ORIGINAL RESEARCH

Do Clinicians Recommend Aspirin to Patients for Primary Prevention of Cardiovascular Disease?

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BACKGROUND: The United States Preventive Services Task Force (USPSTF) released updated guidelines in 2009 recommending aspirin to prevent myocardial infarction among at-risk men and stroke among at-risk women.
OBJECTIVE: Our aim was to examine clinician aspirin recommendation among eligible persons based on cardiovascular risk scores and USPSTF cutoffs.
DESIGN: We used across-sectional analysis of a current nationally representative sample.
PARTICIPANTS: Participants were aged 40 years and older, and in the National Health and Nutrition Examination Survey (NHANES) (2011–2012).
MAIN MEASURES: We determined aspirin eligibility for cardiovascular disease (CVD) prevention for each participant based on reported and assessed cardiovascular risk factors. We assessed men's risk using a published coronary heart disease risk calculator based on Framingham equations, and used a similar calculator for stroke to assess risk for women. We applied the USPSTF risk cutoffs for sex and age that account for offsetting risk for gastrointestinal hemorrhage. We assessed clinician recommendation for aspirin based on participant report.
RESULTS: Among men 45–79 years and women 55–79 years, 87 % of men and 16 % of women were potentially eligible for primary CVD aspirin prevention. Clinician recommendation rates for aspirin among those eligible were low, 34 % for men and 42 % for women. Rates were highest among diabetics (63 %), those 65 to 79 years (52 %) or those in poor health (44 %). In contrast, aspirin recommendation rates were 76 % for CVD secondary prevention. After accounting for patient factors, particularly age, eligibility for aspirin prevention was not significantly associated with receiving a clinician's recommendation for aspirin (AOR 0.99 %; CI 0.7–1.4).
CONCLUSIONS: Despite an "A recommendation" from the USPSTF for aspirin for primary prevention of CVD, the majority of men and women potentially eligible for aspirin did not recall a clinical recommendation from their clinician.

KEY WORDS: aspirin; primary CVD prevention; USPSTF guidelines.
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The United States Preventive Services Task Force (USPSTF) released updated guidelines in 2009 regarding aspirin prophylaxis to prevent myocardial infarction among at-risk men and stroke among at-risk women.[1] This followed a 2002 USPSTF recommendation regarding myocardial infarction prevention in adults.[2] However, determination of aspirin eligibility for primary prevention involves weighing 10-year cardiovascular disease (CVD) risk calculations against gastrointestinal bleeding risks. The USPSTF suggested separate risk calculations for coronary heart disease (CHD) (men) and stroke (women) followed by age-based and sex-based risk cutoffs to balance the reduction in cardiovascular risk and the increased risk from gastrointestinal hemorrhage.[1]

Previous studies have shown that aspirin was frequently recommended among patients with known cardiovascular disease (secondary prevention),[3] but underused among those with CVD risk factors in the absence of overt CVD.[4–9]. The delay in implementation of USPSTF recommendations may reflect lack of clinician awareness of guidelines,[4] uncertainty regarding net benefits,[10] limited time,[11] and competing clinical priorities.[9]

Previous studies have not assessed the extent to which physicians and other clinicians recommend aspirin based on the updated USPSTF guidelines that incorporate CVD risk calculations and age-based risk cutoffs. To assess guideline implementation, we examined clinician recommendations for aspirin among patients eligible for primary prevention based on risk calculations and age cutoffs. Based on previous findings,[4–9] we hypothesized that physicians and other clinicians would frequently not recommend aspirin to persons potentially eligible for primary prevention. We examined this question utilizing a

current nationally representative U.S. sample. We also evaluated the impact of aspirin recommendation on patient use of aspirin.

MATERIALS AND METHODS

Sample

We examined data from the National Health and Nutrition Examination Survey (NHANES) 2011–2012. NHANES uses a stratified multi-stage probability sample of the civilian non-institutionalized population of the United States to provide national estimates of the health of the U.S. population. Since 1999, the survey has been conducted on a continuous basis, with data released in 2-year cycles. Data collection methods include an interviewer-administered questionnaire using Computer-Assisted Personal Interview technology and physical exams performed in Mobile Examination Centers. African Americans, Hispanics, those below the 130 % federal poverty level or those aged 80 years and older were oversampled to improve the precision of estimates for these groups. Our sample included 3,439 individuals aged 40 years and older who participated in the NHANES 2011–2012 standardized physical exam and who completed relevant items on preventive aspirin use. Because our focus is on use of aspirin for primary CVD prevention, we restricted our primary analyses to those without CVD (n=2,969). In secondary analyses, we examined recommendations among those with known CVD (n=470), i.e., history of myocardial infarction, angina or stroke.

Aspirin Recommendation

Aspirin recommendation was based on participant report from the preventive aspirin use component of the in-person home interview. It was based on response to the question, "Doctors and other health care providers sometimes recommend that you take a low-dose aspirin each day to prevent heart attack, strokes, or cancer. Have you ever been told to do this?" For those who refused or answered, "Don't know" (n=3), responses were classified as missing.

CVD Risk Factors

We assessed CVD risk factors necessary to estimate 10-year risk for myocardial infarction in men and 10-year risk for stroke in women without known cardiovascular disease. We categorized age at screening (40–45, 45–55, 55–65, 65–79, and ≥ 80 years), in order to achieve cohorts containing roughly equal numbers of patients. We used participant report to assess current smoking (yes/no), diabetes ("Have you ever been told by a doctor or health professional that you had diabetes or sugar diabetes?"), and current use of anti-hypertensive medications. We used examination data to assess systolic blood pressure (mm Hg) and body mass index (< 25, 25–30, > 30 kg/m^2), and laboratory data to assess HDL and total cholesterol.

Determination of Aspirin Eligibility

We assessed men's risk using a published CHD risk calculator based on Framingham equations.[12] We used a similar calculator for stroke based on Framingham equations to assess risk for women.[13] Links to the calculators and risk factors are shown in Table 1. We determined aspirin eligibility for primary prevention for each participant using the USPSTF suggested risk cutoffs for sex and age.[1] Specifically, we considered male participants to be eligible for primary aspirin prevention based on the following risk categories: 4 %≥ages 45–59; 9 %≥ages 60–69 %; 12 %≥ages 70–79 years. We considered female participants to be eligible for primary aspirin prevention based on the following risk categories: 3 %≥ages 55–59; 8 %≥ages 60–69 %; 11 %≥ages 70–79 years. In sensitivity analyses, we imputed 20 % higher pre-treatment total cholesterol levels (based on current levels) [14] among participants who reporting taking a cholesterol lowering agent. We also examined 1 % lower cutoffs, e.g., from 4 to 3 %. In separate analyses, we examined aspirin use for secondary prevention.

Patient Morbidity

We assessed health conditions that might influence aspirin prescribing. These included self-reported liver conditions, elevated liver enzymes (ALT/AST), kidney disease (eGFR< 60 ml/min), hypertension, and laboratory values indicating platelets < 50,000 cells/uL and anemia (hemoglobin < 12 g/dL in men or<10.5 g/dL women). We also adjusted for morbidity using the Intermountain Index. It is associated with greater morbidity and earlier death.[15,16] We assessed self-reported general health status (excellent, very good, good, fair, poor) as well.

Table 1. Factors Used to Estimate Risk for Men and Women

Myocardial infarction for men	Stroke risk for women
Age	Age
Diabetes	Diabetes
Blood pressure	Blood pressure
Smoking status	Smoking status
Total cholesterol	Cardiovascular disease
HDL cholesterol	*Left ventricular hypertrophy
	*Atrial fibrillation

Not available in NHANES 2011–2012 at time of analyses
****Myocardial risk equation available[12]***
Stroke risk calculator at http://www.westernstroke.org/index.php?header_name=stroke_tools.gif&main=stroke_tools.php
The table for age and sex-specific cutoffs for aspirin is available at http://www.uspreventiveservicestaskforce.org/uspstf09/aspirincvd/aspcvdrsf3.htm

Table 2. Characteristics of Persons Without Known CVD by Aspirin Recommendation

Independent variable	Clinician recommended aspirin		*p* value
	No	Yes	
	% (*n*= 2,054)	% (*n*=915)	
Aspirin eligibility			0.0116
No	73	27	
Yes	65	35	
Age at screening			< 0.0001
40–44	93	7	
45–54	80	20	
55–64	62	38	
65–79	54	46	
≥80	43	57	
Sex			NS
Male	69	31	
Female	71	29	
White, non-Hispanic race			0.0185
No	74	26	
Yes	69	31	
US Citizen			< 0.0001
No	84	16	
Yes	69	31	
Language of interview			0.0073
English	70	30	
Spanish	79	21	
Education			NS
< High school education	70	30	
High school degree	67	33	
> High school education	71	29	
Health Insurance status			< 0.0001
No	85	15	
Yes	68	32	
General health			NS
Excellent	75	25	
Very Good	72	28	
Good	71	29	
Fair	63	37	
Poor	61	39	
Routine place to go for healthcare			< 0.0001
No	88	12	
Yes	68	32	
Primary source for healthcare			0.0465
Clinic or health center	70	30	
Doctor's office or HMO	68	32	
Hospital emergency room	84	16	
Hospital outpatient department	68	32	
Some other place	65	35	
Received healthcare over past year			< 0.0001
No	88	12	
Yes	68	32	
Diabetes			< 0.0001
No	74	26	
Yes	42	58	
eGFR*			< 0.0001
No	72	28	
Yes	53	47	
Platelet count<50,000/mcL			NS
No	70	30	
Yes	100	0	
Anemia (g/dL)			NS
12+ (men) or 10.5+ (women)	70	30	
< 12 (men) or<10.5 (women)	68	32	
Albumin (g/dL)			NS
3+	70	30	
< 3	53	47	
Liver condition			0.0333
No	71	29	
Yes	59	41	
Elevated transaminase**			NS
No	70	30	
Yes	76	24	
Intermountain 5-year mortality risk[45]	mean (standard error)		< 0.0001
	8.2 (0.12)	9.7 (0.22)	

(continued on next page)

Table 2. (continued)

Row percentages reported weighted to the non-institutionalized U.S. population NS=not significant ($p \geq 0.1$)
****eGFR = estimated glomerular filtration rate***
† alanine aminotransferase or aspartate aminotransferase>2 standard deviations above mean

Health Care Access

We assessed a range of factors related to health care access and care. These included race/ethnicity (Non-Hispanic White, All others); citizenship status (US, other); language of interview (English, Spanish); and education (< high school, high school diploma (or equivalent), > high school); health insurance status (yes, no); routine place to go for health care (yes, no); number of times received healthcare in the past year (none, one or more); and hypertension (yes, no). Routine place for healthcare was the self-reported response to the question, "Is there a place that you usually go when you are sick or you need advice about your health?" Having seen a doctor/health care professional in the past year was the self-reported response to the question, "During the past 12 months, how many times have you seen a doctor or other health care professional about your health at a doctor's office, a clinic, hospital emergency room, at home or some other place? Do not include times you were hospitalized overnight." This information was part of the hospital utilization and access-to-care component of the in-person interview.

Statistical Methods

We assessed the number and percent of participants eligible for aspirin prophylaxis and the number and percentage of those reporting an aspirin recommendation from their physician. Chi-square tests were used to determine associations with demographic variables. We used a backwards selection method with logistic regression to assess the independent association of aspirin eligibility with a recommendation after controlling for age, sex, race, ethnicity and factors related to morbidity and health care access. Age, sex, and aspirin eligibility were forced into the model. We incorporated stratum, primary sampling units, and appropriate examination sampling weights to produce unbiased estimates of the non-institutionalized U.S. population [17]. All statistical analyses were conducted using SAS-callable SUDAAN Version 11.0.1 (RTI, Research Triangle Park, NC) and SAS Version 9.3 on the Windows 7 platform (SAS Institute, Cary, NC). A p value of 0.05 or less was considered to be statistically significant. This study was exempted by the University of Rochester Research Subjects Review Board.

Table 3. Persons Eligible for Primary Prevention* by Characteristic and Aspirin Recommendation

	Clinician recommended aspirin		
Independent variable	No % (*n*=713)	Yes % (*n*=409)	*p* value
Age at screening			0.0026
45–54	74	26	
55–64	67	33	
65–79	48	52	
Sex			NS
Male	66	34	
Female	58	42	
Race			NS
Non-White	67	33	
White	64	36	
Citizenship status			0.0032
No	81	19	
Yes	64	36	
Language of interview			0.0839
English	65	35	
Spanish	73	27	
Education			NS
< High school education	62	38	
High school degree	64	36	
> High school education	67	33	
Health Insurance Status			0.0001
No	84	16	
Yes	61	39	
General health condition			NS
Excellent	67	33	
Very good	69	31	
Good	65	35	
Fair	59	41	
Poor	56	44	
Routine place to go for healthcare			0.0001
No	84	16	
Yes	62	38	
Primary source for healthcare			NS
Clinic or health center	60	40	
Doctor's office or HMO	62	38	
Hospital emergency room	79	21	
Hospital outpatient department	66	34	
Some other place	59	41	
Received healthcare in past year			< 0.0001
No	89	11	
Yes	60	40	
Diabetes			< 0.0001
No	70	30	
Yes	37	63	

Row percentages reported weighted to the non-institutionalized U.S. population

****Aspirin eligibility determined based on the 2009 USPTF recommendations for primary prevention of CVD NS = not significant (p ≥ 0.1)***

RESULTS

The characteristics of the sample are shown in Table 2. Among men 45–79 years and women 55–79 years, 87 % and 16 %, respectively were potentially eligible for primary CVD aspirin prevention. Clinician recommendation rates for aspirin among those eligible (Table 3) were low—34 % for men and 42 % for women. Rates of recommendation were highest among diabetics (63 %), those 65 to 79 years (52 %), and those in poor health (44 %) (Table 3).

Recommendation rates were only slightly lower among those who were *not* eligible for CVD prevention, 24 % for men and 28 % for women. After accounting for patient factors including age, morbidity and health care health care access, eligibility for aspirin for primary prevention was not significantly associated with recommendation. (Table 4) Only older age, having a regular source of care, having had a health care visit in the past year, and having a reported liver condition were associated with aspirin recommendation. Accounting for participants who reported taking cholesterol-lowering agents revealed the same results. Similarly, lowering the cutoff by 1 % had little effect. For secondary prevention, i.e., those with known CVD, clinicians recommended aspirin to 76 % of participants.

When we examined reported aspirin use by eligible participants, we found that 68 % of participants reported taking aspirin when it was recommended. In a model that included patient factors, a clinician's recommendation was the single most important determinant of reported aspirin use (15.2 odds ratio; 95 % confidence interval 8–29).

DISCUSSION

Despite national recommendations for aspirin to prevent CHD in men and stroke in women, only a minority of eligible persons reported an aspirin recommendation.[1] After accounting for patient age and access, there was no significant association between eligibility and recommendation. This finding is consistent with earlier studies suggesting that physicians under-recommend aspirin to prevent CVD.[5,6,9]

Consistent with previous studies,[5–9] we observed the higher rates of recommendation for secondary prevention and for diabetics. Clinicians recommended aspirin for primary prevention for 34 % and 42 % of eligible men and women. Our findings mirror previous findings suggesting that clinicians

Table 4. Likelihood of an Aspirin Recommendation Among Persons Without Known CVD

Independent variable	Adjusted odds ratio	95 % Lower CI	95 % Upper CI	*p* value
Aspirin eligibility				0.97
No	1.00	1.00	1.00	
Yes	0.99	0.70	1.42	
Age at screening				< 0.0001
40–<45 (reference)	1.00	1.00	1.00	
45–<55	3.95	2.08	7.51	
55–<65	9.45	4.86	18.38	
65–<80	12.49	6.30	24.76	
80+	18.27	11.44	29.19	
Sex				0.07
Male	1.32	0.98	1.78	
Female	1.00	1.00	1.00	
Routine place to go for healthcare				0.03
Yes	2.04	1.08	3.85	
None	1.00	1.00	1.00	
Received healthcare in past year				0.01
0	1.00	1.00	1.00	
1+	2.42	1.23	4.75	
Liver condition				0.015
No	1.00	1.00	1.00	
Yes	1.88	1.15	3.07	

Age, sex, and aspirin eligibility forced into backwards regression model (n-2,886)

often limit CVD prevention prescribing to those patients at highest risk and do not apply the established guidelines including risk models uniformly to the general population at risk.[18]

Low rates of recommendation likely reflected the complexity of assessing patient eligibility, including weighing benefits and harms in the context of risk calculations and age-based risk cutoffs. In the absence of hand-based or online risk calculators, physicians often misjudge CVD global risk.[19–21] Competing demands and limited time further hinder these complex decisions, [22,23] particularly for the use of aspirin for prevention.[24] Estimates suggest it would take the average physician in the US 7.4 h a day to adequately fulfill the published USPSTF guidelines for a typical panel of patients.[23] Further, the Direct Observation of Primary Care study found that physician's rating of the importance of aspirin had no relationship to physician aspirin recommendations.[25]

Implementation is hindered by clinician uncertainty in determining relative benefits and harms to patients.[26] Published findings and an FDA decision subsequent to the USPSTF recommendation have further undermined primary prevention recommendations. Two independent meta-analyses showed no reduction in mortality. [27,28] Another showed no mortality reduction among diabetes.[29] A third showed absolute harms exceeded benefits.[30] A randomized controlled trial among those without vascular disease showed no benefit.[31] In May, 2014, the FDA again declined to approve an indication for aspirin for primary prevention.[32]

Setting aside the merits of aspirin for primary prevention of CVD, our study findings underscore the challenge clinicians face in implementing any recommendation that requires risk calculation. The American College of Cardiology and American Heart Association guidelines on treatment of cholesterol to reduce CVD risk rely on use of an risk calculator.[33] Potentially, incorporation of automated CVD risk assessments into electronic health records could improve clinicians' estimation of risk and recommendation for prescribing.[34,35] In one randomized trial, electronic prompts more than doubled rates of aspirin prescription.[36] A subsequent systematic review showed a positive effect of prompts on aspirin prescription.[37] In addition, providing patients with global CVD risk assessments seems to improve patient intent to initiate CVD prevention.[38]

Engaging non-clinicians through expanded care teams and standing orders may also prove helpful in reducing the volume of decisions that rest solely with the clinician at the point of care. Sharing care with team members can enhance the concordance between published guidelines, use of risk models and actual practice.[39] Panel management that focuses on population-based care also has the potential to broaden evidence-based practice, especially for the many patients who don't seek office-based consultations.[40]

The strengths of our study include use of data from a current sample representative of the non-institutionalized U.S. population and the use of detailed CVD risk factors. NHANES uses rigorous methodology, including strict quality control procedures, resulting in high quality data. This allowed us to assess the impact of measured (rather than reported) risk factors related to blood pressure, cholesterol, and body mass index.

The study limitations include potential overestimation and underestimation of clinicians' recommendations based on study participants' recall. We lacked data regarding potential contraindications (e.g., severe gastrointestinal bleeding and allergy), use of other antiplatelet agents, and presence of atrial fibrillation and left ventricular hypertrophy. Inclusion of clinician recommendations of aspirin use for cancer prevention in the survey question probably overestimates recommendations for CVD prevention alone. Data were not available on atrial fibrillation (2 % prevalence among persons 50 years and older[41]) or left ventricular hypertrophy (LVH) (7 % prevalence among those 45 years and older [42]).

Data regarding clinician specialty were not available. However, previous data show cardiologists had higher rates of prescribing aspirin than primary care physicians.[6,7] Finally, clinicians might have chosen not to recommend aspirin following a shared decision with patients regarding the potential benefits and harms.[43,44]

Despite an "A recommendation" from the USPTF for aspirin for primary prevention of CVD, a majority of people potentially eligible for aspirin do not recall a clinical recommendation from their clinician to take it. Subsequent evidence regarding aspirin for primary prevention suggests that this caution may be warranted.

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