Contemporary Primary Prevention Aspirin Use by Cardiovascular Disease Risk: Impact of US Preventive Services Task Force Recommendations, 2007—2015: A Serial, Cross-sectional Study

Jeremy R. Van’t Hof, MD; Sue Duval, PhD; Adrienne Walts, MS; Stephen L. Kopecky, MD; Russell V. Luepker, MD, MS; Alan T. Hirsch, MD*

Background—No previous study has evaluated the impact of past US Preventive Services Task Force statements on primary prevention (PP) aspirin use in a primary care setting. The aim of this study was to evaluate temporal changes in PP aspirin use in a primary care population, stratifying patients by their 10-year global cardiovascular disease risk, in response to the 2009 statement.

Methods and Results—This study estimated biannual aspirin use prevalence using electronic health record data from primary care clinics within the Fairview Health System (Minnesota) from 2007 to 2015. A total of 94,270 patient encounters had complete data to estimate a 10-year cardiovascular disease risk score using the 2013 American College of Cardiology/American Heart Association global risk estimator. Patients were stratified into low- (<10%), intermediate- (10–20%), and high- (≥20%) risk groups. Over the 9-year period, PP aspirin use averaged 43%. When stratified by low, intermediate and high risk, average PP aspirin use was 41%, 63%, and 73%, respectively. Average PP aspirin use decreased after the publication of the 2009 US Preventive Services Task Force recommendation statement: from 45% to 40% in the low-risk group; from 66% to 62% in the intermediate-risk group; and from 76% to 73% in the high-risk group, before and after the guideline.

Conclusions—Publication of the 2009 US Preventive Services Task Force recommendation was not associated with an increase in aspirin use. High risk PP patients utilized aspirin at high rates. Patients at intermediate risk were less intensively treated, and patients at low risk used aspirin at relatively high rates. These data may inform future aspirin guideline dissemination. (J Am Heart Assoc. 2017;6:e006328. DOI: 10.1161/JAHA.117.006328.)

Key Words: aspirin • cardiovascular disease • prevention • risk score • US Preventive Services Task Force

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in the United States and worldwide.1 Reductions in CVD morbidity and mortality have been achieved by reducing risk factor exposure with lifestyle and pharmacologic interventions, including use of aspirin.2–15

Aspirin has been demonstrated to prevent a first myocardial infarction (MI) or stroke among individuals at high risk12,13 and to be cost-effective.16,17 It also decreases the risk of subsequent cardiovascular events and death among individuals who have already experienced an MI or stroke.14,15 Regular aspirin use for primary prevention (PP) of CVD has been evaluated in multiple well-designed clinical trials. In 1989, the Physician’s Health Study reported a 44% reduction in risk of a first MI for male participants who received aspirin.12 Regular aspirin use led to a 24% reduction in risk for ischemic stroke in women as demonstrated in the Women’s Health Study in 2005.13 These studies and others18–20 led the US Preventive Services Task Force (USPSTF) in 2009 to develop a class A recommendation for PP aspirin use in men aged 45 to 79 years and women aged 55 to 79 years for whom CVD ischemic event prevention outweighs bleeding risk.21 This recommendation provided a distinctly favorable recommendation for aspirin use compared with the 2002 statement. The 2009 recommendation also offered specific benefit/risk guidance tables to facilitate the use of aspirin for PP, compared with the 2002 statement, which only recommended a discussion between clinicians and patients at
Trends in Aspirin Use by Cardiovascular Disease Risk

Van’t Hof et al

Primary Prevention Project\(^2\)) have since demonstrated studies of PP aspirin use in low-risk cohorts (eg, the Japanese increased risk for CVD ischemic events. Contemporary professionals on the appropriate use of aspirin for PP of cardiovascular ischemic events.\(^2\)) have also released positive recommendations to guide healthcare organizations, including the American Heart Association, the American Stroke Association, and the American Diabetes Association, have also released positive recommendations to guide healthcare professionals on the appropriate use of aspirin for PP of cardiovascular ischemic events.\(^2\)–\(^7\)) Thus, within this time frame, primary care clinicians were offered strong published support for PP aspirin use, in the absence of a national dissemination plan and easy-to-use aspirin prescriptive clinical tools.

Since the publication of the 2009 USPSTF recommendation, examination of the appropriateness of aspirin use (defined as benefit greater than risk) in a primary care outpatient population has been limited. Descriptions of PP aspirin use in this population have not previously been published in association with measurements of individual 10-year CVD risk.

The current investigation was thus designed to: (1) evaluate the temporal trends in PP aspirin use in a large, primary care–based population over a 9-year period (2007–2015); (2) evaluate these trends in subgroups with lower to high CVD risk; (3) compare PP and secondary prevention aspirin treatment intensity; and (4) define the prevalence of selected contraindications to PP aspirin use. We hypothesized that PP aspirin use would increase after publication of the 2009 USPSTF recommendation, particularly in intermediate- and high-risk populations. We also hypothesized that low-risk patients might experience a lower aspirin exposure after the 2009 USPSTF publication.

The recently updated 2016 USPSTF aspirin PP recommendation statement\(^2\) advises use of low-dose aspirin for the PP of CVD and colorectal cancer in adults aged 50 to 69 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years (B and C recommendations). Improved effectiveness of the updated 2016 national aspirin use PP guidelines can be informed by evaluation of past aspirin use trends in real-world practice.

**Methods**

**Study Population and Setting**

This study included men aged 45 to 79 years and women aged 55 to 79 years with one or more primary care encounters at a Fairview Health Services clinic between 2007 and 2015. Encounters were limited to those labeled as “office visit” or “outpatient visit” to delineate a face-to-face visit with a healthcare professional. Fairview Health Services is a nonprofit, integrated health system, based in Minnesota, that includes 6 hospitals and health centers, 43 primary care clinics, and 2500 aligned physicians, with \(\approx\)6.6 million outpatient encounters and 1.6 million clinic visits annually.\(^2\) This health system includes the University of Minnesota Medical Center as its flagship academic hospital. While no single health system can fully represent a national PP clinical population, this health system is representative of the 7 county Twin Cities metropolitan area in demographic characteristics. The Minnesota Heart Survey data set, a random sample of adults, found similar characteristics.\(^3\)

**Data Source and Extraction Method**

Data were extracted from the electronic health record (EHR) for the months of January and July from 2007 to 2015 (18 one-month serial cross-sectional data sets). Patients were included if they consented to EHR data sharing for research (over 97% of patients from Fairview), were in the target age range, and presented for a visit with a primary care provider. Only the first visit in a 1-month time period was included. The EPIC EHR system (Epic Systems) is currently used by Fairview Health Services. Data were placed in an Oracle SQL database on a secure electronic data shelter. A series of manual chart reviews were completed to compare the accuracy of the extracted electronic data with a physician-based individual
EHR review (J.R.V.H.). Iterative adjustments were made to the data extraction code to improve accuracy.

Primary and secondary prevention patients were identified by searching the problem list and encounter diagnosis data fields, at the time of the index encounter, for International Classification of Diseases, 9th Revision (ICD-9), and Current Procedural Terminology codes for atherosclerotic disease. These data fields were also used to assign CVD risk factors and to identify aspirin contraindications, including a documented history of peptic ulcer disease or gastrointestinal bleeding. A third data field contained diagnoses that were not linked to a date, therefore it was not used to identify diagnoses or contraindications. However, this data field was used to exclude from analysis 22,180 persons with any diagnosis of an atherosclerotic event. Figure 1 displays a diagram of patient cohort assembly.

Medication lists at the time of the encounter were queried for aspirin, antihypertensive, antithrombotic, and statin medications. Aspirin doses >325 mg were not considered as indicative of primary or secondary prevention and were therefore excluded from the analysis. Blood pressure was extracted if obtained during the specified encounter. Total cholesterol and high-density lipoprotein cholesterol values were abstracted if drawn within 6 months before the encounter.

Figure 1. Flow diagram for patients included in the study. After duplicates were removed, 274,969 unique encounters were identified. The primary prevention population numbered 220,482. Complete risk score data were available for 94,270 persons and 88,979 of those had no contraindication to aspirin (n*). CVD indicates cardiovascular disease.
Variable Definitions

The secondary prevention (SP) population was defined by a documented history of coronary artery disease, ischemic stroke or peripheral artery disease, or a disease-specific revascularization procedure. Patients excluded from the SP population were defined as the PP population. The PP population was further divided into those with and without complete data required for the cardiovascular risk score calculation (Figure 1). The American College of Cardiology/American Heart Association 2013 global risk estimator was used to estimate 10-year CVD risk as this estimation has effectively replaced the use of the Framingham Risk Score.31 Patients with CVD risk scores were then divided into low-, intermediate-, and high-risk groups, corresponding to a 10-year CVD risk score of <10%, 10% to 20%, and ≥20%, respectively. Contraindications to aspirin use were defined as a documented history of peptic ulcer disease or gastrointestinal bleeding or use of another antithrombotic medication. Allergy to aspirin was unobtainable because of formatting of the EHR, but allergic reactions have been shown to be low in a normal population.32 Thus, appropriate PP aspirin use candidates were defined as individuals within the age and sex targets outlined by the USPSTF who did not have a contraindication to aspirin.

Smoking included current or past tobacco use as identified by ICD-9 codes for tobacco use, Current Procedural Terminology codes for cessation counseling, or use of varenicline. A complete list of ICD-9 and Current Procedural Terminology codes used to identify all diagnoses and procedures is provided in Table 1.

Statistical Analysis

Descriptive demographic data are presented as counts, mean±SD, and percentages. The prevalence of aspirin use was defined as the number of aspirin users within each group divided by the total number of individuals within that group. Aspirin use by PP candidates was further examined by risk category. The prevalence of aspirin use by individuals in the PP population was reported only for those patients without an aspirin contraindication, as defined above. When describing aspirin use in the SP population, all patients were analyzed. Trend analysis using a logistic regression model was used to evaluate the change in aspirin use over time. When examining the change in PP aspirin use by risk group, dummy variables and their interaction effects with time were used to fit the logistic regression model to the entire sample. Logistic regression was used to identify univariate associations between ASA use and patient characteristics. All analyses were performed using Stata version 13 (StataCorp).

The study protocol was reviewed and approved by the University of Minnesota’s institutional review board.

Results

There were 314,434 primary care clinic encounters during the 18 one-month time intervals over the 9-year study period.

---

Table 1. ICD-9 and CPT Codes Used for Data Extraction

| Disease                  | ICD-9 Codes                  | CPT Codes                  |
|--------------------------|------------------------------|----------------------------|
| Coronary artery disease  | 410-410.92, 412, 414-414.9   | 33140, 33141, 33510-33514, 33516-33523, 33530, 33533-33556, 33572, 35600, 92973-92975, 92977, 92980, 92981 |
| Stroke                   | 430-437.1, 437.3-438.9        | 37215, 37216, 35390, 35301, 00757, 0076T |
| Peripheral artery disease| 440.2-440.9, 443.89, 443.9   | 34201, 34203, 35256, 35286, 35302-35306, 35351, 35355, 35361, 35363, 35371-35372, 35452, 35472, 35521, 35533, 35537-35540, 35556, 35558, 35565-35566, 35570-35571, 35583, 35585, 35587, 35621, 35623, 35637-35638, 35646-35647, 35664, 35656, 35661, 35665-35666, 35671, 35700, 35879, 35881, 37220-37235 |
| Peptic ulcer disease     | 530.4, 530.7, 530.82, 531-534.91, 531.01, 535.11, 535.21, 535.31, 535.41, 535.51, 535.61, 535.71, 537.83, 537.84, 569.85, 569.86, 578.9 | na |
| Diabetes mellitus        | 250-250.93, 357.2, 362.01-362.07, 366.41 | na |
| Hyperlipidemia           | 272, 272.2, 272.3, 272.4, 272.9 | na |
| Hypertension             | 401-405.99, 437.2            | na |
| Smoking                  | V15.82, 305.1, 989.84        | 99406, 99407 |

CPT indicates Current Procedural Terminology, ICD-9, International Classification of Diseases, 9th Revision; na, not applicable.
After removing 39,465 duplicates and 22,180 patients with a CVD diagnosis that was not linked to a date, 252,789 patients were included in the study. A total of 220,482 (87%) had no history of CVD, of whom 94,270 had sufficient data available for calculating a CVD risk score (Figure 1). The low- (<10%), intermediate- (10–20%), and high- (≥20%) risk groups included 51,680 (55%), 24,944 (26%), and 17,646 (19%) persons, respectively.

The study population was primarily white, with 45% of women. Demographic data from both the PP and SP groups are displayed in Table 2. Compared with patients in the SP group, patients in the PP group were younger (61±9 versus 67±8) and had a higher prevalence of women (45% versus 37%) and lower prevalence of CVD risk factors. Within the PP sample, age, sex, and race were similar in patients with and without data required to calculate a risk score. Those with a calculated risk score had a higher prevalence of hypertension (52% versus 37%), hyperlipidemia (63% versus 32%), and diabetes mellitus (24% versus 11%) and were prescribed more antihypertensive medications (55% versus 43%) and statins.

### Table 2. Patient Characteristics: January 2007 to July 2015

|                          | Total Population | Primary Prevention | Secondary Prevention |
|--------------------------|------------------|--------------------|----------------------|
|                          | Total            | Incomplete Risk Score Data | Complete Risk Score Data | Total |
| No.                      | 252,789          | 220,482            | 126,212              | 94,270 |
| Age, y                   | 62±9             | 61±9               | 61±9                 | 62±9   |
| Women                    | 113,471 (45)     | 101,596 (46)       | 58,394 (46)          | 43,202 (46) |
| Race                     |                  |                    |                      | 11,875 (37) |
| White                    | 192,019 (87)     | 192,019 (87)       | 109,682 (87)         | 82,337 (87) |
| Black                    | 8367 (3.8)       | 8367 (3.8)         | 4739 (3.8)           | 3628 (3.8) |
| Asian                    | 5965 (2.7)       | 5965 (2.7)         | 2882 (2.3)           | 3083 (3.3) |
| Other/declined           | 14,131 (6)       | 14,131 (6)         | 8909 (7)             | 5222 (6) |
| BMI, kg/m²*              | 30±6             | 30±6               | 30±6                 | 31±6   |
| Total cholesterol, mg/dL†| 184±42           | 188±41             | 187±41               | 188±41 |
| HDL, mg/dL‡              | 50±22            | 51±23              | 50±21                | 51±23  |
| Risk factors             |                  |                    |                      | 46±21  |
| Smoking§                 | 37,080 (15)      | 29,406 (13)        | 17,119 (14)          | 12,287 (13) |
| Hypertension             | 118,755 (47)     | 95,981 (44)        | 46,672 (37)          | 49,309 (52) |
| Hyperlipidemia           | 124,082 (49)     | 100,033 (45)       | 40,695 (32)          | 59,338 (63) |
| Diabetes mellitus        | 47,994 (19)      | 36,712 (17)        | 14,503 (11)          | 22,209 (24) |
| Medications              |                  |                    |                      | 11,282 (35) |
| Antihypertensive         | 131,862 (52)     | 106,579 (48)       | 54,622 (43)          | 51,957 (55) |
| Statin                   | 107,694 (43)     | 82,348 (37)        | 33,796 (27)          | 48,552 (52) |
| Aspirin contraindications|                  |                    |                      | 25,346 (78) |
| PUD or GI bleeding       | 4725 (1.9)       | 3365 (1.5)         | 1971 (1.6)           | 1394 (1.5) |
| Antithrombotic           | 22,313 (8.8)     | 10,838 (4.9)       | 6826 (5)             | 4012 (4.3) |
| History of CVD           |                  |                    |                      | 11,475 (36) |
| CAD                      | 19,582 (8)       | na                 | na                   | 19,582 (61) |
| Stroke or carotid disease| 10,978 (4.3)     | na                 | na                   | 10,978 (34) |
| PAD                      | 6698 (2.7)       | na                 | na                   | 6698 (21) |

Continuous data are reported as mean±SD and categorical data as number (percentage). CAD indicates coronary artery disease; CVD, cardiovascular disease; GI, gastrointestinal; na, not applicable; PUD, peripheral arterial disease.

*Body mass index (BMI) data are available in 218,193; 190,349; 96,165; 94,184; 27,844 patients in each column respectively.

†Total cholesterol data are available in 126,654 of the total study population, 106,438 of the primary prevention population, 12,168 of the primary prevention population without risk score calculated, and 20,216 of the secondary prevention population.

‡High-density lipoprotein (HDL) data are available in 126,890 of the total population, 106,596 of the primary prevention population, 12,326 of the primary prevention population without risk score calculated, and 20,294 of the secondary prevention population.

§Smoking includes current and former smokers.

DOI: 10.1161/JAHA.117.006328
(52% versus 27%) compared with those without a risk score. Prevalence of smoking was similar between the groups.

Characteristics of patients with PP by 10-year CVD risk score are displayed in Table 3. As CVD risk increased, the average age increased from 57 years to 71 years, and the proportion of women decreased from 50% to 39%. In the low-risk group, 65% had 0 or 1 CVD risk factor, whereas over 75% of the high-risk group had ≥2 risk factors. Contraindications to aspirin were low in the PP population. Ulcer or bleeding prevalence was <3% in all groups. However, antithrombotic medication use increased from 2.6% in the low-risk group to 8% in the high-risk group.

Over the 9-year study period, the prevalence of aspirin use among the total PP sample decreased (P for trend <0.0001), varying between 39% and 46%, with a mean of 43%. When stratified by 10-year CVD risk, aspirin use was higher in each progressively higher-risk group (Figure 2). The high-risk sample had a mean prevalence of aspirin use of 73%; nearly as high as aspirin use in the SP population (77%). The intermediate-risk and low-risk samples had a mean prevalence of aspirin use of 63% and 41%, respectively. The PP sample without a risk score had the lowest prevalence of aspirin use, with a mean of 35%. In the years before the 2009 USPSTF recommendation, mean aspirin use in the high-

Table 3. Characteristics of Primary Prevention Sample by CVD Risk Category: January 2007 to July 2015

|                   | Low Risk (<10%) | Intermediate Risk (10–20%) | High Risk (≥20%) |
|-------------------|-----------------|-----------------------------|-----------------|
| No.               | 51 680          | 24 944                      | 17 646          |
| Age, y            | 57±6            | 65±7                        | 71±6            |
| Women             | 25 929 (50)     | 10 368 (42)                 | 6905 (39)       |
| Race              |                 |                             |                 |
| White             | 44 987 (87)     | 21 665 (88)                 | 15 686 (88)     |
| Black             | 1879 (3.6)      | 1247 (5.0)                  | 502 (2.8)       |
| Asian             | 1704 (3.3)      | 732 (3.0)                   | 647 (3.6)       |
| Other/declined    | 3110 (6.0)      | 1300 (5.2)                  | 812 (4.6)       |
| BMI, kg/m²        | 30±6            | 31±7                        | 31±6            |
| Total cholesterol, mg/dL | 192±39   | 187±42                      | 179±43          |
| HDL, mg/dL        | 53±26           | 48±17                       | 47±19           |
| Risk factors      |                 |                             |                 |
| Smoking*          | 4039 (7.8)      | 4799 (19)                   | 3449 (20)       |
| Hypertension      | 20 317 (39)     | 15 550 (62)                 | 13 442 (76)     |
| Hyperlipidemia    | 28 893 (56)     | 17 165 (69)                 | 13 280 (75)     |
| Diabetes mellitus | 6034 (12)       | 6973 (28)                   | 9202 (52)       |
| No. of risk factors |                |                             |                 |
| Zero              | 14 169 (27)     | 2640 (11)                   | 911 (5.2)       |
| One               | 19 875 (38)     | 6866 (28)                   | 3046 (17)       |
| Two               | 13 597 (26)     | 9267 (37)                   | 5948 (33.7)     |
| Three             | 3942 (7.6)      | 5597 (22)                   | 6533 (37)       |
| Four              | 97 (0.2)        | 574 (2.3)                   | 1208 (6.8)      |
| Medications       |                 |                             |                 |
| Antihypertensives | 21 098 (41)     | 16 353 (66)                 | 14 506 (82)     |
| Statins           | 22 706 (44)     | 14 228 (57)                 | 11 618 (66)     |
| Aspirin contraindications |       |                             |                 |
| PUD or GI bleeding| 587 (1.1)       | 393 (1.6)                   | 414 (2.4)       |
| Antithrombotic    | 1357 (2.6)      | 1233 (4.9)                  | 1422 (8.1)      |

Continuous data are reported as mean±SD and categorical data as number (percentage). BMI indicates body mass index; CVD, cardiovascular disease; GI, gastrointestinal; HDL, high-density lipoprotein; PUD, peptic ulcer disease.

*Smoking includes current and former smokers.
intermediate-, and low-risk group was 76%, 66%, and 45%, respectively. In the years following the recommendations, mean aspirin use was 73%, 62%, and 40% for high-, intermediate-, and low-risk groups, respectively. For each PP risk category, there was a significant decrease in aspirin use over the 9-year study (P for trend <0.0001). In the years following the recommendation, 2010 to 2015, the decrease in aspirin use remained significant (P <0.0001). There was no change in SP aspirin use over time.

Univariate analysis identified several strong associations with PP aspirin use (Table 4). Aspirin use increased with age (odds ratio [OR] of 1.36 per 5-year increment; 95% CI, 1.36–1.37). The prevalence of aspirin was lower in men (OR, 0.89; 95% CI, 0.88–0.91) and nonwhite populations. Among CVD risk factors, hypertension (OR, 3.1; 95% CI, 3.04–3.15), hyperlipidemia (OR, 3.05; 95% CI, 3.00–3.11), and diabetes mellitus (OR, 6.88; 95% CI, 6.69–7.08) were all strongly associated with aspirin use, while smoking was weakly associated with aspirin use (OR, 1.04; 95% CI, 1.01–1.17). Aspirin use was higher in individuals taking other medications to decrease CVD risk, including antihypertensive medications (OR, 3.60; 95% CI, 3.54–3.67) and statins (OR, 4.37; 95% CI, 4.28–4.45).

Contraindications to aspirin use were low (6%) in the total PP sample but increased as CVD risk increased. Four percent of the low-risk sample, 6% of the intermediate-risk sample, and 10% of the high-risk sample had a contraindication to aspirin use. This also did not vary over the 9-year study period (data not shown).

Discussion

This study demonstrates that PP aspirin use in this representative population did not increase in response to the publication of the 2009 USPSTF aspirin PP recommendation. These data also demonstrate that aspirin use was higher for individuals with elevated calculated CVD risk. Thus, health professionals were indeed applying the 2009 USPSTF recommendation, in the absence of a health system–based quality improvement initiative, in patients with easily recognized high risk.

Temporal Change in Aspirin Use

Aspirin use at the beginning of the study in January 2007 was 42%, 64%, and 75% in the low-, intermediate-, and high-risk groups, respectively, and 40% overall. By July 2015, aspirin use prevalence was 36%, 59%, and 69% in the low-, intermediate-, and high-risk groups, respectively, and 39% overall. Although a statistically significant decrease, the clinical difference is small, reflecting a lack of major change in aspirin use behavior. A recent national survey described PP...
aspirin use in 47% of adults aged 45 to 75 years, which is similar to the prevalence found in this study. The lack of improvement in PP aspirin use contrasts with the large increase in SP aspirin use observed in response to secondary CVD prevention guideline dissemination. For example, our work from MHS (Minnesota Heart Survey) reported an increase in SP aspirin use among men aged 25 to 75 years living in Minnesota from 19% in 1980 to 1982 to 74% in 2007 to 2009. As is well known, cardiovascular SP efforts have long been embedded into national, regional, and health system quality-improvement initiatives, which have not emphasized PP. Poor uptake of PP recommendations is a well-recognized problem and this study demonstrates that the challenge extends to aspirin use as well.

The 2009 USPSTF recommendation was not effective, in the absence of a dissemination program, in increasing PP aspirin use. As well, the lack of improvement in PP aspirin use may be attributable to the complexity of the recommendation, which varied by age, sex, and risk level. It is unlikely, in a limited primary care visit, that a CVD risk score was formally calculated. High-risk individuals are easily recognized and in this study used aspirin at a rate similar to the SP population, leaving little room for improvement after recommendation publication. However, the intermediate-risk group, which is likely less quickly identified, had suboptimal aspirin use at the beginning of the study and experienced a slight decrease in aspirin use after the 2009 recommendation.

### PP Aspirin Use is Higher With Increased CVD Risk

Aspirin use has previously been shown to increase as the number of CVD risk factors increase. The univariate analysis in Table 4 again shows a strong association between increased aspirin use with an increased number of risk factors. This is the first study to describe PP aspirin prevalence within a primary care population by the calculated 10-year risk score. The high 73% aspirin use in the high-risk (≥20%) PP population is similar to aspirin use in the SP population. The intermediate-risk population (10–20% 10-year risk) had a lower prevalence rate of aspirin use of 63%. The low-risk population (<10% 10-year risk) had a 41% aspirin use prevalence, and the lowest use was seen in the population with incomplete data for risk calculation (35%). Although a risk score was not calculated, this group had fewer risk factors than the low-risk group. This was particularly true for a diagnosis of hyperlipidemia, which was documented in 32% of the no-risk group and 56% of the low-risk group. This may represent a true difference in prevalence of risk factors or simply a lack of screening for hyperlipidemia. Inclusion in the current study required a clinic visit, so these estimates likely overrepresent aspirin use by the general public.

This study used a conservative 10-year CVD risk score of 10% as the threshold to define the intermediate-risk group. This risk score threshold is supported by the recently updated USPSTF recommendation statement, which uses a 10-year CVD risk score of ≥10% as the cutoff for PP aspirin recommendation in adults aged 50 to 59 years (B recommendation) and those aged 60 to 69 years (C recommendation). Future evaluation of PP aspirin use following the 2016 recommendations can be informed by these data as clinicians and researchers seek to use these guidelines to achieve maximal benefit at lowest risk.

This study used the American College of Cardiology/American Heart Association risk estimator to identify 10-year CVD risk. We note that this estimator was not available nor used in clinical practice during the observation period of the current study. Use of CVD risk estimators was not common.

### Table 4. Univariate Analysis of Characteristics Associated With Appropriate Primary Prevention Aspirin Use

| Variable                  | OR (95% CI)* |
|---------------------------|-------------|
| Age (per 5-y increments), y | 1.36 (1.36–1.37) |
| Women                     | 1.12 (1.10–1.14) |
| Race                      |              |
| White                     | Reference    |
| Black                     | 0.85 (0.81–0.89) |
| Asian                     | 0.85 (0.80–0.90) |
| Other/missing/declined    | 0.75 (0.72–0.78) |
| BMI (per 2-kg/m² increment), kg/m² | 1.09 (1.09–1.10) |
| Total cholesterol (per 20-mg/dL increments), mg/dL | 0.81 (0.81–0.82) |
| HDL (per 5-mg/dL increments), mg/dL | 0.96 (0.96–0.97) |
| Risk factors              |              |
| Smoking                   | 1.04 (1.01–1.17) |
| Hypertension              | 3.10 (3.04–3.15) |
| Hyperlipidemia            | 3.05 (3.00–3.11) |
| Diabetes mellitus         | 6.88 (6.69–7.08) |
| No. of risk factors       |              |
| Zero                      | Reference    |
| One                       | 2.31 (2.25–2.36) |
| Two                       | 4.75 (4.63–4.88) |
| Three                     | 11.35 (10.96–11.76) |
| Four                      | 15.53 (14.09–17.13) |
| Medications               |              |
| Antihypertensives         | 3.60 (3.54–3.67) |
| Statins                   | 4.37 (4.28–4.45) |

BMI indicates body mass index; CI, confidence interval; HDL, high-density lipoprotein; OR, odds ratio.

*P<0.001 for all associations.
during the decade of this study.\textsuperscript{41} We cannot determine from the current data source whether the Framingham Risk Score or any other risk estimation was used by clinicians.

**Appropriate Aspirin Use**

Aspirin use is effective in preventing first heart attacks and strokes, although at the cost of an increased risk of bleeding events. A 2012 meta-analysis of the net benefit of aspirin to prevent vascular events reported a 31% excess in nontrivial bleeding (OR, 1.31; 95% CI, 1.14–1.50).\textsuperscript{42} Yet, there is not an identical health impact of a heart attack or stroke and a reversible, nonfatal bleeding event. Thus, “appropriate aspirin use” could be defined as prescription of aspirin to prevent a first cardiovascular ischemic event, when benefit is greater than risk, as informed by patient preferences. To achieve this clinical goal requires thoughtful discussion by an informed clinician who engages an informed “at-risk” patient, on the individual level.

Clinicians may be concerned about “inappropriate” aspirin use in populations with low CVD risk.\textsuperscript{43} In this study, 41% of individuals with a 10-year CVD risk of <10% used aspirin and 33% of those with CVD risk <5% used aspirin. This high prevalence of aspirin use may reflect a lack of consensus on which patients might benefit from aspirin use as reflected by the differing recommendations released by various guideline committees. The 2009 recommendations used different risk thresholds based on age and sex, thus many people with 5% to 10% risk would have met the qualifications for aspirin use. Interestingly, the pattern of aspirin use in the group with 5% to 10% risk was the same as the other risk categories, with a slight decline in aspirin use during the years following the 2009 recommendations. These methods are unable to account for people taking aspirin for pain relief or any other noncardiovascular indication. It also cannot assess individual preference when ascribing value to CVD prevention versus bleeding risk. Thus, it is not possible to discern whether such use in low CVD risk populations is “inappropriate.”

**The Prevention Goal: Improving PP Aspirin Use**

Aspirin use remains suboptimal in an intermediate-risk sample that might yet benefit. Our past work has demonstrated a feasible approach to rapidly improving appropriate PP aspirin use by applying a community-based intervention targeting both patients and healthcare professionals.\textsuperscript{44} This intervention provides the public with self-assessment tools and a media campaign to promote public awareness of individual cardiovascular risk. The intervention also provides primary care practice-based educational interventions and candidacy tools to foster health professional risk/benefit assessments. A cost-effectiveness Markov model to evaluate the impact of this approach on a state-wide level has demonstrated that this approach would likely be clinically effective and also cost-effective in both men and women.\textsuperscript{17}

The updated 2016 USPSTF recommendation has, compared with the 2009 USPSTF recommendation, been simplified with no prescriptive difference by sex and with one well-defined risk threshold proposed. However, to effect change, a dissemination effort will likely be necessary. Routine risk calculation using data from the EHR is one way to correctly identify candidates for PP aspirin use who might otherwise be undertreated.

**Study Limitations**

There are several limitations to this study that are common to all administrative data set studies. The use of EHR data assumes regular updates of the problem lists and medications. This is especially pertinent because aspirin can be obtained without a prescription. While the accuracy of these data cannot be known, misclassification of low-dose aspirin use in an EHR has been shown to be uncommon.\textsuperscript{45} Two studies evaluating PP aspirin use gathered data by surveying participants and reported aspirin use rates similar to those in our study.\textsuperscript{33,46} As noted, this method of analysis does not allow for determination of the indication for aspirin use or how regularly it is used. To decrease the inclusion of individuals who might be using aspirin as a pain reliever, we excluded aspirin doses >325 mg when calculating aspirin prevalence. Finally, this study population was largely white, reflecting the racial demographics of Minnesota, therefore these results may not generalize to nonwhite populations. While the population studied was large and included individuals from many different clinics across a wide geographic region in this state, it cannot be known whether comparable results would be observed in other health systems or in other geographic sites.

**Conclusions**

PP aspirin use did not temporally increase in a large primary care population following the release of the 2009 USPSTF recommendations. Aspirin use was observed to increase with CVD risk and is highly prevalent in a high-risk population but may be underused in those with a 10% to 20% 10-year risk of CVD. As the 2016 USPSTF aspirin PP recommendations are considered for national dissemination, specific interventions to inform patients and health professionals should be implemented in primary care settings to improve PP aspirin use.
Acknowledgments

Thank you to Dr Mickey Edur and Jeffrey Misialek for their roles in article editing and analysis.

Sources of Funding

Philanthropic funding was provided from the Lillehei Heart Institute, University of Minnesota, and a grant from the National Heart, Lung, and Blood Institute (1R01HL126041-01).

Disclosures

Dr Hirsch earned income from serving on a steering committee for an unrelated clinical trial sponsored by Bayer, which has no relationship to this research project. This relationship had been reviewed and managed by the University of Minnesota in accordance with its conflict of interest policies. No other authors report a conflict of interest related to this study.

References

1. Writing Group Members, Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, Das SR, de Ferranti S, Despres JP, Fullerton HJ, Howard VJ, Huffman MD, Iasiri CR, Jiménez MC, Judd SE, Kissela BM, Lichtman JH, Lisabeth LD, Liu S, Mackey RH, Magid DJ, McGuire DK, Mohr ER III, Mory CS, Muntner P, Mussolino ME, Nasir K, Neumar RW, Nichols G, Palaniappan L, Pandey DK, Reeves MJ, Rodriguez CJ, Rosamond W, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Woo D, Yeh RW, Turner MB; American Heart Association Statistics Committee; Stroke Statistics Subcommittee. Executive summary: Heart disease and Stroke Statistics—2016 Update: A Report From the American Heart Association. Circulation. 2016;133:447–454.
2. Cooper R, Cutler J, Desvigne-Nickens P, Fortmann SP, Friedman L, Havlik R, Higgin L, Marlier J, McGovern P, Morosco G, Mosca L, Pearson T, Stamler J, Stryer D, Thom T. Trends and disparities in coronary heart disease, stroke, and other cardiovascular diseases in the United States: findings of the national conference on cardiovascular disease prevention. Circulation. 2000;102:3137–3147.
3. Critchley JA, Capewell S. Mortality risk reduction associated with smoking cessation in patients with coronary heart disease: a systematic review. JAMA. 2003;290:86–97.
4. Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988–2000. JAMA. 2010;303:2043–2050.
5. Rashid P, Leonardi-Jee J, Bath P. Blood pressure reduction and secondary prevention of stroke and other vascular events: a systematic review. Stroke. 2003;34:2741–2748.
6. Hembert PR, Gaziano JM, Chan KS, Hennekens CH. Cholesterol lowering with statin drugs, risk of stroke, and total mortality. An overview of randomized trials. JAMA. 2008;299:315–321.
7. Mihaylova B, Emberson J, Blackwell L, Keech A, Simes J, Barnes EH, Voysey M, Gray A, Collins R, Baigent C. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. Lancet. 2012;380:581–590.
8. LaRosa JC, Grundy SM, Waters DD, Shear C, Barter P, Fruchart JC, Gotto AM, Greten H, Kastelein JJ, Shepherd J, Wenger NK. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. N Engl J Med. 2005;352:1425–1435.
9. Trichopoulos A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med. 2003;348:2599–2608.
10. Lee IM, Paffenbarger RS. Physical activity and stroke incidence: the Harvard Alumni Health Study. Stroke. 1998;29:2049–2054.
11. Berlin JA, Colditz GA. A meta-analysis of physical activity in the prevention of coronary heart disease. Am J Epidemiol. 1990;132:62–68.
31. Goff DC, Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB, Gibbons R, Greenland P, Lackland DT, Levy D, O'Donnell CJ, Robinson JG, Schwartz JS, Shero ST, Smith SC, Sorlie P, Stone NJ, Wilson PF. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63:2935–2959.

32. Settipane RA, Constantine HP, Settipane GA. Aspirin intolerance and recurrent urticaria in normal adults and children. Epidemiology and review. Allergy. 1980;35:149–154.

33. Williams CD, Chan AT, Elman MR, Kristensen AH, Miser WF, Pignone MP, Stafford RS, McGregor JC. Aspirin use among adults in the U.S.: results of a national survey. Am J Prev Med. 2015;48:501–508.

34. Stafford RS. Aspirin use is low among United States outpatients with coronary artery disease. Circulation. 2000;101:1097–1101.

35. Ajani UA, Ford ES, Greenland KJ, Giles WH, Mokdad AH. Aspirin use among U.S. adults: Behavioral Risk Factor Surveillance System. Am J Prev Med. 2006;30:74–77.

36. Shahar E, Folsom AR, Romm FJ, Bisgard KM, Metcalf PA, Crum L, McGovern PG, Hutchinson RG, Heiss G. Patterns of aspirin use in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. Am Heart J. 1996;131:915–922.

37. Cabana MD, Rand CS, Powe NR, Wu AW, Wilson MH, Abboud PA, Rubin HR. Why don’t physicians follow clinical practice guidelines? JAMA. 1999;282:1458.

38. Pokharel Y, Tang F, Jones PG, Namib V, Bittner VA, Hira RS, Nasir K, Chan PS, Maddox TM, Oetgen WJ, Heidenreich PA, Borden WB, Spertus JA, Petersen LA, Ballantyne CM, Virani SS. Adoption of the 2013 American College of Cardiology/American Heart Association Cholesterol Management Guideline in Cardiology Practices Nationwide. JAMA Cardiol. 2017;11:1–23.

39. Yao X, Abraham NS, Alexander GC, Crown W, Montori VM, Sangaralingham LR, Gersh BJ, Shah ND, Noseworthy PA. Effect of adherence to oral anticoagulants on risk of stroke and major bleeding among patients with atrial fibrillation. J Am Heart Assoc. 2016;5:e003074. DOI: 10.1161/JAHA.115.003074.

40. Tchwenko S, Fleming E, Perry GS. Aspirin Use for the Primary Prevention of Myocardial Infarction Among Men in North Carolina, 2013. Prev Chronic Dis. 2015;12:E202.

41. Eichler K, Zoller M, Tschudi P, Steurer J. Barriers to apply cardiovascular prediction rules in primary care: a postal survey. BMC Fam Pract. 2007;8:1.

42. Seshasai SRK, Wijesuriya S, Sivakumaran R, Nethercott S, Erqou S, Sattar N, Ray KK. Effect of aspirin on vascular and nonvascular outcomes: meta-analysis of randomized controlled trials. Arch Intern Med. 2012;172:209–216.

43. Hira RS, Kennedy K, Nambi V, Jneid H, Alam M, Basra SS, Ho PM, Deswal A, Ballantyne CM, Petersen LA, Virani SS. Frequency and practice-level variation in inappropriate aspirin use for the primary prevention of cardiovascular disease: insights from the National Cardiovascular Disease Registry’s Practice Innovation and Clinical Excellence registry. J Am Coll Cardiol. 2015;65:111–121.

44. Oldenburg NC, Duval S, Luepker RV, Finnegan JR, LaMarre H, Peterson KA, Zanteck ND, Jacobs G, Straka RJ, Miller KH, Hirsch AT. A 16-month community-based intervention to increase aspirin use for primary prevention of cardiovascular disease. Prev Chronic Dis. 2014;11:E83.

45. Cea Sóranio L, Sóranio-Gabarró M, García Rodríguez LA. Validation of low-dose aspirin prescription data in The Health Improvement Network: how much misclassification due to over-the-counter use? Pharmacoepidemiol Drug Saf. 2016;25:392–396.

46. Pignone M, Anderson GK, Binns K, Tilson H, Weisman SM. Aspirin use among adults aged 40 and older in the United States: results of a national survey. Am J Prev Med. 2007;32:403–407.