Psychoactive Drugs and the Risk of Injurious Motor Vehicle Crashes in Elderly Drivers

Wayne A. Ray, Randy L. Fought, and Michael D. Decker

To determine whether commonly used psychoactive drugs increase the risk of involvement in motor vehicle crashes for drivers ≥65 years of age, the authors conducted a retrospective cohort study. Data were obtained from computerized files from the Tennessee Medicaid program, driver's license files, and police reports of injurious crashes. Cohort members were Medicaid enrollees 65–84 years of age who had a valid driver's license during the study period 1984–1988 and who met other criteria designed to exclude persons unlikely to be drivers and to ensure availability of necessary study data. There were 16,262 persons in the study cohort with 38,701 person-years of follow-up and involvement in 495 injurious crashes. For four groups of psychoactive drugs (benzodiazepines, cyclic antidepressants, oral opioid analgesics, and antihistamines), the risk of crash involvement was calculated with Poisson regression models that controlled for demographic characteristics and use of medical care as an indicator of health status. The relative risk of injurious crash involvement for current users of any psychoactive drug was 1.5 (95% confidence interval (CI) 1.2–1.9). This increased risk was confined to benzodiazepines (relative risk = 1.5; 95% CI 1.2–1.9) and cyclic antidepressants (relative risk = 2.2; 95% CI 1.3–3.5). For these drugs, the relative risk increased with dose and was substantial for high doses: 2.4 (95% CI 1.3–4.4) for ≥20 mg of diazepam and 5.5 (95% CI 2.6–11.6) for ≥125 mg of amitriptyline. Analysis of data for the crash-involved drivers suggested that these findings were not due to confounding by alcohol use or driving frequency. Am J Epidemiol 1992;136:873–83.

For older persons in the United States today, continuing to drive is frequently essential to maintaining independence. In 1986, 58 percent of persons 65 years of age or older held driver's licenses, and many continue to drive into the ninth decade of life (1). However, the ability of the older driver to safely operate a motor vehicle may be adversely affected by the decreases in sensory, cognitive, and motor function and the increase in prevalence of illness that accompany aging (2, 3). For drivers 65 years of age or older, the rate of involvement in motor vehicle crashes per mile driven increases exponentially with age (4). Thus, there has been considerable recent interest (3–7) in elucidating the factors that influence the safety of older drivers. These data are essential to development of policies regulating testing and relicensing of the older driver, to physician counselling of older patients, and to implementation of preventive measures.
The use of psychoactive drugs may interfere with the older driver’s ability to safely operate a motor vehicle (3, 8-10). These medications are known to produce general psychomotor impairment in persons 65 years of age or older (11-16). For persons less than 65 years of age, there is an extensive body of experimental research that shows that benzodiazepines produce a dose-related impairment in performance on tests of driving-related psychomotor skills, including reaction time (17), stimulus detection (18), hand-eye coordination (19), and simulated driving (20-22). O’Hanlon et al. (23) have demonstrated that a single dose of 10 mg of diazepam given to healthy young males impaired road-tracking ability during uninterrupted high-speed highway driving. Similar adverse effects on performance in the laboratory or on the road have been demonstrated for other benzodiazepines (24-26), barbiturates (26), cyclic antidepressants (27), opioid analgesics (10), and sedating antihistamines (28). There are limited epidemiologic data that suggest that psychoactive drugs increase risk of involvement in crashes (29-31), although this finding is still controversial (32).

However, although psychoactive drugs are among the most frequently used medications in elderly populations (33), little is known concerning their effects on driving performance or on risk of motor vehicle crashes for drivers 65 years of age or older. To address this latter question, we performed a retrospective cohort study of the risk of involvement in injurious motor vehicle crashes in a defined population of older licensed drivers.

MATERIALS AND METHODS

Sources of data

Study design. The study subjects were persons 65–84 years of age who were enrolled in Tennessee Medicaid at some time during the study period 1984–1988 who had a valid driver’s license and met several other entry criteria designed to exclude persons unlikely to be regular drivers and to ensure that necessary study data were available. The study was conducted among elderly Medicaid enrollees because the Medicaid program kept computerized records of prescriptions filled at the pharmacy, providing a detailed and unbiased indicator of the use of psychoactive drugs. However, because the majority of enrollees under 65 years of age consist of children, young women, and the severely disabled (34), this data source is less suitable for studying the effects of psychoactive drugs in younger drivers. Computerized files maintained by the Tennessee Department of Safety were used to identify Medicaid enrollees with driver’s licenses and their involvement in motor vehicle crashes.

Medicaid files. The enrollment file identified persons who were eligible to receive Medicaid benefits. It included each enrollee’s Medicaid number, name, address, social security number, date of birth, dates and basis of Medicaid enrollment, sex, race, county of residence, and date of death (34). The pharmacy file contained a record of each prescription for drugs filled for outpatients and reimbursed by Medicaid. Each record identified the patient’s Medicaid number, the date the prescription was filled, the drug name and quantity dispensed, and the anticipated duration of the prescription (days of supply). Other files contained information on inpatient hospital admissions, emergency room visits, and nursing home stays. The Medicaid data elements used for this study have a high level of accuracy and completeness (35), because they are required for provider payments and thus are subject to periodic audits.

Driving files. The driver’s license file maintained a cumulative record of persons issued a Tennessee driver’s license. The file included each person’s license number, name, address, social security number, sex, date of birth, type of license, most recent renewal (or issue) date, previous renewal date, and termination (expiration, revocation, suspension, or cancellation) date. This file was linked with the Medicaid enrollment file to identify enrollees who held valid driver’s licenses. The Tennessee motor vehicle crash file contained records for crashes reported to the Tennessee Department of Safety. Re-
ports are required by law for crashes that involve injury or property damages of $200 or more. Each record identified the date and time of the crash and the number of involved vehicles. For each of these vehicles, the record further identified the license number of the driver, injury to any occupant or pedestrian, the estimated amount of property damage, an estimate of the speed at which the vehicle was travelling, and whether or not there was evidence of driver use of alcohol (police reports and, for 1987–1988, results of blood alcohol tests). In 1986, the rate of involvement in any reported crash for Tennessee-licensed drivers 65–84 years of age was 38 per 1,000, which was similar to the rate of 40 per 1,000 for all United States-licensed drivers in this age group estimated from the National Accident Sampling System (1).

Study cohort

The cohort inclusion criteria were age 65–84 years, Medicaid enrollment for \( \geq 365 \) days, and holding a valid driver’s license. The exclusion criteria were residence in a nursing home, blindness, medically needy Medicaid enrollment (persons who met all criteria for Medicaid eligibility except income, which, after deduction of allowed medical expenses, fell below the income standard (36)), and treatment consistent with dementia (defined as receipt of more than a single prescription for an antipsychotic drug or a dihydrogenated ergot alkaloid). Although persons qualifying for the study at any time between 1984 and 1988 were included in the cohort, the analysis was confined to that person-time for which all entry criteria were met. Thus, for each person in the cohort, study person-time began on January 1, 1984, or the subsequent first date that all study entry criteria were met. Person-time ended on the earliest of these dates: December 31, 1988, date of first crash in the study, date of death, or first date when any of the study entry criteria ceased to be met. The person-time during and shortly after hospital stays (date of admission through 30 days following discharge) was excluded because records of medications received in the hospital were not present in the Medicaid pharmacy files.

Drug exposure

We studied four classes of psychoactive drugs: benzodiazepines, cyclic antidepressants, oral opioid analgesics, and antihistamines. With the exception of the benzodiazepine hypnotics flurazepam and triazolam, the Medicaid formulary included all drugs in these classes that were commonly used during the study years. We considered other types of drugs with central nervous system effects, including other sedatives, monoamine oxidase inhibitors, lithium, centrally acting skeletal muscle relaxants, injectable opioid analgesics, opioid preparations for treatment of cough or diarrhea, and phenothiazine antiemetics. However, the aggregate rate of use for all of these drugs was only 1.5 percent; therefore, they were not considered in the analysis.

Each person-day of follow-up was classified according to potential use of the study drugs. Current use was defined as the period from the day following the dispensation of the prescription through the day following the last scheduled day of supply. Persons in the cohort were thought to be most likely to be exposed to drug effects during this period. Indeterminate use consisted of the day the prescription was dispensed and the 60 days following the end of current use. Because this period was likely to include days of both drug use and nonuse, it was analyzed separately to reduce misclassification. Former use included the remainder of the 365 days following the end of current use. This period consisted of person-time with a recent history of study drug use, but low likelihood of current use. Nonuse encompassed all other person-time.

Current-use person-time was further classified by dose and duration. For each individual drug, the dose was calculated from the most recently filled prescription for that drug by dividing the total quantity of drug received by the days of supply. With the use of standard conversion factors for the drug

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class (37), the dose was then converted into equivalent units. To obtain the total dose for a drug class, we summed the doses for all individual drugs in the class. Duration was defined as the number of days of uninterrupted current use.

**Injurious crashes**

The study outcome was involvement of a cohort member as a driver in a crash reported to the Tennessee Department of Safety in which someone was injured. We did not study crashes that only resulted in property damage because these may be substantially underreported. To check the completeness of injury reporting, we identified those crashes involving a cohort driver who had an emergency room visit, hospitalization, or death within 1 day following the crash. Of these, 86 percent had an injury report in the crash file.

**Analysis**

Unadjusted rates of crash involvement were calculated by dividing the number of crashes by person-years (person-days/365) of study person-time. Confidence intervals were calculated assuming a Poisson distribution for the number of crashes. The rate of crashes by psychoactive drug use, adjusted for several potential confounders, was estimated from Poisson regression models (38) using the GLIM program (39). The initial model included terms for psychoactive drug use, demographic characteristics, length and basis of Medicaid enrollment, and use of medical care in the previous 365 days. The medical care variables, which provided several indirect measures of health status, consisted of ten terms: one for number of emergency room visits, one for prior hospitalization, and eight for use of nonpsychoactive drugs (antihypertensives, other cardiovascular drugs, hypoglycemic agents, bronchodilators, antiulcer drugs, antimicrobials, nonsteroidal antiinflammatory drugs, and other drugs). This model was simplified through backward elimination to one that included terms for the psychoactive drugs, sex, race, residence in an urban county (defined as a county with a city of 100,000 or larger), age, and calendar year. The estimates of psychoactive drug effects from these two models did not differ materially.

For each category of psychoactive drug use, adjusted rates of crash involvement were calculated by the method of marginal prediction (40), using the regression coefficients from the Poisson model. Relative risk was estimated directly as the antilogarithm of the regression coefficients. The reference exposure category was that of nonuse of any of the study drugs. The test for dose-response trend was performed by calculating for current users the orthogonal linear polynomial contrast of the regression coefficients and its estimated variance (41). Statistical significance was defined as $p$ (two sided) $\leq 0.05$.

To assess whether alcohol use was a confounder, we grouped cohort drivers involved in an injurious crash by psychoactive drug use on the date of the crash. We then calculated the proportions of reported alcohol use in each of these groups of drivers. If alcohol were a confounder, then these proportions would differ (34).

We performed a case-crossover analysis (42) to assess whether other unmeasured factors, such as driving practices, were confounders. This analysis, which was restricted to drivers involved in injurious crashes (cases) who had periods of both use and nonuse of psychoactive drugs, is appropriate for episodic exposures where risk is increased only during periods of exposure. It controls for confounding by subject characteristics that do not change during periods of exposure (42). Each case is considered as a separate stratum. Under the null hypothesis, the probability that the case was exposed at the time of the crash depends upon the ratio of total exposed to total unexposed person-time for that case. Thus, a summary (over all strata) Mantel-Haenszel estimator (43) of the rate ratio (and the estimated variance of its logarithm) can be calculated to estimate the relative risk during periods of exposure.
TABLE 1. Unadjusted rate of involvement in injurious crashes, by demographic characteristics: Tennessee Medicaid crash study, 1984–1988

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Person-years</th>
<th>No. of crashes</th>
<th>Rate per 1,000</th>
<th>95% CI*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire cohort</td>
<td>38,701</td>
<td>495</td>
<td>12.8</td>
<td>11.7–13.9</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>21,403</td>
<td>320</td>
<td>15.0</td>
<td>13.3–16.6</td>
</tr>
<tr>
<td>Female</td>
<td>17,298</td>
<td>175</td>
<td>10.1</td>
<td>8.6–11.6</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>29,408</td>
<td>348</td>
<td>11.8</td>
<td>10.6–13.0</td>
</tr>
<tr>
<td>Black</td>
<td>9,293</td>
<td>147</td>
<td>15.8</td>
<td>13.2–18.4</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>30,649</td>
<td>135</td>
<td>16.8</td>
<td>14.0–19.6</td>
</tr>
<tr>
<td>Nonurban</td>
<td></td>
<td>360</td>
<td>11.7</td>
<td>10.5–12.9</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;75 years</td>
<td>24,559</td>
<td>319</td>
<td>13.0</td>
<td>11.6–14.4</td>
</tr>
<tr>
<td>≥75 years</td>
<td>14,142</td>
<td>176</td>
<td>12.4</td>
<td>10.6–14.2</td>
</tr>
<tr>
<td>Years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1984–1985</td>
<td>15,139</td>
<td>197</td>
<td>13.0</td>
<td>11.2–14.8</td>
</tr>
</tbody>
</table>

* CI, confidence interval.

RESULTS

There were 16,262 persons in the study cohort, who had 38,701 person-years of follow-up. These persons were involved in 495 injurious crashes, a rate of 12.8 per 1,000 person-years (table 1), which was slightly higher than that of 10.6 per 1,000 for all driver’s license holders of comparable age in Tennessee. In the cohort, the incidence of crashes (table 1) was higher in men, nonwhites, and persons living in urban counties. The crashes (table 2) most commonly occurred between 6 a.m. and 7 p.m., were at speeds of less than 45 mph (72 km/hour), involved more than one vehicle, and caused property damage of more than $500.

For current users of psychoactive drugs, the relative risk of involvement in injurious crashes was significantly increased to 1.5 (95 percent confidence interval (CI) 1.2–1.9) (table 3). In contrast, the relative risk for former users was 1.1 (95 percent CI 0.8–1.9), which was not significantly different from 1. The increased risk among current users of psychoactive drugs was due to increased relative risks of 1.5 (95 percent CI 1.1–2.0) for current users of benzodiazepines, 2.2 (95 percent CI 1.3–3.5) for cyclic antidepressants, and 2.1 (95 percent CI 1.1–4.2) for concurrent users of both types of drugs. However, the relative risk for current users of only antihistamines or opioid analgesics was 1.1 (95 percent CI 0.7–1.8). These two classes of drugs were analyzed together because the relative risks for each were similar (relative risk = 1.2 (95 percent CI 0.6–2.4) for current antihistamine use; relative risk = 1.1 (95 percent CI 0.5–2.4) for current opioid analgesic use). There were no dose effects for these drugs and no modification of the effect of other psychoactive drugs.

For current users of benzodiazepines or cyclic antidepressants, the risk of involvement in injurious crashes increased with

<table>
<thead>
<tr>
<th>Psychoactive drug use</th>
<th>Person-years</th>
<th>No. of crashes</th>
<th>Rate* per 1,000</th>
<th>Relative risk</th>
<th>95% Cl†</th>
</tr>
</thead>
<tbody>
<tr>
<td>None in 365 days</td>
<td>21,578</td>
<td>254</td>
<td>11.3</td>
<td>1.0</td>
<td>Reference</td>
</tr>
<tr>
<td>Former use</td>
<td>6,600</td>
<td>77</td>
<td>12.0</td>
<td>1.1</td>
<td>0.8-1.4</td>
</tr>
<tr>
<td>Indeterminate use</td>
<td>4,993</td>
<td>76</td>
<td>16.2</td>
<td>1.4</td>
<td>1.1-1.9</td>
</tr>
<tr>
<td>Current use: any psychoactive drug</td>
<td>5,530</td>
<td>88</td>
<td>17.2</td>
<td>1.5</td>
<td>1.2-1.9</td>
</tr>
<tr>
<td>Benzodiazepine or cyclic antidepressant</td>
<td>4,215</td>
<td>72</td>
<td>18.8</td>
<td>1.7</td>
<td>1.3-2.2</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>2,978</td>
<td>46</td>
<td>16.7</td>
<td>1.5</td>
<td>1.1-2.0</td>
</tr>
<tr>
<td>Cyclic antidepressant</td>
<td>844</td>
<td>18</td>
<td>24.4</td>
<td>2.2</td>
<td>1.3-3.5</td>
</tr>
<tr>
<td>Both benzodiazepine and cyclic antidepressant</td>
<td>393</td>
<td>8</td>
<td>23.9</td>
<td>2.1</td>
<td>1.1-4.2</td>
</tr>
<tr>
<td>Antihistamine or opioid analgesic only</td>
<td>1,315</td>
<td>16</td>
<td>12.5</td>
<td>1.1</td>
<td>0.7-1.8</td>
</tr>
</tbody>
</table>

* Rates adjusted for age, sex, race, county of residence, and calendar year with Poisson regression, using the method of marginal prediction.
† Cl, confidence interval.

Increasing dose. For benzodiazepines (figure 1), the relative risk increased from 1.1 (95 percent CI 0.5–2.2) for the equivalent of 4 mg of diazepam or less to 2.4 (95 percent CI 1.3–4.4) for 20 mg or more (p = 0.05, test for linear trend). For cyclic antidepressants (figure 2), the relative risk increased from 0.8 (95 percent CI 0.3–2.7) for the equivalent of 25 mg of amitriptyline or less to 5.5 (95 percent CI 2.6–11.6) for 125 mg or more (p = 0.01, test for linear trend).
Concurrent use of two different benzodiazepines or two different cyclic antidepressants was associated with a pronounced increase in risk of involvement in an injurious crash (figure 3). For benzodiazepines, the relative risk increased from 1.5 (95 percent CI 1.1–2.0) for current use of a single benzodiazepine to 4.8 (95 percent CI 1.6–14.5) for use of more than one (p = 0.05). For cyclic antidepressants, the risk increased from 2.0 (95 percent CI 1.3–3.1) for current use of a single drug to 9.8 (95 percent CI 2.4–39.5) for use of more than one (p = 0.03).

The risk of crash involvement did not vary significantly with duration of benzodiazepine or cyclic antidepressant use. For benzodiazepines, the duration of drug use was ≤ 30 days for 13 percent of current use, 31–90 days for 9 percent of use, and > 90 days for 78 percent; the respective relative risks were 1.3 (95 percent CI 0.6–2.9), 1.6 (95 percent CI 0.7–3.8), and 1.6 (95 percent CI 1.1–2.2). For cyclic antidepressants, the duration of drug use was ≤ 30 days for 16 percent of current use, 31–90 days for 10 percent of use, and > 90 days for 74 percent; the respective relative risks were 1.6 (95 percent CI 0.5–4.8), 2.5 (95 percent CI 0.8–7.6), and 2.2 (95 percent CI 1.4–3.5). There were no statistically significant differences in risk of crash involvement between the individual drugs. Diazepam accounted for 38 percent of current benzodiazepine use, lorazepam for 29 percent, chlordiazepoxide for 16 percent, clorazepate for 9 percent, and other drugs for 8 percent. Amitriptyline accounted for 50 percent of current cyclic antidepressant use, doxepin for 24 percent, trazodone for 9 percent, imipramine for 6 percent, and other drugs for 11 percent.

The increased risk of injurious crash involvement among current users of cyclic antidepressants or benzodiazepines was present in subgroups of the cohort defined by sex, race, county of residence, age, and calendar year. The risk was increased for various types of crashes (table 4). There were nonsignificant trends of increased risk for crashes that occurred in the morning, involved speeds ≥45 mph, or involved only a single vehicle. For cohort drivers involved in an injurious crash, the proportion with reported alcohol use was 4.6 percent for both current users and nonusers of psychoactive drugs.

To assess whether other driver characteristics that may be associated with crash risk and psychoactive drug use were confounders, we performed a case-crossover analysis. The estimates of relative risk of involvement in injurious crashes from this analysis were 2.2 (95 percent CI 1.0–4.9) for current use of any psychoactive drug, 1.8 (95 percent CI 1.2–2.9) for indeterminate use, and 0.8 (95 percent CI 0.5–1.1) for former use, which were similar to those from the primary analysis.

**DISCUSSION**

In the study cohort of 16,262 elderly driver's license holders, 14 percent of the 38,701 person-years of follow-up consisted of pe-
TABLE 4. Relative risk of involvement in injurious crashes for current users of benzodiazepines and cyclic antidepressants, by characteristics of the crash: Tennessee Medicaid crash study, 1984-1988

<table>
<thead>
<tr>
<th></th>
<th>Only benzodiazepine</th>
<th>Only cyclic antidepressant</th>
<th>Both</th>
<th>Either</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Relative risk</td>
<td>95% CI</td>
<td>Relative risk</td>
<td>95% CI</td>
</tr>
<tr>
<td>Time of day</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 a.m.-12 p.m.</td>
<td>2.0</td>
<td>1.3-3.2</td>
<td>2.1</td>
<td>1.0-4.6</td>
</tr>
<tr>
<td>1 p.m.-7 p.m.</td>
<td>1.1</td>
<td>0.7-1.8</td>
<td>2.2</td>
<td>1.2-4.3</td>
</tr>
<tr>
<td>8 p.m.-5 a.m.</td>
<td>1.4</td>
<td>0.4-4.7</td>
<td>1.7</td>
<td>0.2-12.7</td>
</tr>
<tr>
<td>Speed ≥ 45 mph‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.3</td>
<td>0.9-2.0</td>
<td>1.8</td>
<td>0.9-3.5</td>
</tr>
<tr>
<td>Yes</td>
<td>1.7</td>
<td>1.1-2.8</td>
<td>2.7</td>
<td>1.4-5.5</td>
</tr>
<tr>
<td>Involved single vehicle</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.4</td>
<td>1.0-2.0</td>
<td>1.9</td>
<td>1.1-3.2</td>
</tr>
<tr>
<td>Yes</td>
<td>2.0</td>
<td>0.9-4.7</td>
<td>4.3</td>
<td>1.5-12.5</td>
</tr>
<tr>
<td>Property damage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; $500</td>
<td>1.3</td>
<td>0.6-2.6</td>
<td>2.2</td>
<td>0.8-6.0</td>
</tr>
<tr>
<td></td>
<td>1.5</td>
<td>1.1-2.2</td>
<td>2.1</td>
<td>1.2-3.7</td>
</tr>
</tbody>
</table>

* CI, confidence interval.
† No current drug users in this subgroup were involved in crashes.
‡ Metric conversion: 72 km/hour.

riods of current psychoactive drug use. This exposure was associated with a 50 percent increased rate of involvement in injurious motor vehicle crashes. The increased risk was confined to current use of benzodiazepines (relative risk = 1.5) and cyclic antidepressants (relative risk = 2.2), where there was a pronounced increase in risk with increasing dose of drug. If this association is causal, then our data suggest that, of the 217,000 injurious crashes that occur each year among elderly drivers (1), at least 16,000 are attributable to psychoactive drug use.

When cohort members were grouped by age, sex, race, residence, and indirect measures of health status, the increased risk of crash involvement among users of psychoactive drugs was present within all subgroups, and there was no statistical evidence that the magnitude of the effect differed between subgroups. Similarly, psychoactive drug use increased the risk for all types of crashes, and the risks for users of individual benzodiazepines and cyclic antidepressants did not differ. The consistency of this effect across demographic and health status subgroups suggests that the study findings may be generalizable beyond the population of Medicaid enrollees, who comprise a small proportion of all elderly drivers. However, other factors such as income that are associated with Medicaid enrollment (44) were not studied. Furthermore, even though our study encompassed nearly 500 crashes, the power to detect differences in subgroup analyses was limited. Additional studies in other populations and of how risk is affected by specific subject, crash, and drug characteristics are needed.

Drug use in the cohort was ascertained from computerized records of prescriptions filled at the pharmacy. These data provided sufficient detail to classify each person-day of follow-up with respect to drug exposure and were not subject to the intentional or unintentional underreporting that is a major problem when self-reports of psychoactive drug use are obtained from persons involved in crashes (30). However, noncompliance or use of drugs from other sources would reduce the accuracy of this measure of drug exposure. Because the resulting misclassification would most probably be nondifferential, it would introduce a conservative bias (45), causing our estimates to underestimate the true risk associated with psychoactive drug use. Thus, exposure misclassification is unlikely to explain the increased crash risk among current users of cyclic antidepres-
sants and benzodiazepines. However, our finding of no significantly increased risk for sedating antihistamines should be interpreted cautiously, as these drugs are widely available in over-the-counter products.

We did not have information on whether persons avoided driving after taking drugs, as is usually recommended for sedating medications. Because the individual benzodiazepines and cyclic antidepressants that accounted for most of the use of these drugs had elimination half-lives ranging from 14 hours (lorazepam (46)) to more than 72 hours (diazepam (47)), regular users could not avoid exposure to psychomotor effects. However, refraining from driving while medicated may partially explain the lack of increased risk for opioid analgesics and antihistamines, where the compounds used most commonly by cohort members had half-lives of 3–8 hours (37).

Two thirds of benzodiazepine use in this population were of drugs such as diazepam, chlordiazepoxide, and clorazepate that have prolonged elimination and persistent psychomotor effects in elderly patients (14, 47). Although the metabolism of lorazepam, which accounted for nearly all of the remaining benzodiazepine use, is little affected by aging, its half-life is 14 hours (46) and, thus, it may have residual sedative effects. Because of concerns with the safety of ultra-short half-life agents such as triazolam (48), the use of these long and intermediate half-life benzodiazepines may increase in elderly patients. It will be important to consider their potential effects on the risk of crash involvement and of other injuries (49).

Amitriptyline and doxepin were the most commonly prescribed cyclic antidepressants, which is consistent with national use patterns in the elderly (33). Among drugs in this class, these tertiary amine compounds have a relatively high incidence of sedative and anticholinergic effects (50) and have been shown to impair road-tracking ability during highway driving (27). Secondary amine compounds such as nortriptyline and desipramine currently are the preferred cyclic antidepressants for elderly patients (50). As the use of these drugs and of specific serotonin reuptake inhibitors with few sedative effects (51) increases in older drivers, further studies to evaluate their effects on driving safety are needed.

There were several potential confounders that were not controlled for directly in the primary analysis, including health status, alcohol use, driving frequency, and drug indication. Poor health could be associated with psychoactive drug use and predispose drivers to either increased risk of involvement in crashes or increased likelihood of sustaining an injury during a crash. However, control for surrogate measures of poor health in the multivariate analysis, including recent history of hospitalization or emergency room visits and use of prescribed medications, did not alter our findings. The lack of an association between former use of psychoactive drugs and crash involvement was further evidence that the association with current drug use did not result from confounding by chronic illness.

Alcohol use is a major risk factor for crashes in younger drivers (52). If our findings were due to confounding by alcohol use, then alcohol use among cohort drivers involved in injurious crashes would have been highest for those who were current users of psychoactive drugs (34). Our data that alcohol use was reported for 4.6 percent of crash involvements among both current users and nonusers of psychoactive drugs indicate that this factor was not a confounder. It is possible that alcohol was an effect modifier that potentiated or enhanced the effects of benzodiazepines and antidepressants (10). However, the very low proportion of crashes with reported alcohol use, which is consistent with behavioral risk factor surveys indicating that fewer than 4 percent of elderly drive after using alcohol (53), suggests that synergistic effects were of limited import.

We did not have information on how frequently cohort members drove. This would be a confounder only if current users of psychoactive drugs drove more frequently than other persons in the cohort. Evidence that such confounding did not occur is provided by the lack of increased risk among former users and by the similarity of results obtained from the case-crossover analysis,
which controls for confounding by subject characteristics that do not change during periods of drug use (42).

There is some evidence that the psychiatric disorders leading to the use of these drugs, particularly depression and dementia, may themselves increase the risk of crash involvement. Major depression is often associated with psychomotor retardation, including impaired information processing, learning, memory, and tracking skills (54). Dementia, in which concomitant depressive symptoms or agitation may lead to prescription of an antidepressant or a benzodiazepine, is associated with marked performance impairment and increased risk of crash involvement (55).

Because we did not have information on affect or cognition, we could not assess the extent to which confounding by indication contributed to the increased crash risk among users of cyclic antidepressants and benzodiazepines. There are two lines of indirect evidence that such confounding does not explain our findings. First, there are data suggesting that, among persons with psychiatric illnesses, drug use independently impairs performance. This has been reported in short-term placebo-controlled trials in persons with major depression (56), high levels of anxiety (57), or periodic insomnia (25). A recent observational study of drivers with dementia found that sedative drug use independently increased the risk of crash involvement (58). Second, the concordance of increased crash risk with periods of active drug treatment and higher doses is most consistent with a drug effect. However, further research to delineate the respective contributions of drug and disease should have high priority because current use of cyclic antidepressants or benzodiazepines, whether because of psychiatric illness or direct drug effects, identified elderly drivers with materially increased risk of crash involvement.

REFERENCES


