# Aspirin Use and Counseling About Aspirin Among Patients With Diabetes

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**OBJECTIVE** — Despite being a safe, effective therapy for lowering cardiovascular risk, only 20% of diabetic patients were using aspirin in the early 1990s. This study examines current physician practices and the use of aspirin therapy by individuals with diabetes.

**RESEARCH DESIGN AND METHODS** — A random sample of diabetic patients receiving care in the Department of Veterans Affairs health care system were surveyed during January-March 2000. The association between aspirin counseling, aspirin use, and reported coronary vascular disease (CVD) and classical CVD risk factors were examined using logistic regression. The effect of increasing aspirin use on risk of myocardial infarction (MI) and cardiovascular mortality was demonstrated by simulation.

**RESULTS** — Seventy-one percent of respondents reported being counseled about aspirin use, and 66% were taking daily aspirin. Individuals with known CVD were more likely to be counseled (odds ratio [OR] 4.9, 95% CI 2.9–8.1) and to use aspirin (2.1, 1.2–3.7). The factor most strongly associated with aspirin use was having been counseled about aspirin therapy by a doctor. We estimate that for this population, increasing daily aspirin use to 90% could prevent an additional 11,000 MIs and potentially save >8,000 lives.

**CONCLUSIONS** — Compared with previous reports, a substantial proportion of these diabetic patients have been counseled about and use aspirin. Most clinicians recognize aspirin as an important treatment for patients with preexisting coronary disease. However, since diabetes is now considered a CVD equivalent, it is imperative that clinicians include counseling about aspirin therapy as a care priority for all their diabetic patients, as this simple intervention may prevent many cardiovascular events and deaths.

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Cardiovascular disease is the leading cause of complications and death in people with diabetes (1–3). Middle-aged diabetic subjects are at two to four times higher risk of macrovascular disease (including coronary artery disease, stroke, and peripheral vascular disease) and overall mortality compared with similar nondiabetic individuals (4–8). Due to this elevated risk, the use of proven cardiovascular preventive therapies is imperative for individuals with diabetes.

Perhaps the easiest, safest, and least expensive preventive practice is the use of aspirin (9–12). Research shows that aspirin therapy is effective for both primary and secondary prevention of cardiovascular events and cardiac mortality (9–11,13–16). Studies also suggest that individuals with diabetes receive the same relative benefit from aspirin use as those without diabetes, (9,11,14,16) but due to their markedly higher baseline risk, the absolute benefit of aspirin therapy may be two to four times higher. In addition, aspirin therapy does not increase risk of retinal or vitreous hemorrhage and can be safely used in patients with diabetes who do not have other contraindications (e.g., allergy, bleeding tendency, anticoagulant therapy, active liver disease) (12,16).

In 1997, the American Diabetes Association (ADA) published its first recommendations for the use of low-dose aspirin therapy as a secondary prevention strategy or for primary prevention in high-risk diabetic patients (e.g., individuals with high blood pressure) (12,17). In their January 2000 publication, the ADA explicitly recommended using aspirin as a primary prevention strategy not only for individuals with specific risk factors but for anyone with diabetes who is >30 years of age and has no known contraindications (18).

Despite evidence of the benefits of aspirin use and specific recommendations by the ADA, studies suggest that this important intervention may be underused, especially for primary prevention (19–22). Estimates of the use of aspirin as a secondary prevention strategy range from 37% of the U.S. adult population with diabetes and known coronary vascular disease (CVD) to 62% of Medicare beneficiaries with diabetes discharged after an acute myocardial infarction (MI) to 63% of patients with one or more macrovascular complication who are attending the outpatient diabetes clinics of a large public hospital (20,21,23). On the other hand, only 13% of adults with diabetes who had one or more CVD risk factors but no established CVD were taking aspirin on a regular basis during 1988–1994 (20).

Although this previous research points to the potential need for more aggressive interventions to promote the use of aspirin among patients with diabetes, especially those without known cardio-

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**Abbreviations:** CVD, coronary vascular disease; DQIP, Diabetes Quality Improvement Project; MI, myocardial infarction; OR, odds ratio; VA, Veterans Affairs; VISN, veterans integrated service network.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

vascular disease, data for most studies were collected before the publication of the ADA recommendations. This study uses data from a survey conducted in January-March 2000 to examine aspirin counseling and the current level of adoption of aspirin therapy for both secondary and primary prevention among patients with diabetes receiving care in the Department of Veterans Affairs (VA) health care system, as well as the potential incremental benefit of further increasing aspirin use in this population.

## RESEARCH DESIGN AND METHODS

— This research is part of a larger project to improve diabetes care in the VA health care system as well as improve the care of individuals with other chronic conditions (24). Approval for the use of human subjects was obtained from the VA Ann Arbor Healthcare System Institutional Review Board. Individuals receiving diabetes care at one of 25 VA medical centers located in four veterans integrated service networks (VISNs) were identified using information extracted from each participating VA facility and a national utilization database maintained at a centralized repository (25,26). Because this project was designed to make comparisons across facilities, we purposefully recruited entire VISNs, each consisting of 3–10 medical centers, to participate. The participating VISNs were selected based on the willingness of their administrative leadership to endorse the project, thereby facilitating our ability to collect data from each medical center in the network. Additionally, the geographic location of the participating VISNs was such that it produced a sample of facilities and patients representing three different census regions.

To identify the eligible survey population, we used a modified version of criteria developed with Medicare claims data (27). Specifically, the survey sample consisted of patients who, in fiscal year 1998, had at least one hospitalization with a diabetes-related ICD-9 code (250.x, 357.2, 362.0, or 366.41), had at least two outpatient visits with a diabetes-related ICD-9 code, or received at least one prescription for insulin, an oral hypoglycemic medication, or home glucose monitoring supplies. In addition, individuals had to have one or more VA outpatient encounters of any kind in fiscal year 1999. The study survey was sent to a random sample of 80 eligible patients at each of the 25 study facilities.

Surveys were returned by 1,431 of those sampled, for an overall response rate of 72%. Administrative information available for both the respondents and nonrespondents showed that respondents were older (68 vs. 65 years of age, $P < 0.001$) and tended to have more diabetes-related outpatient visits (4.8 vs. 4.1, $P < 0.001$). Furthermore, ~8% of the respondents were ineligible for the study because they indicated they did not have diabetes ($n = 53$), they left too much of the survey blank to confirm their eligibility ($n = 31$), or they were deceased at the time of the study ($n = 33$). One individual <30 years of age was also eliminated, resulting in a final sample of 1,313 veterans with diabetes, all of whom were eligible for aspirin therapy (in the absence of any contraindications) according to current ADA criteria.

The study questionnaire, based on the patient survey created as part of the Diabetes Quality Improvement Project (DQIP) (28), consisted of ~150 items, including measures of general health, diabetes severity, and socioeconomic status. Questions about aspirin use and counseling were added for this project. The survey data were supplemented using information extracted from VA national databases. The supplemental information included in this study consisted of the number of outpatient clinic visits to primary care and diabetes-related providers and demographic information (e.g., sex).

### Variables

The dependent variables used in our analysis are based on two survey questions. The first question asks individuals whether they have been told by a doctor to take aspirin on a daily basis. The response categories for this item were "yes," "no," and "my doctor told me that I should not take aspirin." In the analysis, those who indicated they were told not to take aspirin were considered as a "yes" for being counseled about aspirin use. The second question asked each respondent if they take aspirin each day. Individuals who had previously indicated that they were told not to take aspirin were excluded from the analysis of aspirin use.

The key independent variables were whether an individual reported having CVD and, in the absence of known CVD, whether they had any of the classical risk factors for CVD. Having CVD was defined as reporting a previous heart attack, angina, coronary artery bypass surgery, coronary angioplasty, chest pain/pressure with exercise more than once a week or almost every week, or chest pain/pressure at rest more than once a week or almost every week (11). Individuals who did not report having CVD were considered to have a CVD risk factor if they reported having high blood pressure, having high cholesterol, or being a current smoker (6). Other variables included in the analyses, to adjust for factors that might influence aspirin use or counseling, included age, race, non-VA insurance coverage, number of outpatient visits, education level, income, time since diagnosis, and VISN (to account for any potential regional effects). Whether the individual had been counseled about the use of aspirin was also included as an independent variable in the aspirin use model.

### Statistical analysis

The data were analyzed using bivariate and multivariable methods. The percent of individuals who had been counseled about aspirin use and who used aspirin are reported by CVD status. Logistic regression was then used to examine the relationship between aspirin counseling, aspirin use, and the presence of known CVD or CVD risk factors while adjusting for other covariates as described above. We also estimated both models with sampling weights to take into account the nonproportional sampling strategy. Because the results did not substantially change when sampling weights were used, we report the results of the unweighted analysis. All analyses were conducted using Stata release 6.0 (29).

A multilevel modeling approach was considered but determined to be unfeasible after an initial examination of the intraclass correlation showed that facility-level cluster effects for aspirin use were <1%. Nonetheless, to account for the clustering of patients within medical centers, the SEs from the logistic models were adjusted using the Huber/White heteroskedastic consistent estimator of the variance/covariance matrix (30,31) with cluster correction, as found in the Stata statistical package (29). The statistical significance of individual parameter estimates was assessed using a $z$-statistic (Wald $\chi^2$) and 95% CIs.

The amount of missing data were gen-

**Table 1—*Sample characteristics***

| | |
|---|---|
| Age | 67 ± 10 |
| Male | 98 |
| White | 84 |
| VA outpatient visits in past 12 months | 5 ± (4) |
| Income <$20,000 | 62 |
| Have other insurance | 74 |
| Education | |
| Less than high school education | 30 |
| High school education | 34 |
| More than high school education | 36 |
| Years since diabetes diagnosis | 12 ± 9.5 |
| Reported CVD* | 42 |
| Reported classical CVD risk factor† | 49 |
| Counseled by doctor about aspirin use | 71 |
| Report taking aspirin on a daily basis‡ | 66 |

Data are means ± SD or %. *Previous heart attack, angina, coronary artery bypass surgery, coronary angioplasty, chest pain/pressure with exercise more than once a week or almost every week, or chest pain/pressure at rest more than once a week or almost every week. †High blood pressure, high cholesterol, or current smoker but no current reported CVD. ‡Excludes those individuals who reported they were told by a doctor not to take aspirin.

erally <5% for most of the study variables. However, to avoid selection bias and inaccurate inferences resulting from listwise deletion, we chose to run both models using Amelia (32), a multiple-imputation procedure for missing data, as described by King et al. (33 ). Amelia uses a computational algorithm to impute values for each missing cell in the data matrix, thereby creating a specified number of data sets in which the observed values remain the same but the missing values are replaced with different imputed values in each data set to reflect the uncertainty about the missing data. Logistic regression is then applied to the data sets with the imputed values (32). The adjusted odds ratios (ORs) and 95% CIs from the imputation models are reported.

To further illustrate the impact of daily aspirin use by individuals with diabetes, we calculated the effect of increasing the percentage of patients using aspirin on risk of MI and total cardiovascular mortality over a period of 25 years. Estimates derived from the Framingham Study (34) and a Weibull regression model were used to generate risk of MI and then cardiovascular mortality, conditional on the current level of specific risk factors such as lipids, blood pressure, age, and sex in the population, thus assuming a static cohort. Mean values for these risk factors were obtained from the study population and from national VA databases (24,25).

Although most studies found a statistically significant reduction in MIs for patients taking aspirin versus placebo, there is considerable variation in the relative risk estimates across studies. To model the potential effect of aspirin use on this population, we attributed a reduction in risk of MI using estimates ranging from 15 to 28 to 61%, as found in the literature (9,13,16). As with MI, the published relative risk estimates for cardiovascular mortality are quite variable. However, the observed decrease in cardiovascular mortality associated with aspirin use has achieved statistical significance in only a few studies, so for simplicity, we elected to use the relatively conservative estimate of 17% reported by the Antiplatelet Trialists' Collaboration (11). The expected proportion of MIs and cardiovascular deaths was then applied to the VA population of ~500,000 patients with diabetes to determine the number of potentially preventable MIs and cardiovascular-related deaths associated with different levels of aspirin use.

**RESULTS** — Characteristics of the study sample are presented in Table 1. The study subjects were, on average, 67 years of age, were diagnosed with diabetes for ~12 years, and were almost exclusively male. These characteristics are similar to those found in another study of patients with diabetes receiving care in VA health care system (25). The study sample is also predominantly white (84%), and >60% reported incomes of <$20,000 per year. Approximately 42% of those surveyed reported having CVD, and another 49% had at least one classical CVD risk factor.

Counseling about aspirin use was reported by 71% of the respondents, of whom 11% indicated that they were told by a doctor not to take aspirin. However,

**Table 2—*Association of CVD status with counseling by a doctor about aspirin therapy and daily aspirin use, showing crude and adjusted ORs***

| Model 1: Counseled by a doctor about aspirin use | Counseled | Not counseled | Crude OR (95% CI)* | Adjusted OR† (95% CI) |
|---|---|---|---|---|
| Reported CVD | 445 (85) | 76 (15) | 5.1 (3.2–8.1) | 4.9 (2.9–8.1)‡ |
| Reported classical CVD risk factor and no CVD | 391 (64) | 218 (36) | 3.7 (0.99–2.3) | 1.5 (0.97–2.3) |
| No CVD or classical CVD risk factor | 59 (54) | 51 (46) | — | — |
| **Model 2: Usually take aspirin each day** | **Take aspirin** | **Don't take aspirin** | **Crude OR (95% CI)*** | **Adjusted OR† (95% CI)** |
| Reported CVD | 379 (79) | 102 (21) | 4.5 (2.8–7.1) | 2.1 (1.2–3.7)‡ |
| Reported classical CVD risk factor and no CVD | 334 (59) | 228 (41) | 1.7 (1.1–2.6) | 1.8 (0.96–3.4) |
| No CVD or classical CVD risk factor | 48 (45) | 58 (55) | — | — |

Data are *n* (%) unless otherwise indicated. *Based on Cornfield approximation. †Adjusted for age, race, insurance status, number of VA outpatient visits, education, income, and time since diagnosis, Veterans Integrated Service Network. Model 2 also adjusted for counseling. ‡$P \leq 0.05$.

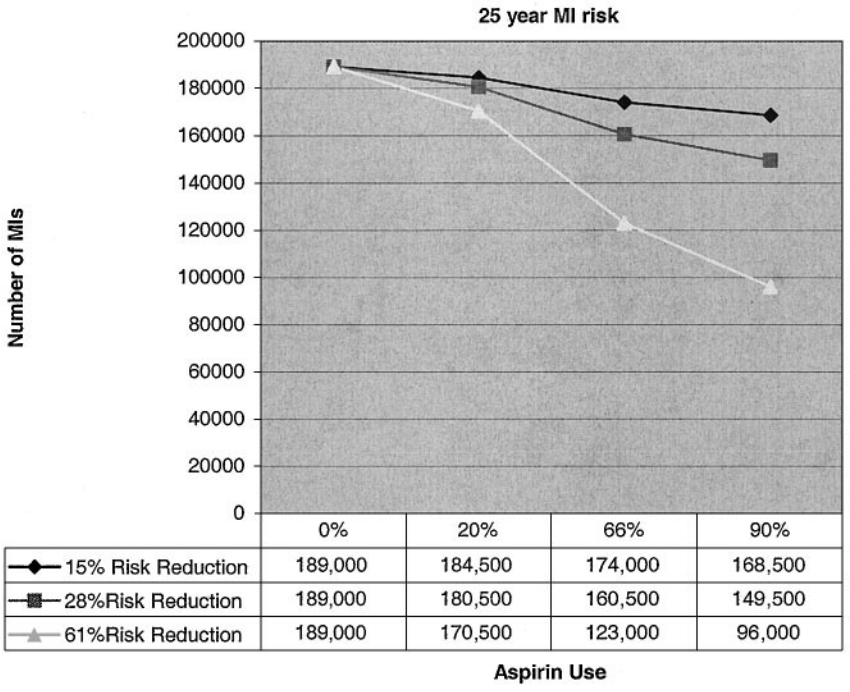


**Figure 1—***Estimated 25-year reduction in MI for 500,000 veterans with diabetes.*

rates of counseling varied by CVD status, as shown in Table 2. Eighty-five percent of veterans with established CVD had been counseled, whereas 64% of those with a CVD risk factor and only 54% of those without CVD or a CVD risk factor reported counseling about aspirin use. Likewise, although 66% of respondents reported using aspirin on a daily basis, this percentage differed by CVD status, ranging from 79% of those with CVD to just 45% of those in the no CVD or CVD risk factor category.

Both crude and adjusted ORs, further describing the relationship between CVD status and counseling about aspirin use (model 1), are also presented in Table 2. After adjustment for possible demographic or social differences using logistic regression, known CVD remains strongly associated with being counseled, with the odds almost fivefold relative to those without known CVD or CVD risk factors. On the other hand, the odds of being counseled about aspirin use for a patient with diabetes and at least one of the classical CVD risk factors is only 1.5 times that of someone without any reported additional risk factors. Other statistically significant variables ($P \leq 0.05$) included having health care insurance coverage in addition to enrollment in the VA health care system and age. The association between counseling and age was not linear, suggesting that the oldest individuals were not as likely to report being counseled about aspirin therapy.

ORs for aspirin use (model 2) are also presented in Table 2. Once again, known CVD is strongly associated with aspirin use, with CVD patients more than twice as likely to report using aspirin compared with individuals without known CVD or CVD risk factors. The presence of a classical CVD risk factor also appears to increase the likelihood of aspirin use. However, by far the variable most strongly associated with aspirin use by veterans with diabetes ($P < 0.001$) was whether their doctor told them to take aspirin on a daily basis (91% of those who had been counseled reported taking aspirin versus 10% of those with no counseling). As in the counseling model, there appears to be a curvilinear relationship between age and the reported use of aspirin therapy.

Figure 1 shows the potential decrease in risk of MI associated with the use of aspirin therapy over a period of 25 years. Based on the simulation model, if no patients with diabetes used aspirin, 189,000 of the 500,000 veterans with diabetes currently receiving care in VA would be expected to have a MI over the next 25 years. Assuming a moderate risk reduction of 28%, aspirin use by 20% of these individuals, which may have been the case several years ago (20), would prevent 8,500 MIs. Increasing the use of aspirin to 66%, as currently observed, would prevent an additional 20,000 MIs over a 25-year period. Likewise, if we increase the percentage of veterans with diabetes who use aspirin from 66 to 90%, which may be a reasonable goal after taking into account those with contraindications, we could prevent another 11,000 MIs. Comparable estimates based on risk reductions of 15 and 61% are also presented in Fig. 1.

The simulation model for cardiovascular mortality yields a similar picture. Over the next 25 years, 262,000 of the ~500,000 veterans with diabetes currently receiving care in VA would be expected to die from cardiovascular complications with no aspirin use. Assuming a risk reduction of 17%, aspirin use by 66% of these individuals could result in 14,500 lives saved, and by increasing the percentage of veterans with diabetes who use aspirin to 90%, over the next 25 years, ~8,500 additional cardiovascular-related deaths could be prevented.

**CONCLUSIONS** — Over the past decade, there has been an increasing amount of research evidence supporting the importance of aspirin therapy in decreasing cardiovascular events and mortality, particularly for individuals with diabetes or known CVD. In 1997, after conducting a review of the evidence (12), the ADA developed practice recommendations that included the use of aspirin as both secondary and primary prevention for individuals with diabetes. Nonetheless, despite the proven efficacy of this generally safe, inexpensive intervention and the published recommendations, there is concern that aspirin prescribing and use has not been fully adopted by many providers and their patients with diabetes.

This study shows that VA clinicians are doing quite well in counseling their patients with diabetes about the use of aspirin and, in the absence of contemporaneous national data, this may serve as a benchmark for other health care organizations. In addition, even though aspirin is readily available over the counter and rarely formally prescribed, our analysis reinforces the importance of counseling about aspirin use by providers (22). Furthermore, assuming the rates of aspirin use among veterans with diabetes in the

early 1990s was similar to the general adult population (20), the use of aspirin therapy by patients with diabetes appears to be increasing, with approximately two-thirds of the study population reporting taking aspirin on a daily basis.

On the other hand, more than one-quarter of the study sample did not report being counseled about aspirin use, suggesting a continuing need for more aggressive education about this important preventive measure. In particular, the study results indicate that both counseling and aspirin use are recognized as very important for patients with preexisting CVD, as found in other studies, and to some extent, those who have at least one classical CVD risk factor. However, there needs to be more emphasis on the importance of aspirin use by all adults with diabetes (who don't have contraindications to its use), due to their increased risk for cardiovascular-related complications and death as well as a heightened awareness by providers that simply talking with their patients about aspirin therapy can be a powerful intervention.

As demonstrated by simulation, increasing aspirin use could significantly reduce MIs and cardiovascular-related deaths among diabetic subjects. The number of MIs (and deaths) prevented depends in part on the amount of risk reduction achieved, for which there is a currently a rather wide range reported in the literature. Nonetheless, even when using fairly conservative estimates, it is clear that much morbidity could be prevented and many lives may be saved by encouraging the adoption of this inexpensive and effective therapy.

There are some limitations with this analysis that should be noted. First, these results are based on patient self-report and are therefore subject to the usual limitations of survey research, such as recall bias. However, because aspirin is inexpensive, readily available, and rarely formally prescribed, survey appears to be the most accurate way to obtain information about aspirin use. In addition, we expect that respondents would be most likely to not recall being counseled about aspirin therapy, and this would result in our actually underestimating the effect of counseling on aspirin use. Second, these results are based on the responses of individuals who are primarily receiving their health care services within one health care system and therefore may not be representative of the activities and practices taking place elsewhere. Third, the simulation results use cross-sectional data; therefore, the estimates are reflective only of the current population. Also, although there may be some differences in benefit based on whether aspirin is being used for secondary or primary prevention, the differential benefit among diabetic patients with and without CVD is currently unknown and therefore was not included as part of the simulation analysis.

In conclusion, this research suggests that the use of aspirin has been adopted by many VA clinicians and their patients with diabetes. Moreover, if the rates of aspirin therapy observed among patients with diabetes in this study reflects its use nationally, then great strides are being made in preventing cardiovascular morbidity and mortality. However, although most providers recognize the importance of aspirin for those patients with diabetes and known CVD, it is imperative that clinicians include counseling about aspirin therapy as a care priority for all of their patients with diabetes. Doing so will likely prevent a significant number of MIs and potential cardiovascular-related deaths.

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