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Zolpidem Use and Motor Vehicle Collisions in Older Drivers

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Abstract

Background/Objectives—Prescription sleep medication use is most prevalent among women and older adults. Morning drowsiness and impaired coordination are side-effects of sleep medications that may affect driving safety. The association between current use of zolpidem-containing medications and motor vehicle collisions (MVCs) was evaluated among very old drivers.

Patients/Methods—Participants were current drivers aged ≥70 years residing in north-central Alabama, spoke English, had a valid driver's license, and drove within the past 3 months (n=2,000). Current zolpidem use was determined by pill-bottle review. Participant's 5-year MVC history was determined from Alabama Department of Public Safety accident reports. The 5-year MVC and at-fault MVC rate ratios (RR) were estimated comparing zolpidem users with nonusers in the overall sample and a-priori defined age and sex subgroups.

Results—The unadjusted RR (95%CI) of MVCs comparing zolpidem users with nonusers was attenuated after adjustment (1.46 [1.02-2.08] and 1.38 [0.97-1.98], respectively). Among women, the unadjusted and adjusted RRs (95%CI) were 1.65 (1.03-2.66) and 1.61 (1.00-2.60), respectively. The unadjusted and adjusted RRs (95%CI) among those aged ≥80 years were 2.24 (1.19-4.57) and 2.35 (1.20-4.61), respectively. There were no statistically significant associations among men or participants <80 years old. Similar patterns were present for at-fault MVCs.

Conclusion—Current zolpidem users, specifically women and individuals aged ≥80 years, had higher MVC rates than nonusers. Practitioners should consider behavioral treatment before initiating low doses of zolpidem and escalating it as needed to achieve restorative sleep in females and individuals aged ≥80 years to reduce the risk of zolpidem-associated MVCs.

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Keywords

geriatrics; elderly; motor vehicle collisions; zolpidem; Ambien

1. Introduction

Prescription sleep aids are a common treatment for sleep problems. The prevalence of prescription sleep medication use in the prior 30 days is approximately 4% in US adults and is highest among women and older adults.(Knutson *et al.* 2009, Chong *et al.* 2013, Bertisch *et al.* 2014) Since the 1990s, prescription zolpidem have become one of the most common medications for sleep problems, specifically insomnia.(Gustavsen *et al.* 2008) Although prescription sedative-hypnotics, such as zolpidem, are effective sleep-inducing agents, morning drowsiness and reduced coordination are important side effects that have been identified as hazards to safe driving.(Bocca *et al.* 2011, Anon 2013c)

There is a large body of evidence for the association between prescription zolpidem use and injuries, several of which have focused specifically on motor vehicle collisions (MVCs). (Gustavsen *et al.* 2008, Orriols *et al.* 2011, Yang *et al.* 2011, Chung *et al.* 2013, Lai *et al.* 2014) Gustavsen et. al. and Orriols et. al. reported a higher incidence of MVCs among individuals using prescription sedative-hypnotics, including zolpidem.(Gustavsen *et al.* 2008, Orriols *et al.* 2011) Additionally, a positive association between MVCs and prescription zolpidem use one day earlier was reported in a case-crossover study.(Yang *et al.* 2011) However, these studies failed to evaluate this association in drivers aged > 65 years and did not consider the potential role of sex as an effect modifier and account for driving behaviors. These are important limitations since the pharmacokinetics of zolpidem differs by age and sex (Greenblatt *et al.* 2013, Greenblatt *et al.* 2014) and the rate of MVC-related deaths per mile driven is highest in older adults. Additionally, few studies have considered whether individuals with versus without sleep problems may drive less frequently due to being sleepy, thereby reducing the opportunity for MVCs. Therefore, accounting for these limitations, the current study will evaluate the association between prescription zolpidem use and MVCs among drivers ≥ 70 years of age residing in Alabama.

2. Methods

2.1 Study Population and Design

The source population for the current cross-sectional study has been described previously. (Owsley *et al.* 2013) Briefly, the data were collected with the purpose of examining the prevalence of vision impairment and major ophthalmological conditions among drivers aged ≥ 70 years. Adults aged ≥ 70 years residing in north-central Alabama were enrolled between October 2008 and August 2011. Potential participants were randomly identified using a direct marketing company's list of contacts. There were 18,544 individuals verified to have a valid Alabama driver's license in the Alabama Department of Public Safety (AL DPS) database that were initially contacted by mail through an informative letter and 61% were successfully interviewed by telephone (n=11,267 of 18,544). Among the 30% of individuals that completed the telephone screener (n=3,412 of 11,267), 70% spoke English and reported

driving in the past 3 months (n=2,389 of 3,412). These individuals were subsequently invited to enroll and participate in a clinical exam visit consisting of two components: interviewer-administered questionnaires and a visual screening test. At the end of the recruitment period, 2,000 drivers were enrolled in the study. The racial distribution of enrolled participants was reflective of the area from which they were recruited. Eligible participants were on average 1 year younger than those who declined participation (77 and 78 years old, respectively) and more likely to be male. This study was approved by the University of Alabama at Birmingham Institutional Review Board in agreement with the Declaration of Helsinki.

2.2 Study Procedures

Information relevant to the current study is described herein. More detailed information is provided elsewhere.(Owsley *et al.* 2013) Participants self-reported their gender, race/ethnicity, marital status, retirement status, current occupation or occupation prior to retirement, alcohol consumption, smoking status, highest level of education completed and presence of physician diagnosed chronic medical conditions (e.g., diabetes, neurological complications, hearing impairment, osteoporosis, etc.) via questionnaires at the baseline clinical visit. Mental health status was assessed using the mini-mental state examination (MMSE). Annual mileage driven, destinations and frequency of driving during the prior 5 years were determined using The Driving Habits Questionnaire. Additionally, participants were instructed to bring current prescription and over-the-counter medications to the baseline clinical visit. The name and frequency, dosage and method of administration for each medication that participants brought with them were recorded.

Age was categorized into two age groups: 70 to 79 and ≥ 80 years. Race/ethnicity was defined as white and non-white. Level of education was categorized as less than high school or received a high school/general education diploma, 1 to 4 years of college and post-graduate degree. Marital status was defined as married or not married. Participants were considered to be not married if they were single, divorced, widowed or living separately but not legally divorced. Smoking status was defined as never, former and current. Former smokers were participants that indicated they smoked ≥ 100 cigarettes in their lifetime but do not currently smoke. Alcohol consumption was defined in categories as none, 0.5 to 6, and 7 or more drinks per week. The number of chronic medical comorbidities was calculated as the sum of physician diagnosed chronic medical conditions reported. The categories of none, 1 to 2, 3 to 4 and ≥ 5 chronic medical conditions were analyzed as a continuous variable. Normal and reduced cognitive status was defined by using standardized MMSE cut-point scores of > 23 and ≤ 23, respectively. The number of medications being taken was calculated by summing each medication recorded during the pill bottle review, minus zolpidem-containing medications (i.e., the exposure of interest), and analyzed as a continuous variable. Prescription sleep medication use, minus zolpidem-containing medications (i.e., the exposure of interest), and separately, over-the-counter sleep medication use were defined as “yes” and “no”, respectively. The number of falls within the past 12-months was categorized as none, 1 and ≥ 2 and analyzed as a continuous variable.

2.2.1 Exposure—Participants were dichotomized as current zolpidem users or nonusers. Current zolpidem users were participants with a recorded medication containing zolpidem (i.e., Ambien, Ambien CR, Intermezzo, Stilnox, Stilnoct, Sublinox, Hypnogen, Zolsana).

2.2.2 Outcome—The primary and secondary outcomes were MVCs, overall, and at-fault MVCs, respectively, during the prior 5 years. Each participant's five-year MVC history was determined from accident police reports provided by AL DPS dating from their enrollment date. Reports were limited to accidents involving participants as a driver. Information on the date of occurrence and at-fault status were recorded. This approach for determining at-fault status has been used in prior research whereby outstanding inter-rater agreement has been demonstrated.(Huisingh *et al.* 2014)

3. Statistical Analysis

Participant characteristics were determined overall and by status of current zolpidem use. Chi-square and *t*-tests were used to compare characteristics of zolpidem users and nonusers, as appropriate. Analyses described below are for MVCs overall (primary outcome). Identical analyses were repeated for at-fault MVCs (secondary outcome) and subgroups characterized a-priori by sex and age (< 80 and ≥ 80 years old).

MVC rates during the past 5 years were calculated per 1,000,000 person-miles driven. Rate ratios (RRs) and 95% confidence intervals (95% CI) were calculated to evaluate the association between status of current zolpidem use and MVCs during the prior 5 years using Poisson models offset by the number of miles driven annually during the prior 5 years. Initial unadjusted RRs (95% CIs) were adjusted for selected confounders (see Table 1) that were identified using a step-wise process. First, each participant characteristic was substituted into a separate model estimating the association between status of current zolpidem use and MVCs (i.e., MVC = (participant characteristic) + status of zolpidem use). Next, the percent change in the estimated beta coefficients between the distinct models for each participant characteristic and the unadjusted model for the association between status of current zolpidem use and MVCs during the prior 5 years was calculated as (((unadjusted beta estimate – adjusted beta estimate) / unadjusted beta estimate)*(100)). Participant characteristics that changed the unadjusted estimated beta coefficient by ≥ 10% were considered confounders and selected as covariates for the adjusted model.(Mickey and Greenland 1989) This method for identifying confounders was initially described for case-control study designs but it is also appropriate for cross-sectional studies. The only confounder identified for the primary analysis was current number of medications being taken. This covariate was subsequently included in the adjusted model for the secondary outcome (at-fault MVCs) and stratified analyses (sex and age). Additionally, since many patients taking sleep medication for insomnia use another sedation medication, we also evaluated the association of zolpidem use with MVCs, overall, and at-fault MVCs during the prior 5 years, respectively, after further adjustment for prescription and over-the-counter sleep medication use in the full sample. There was no evidence of over-dispersion due to few MVCs occurring during participants' five-year history. P-values ≤ 0.05 were considered statistically significant. Analyses were performed using SAS version 9.3 (SAS Institute, Inc., Cary, NC).

4. Results

Current zolpidem users represented 3.8% of the sample. Compared to nonusers, current zolpidem users were significantly more likely to be former or current smokers, had a greater number of chronic medical conditions, falls within the past 12 months and medications (excluding zolpidem) currently being taken and drove fewer miles annually (Table 1).

In the primary analysis, the unadjusted RR (95% CI) for all MVCs comparing current zolpidem users with nonusers was 1.46 (1.02 - 2.08). The sex-stratified unadjusted RRs (95% CIs) were 1.65 (1.03 - 2.66) for females and 1.23 (0.72 - 2.09) for males. The age-stratified unadjusted RRs (95% CIs) for those < 80 and ≥ 80 years old were 1.27 (0.84 - 1.92) and 2.24 (1.19 - 4.57), respectively (Table 2a). Adjustment attenuated these models but similar patterns were present. The RRs for females and individuals aged ≥ 80 years remained statistically significant.

In the secondary analysis, similar patterns were observed for the association of at-fault MVCs comparing current zolpidem users to nonusers (Table 2b). However, there were no statistically significant associations, likely attributable to the small number of events.

In the primary and secondary analyses, prescription and over-the-counter sleep medication use were also assessed as confounders of the association between zolpidem use and MVCs. However, adjustment for these co-variables did not qualitatively change the beta coefficient for the association between zolpidem and MVC (i.e., the beta coefficient changed <10%). Therefore, prescription and over-the-counter sleep medication use were not included in the final model.

5. Discussion

In the current study, older drivers currently taking zolpidem had an increased rate of MVCs during the prior 5 years compared to nonusers. Notably, the 5-year rates of MVCs were significantly higher among females and individuals aged ≥ 80 years who were current zolpidem users. Although adjustment for the current number of medications being taken attenuated these associations, there were similar patterns. It should be noted however that given the cross-sectional nature of the study design, the temporal relationship between MVC occurrence during the prior 5 years and zolpidem use cannot be firmly established.

Zolpidem use by pill bottle review in the current study was lower than has been self-reported for any prescription sedative medication use in the US population (3.8% versus 4.0%). (Knutson *et al.* 2009, Chong *et al.* 2013, Bertisch *et al.* 2014) Prior observational studies suggest the risk of MVCs is elevated after prescription sedative-hypnotic medication use, including zolpidem. Yang et. al. conducted a case-crossover study using data from a national health insurance database in Taiwan. The odds of a next-day MVC hospitalization were 1.5-times higher among zolipdem users than nonusers, with a stronger association in males. (Yang *et al.* 2011) Additionally, among a large Norwegian cohort selected from population-based registries, the standardized incidence of MVCs was more than 2-times higher among zolpidem users compared with nonusers.(Gustavsen *et al.* 2008) In each of these studies, the association was stronger in males than females. However, these prior studies included a

limited number of older drivers. The current study extends the literature by reporting an association between current zolpidem use and MVCs during the prior 5 years in drivers aged ≥ 70 years. Furthermore, the oldest of older drivers were identified to have the highest 5-year rate of MVCs. In contrast with prior studies, there was a stronger association in females than males. Evidence supporting this finding is provided by randomized, crossover pharmacologic studies that report zolpidem clearance being up to 40 - 50% lower in females than males administrated the same dosage.(Greenblatt *et al.* 2013, Greenblatt *et al.* 2014) Results of the clinical studies led to a US Federal Drug Safety communication indicating men, and particularly women, are susceptible to next-morning impairment for activities requiring complete mental alertness, including driving.(Anon 2013c, a) This discordance of the current and prior studies may be attributable to differences in the selected sample between the prior and current studies (e.g., demographics).

The association between current zolpidem use and MVCs during the prior 5 years is plausible. Intervention studies have detected clinically relevant elevated plasma concentrations of zolpidem the morning after taking zolpidem-containing medication.(Bocca *et al.* 2011, Anon 2013c, a) As such, enduring drowsiness, loss of coordination and impaired alertness may contribute to the risk of MVCs.(Logan and Couper 2001, Hossain and Shapiro 2002) Additionally, well-controlled driving simulation studies provide evidence that zolpidem use is a risk factor for MVCs, even when recommended dosing was administered. For example, zolpidem use was associated with an inconsistent rate of speed, an increased number of lane departures in monotonous driving environment simulations and a modified lateral vehicle position in urban driving situations with accident scenarios.(Meskali *et al.* 2009, Bocca *et al.* 2011) Furthermore, it was not surprising that the strongest associations in the current study were among females and participants aged ≥ 80 years. Older adults and women have lower clearance rates and higher plasma concentrations for a given zolpidem dose compared to younger adults and men, respectively.(Greenblatt *et al.* 2014)

Sleep disorders are associated with significant morbidity, reduced quality of life, lost income and increased risk for MVCs.(Stoller 1994, Hossain and Shapiro 2002, Colten *et al.* 2006, Anon 2013b, de Mello *et al.* 2013) Restorative sleep can be achieved and quality of life and sleep disorder-related morbidities may be improved by taking sleep medications if behavior modification, the first-line treatment recommendation in guidelines, is unsuccessful.(Stoller 1994, Dang *et al.* 2011) In the current study, some MVCs during the prior 5 years detected among zolpidem users may have been attributable to sleep disorders, not the sleep medication itself. For example, zolpidem may not have been taken the night before a MVC or the MVC may have occurred long-after awakening from sleep. Future studies should be conducted to specifically address how sleep medication affects the risk for MVCs among individuals with and without sleep problems.

Results from the current study should be interpreted in the context of known limitations. First, the timing of zolpidem use compared with when MVCs occurred and the dosage and form of zolpidem and duration of use were unavailable. Thus, a temporal relationship between zolpidem use and MVCs cannot be determined due to the cross-sectional study design. Specifically, zolpidem may not have been taken by current users on the night before their MVC. As such, zolpidem use may be only a marker of older adults with higher risk for

MVCs. Second, although the current results may be attributed to survival bias, we are unaware of evidence suggesting that current zolpidem users are more likely to survive or be involved in less severe MVCs than nonusers. Third, there may have been bias by indication as some participants could have changed their sleep medication to zolpidem post-MVC since there may be less drowsiness the morning following its use. Furthermore, if participants did not bring all of their medication bottles to the baseline clinical visit, some zolpidem users may have been misclassified as nonusers, resulting in bias toward the null. Fourth, the data were not available on participants' sleep pattern. For example, sleeping during the day and driving during the night may increase the risk for MVCs. Fifth, information on whether behavior modification was used prior to zolpidem prescription use as a means to prevent MVC-associated risks was unavailable. Sixth, MVCs without a police report were not included in the current analysis. Seventh, information on the timing, length, frequency and purpose of travel and trips were not collected. Eighth, information on hepatic and renal function, which may affect zolpidem clearance in older adults, was unavailable.

In contrast, the current study has several notable strengths. First, the current study included a large sample of very old drivers, a subgroup known to have a higher prevalence of sleep disorders(Dijk *et al.* 2000), higher plasma concentrations of zolpidem the morning after use and a lower rate of its clearance.(Olubodun *et al.* 2003) Second, in contrast with prior studies, information collected at the baseline clinical visit permitted the current study to identify and adjust for confounders. Most importantly, since current zolpidem users drove fewer miles annually than nonusers, having information on the annual miles driven permitted the current study to account for participant's time at risk for MVCs during the prior 5 years.

6. Conclusion

The current study highlights the need for individuals' ≥ 70 years of age who take zolpidem to cautiously decide when to drive. Practitioners should be encouraged to prescribe low doses of zolpidem and escalate it as needed, particularly among females and individuals aged ≥ 80 years since they have a lower clearance rate and higher risk for next-morning impairment compared to men and younger adults, respectively. Additionally, individuals aged ≥ 70 years, and particularly those aged ≥ 80 years, taking zolpidem should be advised to avoid activities requiring unimpaired alertness, judgment and coordination, such as driving, until they are fully awake.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

Anon. Fda drug safety communication: Risk of next-morning impairment after use of insomnia drugs; fda requires lower recommended doses for certain drugs containing zolpidem (ambien, ambien cr, edluar, and zolpimist). 2013a

Anon. Prescription sleep aid use is most common among women, older adults. JAMA Intern Med. 2013b; 310(15):1552.

Anon. Zolpidem containing products: Drug safety communication - fda requires lower recommended doses. 2013c

Bertisch SM, Herzig SJ, Winkelman JW, Buettner C. National use of prescription medications for insomnia: Nhanes 1999-2010. Sleep. 2014; 37(2):343–9. [PubMed: 24497662]

Bocca ML, Marie S, Lelong-Boulouard V, Bertran F, Couque C, Desfemmes T, Berthelon C, Amato JN, Moessinger M, Paillet-Loilier M, Coquerel A, Denise P. Zolpidem and zopiclone impair similarly monotonous driving performance after a single nighttime intake in aged subjects. Psychopharmacology (Berl). 2011; 214(3):699–706. [PubMed: 21086117]

Chong Y, Fryer CD, Gu Q. Prescription sleep aid use among adults: United states, 2005-2010. NCHS Data Brief. 2013; 127:1–8. [PubMed: 24152538]

Chung SD, Lin CC, Wang LH, Lin HC, Kang JH. Zolpidem use and the risk of injury: A population-based follow-up study. PLoS One. 2013; 8(6):e67459. [PubMed: 23826304]

Colten, HR.; Altevogt, BM. Sleep disorders and sleep deprivation : An unmet public health problem Institute of Medicine. National Academies Press; Washington, DC: 2006. Institute of Medicine (U.S.). Committee on Sleep Medicine and Research.

Dang A, Garg A, Rataboli PV. Role of zolpidem in the management of insomnia. CNS Neurosci Ther. 2011; 17(5):387–97. [PubMed: 20553305]

De Mello MT, Narciso FV, Tufik S, Paiva T, Spence DW, Bahammam AS, Verster JC, Pandi-Perumal SR. Sleep disorders as a cause of motor vehicle collisions. Int J Prev Med. 2013; 4(3):246–57. [PubMed: 23626880]

Dijk DJ, Duffy JF, Czeisler CA. Contribution of circadian physiology and sleep homeostasis to age-related changes in human sleep. Chronobiol Int. 2000; 17(3):285–311. [PubMed: 10841208]

Greenblatt DJ, Harmatz JS, Roth T, Singh NN, Moline ML, Harris SC, Kapil RP. Comparison of pharmacokinetic profiles of zolpidem buffered sublingual tablet and zolpidem oral immediate-release tablet: Results from a single-center, single-dose, randomized, open-label crossover study in healthy adults. Clin Ther. 2013; 35(5):604–11. [PubMed: 23541711]

Greenblatt DJ, Harmatz JS, Singh NN, Steinberg F, Roth T, Moline ML, Harris SC, Kapil RP. Gender differences in pharmacokinetics and pharmacodynamics of zolpidem following sublingual administration. J Clin Pharmacol. 2014; 54(3):282–90. [PubMed: 24203450]

Gustavsen I, Bramness JG, Skurtveit S, Engeland A, Neutel I, Morland J. Road traffic accident risk related to prescriptions of the hypnotics zopiclone, zolpidem, flunitrazepam and nitrazepam. Sleep Med. 2008; 9(8):818–22. [PubMed: 18226959]

Hossain JL, Shapiro CM. The prevalence, cost implications, and management of sleep disorders: An overview. Sleep Breath. 2002; 6(2):85–102. [PubMed: 12075483]

Huisingh C, Mcgwin G Jr, Orman KA, Owsley C. Frequent falling and motor vehicle collision involvement of older drivers. J Am Geriatr Soc. 2014; 62(1):123–9. [PubMed: 24279730]

Knutson KL, Van Cauter E, Rathouz PJ, Yan LJL, Hulley SB, Liu K, Lauderdale DS. Association between sleep and blood pressure in midlife the cardia sleep study. Arch Intern Med. 2009; 169(11):1055–1061. [PubMed: 19506175]

Lai MM, Lin CC, Lin CC, Liu CS, Li TC, Kao CH. Long-term use of zolpidem increases the risk of major injury: A population-based cohort study. Mayo Clin Proc. 2014; 89(5):589–94. [PubMed: 24684782]

Logan BK, Couper FJ. Zolpidem and driving impairment. J Forensic Sci. 2001; 46(1):105–10. [PubMed: 11210892]

Meskali M, Berthelon C, Marie S, Denise P, Bocca ML. Residual effects of hypnotic drugs in aging drivers submitted to simulated accident scenarios: An exploratory study. Psychopharmacology (Berl). 2009; 207(3):461–7. [PubMed: 19798483]

Mickey RM, Greenland S. The impact of confounder selection criteria on effect estimation. Am J Epidemiol. 1989; 129(1):125–37. [PubMed: 2910056]

Olubodun JO, Ochs HR, Von Moltke LL, Roubenoff R, Hesse LM, Harmatz JS, Shader RI, Greenblatt DJ. Pharmacokinetic properties of zolpidem in elderly and young adults: Possible modulation by testosterone in men. Br J Clin Pharmacol. 2003; 56(3):297–304. [PubMed: 12919178]

Orriols L, Philip P, Moore N, Castot A, Gadegbeku B, Delorme B, Mallaret M, Lagarde E, Group CR. Benzodiazepine-like hypnotics and the associated risk of road traffic accidents. Clin Pharmacol Ther. 2011; 89(4):595–601. [PubMed: 21368756]

Owsley C, Mcgwin G Jr, Searcey K. A population-based examination of the visual and ophthalmological characteristics of licensed drivers aged 70 and older. J Gerontol A Biol Sci Med Sci. 2013; 68(5):567–73. [PubMed: 22982690]

Stoller MK. Economic effects of insomnia. Clin Ther. 1994; 16(5):873–97. discussion 854. [PubMed: 7859246]

Yang YH, Lai JN, Lee CH, Wang JD, Chen PC. Increased risk of hospitalization related to motor vehicle accidents among people taking zolpidem: A case-crossover study. J Epidemiol. 2011; 21(1):37–43. [PubMed: 21030794]

Highlights

- Prescribed sleep medicine use in the past 30 days is highest in women/older adults
- Side effects that can affect driving safety are drowsiness/impaired coordination
- Assess zolpidem use and motor vehicle collisions (MVC) over 5 years in old drivers
- Zolpidem use was associated with higher MVC rates in women and adults ≥80 years old
- Zolpidem-related MVCs may be avoided by initiating low doses, escalating as needed

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Table 1

Demographic, Health and Driving Characteristics of Older Drivers by Zolpidem Use

Characteristic	**Overall N = 2,000**	**Current zolpidem use n = 75**	**Zolpidem nonuse n = 1,925**	**p-value**
Characteristic	Overall N = 2,000	Current zolpidem use n = 75	Zolpidem nonuse n = 1,925	p-value
Age group, n (%)				
70 - 79	1,433 (71.7)	58 (77.3)	1,375 (71.4)	0.161
≥ 80	567 (28.4)	17 (22.7)	550 (28.6)	
Sex, n (%)				
Female	870 (43.5)	31 (41.3)	839 (43.6)	0.700
Male	1,130 (56.5)	44 (58.7)	1,086 (55.4)	
Race, n (%)				
Non-white	360 (18.0)	11 (14.7)	349 (18.1)	0.444
White	1,640 (82.0)	64 (85.3)	1,576 (81.9)	
Education level, n (%)	1,092 (54.6)	42 (56.0)	1,050 (54.5)	0.804
≤ High School or GED	683 (34.2)	22 (29.3)	661 (34.4)	0.149
College (1 – 4 Years)	1,018 (50.9)	36 (48.0)	982 (51.0)	
Postgraduate degree	298 (14.9)	17 (22.7)	281 (14.6)	
Marital status, n (%)				
Married	1,092 (54.6)	42 (56.0)	1,050 (54.5)	0.804
Not married	908 (45.4)	33 (44.0)	875 (45.5)	
Smoking, n (%)				
Never	944 (47.3)	27 (36.0)	917 (47.8)	0.022
Former	958 (48.0)	41 (54.7)	917 (47.8)	
Current	93 (4.7)	7 (9.3)	86 (4.5)	
Alcohol consumption, drinks/week, n (%)				
None	947 (47.4)	28 (37.3)	919 (47.7)	0.184
0.5 - 7	856 (42.8)	37 (49.3)	819 (42.6)	
≥ 7.5	120 (6.0)	10 (13.3)	187 (9.7)	
Mean ± SD	2.1 ± 4.7	2.6 ± 4.1	2.1 ± 4.7	0.331
Number of chronic medical conditions, n (%)				

Characteristic	Overall N = 2,000	Current zolpidem use n = 75	Zolpidem nonuse n = 1,925	p-value
None	55 (2.8)	2 (2.7)	53 (2.8)	0.002
1-2	440 (22.0)	9 (12.0)	431 (22.4)	
3-4	795 (39.8)	22 (29.3)	773 (40.2)	
≥ 5	710 (35.6)	42 (56.0)	668 (34.7)	
Mean ± SD	4.0 ± 2.0	4.9 ± 2.2	3.9 ± 2.0	<0.001
MMSE score, n (%)				
≤ 23	47 (2.4)	2 (2.7)	45 (2.3)	0.854
> 23	1,953 (97.7)	73 (97.3)	1,880 (97.7)	
Number of falls, n (%)				
None	1,535 (76.8)	47 (62.7)	1,488 (77.3)	0.013
1	291 (14.6)	17 (22.7)	274 (14.2)	
≥ 2	174 (8.7)	11 (14.7)	163 (8.5)	
Mean ± SD	0.4 ± 1.1	0.7 ± 1.5	0.4 ± 1.1	0.015
Number of medications, n (%)				
None	104 (5.2)	0 (0.0)	104 (5.4)	<0.001
1-3	565 (28.3)	8 (10.7)	567 (28.9)	
≥4	1,331 (66.6)	67 (89.3)	1,264 (65.7)	
Mean ± SD	5.3 ± 3.5	8.1 ± 3.2	5.2 ± 3.5	<0.001
Prescription sleep medication use (minus zolpidem-containing drugs), n (%)	73 (3.7)	2 (2.7)	71 (3.7)	
Over-the-counter sleep medication use, n (%)	181 (9.1)	49 (65.3)	132 (6.9)	
Annual Mileage, Mean ± SD	9,528 ± 9,420	8,382 ± 5,574	9,572 ± 9,537	0.283

SD = Standard Deviation

MMSE = Mini–Mental State Examination

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Table 2a

Five-Year Crash Rates (All Collisions), Unadjusted and Adjusted Rate ratios

	Current Zolpidem Use	MVC (n)	Person-Miles	Crash Rate[a]	Unadjusted RR (95% CI)	Adjusted[b] RR (95% CI)
All	Yes	32	4,087,233	7.83	1.46 (1.02 - 2.08)	1.38 (0.97 -1.98)
	No	649	120,626,847	5.38	Ref	Ref
Female	Yes	18	1,363,443	13.20	1.65 (1.03 - 2.66)	1.61 (1.00 - 2.60)
	No	302	37,816,638	7.99	Ref	Ref
Male	Yes	14	2,723,790	5.14	1.23 (0.72 - 2.09)	1.15 (0.67 - 1.98)
	No	347	82,810,209	4.19	Ref	Ref
Age < 80	Yes	23	3,380,968	6.80	1.27 (0.84 - 1.92)	1.18 (0.77 - 1.80)
	No	491	91,641,996	5.36	Ref	Ref
Age ≥ 80	Yes	9	706,264	12.74	2.24 (1.19 - 4.57)	2.35 (1.20 - 4.61)
	No	158	28,984,851	5.45	Ref	Ref

[a] Crash Rates are reported as number of motor vehicle crashes per 1,000,000 person-miles.

[b] Adjusted for current number of medications.

RR: Rate Ratio, CI: Confidence Interval, MVC: number of motor vehicle collisions within 5 years prior to baseline.

Table 2b

Five year crash rates (at-fault collisions), unadjusted and adjusted rate ratios.

	Current Zolpidem Use	MVC (n)	Person-Miles	Crash Rate[a]	Unadjusted RR (95% CI)	Adjusted[b] RR (95% CI)
All	Yes	14	4,087,233	3.43	1.41 (0.82 - 2.40)	1.29 (0.75 - 2.21)
	No	294	120,626,847	2.44	Ref	Ref
Female	Yes	8	1,363,443	5.87	1.46 (0.72 - 2.97)	1.40 (0.69 - 2.85)
	No	152	37,816,638	4.02	Ref	Ref
Male	Yes	6	2,723,790	2.20	1.28 (0.57 - 2.91)	1.20 (0.52 – 2.74)
	No	142	82,810,209	1.71	Ref	Ref
Age < 80	Yes	11	3,380,968	3.25	1.41 (0.77 - 2.59)	1.24 (0.67 - 2.29)
	No	211	91,641,996	2.30	Ref	Ref
Age ≥ 80	Yes	3	706,264	4.25	1.48 (0.47 - 4.69)	1.48 (0.47 - 4.71)
	No	83	28,984,851	2.86	Ref	Ref

[a] Crash Rates are reported as number of motor vehicle crashes per 1,000,000 person-miles.

[b] Adjusted for current number of medications.

RR: Rate Ratio, CI: Confidence Interval, MVC: number of motor vehicle collisions within 5 years prior to baseline.