Aspirin Use Among Adults With Diabetes

Recent Trends and Emerging Sex Disparities

Stephen D. Persell, MD, MPH; David W. Baker, MD, MPH

Background: Despite high cardiovascular risk among adults with diabetes mellitus, aspirin use has been low.

Methods: To assess recent self-reported regular aspirin use among adults 35 years or older with diabetes, we used statewide telephone surveys conducted in 7 states in 1997 and 20 states in 1999 and 2001 including 875, 3205, and 4272 subjects in 1997, 1999, and 2001, respectively.

Results: Aspirin use increased from 37.5% in 1997 to 48.7% in 2001. In 2001, 74.2% (95% confidence interval [CI], 70.9%-77.5%) of diabetic adults with cardiovascular disease, but only 37.9% (95% CI, 35.1%-40.7%) of those without cardiovascular disease, used aspirin regularly, including less than 40% with diagnosed hypertension or hypercholesterolemia or who smoked. After adjusting for cardiac risk factors and socioeconomic characteristics, among those without cardiovascular disease, aspirin use was less common in women aged 35 to 49 years (adjusted rate ratio [RR], 0.35; 95% CI, 0.24-0.51) and 50 to 64 years (RR, 0.69; 95% CI, 0.53-0.88) and in men aged 35 to 49 years (RR, 0.62; 95% CI, 0.43-0.85) compared with men 65 years and older. For those with diagnosed cardiovascular disease, aspirin use was lower among women (RR, 0.81 compared with men; 95% CI, 0.70-0.90) and adults younger than 50 years (RR compared with those ≥65 years, 0.81; 95% CI, 0.61-0.98). The disparity in aspirin use between men and women appeared between 1997 and 2001.

Conclusions: Aspirin use among adults with diabetes has increased. However, many high-risk individuals, especially women and those younger than 50 years, do not use this effective and inexpensive therapy.

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The Risk of Cardiovascular Disease (CVD) is very high among adults with diabetes mellitus.1-3 Adults with diabetes but no clinical CVD may have risk of CVD events similar to that of non-diabetic adults with established CVD.2,5 Although there has been a decline in CVD mortality in recent decades, adults with diabetes have not seen the same improvements as those without this disease, and CVD mortality among women with diabetes actually increased during a time when it fell among nondiabetic women.7

Despite this high risk of CVD, strategies to prevent cardiovascular events in persons with diabetes are underused.8-11 Aspirin, which effectively reduces the risk of first and subsequent myocardial infarction,12-14 can be taken safely by adults with diabetes who lack contraindications to its use.15-17 However, many adults with diabetes do not use this widely available and inexpensive therapy. Among adults with diabetes in the United States during 1988 through 1994, regular aspirin use was reported by only 37% of those with CVD and by 13% of those with cardiac risk factors only.18 To address this problem, the American Diabetes Association published a position statement in 1997 recommending that aspirin be considered for prevention of CVD events in any high-risk adult older than 30 years with diabetes. This included both individuals with established CVD and those with risk factors in addition to diabetes (ie, a family history of CVD, smoking, hypertension, obesity, albuminuria, or dyslipidemia) who did not yet have overt CVD.19,20

Prior to this study, it is not clear whether aspirin use increased after the 1997 American Diabetes Association position statement. Our goals were to determine changes in aspirin use from 1997 to 2001 and to determine current disparities in aspirin use by means of recent survey data.
DATA SOURCE

We analyzed data from the 1997, 1999, and 2001 Behavioral Risk Factor Surveillance System, a federally funded telephone survey of noninstitutionalized adults in the United States. The survey methods, including the complex survey design and weighting adjustments used to adjust for nonresponse and noncoverage, are described elsewhere.24 We analyzed responses to questions in a CVD module administered to adults 35 years and older in 7 states (Arizona, Iowa, Louisiana, Oklahoma, Pennsylvania, Virginia, and Wyoming) in 1997; 19 states (Alabama, Arizona, Georgia, Indiana, Iowa, Kentucky, Louisiana, Maine, Mississippi, Montana, New Mexico, New York, North Carolina, North Dakota, Ohio, Oklahoma, South Carolina, Virginia, and Wisconsin) and Washington, DC, in 1999; and 19 states (Alabama, Arkansas, Colorado, Iowa, Minnesota, Mississippi, Missouri, Montana, New York, North Dakota, Ohio, Oklahoma, South Carolina, Tennessee, Utah, Virginia, Washington, West Virginia, and Wyoming) and Washington, DC, in 2001.

STUDY POPULATION AND CARDIOVASCULAR RISK FACTORS

Respondents who were 35 years and older were eligible for this analysis if they said a doctor had told them they had diabetes, excluding women who said they had diabetes only during pregnancy. Respondents were considered to have CVD if they reported that a doctor told them they had had a heart attack, myocardial infarction, angina, coronary heart disease, or stroke. We classified respondents as being at high risk for CVD if, in addition to their diabetes, they reported hypertension, hypercholesterolemia, or current cigarette smoking.

ASPIRIN USE

We considered respondents to be aspirin users if they answered yes to the question, “Do you take aspirin daily or every other day?” We then calculated the prevalence of aspirin use among adults with diabetes, stratified according to whether patients had been diagnosed as having CVD. The prevalence of aspirin use was also determined for individuals without known CVD but with other risk factors for CVD besides diabetes (smoking, hypertension, or hypercholesterolemia). We also determined the prevalence of aspirin use among individuals with and without CVD for each state that administered the CVD module in 1997, 1999, or 2001.

STATISTICAL ANALYSIS

Analyses were performed with SAS (version 8.2; SAS Institute Inc, Cary, NC) and SUDAAN (release 8.0; Research Triangle Institute Inc, Research Triangle Park, NC) software to adjust statistical analyses for the complex survey design. The tables show the actual number of participants, but all frequencies are weighted to account for the sampling design. We calculated the change in aspirin use across 2-year intervals by comparing the pooled data for states that participated in consecutive 2-year periods; 5 states participated in both 1997 and 1999, and 11 states participated in both 1999 and 2001. Statistical significance was determined with the 2-sample z test.

To determine individual characteristics associated with aspirin use, we analyzed the responses from 4272 individuals surveyed in 19 states and Washington, DC, in 2001. We first determined bivariate associations between aspirin use and sex, age, race, education, income, insurance status, smoking, hypertension, and hypercholesterolemia. Analyses were stratified by whether participants had CVD. Associations between aspirin use and the type of CVD (ie, myocardial infarction, coronary heart disease without myocardial infarction, and stroke) were determined for the stratum with CVD. We used an indicator variable to denote individuals with missing income data (21.1%) and designated 17 subjects with missing education data as having a high school education.

We then performed multivariable logistic regression to determine independent predictors of aspirin use among those with and without diagnosed CVD, including all covariates listed previously in multivariable models. Because preliminary analyses suggested a possible interaction between age and sex, we introduced interaction terms into the regression models. The interaction terms significantly improved the model predicting aspirin use for adults without CVD. We therefore included 5 age × sex indicator variables in the final model for patients without CVD, with men 65 years and older used as the reference group. There was no significant age × sex interaction among the group with CVD. A P value of .05 was used to determine statistical significance of variables in the final model. We converted multivariable odds ratios to rate ratios (RRs) by means of a published formula.22

To examine trends in the lower use of aspirin among women, we calculated the adjusted rate ratios of aspirin use for women relative to men in 1997, 1999, and 2001 by using only data from the groups of states for which data were available at 2 consecutive 2-year intervals. Because of the smaller sample size, final models included participants with and without CVD, and we included only CVD and age as covariates.

RESULTS

The characteristics of participants surveyed in 1997, 1999, and 2001 are described in Table 1. The presence of CVD was reported by 28.0%, 27.5%, and 29.7% of subjects in 1997, 1999, and 2001, respectively. The prevalence of physician-diagnosed hypertension and hypercholesterolemia increased dramatically between 1997 and 2001. Hypertension was reported by 43.2% of subjects in 1997 and 66.9% in 2001. Hypercholesterolemia was reported by 35.2% in 1997 and 50.6% in 2001. The prevalence of smoking was similar in all 3 years.

Among participants 35 years or older with diabetes, regular aspirin use was reported by 37.5% in 1997, 38.8% in 1999, and 48.7% in 2001 (Table 2). Aspirin use was approximately twice as high among participants with CVD than among those without diagnosed CVD (Table 2). Among adults without CVD who had other cardiac risk factors besides diabetes (ie, hypertension, hypercholesterolemia, or smoking), aspirin was used by 31.9%, 31.4%, and 39.8% in 1997, 1999, and 2001, respectively.

Statewide frequencies of aspirin use by CVD status are depicted in the Figure for patients with and without known CVD. State-to-state variation in aspirin use among participants without CVD was significant in 1999 (χ², P < .001; otherwise P > .20) but was not significant for other years and was not significant in any study year for participants with CVD.

Among the 5 states with data available in both 1997 and 1999, there was a nonsignificant 5.6% (95% confi-
Among adults with diagnosed CVD, aspirin use was less likely in women aged 35 to 49 years compared with men 65 years or older (Table 4). Aspirin use tended to be higher among persons with diagnosed hypertension or hypercholesterolemia and lower in smokers, but these associations did not reach statistical significance.

In multivariable adjusted analyses for adults with diagnosed CVD, aspirin use was less likely for women (RR, 0.81; 95% CI, 0.70-0.90), those younger than 50 years (RR compared with those ≥65 years, 0.81; 95% CI, 0.61-0.98), the uninsured (RR, 0.77; 95% CI, 0.56-0.96), and those with a previous stroke (RR compared with the previous myocardial infarction, 0.86; 95% CI, 0.74-0.97). Aspirin use was significantly more likely for those with diagnosed hypercholesterolemia (RR, 1.13; 95% CI, 1.02-1.22).

Among adults with diabetes from 5 states with data available in both 1997 and 1999, the adjusted RR for aspirin use in women compared with men was 0.97 (95% CI, 0.71-1.26) in 1997 and 0.91 (95% CI, 0.61-1.23) in 1999. In the 11 states with data from both 1999 and 2001, the adjusted RR for aspirin use in women compared with men in 1999 was 0.81 (95% CI, 0.63-1.01) and 0.73 (95% CI, 0.61-0.85) in 2001.

Our results show an encouraging increase in aspirin use among adults with diabetes mellitus in recent years. Nevertheless, aspirin use remains less than ideal for patients with CVD, with a quarter of individuals known to have heart disease or stroke not using aspirin. Moreover, almost two thirds of adults with diabetes without diagnosed CVD do not use this widely available and inexpensive therapy. Even among adults with diabetes who smoke, have diagnosed hypertension, or have diag-
nosed hypercholesterolemia (but who do not as yet have
diagnosed CVD), 60% do not use aspirin regularly.

Low rates of aspirin use in the past among adults with
diabetes may have been due to concerns about aspi-
rin’s safety. Regular aspirin is known to increase the risk
of nonfatal bleeding in all users by a factor of 1.5 to 2.0. However, randomized trials that have included many pa-
tients with diabetes have not shown aspirin to be espe-
cially dangerous in this group.

Aspirin may also be underused because patients and
physicians underappreciate the CVD risk associated with
diabetes. Increasing awareness of this risk may be con-
tributing to the recent increase in usage we observed. Al-
though diabetes has been known to be an important CVD
risk factor for decades, the magnitude of this risk has
become increasingly clear during recent years. A recent national survey of patients
and physicians showed that many people with diabetes
do not appreciate their CVD risk, and although physi-
cians do understand the high CVD risk associated with
diabetes, they place greater importance on glucose con-
trol than on blood pressure management, cholesterol low-
ering, or aspirin use as means of reducing CVD risk. The
identification of diabetes as a CVD risk equivalent
by the National Cholesterol Education Program and
educational efforts such as “Be Smart About Your Heart,”
began in 2001 by the National Diabetes Education Pro-
gram of the National Institutes of Health, and the “Make
the Link!” campaign of the American Diabetes Asso-
ciation and American College of Cardiology begun in 2002
may further increase the attention to CVD risk reduc-
tion in adults with diabetes and continue to increase as-
pirin use.

Physicians may not recommend aspirin to patients with
diabetes because of concerns that aspirin may not be as
effective for the prevention of CVD events in patients with
diabetes as in other high-risk adults. The protective effect
of antiplatelet agents in adults who have established CVD
appears to be similar in adults with and without dia-
abetes, but until recently there has not been much infor-
mation specifically addressing the impact of aspirin on
initial CVD events in people with diabetes. A large trial
using aspirin in patients with treated hypertension re-
ported that the benefits of aspirin were similar in pa-
tients with diabetes and in the entire cohort. A 2002
meta-analysis examining antiplatelet studies published
before September 1997 found that antiplatelet agents pro-
duced a nonsignificant reduction in the risk of major CVD
events from 16.7% to 15.7% (relative risk with antiplate-
let agent, 0.94) among several high-risk groups includ-
ing a large number of subjects with diabetes. A later pri-
mary prevention trial comparing aspirin with placebo that
included 1031 subjects with diabetes reported a relative
risk reduction in the combined cardiovascular end point
(cardiovascular death, nonfatal myocardial infarction, or
nonfatal stroke) of only 0.90 (95% CI, 0.50-1.62) in sub-
There are several possible explanations for low use of aspirin among women. Physicians may not counsel women with diabetes to use aspirin if the physicians underestimate women’s risk of CVD events. Although women are at lower risk of new-onset CVD than men, diabetes greatly reduces this female advantage. The very low use of aspirin we observed among women aged 35 to 49 years without diagnosed CVD may reflect the low absolute risk in the youngest women, or the concern about using aspirin in women who may become pregnant. However, these 2 potential reasons cannot explain the disparity now exists for the use of aspirin for primary and secondary CVD prevention in diabetes.

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Finally, physicians may have concerns that aspirin is less efficacious for women than men in primary prevention of CVD events. Although observational data suggest that aspirin prevents initial myocardial infarction in women, women were not well represented in early randomized trials of aspirin for the prevention of initial CVD events. Only 1 study among 4 major randomized trials of aspirin for the primary prevention of CVD published procedures and effective medications for acute myocardial infarction, including thrombolytics, β-blockers, and aspirin, in women compared with men. A similar disparity now exists for the use of aspirin for primary and secondary CVD prevention in diabetes.

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between 1988 and 1998,17,42-44 and 1 trial published since then,45 included any women. Prevention guidelines published during the 1990s acknowledged the lack of available information about aspirin for primary prevention of CVD in women.46,47 Data from the 2 primary prevention trials that did include women, the Primary Prevention Project45 and the Hypertension Optimal Treatment study,17,48 suggest that reductions in major cardiovascular events in women and men are similar, but do not establish the benefits of aspirin in women with statistical certainty. However, aspirin has similar cardiovascular benefits in men and women with established CVD,28 so it is not clear that physician concern about aspirin’s lack of efficacy in women is responsible for lower aspirin use in women.

The low use of aspirin associated with younger age is also noteworthy. Physicians or patients may think that the risk of CVD in younger diabetic adults is too low to justify using aspirin. This conception may be true for some patients in their 30s and early 40s who lack other CVD risk factors and whose short-term cardiovascular risk is low enough that the potential harms of aspirin may outweigh the benefits.38,49 However, even without other CVD risk factors, men and women 45 to 49 years old with diabetes have an estimated 7% 10-year risk of major CVD events,36 a risk that is sufficient to justify the consideration of aspirin,39 and younger adults with diabetes who have CVD risk factors in addition to diabetes may also have sufficient short-term CVD risk to warrant the use of aspirin. Yet, our results show that the opportunity to prevent CVD events with aspirin is missed in the majority of younger patients. In addition, the risk of bleeding from aspirin is lower in younger adults than in the elderly population, which further supports the recommendation to use aspirin even in younger patients with a lower absolute risk of CVD.13

Our study has several potential limitations. Our data were self-reported. Previous studies have shown good reliability for the self-reported diagnosis of diabetes, but other cardiovascular risk factors, such as diagnosed hypertension and hypercholesterolemia, are more likely to be underreported.50-53 The Behavioral Risk Factor Surveillance System adjusts the final sample weights to adjust for nonresponse and the final sample is weighted to yield estimates that are demographically representative of state populations, but our prevalence estimates could be biased if aspirin use by responders and nonresponders differs. We did not have information on use of other antiplaese or anticoagulant use and could not identify which patients had important contraindications to aspirin. We could only estimate aspirin use among adults with diagnosed diabetes. Since about 29% of adults with diabetes are undiagnosed,44 aspirin use in the overall American population with diabetes is probably lower. We also lacked detailed information on CVD diagnoses and could not distinguish strokes associated with atherosclerosis from other kinds of stroke.

Although aspirin use among adults with diabetes mellitus has increased, our findings suggest that current usage is not optimal, especially for women, younger adults, and those with major CVD risk factors who have not yet had clinically diagnosed CVD. Health professionals may have a large role to play in increasing appropriate aspirin use among adults with diabetes. Simple interventions such as offering professional advice about aspirin may be adequate to increase appropriate usage given that past studies have shown a strong association between current aspirin use and report of professional counseling.24,56 Health professionals are also in the position to help identify patients for whom the risk of aspirin may outweigh the benefits. Interventions that aim to increase professional counseling about aspirin for women, as well as young and middle-aged adults, may be especially helpful.

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Correspondence: Stephen D. Persell, MD, MPH, Division of General Internal Medicine, Northwestern University, 676 N St Clair St, Suite 200, Chicago, IL 60611-2927 (spersell@nmff.org).

REFERENCES

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