396 (7%)	$272 061
Pre-diabetes: FPG <110 mg/dL	−3686 (−9%)	−322 (−1%)	25 443 (1%)	42 617 (1%)	819 873 408	−231 927 737 (−2%)	587 945 671 (6%)	$17 478
Smoking: stop	−3311 (−8%)	−1387 (−4%)	28 142 (1%)	27 597 (1%)	25 279 854	−72 490 798 (−1%)	−47 210 943 (0%)	−$1755

Data are means±SEM or n (%) unless otherwise indicated. FPG, fasting plasma glucose.

prevention activities continues at current levels (top row) and the differences in outcomes that could theoretically be achieved if prevention activities were adopted with 100% performance, compliance, and effectiveness. These entries show the maximum potential of prevention in reducing clinical outcomes of CVD. For example, if prevention continues at its current level, today's adults in the United States can expect to have ≈43 million MIs. If everyone adopted the prevention activities for which they are indicated, ≈27.4 million (63%) of those MIs could be prevented. Other columns show the effects on stroke, life-years, and QALYs.

Table 3 also shows the effects on health care costs. The cost of caring for CVD, diabetes, and CHD over the coming 30 years will be in the order of $9.5 trillion. If all the recommended prevention activities were applied with 100% success, those costs would be reduced by ≈$904 billion, or almost 10%. However, assuming the costs shown in Table 2, the prevention activities themselves would cost ≈$8.5 trillion, offsetting the savings by a factor of almost 10 and increasing total medical costs by ≈$7.6 trillion (162%).

The far right column of Table 3 shows the cost per QALY for each activity, assuming the reference costs in Table 2. Smoking cessation is the only prevention activity that can be expected to save money, with the reductions in costs of events more than offsetting the cost of the smoking cessation programs. Next in cost-effectiveness is the use of aspirin in high-risk individuals. The effects on the same outcomes using the maximum feasible levels of prevention activities are shown in Table 4.

Tables 3 and 4 show the effect of the prevention activities on the US population as a whole. The effects take into account two factors, the number of people who are candidates for a particular activity and the effect of the activity on those who are candidates (ie, effect/person×number of people). Table 5 shows the benefits of prevention from the perspective of the individuals who have particular risk factors. Each row shows the absolute risk reduction or magnitude of the outcome over 30 years and, where applicable (ie, for MI and stroke), the number needed to treat (NNT) to prevent one event (30-year NNT). The table also shows the increase in life expectancy, with and without adjustment for quality of life, for those who are candidates for each activity. In some cases, the prevention activity increases a person's length of life by an amount sufficient to then increase their risk of an adverse outcome (eg, A1C control on strokes).

Sensitivity Analysis

Table 6 summarizes the results of the sensitivity analysis on cost per QALY for a range of assumptions about the cost of the prevention activities (±20%), quality-of-life weights (±20%), unrelated medical costs ($0 to $10 000/person/year), the cost of dying ($0 to $40 000), the cost of general medical care (±20%), and discount rates (0 to 6%). The most important determinants of the costs and cost per QALY are the costs of the prevention activities themselves (Table 7).

Table 4. Effect of Interventions Over 30 Years on Outcomes and Costs (Thousands) in the US Population, Assuming Maximum Feasible Performance

	MI Total	Stroke Total	Life-Years Total	QALYs	Cost of Prevention Intervention(s)	Cost of All Medical Activities Except Prevention Interventions	Cost of Total Medical	Cost/QALY
Baseline (without interventions)	43 208±736	33 138±665	4 870 695	4 459 603	—	$9 504 964 366	$9 504 964 366	NA
Difference caused by prevention activities (thousands)								
Do everything, feasible performance	−15 527 (−36%)	−6718 (−20%)	131 543 (3%)	147 161 (3%)	5 848 702 328	−495 593 170 (−5%)	5 353 109 158 (56%)	$42 249
Aspirin to high-risk individuals	−1705 (−4%)	166 (0%)	8708 (0%)	8503 (0%)	25 047 387	302 412 (0%)	25 349 799 (0%)	$2779
BMI <30 kg/m^2	−1427 (−3%)	−217 (−1%)	11 040 (0%)	13 156 (0%)	240 818 387	−38 571 245 (0%)	202 247 142 (2%)	$18 941
Blood pressure <140/90 mm Hg in nondiabetic individuals	−2138 (−5%)	−3431 (−10%)	29 343 (1%)	29 053 (1%)	1 480 476 628	−138 771 963 (−1%)	1 341 704 665 (14%)	$52 983
CAD: LDL cholesterol <100 mg/dL	−1572 (−4%)	−123 (0%)	9837 (0%)	7689 (0%)	257 346 368	15 979 467 (0%)	273 325 835 (3%)	$39 130
Diabetes: blood pressure <130/80 mm Hg	−2013 (−5%)	−1402 (−4%)	18 591 (0%)	19 576 (0%)	494 668 638	−60 332 888 (−1%)	434 335 750 (5%)	$25 317
Diabetes: A1C <7%	−652 (−2%)	158 (0%)	15 169 (0%)	23 034 (1%)	1 068 138 749	−139 181 499 (−1%)	928 957 250 (10%)	$48 759
Diabetes: LDL cholesterol <100 mg/dL	−2882 (−7%)	−494 (−1%)	11 723 (0%)	11 927 (0%)	700 215 816	−15 696 203 (0%)	684 519 612 (7%)	$67 199
High-risk CAD: LDL cholesterol <130 mg/dL	−2166 (−5%)	−1145 (−3%)	15 068 (0%)	14 855 (0%)	1 084 429 204	−12 511 890 (0%)	1 071 917 314 (11%)	$83 327
Low-risk CAD: LDL cholesterol <160 mg/dL	−693 (−2%)	−415 (−1%)	2780 (0%)	2993 (0%)	552 024 124	−39 926 827 (0%)	512 097 297 (5%)	$272 061
Pre-diabetes: FPG <110 mg/dL	−2212 (−5%)	−193 (−1%)	15 266 (0%)	25 570 (1%)	491 924 045	−139 156 642 (−1%)	352 767 402 (4%)	$17 478
Smoking: stop	−993 (−2%)	−416 (−1%)	8443 (0%)	8279 (0%)	7 583 956	−21 747 239 (0%)	−14 163 283 (0%)	−$1755

Data are means±SEM and n (%) unless otherwise indicated. FPG, fasting plasma glucose.

Conclusions

Our results lead to seven main conclusions. First, there are large gaps in the application of prevention, and thus large opportunities to reduce the morbidity and mortality of CVD. Even after taking into account current use of prevention activities, the great majority of adults in the United States today (78%) still meet the indications for at least 1 of the 11 prevention activities we studied (Table 1). If every person

Table 5. Effect of Interventions on Absolute Difference in Risk (and NNT) or Magnitude of Outcomes Over Remaining Lifetime per Person Who Is or Becomes a Candidate for That Intervention Over the Remainder of Their Lifetime Up to 30 Years, Assuming 100% Performance

	Proportion of Adult Population With Condition at Start	MI Total (NNT)	Stroke Total (NNT)	Life-Years Gained	QALYs	Cost of Prevention Intervention(s)	Cost of All Medical Activities Except Prevention Interventions	Cost of Total Medical	Cost/QALY
Do everything, 100% performance	100%	−16.17% (6)	−6.02% (17)	1.30	1.44	$50 289	$5330	$44 958	$36 380
Aspirin to high-risk individuals	5.82%	−18.58% (5)	1.81% (−55)	0.95	0.93	$2730	$33	$2763	$2779
BMI <30 kg/m^2	28.75%	−11.94% (8)	−1.81% (55)	0.92	1.10	$20 160	−$3229	$16 931	$18 941
Blood pressure <140/90 mm Hg in nondiabetic individuals	14.21%	−6.85% (15)	−11.00% (9)	0.94	0.93	$47 463	−$4449	$43 014	$52 983
CAD: LDL cholesterol <100 mg/dL	1.53%	−39.23% (3)	−3.07% (33)	2.45	1.92	$64 205	$3987	$68 192	$39 130
Diabetes: blood pressure <130/80 mm Hg	5.99%	−19.32% (5)	−13.45% (7)	1.78	1.88	$47 463	−$5789	$41 674	$25 317
Diabetes: A1C <7%	2.85%	−6.52% (15)	1.58% (−63)	1.52	2.31	$106 906	−$13 930	$92 976	$48 759
Diabetes: LDL cholesterol <100 mg/dL	6.29%	−26.43% (4)	−4.53% (22)	1.07	1.09	$64 205	−$1439	$62 766	$67 199
High-risk CAD: LDL cholesterol <130 mg/dL	8.29%	−10.88% (9)	−5.75% (17)	0.76	0.75	$54 485	−$629	$53 857	$83 327
Low-risk CAD: LDL cholesterol <160 mg/dL	7.29%	−4.82% (21)	−2.89% (35)	0.19	0.21	$38 424	−$2779	$35 645	$272 061
Pre-diabetes: FPG <110 mg/dL	7.76%	−9.88% (10)	−0.86% (116)	0.68	1.14	$21 965	−$6214	$15 752	$17 478
Smoking: stop	23.76%	−7.82% (13)	−3.28% (31)	0.66	0.65	$597	−$1712	−$1115	−$1755

Table 6. Sensitivity Analysis: 30-Year Cost/QALY for Ranges of Assumptions About Selected Parameters

		Cost of Interventions		Quality Weights		Unrelated Medical Costs		Cost of Dying		General Medical Costs		Discount Rates	
	Ref.	−20%	+20%	−20%	+20%	$5000	$10 000	$20 000	$40 000	−20%	+20%	0%	6%
Do everything, 100% performance	$36 380	$28 203	$44 557	$37 128	$35 641	$39 196	$42 012	$34 913	$33 445	$37 281	$35 479	$31 264	$42 936
Do everything, feasible performance	$42 249	$32 981	$51 516	$43 214	$41 299	$44 892	$47 536	$40 740	$39 232	$43 066	$41 431	$36 376	$49 777
Aspirin to high-risk individuals	$2779	$2122	$3436	$2765	$2794	$7380	$11 981	$1294	−$192	$2881	$2677	$2981	$2626
BMI <30 kg/m^2	$18 941	$14 463	$23 420	$19 610	$18 305	$20 667	$22 392	$17 495	$16 048	$19 631	$18 251	$15 373	$23 625
Blood pressure <140/90 mm Hg in nondiabetic individuals	$52 983	$41 263	$64 702	$52 880	$53 073	$57 473	$61 964	$51 338	$49 693	$54 105	$51 860	$46 182	$61 562
CAD: LDL cholesterol <100 mg/dL	$39 130	$31 670	$46 590	$36 978	$41 550	$50 274	$61 419	$37 497	$35 865	$38 764	$39 496	$35 546	$44 093
Diabetes: blood pressure <130/80 mm Hg	$25 317	$19 499	$31 134	$25 667	$24 933	$28 653	$31 989	$23 883	$22 450	$26 071	$24 562	$22 187	$29 406
Diabetes: A1C <7%	$48 759	$37 468	$60 050	$52 590	$45 464	$46 828	$44 897	$47 183	$45 606	$50 298	$47 220	$40 331	$60 796
Diabetes: LDL cholesterol <100 mg/dL	$67 199	$53 518	$80 880	$67 703	$66 602	$71 062	$74 924	$65 547	$63 894	$67 440	$66 957	$57 391	$80 119
High-risk CAD: LDL cholesterol <130 mg/dL	$83 327	$66 585	$100 069	$83 053	$83 613	$87 567	$91 806	$81 481	$79 636	$83 404	$83 250	$72 157	$97 117
Low-risk CAD: LDL cholesterol <160 mg/dL	$272 061	$213 877	$330 245	$279 391	$264 971	$275 202	$278 343	$269 078	$266 096	$275 833	$268 289	$171 106	$550 886
Pre-diabetes: FPG <110 mg/dL	$17 478	$12 860	$22 096	$19 128	$16 054	$15 145	$12 812	$16 082	$14 685	$18 601	$16 355	$13 796	$22 585
Smoking: stop	−$1755	−$2068	−$1442	−$1751	−$1758	$2516	$6787	−$3163	−$4571	−$1091	−$2419	−$1711	−$1529

could receive the prevention activities for which he or she is a candidate, MIs could be reduced >60% (from ≈43 million over 30 years to ≈16 million), strokes could be reduced 30% (from ≈33 million over 30 years to ≈23 million), and everyone's life expectancies could be increased an average of 1.3 years and at a higher quality of life than currently experienced.

Second, even if the full potential of prevention cannot be achieved because of incomplete performance, compliance, and effectiveness, the benefits of aggressive but feasible levels of performance are still large. If performance levels could be uniformly raised to those achieved by the best health care delivery systems (Table 1), 36% of heart attacks and 20% of strokes would be prevented, and life expectancies would be increased an average of 0.7 years.

Third, the 11 prevention activities vary widely in their effectiveness. Viewed from the perspective of the US population as a whole (Table 3), the effects on MIs range from prevention of ≈7.1 million with weight control (BMI <30

Table 7. Annual Cost of Prevention Activities Required to Achieve Various Levels of Cost/QALY

	Cost/QALY					
	$0	$10 000	$20 000	$30 000	$40 000	$50 000
Aspirin to high-risk individuals	$13	$262	$511	$760	$1009	$1258
BMI <30 kg/m^2	$219	$855	$1491	$2127	$2763	$3399
Blood pressure <140/90 mm Hg in nondiabetic individuals	$136	$379	$622	$865	$1108	$1351
CAD: LDL cholesterol <100 mg/dL	−$32	$144	$321	$498	$674	$851
Diabetes: blood pressure <130/80 mm Hg	$416	$1518	$2621	$3724	$4826	$5929
Diabetes: A1C <7%	$157	$361	$565	$770	$974	$1178
Diabetes: LDL cholesterol <100 mg/dL	$29	$268	$507	$746	$985	$1224
High-risk CAD: LDL cholesterol <130 mg/dL	$9	$239	$469	$699	$929	$1159
Low-risk CAD: LDL cholesterol <160 mg/dL	$125	$191	$257	$323	$390	—
Pre-diabetes: FPG <110 mg/dL	$147	$409	$671	$933	$1195	$1457
Smoking: stop	$971	$3896	$6821	$9746	$12 671	$15 596

kg/m^2) to <1 million for cholesterol treatment in low-risk people (LDL cholesterol <160 mg/dL). From the perspectives of individuals who are candidates for particular prevention activities (Table 5), the benefits range from an absolute reduction of MI by 39% (30-year NNT = 3) by control of LDL cholesterol <100 mg/dL in people with established CAD to a decrease in the chance of an MI by an absolute 5% (30-year NNT = 21) by control of LDL cholesterol in people who are at low risk.

Fourth, as they are currently delivered, almost all of the prevention activities are expensive. If applied fully, using current protocols and the reference assumptions about costs (Table 2), they would increase health care costs by ≈$8.5 trillion over 30 years (Table 3), or ≈$283 billion per year, or ≈$1700 per person per year (data not shown). The only cost-saving activity is smoking cessation. Even if $600 is spent annually (versus $350, as shown in Table 2) helping a smoker quit, the savings from preventing downstream CVD events more than offset those costs, yielding a net savings. Aspirin use is relatively inexpensive even if delivered with annual visits; net costs are ≈$50 billion over 30 years, or ≈$90 per candidate per year (Table 3). The other 11 activities increase costs from $0.4 trillion to $1.8 trillion over 30 years (Table 4).

Fifth, the activities vary widely in the value they provide, as measured by cost per QALY (Table 3). Only smoking cessation can be expected to save money over the 30-year follow-up period, and even that does not begin to save money until after 8 years (data not shown). Aspirin for high-risk people has a low cost per QALY (<$3000). Weight control and control of pre-diabetes (fasting plasma glucose <110 mg/dL) have costs per QALY of ≈$18 000. The next five—blood pressure control in diabetic and nondiabetic people and LDL cholesterol control in high-risk people and people with CAD or diabetes—have cost per QALY between $20 000 and the often-cited but arbitrary threshold of $50 000. The lowest value is provided by LDL cholesterol control in low-risk people, ≈$270 000/QALY. The latter has important policy and clinical implications, as it is currently one of the most heavily promoted of all the prevention activities. If the objective is to prevent CVD, then smoking cessation, aspirin, and control of pre-diabetes and weight would be better uses of resources.

Sixth, the "importance" of the prevention activities, in terms of MI and stroke reduction, varies depending on whether the benefits are viewed from the perspective of the population as a whole (Tables 3 and 4) or the individuals who are candidates (Table 5). The former takes into account the number of people who are candidates for an activity, as well as the amount of benefit per candidate. The latter measures only the amount of benefit per candidate. A case in point is LDL cholesterol control in people with established CAD. The benefits of treatment of individuals with CAD who have LDL cholesterol >100 mg/dL are the largest of all the prevention activities (an absolute reduction of MI risk of 40%). However, for the population as a whole, this activity ranks 7th in terms of the number of MIs prevented. Although the per-person benefits are large, only a small proportion (≈1.6%) of the population is a candidate for this activity.

Seventh, for the purposes of reducing the costs of the prevention activities, the most important component is the cost of the interventions themselves: the drugs, weight loss programs, and smoking cessation programs. If ways could be found to reduce the costs of the interventions, overall costs could be reduced and value could be increased to reach more acceptable levels (Table 7).

All of these conclusions are very robust to a wide range of assumptions (Table 6). However, as with any cost-effectiveness analysis or clinical trial, the specific results in the tables should be considered only approximate, for several reasons. First, because risk factors, behaviors, practice protocols, performance levels, and costs vary widely across the country, there is no single set of results that will be accurate in every setting. Second, behaviors, tests, treatments, and other factors will inevitably change in ways that cannot be predicted today. Third, actual practices will deviate from the scenarios we have analyzed. For example, while we analyzed the effect of treating a variable to the goal specified in national guidelines, some people will be treated to lower levels, while others will not reach the specified goals. Fourth, some prevention activities have effects that go beyond the boundaries of our analysis. For example, we did not include nonmedical costs such as lost productivity and absenteeism, nor do our estimates of savings and effectiveness include the effects of the prevention activities on non-CVD and nondiabetes outcomes, such as the effects of smoking on cancer. Fifth, there is some degree of uncertainty when risk factors are modified in either a real or simulated clinical trial. There is further uncertainty when one carries them out for 30 years. However, we have based the effects of modifying risk factors on the data available in the literature on both natural history and from therapeutic trials. We would hope that our ability to have more cost-effective therapies will improve in the future.

Last, we did not consider the costs associated with screening to detect individuals with abnormal values. However, for some of the prevention services studied (eg, those in people with diabetes), monitoring is routine and there is no need for additional testing. For the others, screening adds costs, but since such testing occurs infrequently (ie, every 3–5 years), the associated costs are not likely to change the relative value of prevention services. Moreover, if screening is bundled at a single office visit (eg, lipid profile, blood pressure measurement, weight, and smoking status), the overall impact of screening is likely to be negligible.

To our knowledge, only one other study, conducted by the National Commission on Prevention Priorities (NCCP), has tried to analyze a broad range of prevention activities.[44] In that study, each activity was assigned 1–5 points on each of two measures—clinically preventable burden of disease and cost effectiveness—for a total score ranging from 2 to 10. The study also found that for CVD prevention, smoking cessation and aspirin received high scores. However, our analysis differs in many ways: we report the actual number of people who are candidates for each activity, the effects of each activity one by one and in combination, and the numbers of CVD events, costs, and cost per QALY. Other differences are that our analysis is based on a single integrated model and consistent methodology that includes a representative sample

of the US population, current use of prevention activities, representative costs, the recommended treatment goals for prevention activities, and a comprehensive sensitivity analysis. The NCCP's analysis was based on the results of cost-effectiveness analyses done separately for each of the prevention activities. Each of the analyses was done by different investigators, using different models, different sets of assumptions, and different populations. None of the populations was a representative sample of the US population, and none of the treatments in the analyses precisely matched the recommended prevention activities.

In summary, approximately three-fourths of US adults would benefit from at least one recommended prevention activity to reduce the incidence of CVD. Full deployment of these interventions could potentially prevent approximately two-thirds of MIs and one-third of strokes. However, as they are currently delivered, most of the interventions will substantially increase costs. If our health care system were able to reduce the cost of prevention activities, then the full potential for reducing the burden of CVD could be realized.

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Rose Marie Robertson	American Heart Association	None	None	None	None	None	None	None
Robert Smith	American Cancer Society	None	None	None	None	None	None	None
David Eddy	Archimedes, Inc.	None	None	None	None	None	None	None

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The Impact of Prevention on Reducing the Burden of Cardiovascular Disease

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