Cardiovascular disease (CVD), including myocardial infarction and stroke, is the leading cause of morbidity and mortality in the US. A broad array of randomized trials have demonstrated the benefits of low doses of aspirin (75–325mg) for both the primary and secondary prevention of CVD. Most trials demonstrate a 15–40% reduction in cardiovascular events with chronic aspirin use. Aspirin is unequivocally recommended as a secondary prevention strategy in non-contraindicated patients with known CVD. As for primary prevention, the American Diabetic Association recommends regular aspirin for men and women with diabetes mellitus (DM) who are older than 40 years or have additional cardiovascular risk factors. In addition, aspirin is indicated for apparently healthy individuals without CVD or DM but otherwise with an increased cardiovascular risk, which is defined as a 3% or greater risk in five years by the US Preventive Services Task Force or a 10% or greater risk in 10 years by the American Heart Association. However, the latest results from the Women’s Health Study suggest that careful ascertainment of the absolute benefit and risk on a case-by-case basis is essential to deciding on the use of aspirin therapy in men and, even more so, in women who have shown no clinical manifestations of CVD or diabetes.

Despite the proven benefits of aspirin therapy for reducing cardiovascular risk, aspirin use falls considerably short of recommendations. National surveys of the prescribing of cardiac medications found that aspirin use in visits by patients with coronary heart disease (CHD) increased significantly from 5% in 1980 to 32% in 1995, but then remained unchanged or even declined in subsequent years. The Third National Health and Nutrition Examination Survey (also called NHANES III) data showed that among patients with DM, only 37% of those with CHD and 13% of those with risk factors for CHD were regular aspirin users. While aspirin underutilization is also present in other countries, some evidence suggests that the problem is more prominent in the US. For instance, outpatient use of aspirin for secondary prevention ranged from approximately 40–90% in many European countries, in comparison to approximately 24% in the US. Greater aspirin use is associated with middle to older age (55–75 years old), male gender, diagnosis of hyperlipidemia, smoking, having medical insurance, revascularization or coronary angioplasty, and use of other medications.

Despite ample evidence of aspirin underutilization, research on national trends of outpatient aspirin use by CVD risk category is limited. Using two companion national datasets on ambulatory care in the US, our study tracked changes from 1993–2003 in reported aspirin use by CVD risk status, distinguishing between secondary and primary prevention. Multiple reasons may account for the widespread aspirin underutilization, one being lower priority assigned to aspirin therapy compared to other medications available for CVD risk reduction. To explore this possibility, we examined the priority given to aspirin in comparison to statins. We also examined patient and physician contributors to shortfalls in aspirin use.

**Methods**

The Stanford University Institutional Review Board determined that this study was exempt from “human subjects” requirements.

**Data Sources**

We obtained annual data 1993–2003 from the National Ambulatory Medical Care Survey (NAMCS) and the Outpatient Department component of the National Hospital Ambulatory Medical Care Survey (NHAMCS). The National Center for Health Statistics provides complete descriptions of both surveys and yearly data at http://www.cdc.gov/nchs/about/major/ahcd/ahcd1.htm These surveys, particularly NAMCS, have been validated against other data sources and utilized in past research on aspirin use for CVD risk reduction.

In brief, NAMCS captured healthcare services provided by private office-based physicians, while NHAMCS captured services offered at hospital outpatient departments. The sampling universe for NAMCS was
office-based, patient-care physicians in 15 specialty strata from the master files maintained by the American Medical Association and American Osteopathic Association. The sampling frame for NHAMCS included short-stay (shorter than 30 days) hospitals, or general-specialty (medical or surgical) or children’s general hospitals. Both surveys utilized multistage probability sampling procedures, which enable researchers to generate nationally representative estimates. Between 1993 and 2003, annual participation rates among physicians selected for NAMCS averaged 70%, while the participation rate of selected hospitals with outpatient departments was 90% in NHAMCS. Standard encounter forms were completed for a systematic random sample of patient visits during randomly assigned reporting periods. Yearly encounter forms varied slightly between NAMCS and NHAMCS and were revised every two years. We based this study on variables common to NAMCS and NHAMCS over time, including patient demographics, visit characteristics, reasons for visit (up to three), diagnoses (up to three), and new and continuing medications (up to five in 1993–1994, six in 1995–2002, and eight in 2003). Item non-response rates were mostly 5% or less in both surveys for all years.

Patients

**CHD Risk Categorization**

We defined four mutually exclusive categories of CVD risk based on the presence of specific diagnoses and risk factors. The presence of CHD, myocardial infarction, stroke or transient ischemic attack, peripheral vascular disease, claudication, or angina defined high CVD risk. In the absence of known CVD, visits by patients with DM who were older than 40 years or had additional risk factors (i.e. hypertension, smoking, dyslipidemia, and/or albuminuria) were defined as intermediate risk. The remaining patients were defined in a second intermediate risk category if they met either of the following criteria:

1. two or more major CVD risk factors (i.e. hypertension, smoking, and/or dyslipidemia) among men age 45–54 and women age 55–64; or
2. one or more risk factors among men older than 55 and women older than 65.

Patient visits ineligible for any of the former three categories were considered low risk. The absence of data elements such as family history of premature CHD or levels of high-density lipoprotein cholesterol precluded more accurate risk stratification according to the Framingham risk scoring.

**Patient Visit Characteristics**

We included the following patient visit characteristics: patient age, gender, race/ethnicity, healthcare insurance status, visit status, US census region, metropolitan area status, and physician specialty. Healthcare insurance was classified as private/commercial insurance, public insurance (i.e. Medicare and Medicaid), and other insurance (e.g. workers’ compensation and self-pay). Visit status distinguished first-time visits from return visits to a physician’s practice. Physician specialty was available only from NAMCS, which contributed more than 90% of the total weighted visits for each of the study years. We categorized physician specialties into cardiology, internal medicine, general and family practice, and a category encompassing all others.

**Measures**

Our primary analytic goals were to assess the probability of aspirin use by CVD risk and its relationship to patient visit characteristics. The probability of aspirin use was defined as the proportion of non-contraindicated patient visits in which aspirin or a therapeutically equivalent medication was reported as a new or continuing medication. Measuring the probability of use by CVD risk provided a means to estimate the gaps between current practice and evidence-based medicine regarding aspirin therapy. We defined aspirin therapy as reported use of generic or brand name forms of aspirin, clopidogrel, ticlopidine, or non-narcotic combination analgesics containing aspirin. The number of patient visits in which clopidogrel or ticlopidine was reported is too small to allow their use over time being tracked separately. Oral anticoagulants are not considered aspirin equivalents and are not recommended for the primary or secondary prevention of CVD in a vast majority of patients. Moreover, judging the appropriateness of using or avoiding aspirin for someone who is already on anticoagulant therapy required more clinical detail than our data sources can provide. Therefore, we felt it was appropriate to exclude patients on anticoagulant therapy. We were unable to assess patients’ use of over-the-counter aspirin if it was not reported on the encounter form. We excluded visits by patients younger than 21 years and those with bleeding tendency, gastrointestinal bleeding, anticoagulant therapy, or clinically active hepatic disease.

**Statistical Analyses**

Statistical analyses accounting for sampling weights and the complex sample designs of NAMCS and NHAMCS were performed using SAS for Windows software (SAS Institute, Cary, North Carolina, US) and SAS-callable SUDAAN software (RTI, Research Triangle Park, North
Underutilization of Aspirin in US Ambulatory Care for the Prevention of CVD

The unit of analysis in both surveys was the patient visit. Comparisons of NAMCS and NHAMCS suggested limited differences on key outcome measures. We therefore combined the two surveys to obtain a wider range of outpatient settings and a broader socioeconomic spectrum of patients seeking ambulatory care. Also, to minimize random fluctuations between years, we analyzed data in two-year groupings, except for 2003, for depicting temporal trends in aspirin use. The SAS SURVEYMEANS procedure was performed, which generated national estimates of the probability of aspirin use by CVD risk and corresponding 99% confidence intervals (CIs). We chose to report 99% CIs in following National Center for Health Statistics analytical guidelines and also as a conservative measure to avoid over-interpretation of the findings. Chi-square tests were performed using PROC CROSSTAB in SUDAAN to examine the association of aspirin use with each patient visit characteristic based on combined 1993–2003 NAMCS and NHAMCS data.

The independent effect of each patient visit characteristic on aspirin use after controlling for all other characteristics was assessed with a multivariate logistic regression model using PROC RLOGISTIC in SUDAAN. The model produced adjusted odds ratios and 99% CIs.

**Results**

The volume of outpatient visits by patients identified as being at elevated risk for future CVD events, particularly those at intermediate risk, rose markedly over the study period. The number of high-risk patient visits increased by 33% from 44.2 (99% CI, 41.0–47.4) million in 1993–1994 to 58.8 (54.0–63.6) million in 2001–2002. The number of intermediate-risk patient visits in which a diagnosis of DM was noted more than doubled, from 40.5 (37.1–43.9) million to 83.3 (77.4–89.3) million, and for those with multiple risk factors the increase was 57%, from 70.2 (65.7–74.7) million to 110.4 (102.8–118.0) million. The number of low-risk patient visits rose by 23%, from 975.4 (962.6–988.2) million to 1.20 (1.18–1.22) billion. In 2003, the number of patient visits in each of the four CVD risk categories was 29.5 (22.5–36.6) million for high-risk patients, 39.9 (32.0–47.9) million for intermediate-risk patients, 55.8 (45.5–66.2) million for those with multiple risk factors, and 626.9 (537.1–716.7) million for those with low risk.

Trends over time showed improved, though still substantially suboptimal, aspirin use in the high and intermediate risk categories, with sustained improvements seen beginning in 1999–2000. The probability of aspirin use among patient visits in 1993–1994 was 21.7% (18.8–24.6%) for the high-risk category, 3.5% (2.0–5.0%) for the diabetic, intermediate-risk category, and 3.6% (2.6–4.6%) for the other intermediate-risk category. The probabilities for these three risk categories fluctuated somewhat but remained essentially unchanged through 1999–2000. Increases were observed in 2001–2002 and persisted in 2003. The probability of aspirin use in 2003 was 32.8% (25.2–40.4%) for the high-risk category, 11.7% (7.8–15.7%) for the diabetic, intermediate-risk category, and 16.3% (11.4–21.2%) for the other intermediate-risk category. Aspirin use remained 1%–3% among low-risk patient visits.

To explore the relative priority assigned to aspirin and statins, we examined trends in the co-prescribing of the medications. For this series of analyses, the number of visits by patients with DM was relatively small and were therefore grouped with those with known CVD to compose the high-risk category. Both aspirin and statins were used more frequently when the other therapy was present; however, improvements over time were more evident for statin use among aspirin-treated patient visits than for aspirin use among statin-treated patients. Specifically, the proportion of visits by high-risk patients on aspirin while a statin was used declined modestly from 36.5% (24.9–48.2%) in 1993–1994 to 25.6% (20.1–31.1%) in 1999–2000 but then rebounded to 43.9% (35.1–52.8%) in 2003. In contrast, statin use among visits by high-risk patients on aspirin grew successively from 11.6% (7.4–15.7%) to 54.3% (45.7–63.0%). Of visits by intermediate-risk patients, the probability of aspirin use when on a statin increased from 6.0% (1.4–10.6%) in 1993–1994 to 33.8% (21.5–46.0%) in 2003, while the probability of statin use when on aspirin rose from 8.8% (2.2–15.3%) to 48.1% (35.2–61.0%).

The association of greater aspirin use with higher CVD risk was confirmed by multivariate logistic regression. After adjusting for patient visit characteristics and the number of medications reported, aspirin use was over four times as likely among visits by high-risk patients and approximately two times as likely among visits by patients with multiple risk factors as it was among low-risk patient visits. The odds ratio was marginally significant for the diabetic, intermediate-risk category. The significance of increases in aspirin use over time did not sustain in the multivariate logistic regression.