Identifying Opportunities to Improve Aspirin Utilization for the Primary Prevention of Cardiovascular Disease in a Regional Health Care System

Jeffrey J. VanWormer, PhD; Aaron W. Miller, PhD; Shereif H. Rezkalla, MD

ABSTRACT

Objective: Aspirin is an important part of primary cardiovascular disease prevention, but little is known about aspirin use patterns in regional health care systems. This study used electronic health records from Marshfield Clinic to identify demographic, geographic, and clinical predictors of aspirin utilization in central Wisconsin adults without cardiovascular disease.

Methods: A cross-sectional design was employed using 2010-2012 data from patients in the Marshfield Epidemiologic Study Area. Individuals who took aspirin-containing medication daily or every other day were considered regular aspirin users. There were a total of 6678 adults in the target region who were clinically indicated for aspirin therapy for primary cardiovascular disease prevention, per national guidelines.

Results: Aspirin was generally underutilized in this population, with 35% of all clinically indicated adults taking it regularly. Adjusted models found that individuals who were younger, female, not covered by health insurance, did not visit a medical provider regularly, smokers, were not obese, or did not have diabetes were least likely to take aspirin. In addition, there was some local variation in that aspirin use was less common in northeastern communities within the regional service area.

Conclusion: Several aspirin use disparities were identified in central Wisconsin adults without cardiovascular disease, with particularly low utilization observed in those without diabetes and/or without regular physician contact. Methods of using electronic health records to conduct primary care surveillance as outlined here can be adopted by other large health care systems in the state to optimize future cardiovascular disease prevention initiatives.

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INTRODUCTION

Cardiovascular disease (CVD) is the principle driver of mortality in the United States.[1] Despite steady reductions in both incidence and mortality[2] over recent decades, the overall prevalence of CVD is expected to rise due to an aging population and increased diabetes comorbidities.[3] Without further reductions in new CVD cases, the health care resources required to manage CVD are feared to outstrip financial capacity. CVD preventive medical care focuses on risk factor modification, namely control of elevated blood pressure and lipids.[4] Control of platelet aggregation via low-dose aspirin is also important for those at high risk of experiencing a CVD event.[5,6] Though aspirin therapy for primary CVD prevention remains controversial,[7,8] meta-analytic evidence suggests that it lowers CVD risk by nearly 15% over 7 years.[9]

Aspirin use has been increasing in the United States overall,[10,11] with at least 41% of all US adults over age 40 now taking it regularly.[12] Aspirin is routinely recommended and well utilized in Wisconsin's secondary prevention population with active CVD,[13] but pharmacoepidemiologic research on aspirin use in primary CVD prevention populations is much less common. The most recent statewide research found that about one-third of Wisconsin adults age 35 to 74 years without CVD or diabetes are clinically indicated for aspirin therapy, and of these, just 31% report taking aspirin regularly.[14] Consistent with other previous research, Wisconsinites in older age groups are most likely to use aspirin.

State- and national-level studies are helpful in detecting broad trends in aspirin utilization, but they are less relevant at local levels where targeted health initiatives are more likely to occur. The recent widespread adoption of electronic health records

(EHR) by large health care delivery systems presents opportunities to reuse clinical data for community-level epidemiologic research. There are at least some burgeoning EHR models that can inform regional CVD risk factor surveillance and pharmacoepidemiology,[15-17] but none have specifically examined aspirin at a population level. In order to help regional health care systems leverage their own data to direct primary care initiatives toward patients most likely to benefit, this is an important research gap to address. The purpose of this study was to characterize regular aspirin use in central Wisconsin adults without CVD (who are clinically indicated for aspirin), as well as to identify regional demographic and clinical disparities in aspirin use.

METHODS

Design and Setting

A cross-sectional analysis was performed using data extracted from the Marshfield Clinic research data warehouse, which stores medical and administrative information captured within the system EHR during clinical encounters. The target population was the central portion of the Marshfield Epidemiologic Study Area (MESA). As described in more detail elsewhere,[18] MESA is a regional population-based health research resource that includes patients (and their associated family members) who received care from Marshfield Clinic and reside in 1 of the ZIP codes that surround the primary service area in central Wisconsin. This region is predominantly rural, covering over 1000 square miles, with about 56,000 total residents who receive over 90% of their inpatient and outpatient health care from Marshfield Clinic.[19]

Sample

All data were collected over a 3-year timeframe between January 1, 2010 and December 31, 2012. Eligibility criteria for this analysis were, as of December 31, 2012: (1) current living status in MESA Central, (2) ≥ 1 ambulatory encounter with a Marshfield Clinic medical provider during the study timeframe, (3) no personal history of ischemic vascular disease (ie, myocardial infarction, angina, ischemic stroke—specific diagnostic codes available upon request), and (4) clinically indicated for aspirin therapy for primary CVD prevention, per the US Preventive Services Task Force (USPSTF)[6] and, for those with diabetes, the American Diabetes Association (ADA)[20] guidelines as detailed below. Because this was a retrospective analysis of existing health care data, the study was approved by the Marshfield Clinic Institutional Review Board (IRB) with a waiver of informed consent.

Indication for Aspirin Therapy

The clinical indication for aspirin therapy for primary CVD prevention was determined for all subjects based on current USPSTF[6] and ADA[20] guidelines. Among patients without diabetes, those indicated for aspirin included men in the following age-risk categories for coronary heart disease: 45 to 59 years and ≥ 4% risk, 60 to 69 years and ≥ 9% risk, and 70 to 79 years and ≥ 12% risk; and women in the following age-risk categories for stroke: 55 to 59 years and ≥ 3% risk, 60 to 69 years and ≥ 8% risk, and 70 to 79 years and ≥ 11% risk. For patients with diabetes, men and women with ≥ 10% risk of CVD are indicated for aspirin therapy. Assuming no contraindications, the USPSTF and ADA recommend aspirin in these groups because the probability of cardioprotection outweighs that of major gastrointestinal or intracranial hemorrhage. A 10-year risk of CVD, coronary heart disease, or stroke was calculated for each individual using the global CVD risk equation from the Framingham Heart Study.[21] This method estimates the risk of all CVD using information on age, sex, smoking, systolic blood pressure, total cholesterol, high-density lipoprotein (HDL) cholesterol, and diabetes. The global CVD risk score can then be multiplied by a correction factor to determine the specific 10-year risk for coronary heart disease (for men without diabetes) and stroke (for women without diabetes). Those with a known aspirin contraindication were not indicated for aspirin therapy under the USPSTF and ADA guidelines. Comprehensive assessment of aspirin contraindications using administrative data is not well established, however, because clinical judgment is often needed to determine the severity of a given health condition in this context. As such, only select aspirin contraindicative diagnostic codes were screened for in the EHR based on previous recommendations.[22,23] These included a previous history of a salicylate adverse events, gastrointestinal bleeding, intracranial bleeding, or severe liver disease. Other, more relative potential contraindications such as concurrent use of anticoagulants or nonsteroidal anti-inflammatory drugs (NSAIDS), poorly controlled hypertension, and/or gastroesophogeal reflux were not considered in this study.

Measures

Outcome

Based on previous state-level methods developed for standard health care quality reporting,[13,22] the primary outcome was regular use of aspirin-containing medication. Known initiation/discontinuation dates, dose, and frequency of all patient reported medications were collected in patient interviews conducted as part of the routine workflow during Marshfield Clinic encounters and stored in the system EHR. There are no known objective validation studies of EHR-derived aspirin use, but 1 previous study found strong agreement between manual chart-audited and EHR-automated text-derived aspirin use in adults with diabetes.[16] Another study showed strong agreement between self-reported regular aspirin use and a blood byproduct of salicylates.[24]

In this study, EHR-derived medications were first linked to the therapeutic classification system of the American Society of

Table 1. Descriptive Characteristics, Stratified by Regular Aspirin Use

Characteristics	Regular Aspirin Use n = 2,346	Irregular or No Aspirin Use n = 4,332	*p*
Age (y)	61.6 ±8.5	56.5 ±8.0	<0.001
Sex			
Female	339 (14%)	364 (8%)	<0.001
Male	2,007 (86%)	3,968 (92%)	
Race/Ethnicity			
White, non-Hispanic	2,253 (96%)	4,078 (94%)	0.001
Non-white, non-Hispanic	35 (1%)	64 (1%)	
Hispanic	26 (1%)	73 (2%)	
Unknown	32 (1%)	117 (3%)	
Health Insurance			
Commercial only	1,456 (62%)	3,022 (70%)	<0.001
Public assisted	828 (35%)	1,042 (24%)	
None	62 (3%)	268 (6%)	
Residential Community (ZIP code)			
Dorchester	52 (2%)	121 (3%)	0.097
Abbotsford	108 (5%)	200 (5%)	
Colby	113 (5%)	238 (5%)	
Stratford	202 (9%)	434 (10%)	
Unity	62 (3%)	79 (2%)	
Spencer	172 (7%)	303 (7%)	
Hewitt	45 (2%)	73 (2%)	
Auburndale	96 (4%)	207 (5%)	
Arpin	78 (3%)	166 (4%)	
Milladore	50 (2%)	81 (2%)	
Chili	45 (2%)	100 (2%)	
Pittsville	133 (6%)	217 (5%)	
Marshfield	1,190 (51%)	2,113 (49%)	
Number of Ambulatory Visits in the Past 3 Years	12.4 ±9.8	9.0 ±8.4	<0.001
Smoking			
Current	336 (14%)	1,000 (23%)	<0.001
Former	930 (40%)	1,322 (31%)	
Never	1,080 (46%)	2,010 (46%)	
Body Mass Index (kg/m2)	32.4 ±6.7	30.9 ±6.4	<0.001
Diabetes			
Yes	755 (32%)	559 (13%)	<0.001
No	1,591 (68%)	3,773 (87%)	

Table shows descriptive characteristics of central Wisconsin adults who were clinically indicated for aspirin therapy for the primary prevention of cardiovascular disease in 2012, stratified by regular aspirin use.
All values are reported as mean ±standard deviation or frequency (% of total).
P-value corresponds to the difference between the 2 groups.

Health-System Pharmacists.[25] All salicylate class medications were reviewed and the generic names of aspirin-containing medications screened for during data extraction, including aspirin, aspirin/calcium carb, aspirin/magnesium carb/al aminoacet, aspirin/magnesium hydrox/al hydrox, and aspirin/calcium carb/magnesium/al hydrox. Per standard practice,[22] combined aspirin-narcotic medications (eg, aspirin plus codeine) were not considered due to the transient nature of such therapies. Also, other prescription antiplatelet agents such as clopidogrel were not considered as they typically are reserved only for secondary CVD prevention. Individuals who took aspirin-containing medication daily or every other day at their most recent encounter within the study timeframe were considered current regular aspirin users. Participants who did not take (or discontinued) aspirin at their most recent encounter, took aspirin as needed (PRN), or otherwise took aspirin less frequently than every other day were considered irregular aspirin users. Aspirin dose was reported descriptively where available, but could not be considered in the outcome definition due to incomplete data.

Exposures.
Several exposures were considered to identify the best independent predictors of regular aspirin use. These included age, sex, race/ethnicity, health insurance status, residential community, number of ambulatory care encounters over the previous 3 years, smoking, body mass index (BMI), and diabetes. Community was based on the ZIP code of residence within MESA. BMI was calculated as weight in kg divided by height in meters squared. Diabetes was established by the presence of ≥ 2 diagnostic code in 250.xxx occurring before December 31, 2012. All clinical variables were collected by trained staff following standard Marshfield Clinic office-based physical exam and laboratory procedures.

Analyses
All analytical procedures were conducted with SAS Version 9.3 (SAS Institute, Cary, North Carolina). For individuals with missing total or HDL cholesterol, the 10-year CVD risk estimate was calculated using body mass index (BMI) in place of blood lipids, per methods outlined by D'Agostino and colleagues.[21] This method provides a reasonable approximation of CVD risk in the absence of laboratory values. Univariate and multivariable logistic regression was used to examine the association between all exposures and regular aspirin use. An initial multicollinearity check between exposures found no issues, thus all exposures were considered simultaneously in a fully adjusted model. Given the exploratory nature of this analysis, no model reduction techniques were applied. Also, because there is near complete capture of medical care data within the target MESA population, no sample weighting techniques were used.

RESULTS
There were 6,678 individuals identified as clinically indicated for aspirin therapy and meeting all study eligibility criteria. Descriptive characteristics of the analytical sample are outlined in Table 1. As expected, the sample was predominantly male and non-Hispanic white, with the majority residing in the Marshfield community. There were 2,346 (35%) individuals who took aspirin regularly. Among regular aspirin users, 98% indicated daily use. Full aspirin dose information was available only on 530 aspi-

rin users, with an average daily dose of 81mg being most common (77%), followed by ≥325 mg (21%) and 162 mg (2%).

All exposures except residential community were significantly associated with aspirin use in unadjusted models (Table 1). The fully adjusted multivariable model found that adults who were older, male, commercially insured, visited a medical provider regularly, were nonsmokers, had a higher BMI, or had diabetes had significantly higher odds of aspirin use (Table 2). Residential community was modestly associated with aspirin use (Figure). After adjustment for other exposures, rates of aspirin utilization by community ranged from a low of 29% in Dorchester to a high of 45% in Unity. A sensitivity analysis also was conducted using residential census tract (in lieu of ZIP code) in order to view local variation at a more granular level. Parameter estimates from this analysis were very similar to those observed in the main findings (results not shown).

Table 2. Multivariable Association Between Patient Exposures and Regular Aspirin Use

Exposures	Regular Aspirin Use (Yes vs No)	
Age (y)	1.07 (1.06, 1.08)	*P*<0.001
Sex		
Female vs male	0.56 (0.45, 0.68)	*P*<0.001
Race/Ethnicity		
Non-white, non-Hispanic vs white, non-Hispanic	1.26 (0.81, 1.97)	*P*=0.307
Hispanic vs white, non-Hispanic	0.72 (0.44, 1.17)	*P*=0.185
Unknown vs white, non-Hispanic	0.73 (0.48, 1.11)	*P*=0.142
Health Insurance		
Publicly insured vs commercially insured	0.72 (0.63, 0.83)	*P*<0.001
Not insured vs commercially insured	0.62 (0.46, 0.83)	*P*=0.001
Residential Community		
Dorchester vs Marshfield	0.77 (0.54, 1.11)	*P*=0.168
Abbotsford vs Marshfield	0.88 (0.68, 1.15)	*P*=0.345
Colby vs Marshfield	0.85 (0.66, 1.09)	*P*=0.200
Stratford vs Marshfield	0.85 (0.70, 1.04)	*P*=0.109
Unity vs Marshfield	1.55 (1.08, 2.23)	*P*=0.018
Spencer vs Marshfield	1.01 (0.81, 1.25)	*P*=0.952
Hewitt vs Marshfield	1.19 (0.80, 1.78)	*P*=0.395
Auburndale vs Marshfield	0.86 (0.66, 1.13)	*P*=0.277
Arpin vs Marshfield	0.93 (0.69, 1.25)	*P*=0.625
Milladore vs Marshfield	1.00 (0.68, 1.48)	*P*=0.982
Chili vs Marshfield	0.91 (0.62, 1.33)	*P*=0.628
Pittsville vs Marshfield	1.03 (0.81, 1.32)	*P*=0.812
Number of Ambulatory Visits in the Past 3 Years	1.02 (1.01, 1.03)	*P*<0.001
Smoking		
Current vs former or never	0.80 (0.69, 0.93)	*P*=0.003
Body Mass Index (kg/m2)	1.02 (1.01, 1.03)	*P*<0.001
Diabetes		
Yes vs no	2.41 (2.05, 2.82)	*P*<0.001

Table shows multivariable association between patient exposures and regular aspirin use among central Wisconsin adults who were clinically indicated for aspirin therapy for the primary prevention of cardiovascular disease (N = 6678). Values are reported as odds ratio (95% confidence interval) of regular aspirin use. Values less than 1 indicate that as the exposure variable increased (or relative to the reference category for categorical exposures), the odds of aspirin use decreased.

DISCUSSION

Aspirin is underutilized in central Wisconsin, with 35% of adults clinically indicated to take it for primary CVD prevention actually doing so. Adjusted models found that patients who were younger, female, not covered by health insurance, did not visit a medical provider regularly, smokers, were not obese, or did not have diabetes were least likely to take aspirin. Race had limited influence on aspirin use, unlike 1 other study.[11] Otherwise demographic patterns of aspirin use in this study were largely consistent with other previous findings,[10-12] with the overall rate of aspirin use in this study area slightly higher than that observed statewide in 2008-2010.[14]

Clinical factors were notably strong markers of aspirin use in this study. In particular, adults with diabetes had 2.4 times greater odds of taking aspirin relative to those without. In addition, those with private health insurance and who visited the clinic frequently were much more apt to take aspirin. Taken collectively, such factors underscore previous observations that, according to patients, a physician conversation where aspirin is recommended is the most motivating factor for taking aspirin regularly.[12] It seems logical to conclude that patients who are clinically identified as being in poor health (eg, diabetes, obese) and have reasonable access to and utilization of health care (eg, insured, regular physician visits) are more likely to receive such medical advice relative to healthy young adults or those without health insurance who cannot visit the clinic often.

There also was a modest degree of local variation in that several communities north and east of the main Marshfield Clinic campus were least likely to take aspirin. Reasons for this were unclear and did not obviously track with socioeconomic factors. US census data indicate that education and income levels, as well as professional-oriented occupations predictably drop in all directions further away from the population center of Marshfield. Distance from medical care also did not appear to be a strong factor as has been observed in some previous regional research on care for other health conditions.[26] In addition to the main central clinic in Marshfield, there are 2 satellite clinics that deliver primary care in the northern communities, which serve the lowest aspirin use areas. This may present opportunities to focus specific primary care outreach efforts in those locations in order to improve rates of aspirin use across MESA.

Measurement bias was the main study limitation in that aspirin use was reported during patient interviews as part of usual care and precise dosage information was often lacking, presumably because it could not be recalled by patients. Validation studies are scarce on self-reported aspirin use, but indicate generally good

Figure. Prevalence of Regular Aspirin Use

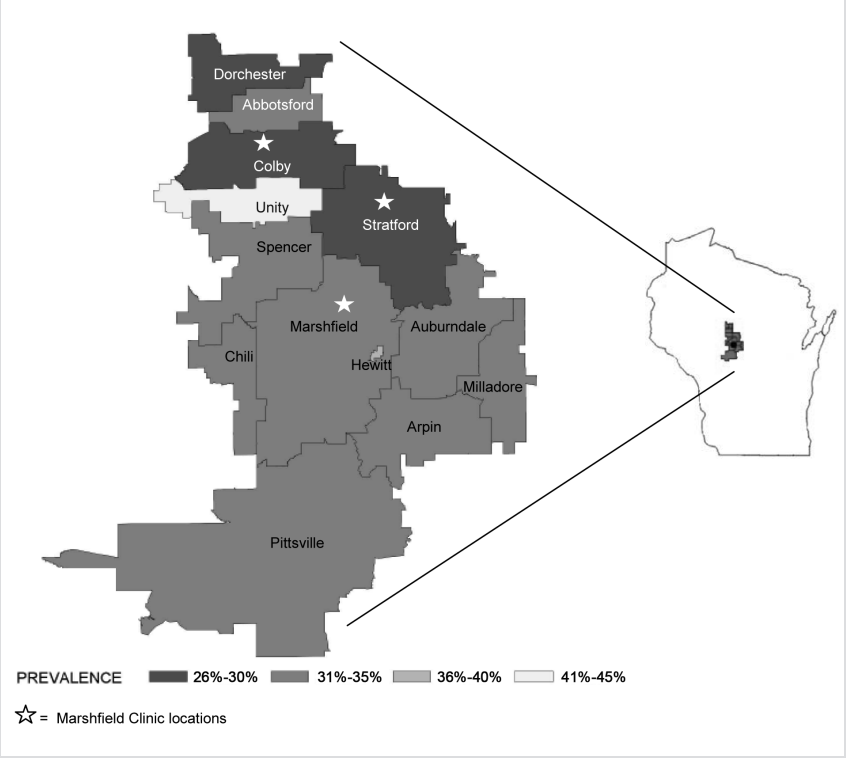

Figure shows regular aspirin use among adults clinically indicated for aspirin for primary cardiovascular disease prevention, stratified by residential community within the Marshfield Epidemiologic Study Area.

accuracy and correlation with biomarkers.[24] The timing of the aspirin assessment at the most recent visit also may be an unstable marker of long-term regular aspirin use for some patients who may only be temporarily using aspirin regularly. More objective and longitudinal sources of medication possession (eg, pharmacy claims) might help augment gaps in self-reported medication use. Despite the general advantages of EHR data in epidemiologic research, more subjective elements of the medical chart are often difficult to query, including direct physician advice to take aspirin, clinical judgments on some potential aspirin contraindications, and patients' primary intent of regular aspirin use (eg, CVD prevention, pain management). Future research would benefit from advancing methods to readily account for this information. Other limitations were the limited racial diversity of the source population relative to other parts of the country or more urban areas of the state.

This study is the first EHR-based examination of the pharmacoepidemiology of aspirin use for primary CVD prevention in the region. Several aspirin disparities were identified, which may help inform a profile of where and for whom future primary CVD care quality improvement initiatives (eg, academic detailing, clinical decision aids) could be optimally targeted. As EHRs become ubiquitous, primary CVD prevention surveillance methods outlined here could be further refined and adopted by other large health care systems, including those with geographically extensive service areas commonly found in Wisconsin and throughout the rural Midwest.[27] As part of the coming wave of American health care reforms, all health care systems will, in addition to providing high-quality care for sick patients, experience mounting expectations to monitor and improve the health of the entire populations they serve.

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