Health Benefits and Cost-Effectiveness of Asymptomatic Screening for Hypertension and High Cholesterol and Aspirin Counseling for Primary Prevention

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ABSTRACT

PURPOSE Our aim was to update estimates of the health and economic impact of clinical services recommended for the primary prevention of cardiovascular disease (CVD) for the comparative rankings of the National Commission on Prevention Priorities, and to explore differences in outcomes by sex and race/ethnicity.

METHODS We used a single, integrated, microsimulation model to generate comparable results for 3 services recommended by the US Preventive Services Task Force: aspirin counseling for the primary prevention of CVD and colorectal cancer, screening and treatment for lipid disorders (usually high cholesterol), and screening and treatment for hypertension. Analyses compare lifetime outcomes from the societal perspective for a US-representative birth cohort of 100,000 persons with and without access to each clinical preventive service. Primary outcomes are health impact, measured by the net difference in lifetime quality-adjusted life years (QALYs), and cost-effectiveness, measured in incremental cost per QALY or cost savings per person in 2012 dollars. Results are also presented for population subgroups defined by sex and race/ethnicity.

RESULTS Health impact is highest for hypertension screening and treatment (15,600 QALYs), but is closely followed by cholesterol screening and treatment (14,300 QALYs). Aspirin counseling has a lower health impact (2,200 QALYs) but is found to be cost saving ($31 saved per person). Cost-effectiveness for cholesterol and hypertension screening and treatment is $33,800 per QALY and $48,500 per QALY, respectively. Findings favor hypertension over cholesterol screening and treatment for women, and opportunities to reduce disease burden across all services are greatest for the non-Hispanic black population.

CONCLUSIONS All 3 CVD preventive services continue to rank highly among other recommended preventive services for US adults, but individual priorities can be tailored in practice by taking a patient's demographic characteristics and clinical objectives into account.

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INTRODUCTION

In 1950 the rate of mortality from cardiovascular disease (CVD) in the United States was more than twice what it is today.[1] Some of this reduction is attributable to new technologies and improvements in the treatment of CVD, but as much as one-half is due to prevention efforts.[2] Nevertheless, CVD remains the leading cause of death and among the greatest causes of morbidity in the United States today.[3,4] Each year, more than 1.2 million first-time CVD events are suffered, and persons younger than 75 years will die of a cardiovascular-related cause at approximately twice the rate of leading nations—a statistic that ranks 23rd among major countries.[5] Total direct and indirect costs of CVD are estimated to exceed $300 billion annually, and total direct medical costs are projected to triple by 2030, when more than 40% of the US population is projected to have some form of CVD.[5,6] Indeed, despite prior successes, only a small percentage of the

US population meets criteria for ideal cardiovascular health,[7] cholesterol and blood pressure management remain major sources of preventable burden,[8] and sizable persisting disparities in CVD outcomes based on sex, race/ethnicity, and geography can be explained by disparities in cardiometabolic risk factors.[9,10]

Although the case for sustained and improved CVD prevention efforts would appear to be strong, a core focus of the National Commission on Prevention Priorities has been to evaluate and identify the relative value of primary prevention activities in the context of a wide spectrum of health conditions and diseases.[11] In 2006 the commission ranked using aspirin for the primary prevention of CVD, screening for lipid disorders, and hypertension screening—all 3 recommended with an A or B grade by the US Preventive Services Task Force (USPSTF)[12-14]—in the top one-half of clinical preventive services as measured by population health impact and cost-effectiveness.[15] All 3 recommendations have since been updated by the USPSTF,[16-18] pharmacy costs of treating cholesterol and blood pressure have seen sustained declines,[19,20] the Million Hearts initiative has been introduced,[21] and CVD risk factor trends have continued to gradually evolve.[22,23]

In this study, we use microsimulation modeling to estimate the health impact and cost-effectiveness of these leading CVD clinical preventive services for an updated ranking[24] and provide new data on the relative impact of these services among population subgroups defined by sex and race/ethnicity. Adequate understanding of the relative priority of these services in busy primary care offices requires updated estimates that reflect changes in population disease-risk profiles, costs, and the evidence base supporting the services. In addition, physicians who seek to tailor priorities to the demographics of their clinical practice or to individual patients need to understand the value of these services for specific population groups.

METHODS

Analyses in this study were conducted using the Health-Partners Institute ModelHealth™: Cardiovascular Disease (ModelHealth: CVD) microsimulation model. Brief descriptions of how the preventive services are implemented in the model and the model itself are described below, and comprehensive details of our methods are provided in the Supplemental Appendix, available at http://www.annfammed.org/content/15/1/23/suppl/DC1.

Aspirin Counseling to Prevent Cardiovascular Disease and Cancer

The USPSTF has substantially revised its recommendations regarding aspirin counseling for the primary

prevention of CVD and colorectal cancer.[16,25,26] The Task Force now recommends use of low-dose aspirin among men and women aged 50 to 59 years with 10% or greater 10-year CVD risk (B recommendation). With its updated evidence review, aspirin is found to reduce the risk of nonfatal myocardial infarction and ischemic stroke—no longer differing by sex—and to lower the risk of colorectal cancer incidence after 10 years of use (Table 1). The USPSTF review also reaffirmed aspirin's role in increasing risk for major gastrointestinal bleeding and hemorrhagic stroke.

For our analysis, the proportion of persons for whom aspirin use is consistent with the new USPSTF recommendation was estimated using data from the National Health Interview Survey.[51] The per incident cost of CVD risk assessment and discussion regarding aspirin use is estimated to be $29.23, and the cost of a year's supply of low-dose aspirin is estimated to be $18.23. We assume that a clinical screening test and discussion may occur up to 3 times between ages 50 to 59 years.

Cholesterol Screening

In 2008 the USPSTF updated its 2001 recommendation for lipid disorder screening among adults aged 20 years and older.[13,17] The Task Force found good evidence that drug therapy can significantly lower heart disease risk in persons with abnormal lipid levels.[59] The USPSTF recommends screening men aged 35 years and older for lipid disorders regardless of risk factors (A recommendation) and men aged 20 to 35 years (B recommendation) if they are at increased risk for heart disease. For women, the Task Force recommends screening those aged 45 years and older (A recommendation) and those aged 20 to 45 years (B recommendation), in both cases, when at increased risk for heart disease. Upon detection of lipid disorders, standard treatment and management guidelines should be followed.[17,61]

For our analysis, the proportion of persons treating high cholesterol levels with medications as prescribed was estimated using data from the National Health and Nutrition Examination Survey (NHANES) (Table 1).[52-56] The efficacy of medications for treating lipid disorders was estimated using data from large randomized controlled trials.[33-41] The per incident cost of clinical screening and discussion regarding statin use is estimated to be $55.56, and the annual medication cost is estimated to be $528.00. We assume that a cholesterol screening test may occur up to once every 5 years.

Hypertension Screening

In 2007 the USPSTF published a reaffirmation of its 2003 A recommendation to screen for hypertension among all adults aged 18 years and older.[14,18] The Task

Table 1. Key Model Parameters

Parameter	Value	Sensitivity Range[a]	Source
Aspirin for primary prevention of CVD and colorectal cancer			
Colorectal cancer incidence >10 y, RR	0.60	0.76/0.47	Chubak[27,28]
Cardiovascular disease death, RR	1.00	1.00/0.97	Guirguis-Blake[29,30]
Gastrointestinal bleed, RR	1.58	1.95/1.29	Whitlock[31,32]
Hemorrhagic stroke, RR	1.27	1.68/1.00	Whitlock[31,32]
Ischemic stroke, nonfatal, RR	0.86	0.98/0.76	Guirguis-Blake[29,30]
Myocardial infarction, nonfatal, RR	0.83	0.94/0.74	Guirguis-Blake[29,30]
Cost per screening, $	29.23	± 25%	See text
Treatment cost, annual, $	18.23	± 25%	See text
Cholesterol screening			
High-density lipoprotein, median treatment efficacy, mg/dL	+1.6	Not considered	4S,[33] Downs,[34] Holdaas,[32] Sever,[33] Knopp,[37] MRC/BHF,[38] LIPID,[39] Shepherd[40,41]
Low-density lipoprotein, median treatment efficacy, mg/dL	−49.9	Not considered	4S,[33] Downs,[34] Holdaas,[32] Sever,[33] Knopp,[37] MRC/BHF,[38] LIPID,[39] Shepherd[40,41]
Cost per screening, $	55.56	± 25%	See text
Treatment and management cost, annual, $	528.00	± 25%	See text
Hypertension screening			
Systolic blood pressure, median treatment efficacy, mm Hg	−6.5	Not considered	Liu,[42] Beckett,[43] MRC,[44] MRC,[45] PROGRESS,[46] SHEP,[47] Dahlof,[48] Liu,[49] Staessen[50]
Cost per screening, $	29.23	± 25%	See text
Treatment and management annual cost, $	278.52	± 25%	See text
All services			
Aspirin use rate, primary/ secondary prevention, %	77/86	± 10% points	NHIS[51]
Blood pressure and lipid medication use rates, primary/secondary prevention, %			
Age 18-39 y	62/77	± 10% points	NHANES[52-56]
Age 40-64 y	84/89	± 10% points	NHANES[52-56]
Age >65 y	94/97	± 10% points	NHANES[52-56]
Myocardial infarction cost, 1st y/ongoing, $	37,095/2,490	± 25%	AHRQ/MEPS[57]
Myocardial infarction QALY decrement, 1st y/ongoing	0.3 (3 mo)/0.0	± 0.1 QALY	Maciosek[58]
Screening and counseling acceptance rate, %	90	± 10% points	Assumed
Stroke cost, 1st y/ongoing, $	18,192/5,389	± 25%	AHRQ/MEPS[57]
Stroke QALY decrement, 1st y/ongoing	0.4/0.4	± 0.1 QALY	Maciosek[58]
Treatment effectiveness, %	70	± 10% points	Calibrated assumption

4S = Scandinavian Simvastatin Survival Study; AHRQ = Agency for Healthcare Research and Quality; CVD = cardiovascular disease; MEPS = Medical Expenditure Panel Survey; NCEP = National Cholesterol Education Program; NCHS = National Center for Health Statistics; NHANES = National Health and Nutrition Examination Survey; QALY = quality-adjusted life years; RR = relative risk; SHEP = Systolic Hypertension in the Elderly Program.

[a] The sensivity range indicates the lower and upper bounds (ie, worst case/best case) used in the deterministic sensitivity analysis.

Force found good evidence that treatment of high blood pressure in adults can substantially decrease risk of cardiovascular disease.[61] Upon detection of high blood pressure, standard treatment and management guidelines should be followed.[18,62]

For our analysis, the proportion of persons treating blood pressure with medications as prescribed was estimated using data from NHANES (Table 1).[52-56] The efficacy of medications for treating hypertension was estimated from large randomized controlled trials.[42-50] The per incident cost of a blood pressure screen for hypertension is estimated to be $29.23, and the annual medication cost is estimated to be $278.52. We assume blood pressure screening will occur annually for persons with a previously measured systolic blood pressure of at least 120 mm Hg and biannually for everyone else.

Model Design

ModelHealth: CVD is an annual-cycle microsimulation model designed to estimate the lifetime incidence of CVD events and associated costs in a birth cohort of individuals representative of the US population. The model was designed to ensure consistency for compar-

Table 2. Baseline ModelHealth: CVD Risk and Event Prevalence

Variable	Total, %	Men, %	Women, %	Non-Hispanic White, %	Non-Hispanic Black, %	Hispanic %
Hypertension						
ModelHealth: CVD	29.2	30.0	28.4	26.1	45.0	27.5
NHANES (2007-2010)[72]	29.6	30.5	28.6	28.6	41.3	27.7
Elevated lipid levels (LDL ≥130)						
ModelHealth: CVD	29.8	27.8	31.6	29.6	29.9	30.2
NHANES (2009-2012)[5]	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)[73]	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)[74]	2.6	2.7	2.6	2.4	3.9	2.5

BRFSS = Behavioral Risk Factor Surveillance System; CVD = cardiovascular disease; LDL = low-density lipoprotein; NHANES = National Health and Nutrition Examination Survey.

Note: Risk factor and event prevalence rates are age-adjusted. ModelHealth: CVD data are generated from a birth cohort starting at age 18 years.

ing outcomes across a wide range of clinical preventive services recommended by the USPSTF and the Advisory Committee on Immunization Practices.[24,58] Disease outcomes include incidence of myocardial infarction, stroke, congestive heart failure, angina pectoris, intermittent claudication, diabetes, and CVD-related death, as well as for assessment of aspirin, incidence of colorectal cancer. Cardiovascular disease events are predicted by 1-year risk equations estimated specifically for the model from Framingham Heart Study data.[63,64] Event risk is based on a person's age, sex, body mass index, systolic blood pressure, high- and low-density lipoprotein cholesterol, smoking status, and history of CVD. Baseline colorectal cancer incidence is derived from US cancer surveillance data.[65,66] Disease costs are estimated from the Medical Expenditure Panel Survey[57] and published literature,[67] with first-year and ongoing disease costs accounted for separately.

The annual progression of body mass index is derived from recall data reported in the Behavioral Risk Factor Surveillance System,[68] and the natural history of systolic blood pressure and cholesterol is estimated using Framingham Heart Study data.[63,64] Tobacco initiation and cessation probabilities are derived from the National Health Interview Survey data[69] and published estimates from longitudinal studies.[70,71] Screening and treatment for hypertension and dyslipidemia in the model are consistent with national clinical guidelines,[60,62] and identification and treatment adherence patterns are consistent with the rates observed within NHANES.[52-56] Use of antihypertensive drugs and lipid-acting agents is modeled as an exogenous treatment effect on systolic blood pressure and cholesterol levels, respectively, and alters disease

risk accordingly. Table 2 displays age-adjusted rates of elevated low-density lipoprotein cholesterol level, hypertension, coronary heart disease, and stroke for the baseline model population, stratified by sex and race/ethnicity, and compares them with their respective nationwide indicators.

Analysis Design

Analyses were conducted from the societal perspective, which includes patient time costs, and in accordance with the reference case of the Panel on Cost-effectiveness in Health and Medicine.[75] All analyses compare outcomes for a simulated population—a 100,000-person birth cohort with demographic and underlying health characteristics representative of the US population of persons aged 18 years—with access to a specified clinical preventive service to the same population, all else held equal, without access to this service. The acceptance rate of the clinical preventive service is assumed to be 90%.

Aspirin use affects the relative risk of myocardial infarction, ischemic stroke, hemorrhagic stroke, incidence of colorectal cancer, major gastrointestinal bleeding, and, in sensitivity analysis, CVD-related mortality. Screening and treatment for lipid disorders affects low- and high-density lipoprotein cholesterol levels. Screening and treatment for hypertension affects systolic blood pressure. Key model parameters are summarized in Table 1, and the effectiveness of treatment is based on calibration to population risk profiles and event rates (Table 2) to account for typical adherence patterns.

Primary outcomes are health impact and cost-effectiveness. Health impact is defined as the lifetime net difference, with and without the preventive

service, in quality-adjusted life years (QALYs) for a 100,000-person birth cohort. When a preventive service increases overall costs, cost-effectiveness is measured in costs per QALY gained and is calculated by the lifetime net difference in discounted costs divided by the lifetime net difference in discounted

Table 3. Predicted Lifetime Health and Cost Outcomes of CVD Clinical Preventive Services in US Population Groups

Preventive Service	US Adults	Men			Women		
		Non-Hispanic White	Non-Hispanic Black	Hispanic	Non-Hispanic White	Non-Hispanic Black	Hispanic
Aspirin for primary prevention							
Health impact, QALY	2,200	2,700	6,800	2,300	300	5,000	100
Cost-effectiveness, $	31 saved pp	50 saved pp	166 saved pp	47 saved pp	16,700/QALY	14 saved pp	60,200/QALY
CVD events, No.	−530	−750	−2,030	−840	−20	−530	−20
MI events	−300	−470	−930	−530	−20	−190	−10
Stroke events	−100	−110	−420	−110	Longevity[a]	−240	−10
CVD deaths	−80	−110	−340	−150	−10	−100	−10
CRC cases, No.	−280	−370	−860	−390	−80	−370	−20
Persons treated for primary prevention, No.	15,600	22,000	39,200	27,500	2,300	21,000	2,200
Total costs, $ million	−3.1	−5.0	−16.6	−4.7	0.8	−1.4	1.1
Disease costs	−5.5	−7.9	−21.7	−8.3	−0.3	−4.8	−0.2
Screening costs	1.1	1.1	1.1	1.3	0.8	1.1	1.1
Treatment costs	1.4	1.8	4.0	2.3	0.2	2.3	0.2
Cholesterol screening							
Health impact, QALY	14,300	17,500	25,600	19,700	7,900	14,200	9,100
Cost-effectiveness, $/QALY	33,800	29,400	22,900	25,600	56,500	42,100	48,900
CVD events, No.	−3,960	−5,090	−6,630	−5,320	−2,150	−3,520	−2,940
MI events	−1,500	−2,150	−2,860	−2,070	−700	−960	−930
Stroke events	−40	−150	Longevity[a]	−40	Longevity[a]	−130	−20
CVD deaths	−1,010	−1,120	−1,450	−1,220	−820	−1,120	−630
Persons treated for primary prevention, No.	40,100	43,300	51,400	45,500	32,500	43,100	36,000
Total costs, $ million	80.1	89.0	106.4	90.1	61.3	90.9	65.1
Disease costs	−36.3	−51.5	−76.4	−58.8	−12.1	−22.6	−21.9
Screening costs	16.1	17.7	18.6	18.5	13.1	18.2	14.4
Treatment and management costs	100.3	122.8	164.3	130.3	60.2	95.4	72.5
Hypertension screening							
Health impact, QALY	15,600	11,800	17,000	14,900	16,500	24,700	16,300
Cost-effectiveness, $/QALY	48,500	52,200	60,600	40,800	48,300	42,100	49,500
CVD events, No.	−4,000	−3,460	−3,740	−4,060	−3,920	−5,930	−4,610
MI events	−750	−880	−970	−860	−600	−630	−690
Stroke events	−1,020	−680	−860	−720	−1,100	−2,250	−1,180
CVD deaths	−1,010	−780	−1,080	−1,040	−1,070	−1,480	−1,080
Persons treated for primary prevention, No.	53,400	46,200	58,900	47,900	56,700	64,700	59,000
Total costs, $ million	122.9	105.7	184.6	102.7	119.7	176.4	121.6
Disease costs	−34.8	−33.6	−37.5	−31.6	−30.7	−58.2	−38.0
Screening costs	33.8	34.2	27.4	34.4	35.4	28.8	34.9
Treatment and management costs	124.0	105.1	194.7	99.9	115.0	205.9	124.8

CRC = colorectal cancer; CVD = cardiovascular disease; MI = myocardial infarction; pp = per person; QALY = quality-adjusted life year.

Note: All outcomes are standardized for comparison purposes to reflect the lifetime of a 100,000 person US-representative birth cohort within each respective group starting at age 18 years. Cost-effectiveness is expressed in terms of incremental costs per QALY, unless a preventive service is cost-saving overall, in which case, it is expressed in terms of costs saved per person. All costs are expressed in 2012 US dollars.

[a] Population rates in the outcome are projected to stay the same or increase slightly due to increases in life expectancy attributable to the clinical preventive service.

QALYs. When a preventive service is cost saving (ie, the lifetime net difference in costs is negative), cost-effectiveness is measured in costs saved per person. All costs are denominated in 2012 US dollars, and the discount rate for calculating cost-effectiveness is 3%. Deterministic (one-way) sensitivity analyses of key parameters (Table 1) were conducted by replicating simulations with all other parameters, probabilities, and population characteristics held equal.

This study was granted an exemption by the HealthPartners Institutional Review Board.

RESULTS

Results from our base case analysis are summarized in Table 3. We estimate that aspirin counseling will save 2,200 QALYs, cholesterol screening and treatment will save 14,300 QALYs, and hypertension screening and treatment will save 15,600 QALYs over the lifetime of a 100,000 person birth cohort in the United States. The health impact of the aspirin, cholesterol, and hypertension services when scaled to a typical US birth cohort size of 4,000,000 persons—also referred to as the "clinically preventable burden"[76]—would be approximately 88,000, 572,000, and 624,000 QALYs, respectively. We find that aspirin counseling is cost saving (–$31 per person), cholesterol screening costs $33,800 per QALY saved, and hypertension screening costs $48,500 per QALY saved.

The aspirin counseling service reaches the fewest people (15,600 thousand persons in a 100,000 person birth cohort, compared with 40,100 and 53,400 for cholesterol and hypertension screening, respectively) and thereby has a lower overall impact on preventing disease. Cholesterol and hypertension screening are very similar in prevention of overall CVD events (about 4,000 each) and mortality (about 1,000 each), but we find that hypertension screening prevents far more lifetime stroke events (1,020 vs 40) for this population, contributing to the difference in health impact.

Costs of screening and treatment for the aspirin service are relatively small in comparison to averted disease, resulting in a net cost savings of $3.1 million over the lifetime of the birth cohort. For the cholesterol and hypertension services, cost savings from averted disease are substantial—at about $35 million each—and exceed the costs of screening, but we estimate the ongoing costs of treating and managing the conditions surpass $100 million in each case.

Table 3 also shows that population subgroup outcomes can in many cases diverge in meaningful ways from the population average. For example, aspirin counseling is not expected to be cost saving for white and Hispanic women, primarily because of the small share (less than 2.5%) of these women expected to meet USPSTF criteria for routine aspirin use. More-

Table 4. Relative Value of Clinical Preventive Services for CVD, by Outcome, for US Population Group

| Outcome | US Adults | Men | | |
		Non-Hispanic White	Non-Hispanic Black	Hispanic
Largest health impact (QALY)	Hypertension[a] (15,600) Cholesterol[b] (14,300) Aspirin[c] (2,200)	Cholesterol (17,500) Hypertension (11,800) Aspirin (2,700)	Cholesterol (25,600) Hypertension (17,000) Aspirin (6,800)	Cholesterol (19,700) Hypertension (14,900) Aspirin (2,300)
Highest cost-effectiveness ($ saved pp, or $ per QALY)	Aspirin (31 pp) Cholesterol (33,800/QALY) Hypertension (48,500/QALY)	Aspirin (50 pp) Cholesterol (29,400/QALY) Hypertension (52,200/QALY)	Aspirin (166 pp) Cholesterol (22,900/QALY) Hypertension (60,600/QALY)	Aspirin (47 pp) Cholesterol (25,600/QALY) Hypertension (40,800/QALY)
Most prevented myocardial infarctions (No.)	Cholesterol (1,500) Hypertension (750) Aspirin (300)	Cholesterol (2,150) Hypertension (880) Aspirin (470)	Cholesterol (2,860) Hypertension (970) Aspirin (930)	Cholesterol (2,070) Hypertension (860) Aspirin (530)
Most prevented strokes (No.)	Hypertension (1,020) Aspirin (100) Cholesterol (40)	Hypertension (680) Cholesterol (150) Aspirin (110)	Hypertension (860) Aspirin (420) Cholesterol (longevity[d])	Hypertension (720) Aspirin (110) Cholesterol (40)

CVD = cardiovascular disease; pp = per person; QALY = quality-adjusted life year.

Note: Preventive services are aspirin counseling, hypertension screening, and cholesterol screening. All outcomes are for the lifetime of a 100,000-person US-representative birth cohort within each respective group starting at age 18 years. Cost-effectiveness is expressed in terms of incremental costs per QALY, unless a preventive service is cost saving overall, in which case, it is expressed in terms of costs saved per person. All costs expressed in 2012 US dollars.

[a] Hypertension screening and management in adults.

[b] Lipid disorder screening and management in adults.

[c] Aspirin for the primary prevention of cardiovascular disease and colorectal cancer.

[d] Population rates in the outcome are projected to stay the same or increase slightly because of increases in life expectancy attributable to the clinical preventive service.

over, because of differences in CVD risk profiles at ages 50 to 59 years, approximately one-tenth of non-Hispanic white and Hispanic women and one-half of non-Hispanic black women meet recommended guidelines for initiating use of aspirin for primary prevention compared with their male counterparts. Differences in risk factor and disease prevalence (Table 2) also help to explain why non-Hispanic black men and women are generally expected to see the largest benefits across all 3 services, why men are shown to benefit more from cholesterol screening (which has a primary benefit in preventing heart disease), and why women overall are expected to benefit slightly more from hypertension screening (which also has substantial benefits in preventing stroke, for which longer life expectancy contributes to higher lifetime incidence in women[77,78]).

These trends are made even clearer in Table 4, which translates the results in Table 3 into a relative value ordering for the overall population and for each sex and race/ethnicity subgroup based on health impact or cost-effectiveness. In addition, Table 4 includes two clinical outcome objectives most likely to resonate with patient preferences, the most prevented myocardial infarctions or strokes.[79] Top services for these outcomes are clear: cholesterol screening has the most potential to prevent myocardial infarctions and hypertension screening has the most potential to prevent strokes—for all groups.

Results of Sensitivity Analysis

Findings can vary substantially with alternative assumptions on key model parameters (Table 5). Results for the aspirin service are most sensitive overall, because of the uncertainty in the scale (eg, how much long-term use increases the relative risk for hemorrhagic stroke) and scope (eg, whether aspirin for primary prevention can reduce CVD mortality) of aspirin's effects. Health impact estimates for aspirin counseling range from approximately 200 to 4,000 QALYs, and cost-effectiveness in the worst case is about $92,000/QALY saved. Also noteworthy is the sensitivity in cost-effectiveness for cholesterol and hypertension screening associated with the cost of medications. If all patients were able to take advantage of the lowest cost cholesterol and blood pressure drugs, cost-effectiveness could improve to nearly $5,000/QALY for cholesterol screening and $26,000/QALY for hypertension screening.

DISCUSSION

The case for prevention can sometimes be a challenging one; benefits often accrue far in the future, and costs tend to be highest upfront. Nevertheless, our analysis indicates that clinical services for the primary prevention of CVD can avert substantial disease burden and potentially save costs. In our accompanying comparison across all clinical preventive services, estimates of health impact for a 100,000-person birth cohort range from 100 to 83,200 (median = 2,900) QALYs, and estimates of cost-effectiveness range from cost saving to $782,600 (median = $36,800) per QALY saved.[24] In this study, we find that initiation of aspirin use among adults at elevated CVD risk and aged 50 to 59 years has a moderate health impact (2,200 QALYs) but is also among the few services expected to save costs overall. Screenings for lipid disorders and hypertension are among the top services for health impact (at 14,300 and 15,600 QALYs, respectively) and rank in the middle of the pack for cost-effectiveness (at $33,800 and $48,500 per QALY, respectively—both of which also compare favorably with the most commonly cited cost-effectiveness

| | Women | |
Non-Hispanic White	Non-Hispanic Black	Hispanic
Hypertension (16,500)	Hypertension (24,700)	Hypertension (16,300)
Cholesterol (7,900)	Cholesterol (14,200)	Cholesterol (9,100)
Aspirin (300)	Aspirin (5,000)	Aspirin (100)
Aspirin (16,700/QALY)	Aspirin (14 pp)	Cholesterol (48,900/QALY)
Hypertension (48,300/QALY)	Cholesterol (42,100/QALY)	Hypertension (49,500/QALY)
Cholesterol (56,500/QALY)	Hypertension (42,100/QALY)	Aspirin (60,200/QALY)
Cholesterol (700)	Cholesterol (960)	Cholesterol (930)
Hypertension (600)	Hypertension (630)	Hypertension (690)
Aspirin (20)	Aspirin (190)	Aspirin (10)
Hypertension (860)	Hypertension (2,250)	Hypertension (1,180)
Aspirin (longevity[d])	Aspirin (240)	Cholesterol (20)
Cholesterol (longevity[d])	Cholesterol (130)	Aspirin (10)

Table 5. Sensitivity to Key Parameter Changes

Parameter	Health Impact QALY	Cost-Effectiveness $	Cardiovascular Disease Event, No.	Total Cost $ Million
Aspirin for primary prevention				
Base case	2,200	31 saved pp	−530	−3.1
Treatment efficacy				
Low	200	91,700/QALY	−50	2.5
High	4,000	68 saved pp	−910	−6.8
Treatment effectiveness				
−10% (60% effectiveness)	1,800	18 saved pp	−370	−1.8
+10% (80% effectiveness)	2,600	45 saved pp	−720	−4.5
Disease costs				
−25%	2,200	17 saved pp	−530	−1.7
+25%	2,200	45 saved pp	−530	−4.5
Screening and medication costs				
Screening (clinic) costs, −25%	2,200	32 saved pp	−530	−3.2
Screening (clinic) costs, +25%	2,200	30 saved pp	−530	−3.0
Bulk aspirin (−35%), $11.93/y	2,200	36 saved pp	−530	−3.6
Name brand aspirin (+32%), $24.04/y	2,200	27 saved pp	−530	−2.7
No patient time cost	2,200	37 saved pp	−530	−3.7
QALY decrements				
−0.10 QALY	2,100	31 saved pp	−530	−3.1
+0.10 QALY	2,300	31 saved pp	−530	−3.1
Cholesterol screening				
Base case	14,300	33,800/QALY	−3,960	80.1
Treatment effectiveness				
−10% (60% effectiveness)	12,400	35,100/QALY	−3,510	71.8
+10% (80% effectiveness)	18,300	27,200/QALY	−5,140	81.9
Disease costs				
−25%	14,300	37,600/QALY	−3,960	89.2
+25%	14,300	30,000/QALY	−3,960	71.0
Screening, management, and medication costs				
Screening and management (clinic) costs, −25%	14,300	30,800/QALY	−3,960	73.0
Screening and management (clinic) costs, +25%	14,300	36,800/QALY	−3,960	87.2
Discount generic medications (−91%), $36.70/y	14,300	5,300/QALY	−3,960	12.6
Name brand medications (+804%), $3,818.73/y	14,300	284,800/QALY	−3,960	675.1
No patient time cost	14,300	28,000/QALY	−3,960	66.4
QALY decrements				
−0.10 QALY	13,400	37,400/QALY	−3,960	80.1
+0.10 QALY	15,000	31,400/QALY	−3,960	80.1
Hypertension screening				
Base case	15,600	48,500/QALY	−4,000	122.9
Treatment effectiveness				
−10% (60% effectiveness)	11,800	60,300/QALY	−3,060	115.7
+10% (80% effectiveness)	19,800	39,700/QALY	−5,100	127.1
Disease costs				
−25%	15,600	52,000/QALY	−4,000	131.6
+25%	15,600	45,100/QALY	−4,000	114.2
Screening, management, and medication costs				
Screening and management (clinic) costs, −25%	15,600	44,400/QALY	−4,000	112.5
Screening and management (clinic) costs, +25%	15,600	52,500/QALY	−4,000	133.1
Discount generic medications (−82%), $36.70/y	15,600	26,200/QALY	−4,000	66.5
Name brand medications (+1,973%), $4,216.16/y	15,600	584,600/QALY	−4,000	1,481.0
No patient time cost	15,600	34,200/QALY	−4,000	86.6
QALY decrements				
−0.10 QALY	14,900	52,300/QALY	−4,000	122.9
+0.10 QALY	15,700	46,800/QALY	−4,000	122.9

CE = cost-effectiveness; CVD = cardiovascular disease; pp = per person; QALY = quality-adjusted life years.

Note: Cost-effectiveness is expressed in terms of incremental costs per QALY, unless a preventive service is cost-saving overall, in which case, it is expressed in terms of costs saved per person. Sources for the sensitivity ranges for medication costs are described in the Supplemental Appendix (Supplemental Appendix http://www.annfa-mmed.org/content/15/1/23/suppl/DC1). All costs are expressed in 2012 US dollars.

thresholds of $50,000 and $100,000 per QALY[80]). As a result, all 3 CVD services rank highly among other clinical preventive services, scoring at least 7 of 10 possible points on combined health impact and cost-effectiveness.[24]

This comparative analysis is the first of its kind to use an integrated, validated microsimulation model to estimate the lifetime impacts from USPSTF-recommended CVD prevention activities for a US-representative birth cohort, and this novel approach lends multiple strengths. The first strength is that microsimulation allows for the assessment of clinical services targeted to persons with specific characteristics, such as by age, sex, and underlying cardiovascular risk factors. Age, sex, and race/ethnicity are correlated with CVD risk profiles that may indicate both eligibility for a preventive service and the likelihood of benefit from prevention activities. This relationship is most notably important for aspirin, where relatively few women aged 50 to 59 years (a ratio of 1:5 compared with men) meet the 10% 10-year CVD risk threshold identified by the USPSTF, and across all services for the non-Hispanic black population, which tends to have greater CVD risk at younger ages compared with other population groups.

As such, an important second benefit of our analysis is the stratification of results by population subgroups, and our analysis shows that a population-wide assessment of prevention activities can mask notable differences in the health impact and cost-effectiveness by sex and race/ethnicity. For example, contrary to our findings for the overall population (and for men), women are generally expected to benefit more from screening for hypertension than for dyslipidemia. Also notable is that cost savings of aspirin are not found for white and Hispanic women and that non-Hispanic black Americans have the greatest overall opportunities for reducing disease burden. These stratified results support tailoring prevention priorities to individual patient preferences and needs and highlight opportunities to reduce health disparities.

A third notable strength of our approach is that the microsimulation model used in our analysis accounts for the dynamics of competing risks among nonfatal and fatal CVD and other causes of death in quantifying net benefits. The model also accounts for background use of other primary prevention activities and secondary prevention subsequent to a CVD event. When the first nonfatal CVD event of a simulated person is prevented or delayed as a result of a clinical preventive service, their use of aspirin, statins, and/ or antihypertensive medications for primary or secondary prevention also may be prevented or delayed. The prevention or delay of an initial nonfatal event

also changes the risk of subsequent nonfatal and fatal events. This approach provides a more realistic estimate of the marginal value of a clinical service for primary prevention relative to secondary prevention.

Our findings do not depart dramatically or unexpectedly from previous National Commission on Prevention Priorities rankings. Previously, cholesterol and hypertension screening scored highly for health impact and scored in the middle to lower half of services for cost-effectiveness, as they still do.[15,81] Aspirin counseling was similarly found to be cost-saving, but it also previously scored very highly for health impact.[15] The lower potential net health benefit from aspirin counseling in our analysis is largely a result of the substantially narrowed target population for the service in the current recommendation and the changes to the underlying evidence of aspirin's benefits and harms, including lower expected effectiveness in preventing nonfatal myocardial infarction and stroke—which no longer differ by sex—and accounting for fatalities from aspirin-induced bleeding.[27,32,82,83]

This study contributes to a broader evidence base that uses modeling to assess the incremental and comparative effectiveness of clinical services for the primary prevention of CVD. Direct comparisons are often difficult because of differing research questions and methods. For example, an analysis by Kahn and colleagues[84] using the Archimedes model shares many similarities with ours—both use a single integrated microsimulation to evaluate individual CVD prevention activities targeted to and treating person-level characteristics for the US population with concurrent use of other prevention activities at contemporary levels—but results are difficult to compare because their evaluation was based on a cross-section of the US population over 30 years, estimated the marginal benefit of ideal prevention to current care, and did not include population screening costs. Similarly, other studies differ from ours in some of the following ways: they evaluate an increase in utilization or adherence to clinical preventive services from contemporary levels,[85-94] the modeling unit is higher than person level (eg, population cohort or system dynamics modeling),[85-88,90-107] the modeled population is cross-sectional rather than a birth cohort,[*] the modeled population is not US based,[†] the time horizon is less than lifetime,[‡] results are not stratified by sex or race/ethnicity,[§] and/or the evaluation focuses on the value of a single or combined composite CVD preventive service.[**] Nevertheless,

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* References 85-91, 93, 94, 101, 104, 106, 108.
† References 91-94, 98, 101-106, 108, 109.
‡ References 85-90, 92-94 ,101, 104, 108.
§ References 85-90, 95, 100, 101, 104, 106, 108.
** References 87-89, 91, 92, 95-103, 105-109.

common threads across these evaluations include the sizable disease prevention potential for screening for and treating lipid disorders and hypertension and good cost-effectiveness for aspirin chemoprophylaxis.

The microsimulation model design and the results of these analyses are limited by the quality of data and evidence used to inform them. Our sensitivity analysis results indicate that health impact estimates are especially sensitive to the fidelity and adherence to treatment plans for all services. Uncertainty in the efficacy of aspirin with respect to benefits and harms also limits the precision of our results. For patients treating lipid disorders or hypertension, the cost-effectiveness proposition is highly dependent on the cost of medications. The marginal benefit of a clinical preventive service is also dependent on baseline risk factors and disease rates, but ModelHealth: CVD is shown to validate well with US data (Table 2).

Clinical prevention and practice recommendations, treatments, and effectiveness evidence are continually in flux. Since the conduct of these analyses, the USPSTF updated its recommendation for blood pressure screening.[110] In its update, the Task Force recommends the use of ambulatory or home blood pressure monitoring before initiating treatment—a change that some evidence suggests could lower the overall cost of the service based on improved hypertension diagnosis.[111,112] Practice guidelines for managing high cholesterol levels and hypertension have also recently been revised,[113,114] although evidence is not yet clear how and whether clinical practice patterns have shifted as a result. Proprotein convertase subtilisin–kexin type 9 (PCSK9) inhibitors are emerging as a new drug class for the treatment of lipid disorders,[115,116] and several ongoing aspirin trials may reveal new benefits or harms.[30,32, 117-120] The evolving environment will continue to affect the impact and value of clinical preventive services for CVD.

Policy makers are often interested in prioritizing efforts and investments to increase prevention utilization from contemporary rates. In cases where use is relatively high, such as with screening for hypertension and lipid disorders,[121] incremental gains may be modest. Still, almost one-half of those with a diagnosis of hypertension do not meet recommended blood pressure goals,[122] and our sensitivity analysis, along with the findings of others,[84] indicates that major reductions in disease and cost burdens can be realized with improvements in treatment effectiveness. Our findings also highlight opportunities for closing gaps among populations for which persistent care access and quality disparities have hindered uptake of effective preventive services[123-127] and advance the case toward a personalized approach to quantitative prior-

ity setting.[128] Overall, our findings affirm that aspirin counseling for primary prevention and asymptomatic screening and treatment of hypertension and lipid disorders should remain among the top prevention priorities for adults in primary care.

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