



## Drug use and fatal motor vehicle crashes: A case-control study



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### ABSTRACT

Drugged driving is a serious safety concern, but its role in motor vehicle crashes has not been adequately studied. Using a case-control design, the authors assessed the association between drug use and fatal crash risk. Cases ( $n = 737$ ) were drivers who were involved in fatal motor vehicle crashes in the continental United States during specific time periods in 2007, and controls ( $n = 7719$ ) were participants of the 2007 National Roadside Survey of Alcohol and Drug Use by Drivers. Overall, 31.9% of the cases and 13.7% of the controls tested positive for at least one non-alcohol drug. The estimated odds ratios of fatal crash involvement associated with specific drug categories were 1.83 [95% confidence interval (CI): 1.39, 2.39] for marijuana, 3.03 (95% CI: 2.00, 4.48) for narcotics, 3.57 (95% CI: 2.63, 4.76) for stimulants, and 4.83 (95% CI: 3.18, 7.21) for depressants. Drivers who tested positive for both alcohol and drugs were at substantially heightened risk relative to those using neither alcohol nor drugs (Odds Ratio = 23.24; 95% CI: 17.79, 30.28). These results indicate that drug use is associated with a significantly increased risk of fatal crash involvement, particularly when used in combination with alcohol.

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### 1. Introduction

Drugged driving has become a safety issue of increasing public concern in the United States and many other countries (Brady and Li, 2013; Dupont et al., 2012; Legrand et al., 2013). Driving performance can be impaired by a wide array of illicit and prescription drugs. Among non-alcohol drugs, marijuana is the most frequently detected substance in the general driver population as well as in drivers being involved in crashes (Arria et al., 2011; Brady and Li, 2013; Jones et al., 2003; Kaplan et al., 2006; Kelly et al., 2004; Lacey et al., 2009a; Walsh et al., 2005). There is mounting evidence that use of marijuana impairs cognitive functions and driving performance, such as psychomotor skills, divided attention, and lane tracking (Battistella et al., 2013; Hartman and Huestis, 2013), and doubles the risk of being involved in a motor vehicle crash (Asbridge et al., 2012; Li et al., 2012). Benzodiazepines have also been frequently detected in drivers (Kelly et al., 2004; Walsh et al., 2004a) and have been consistently found to be associated with a significantly increased risk of crash involvement and crash culpability (Dassanayake et al., 2011; Dubois et al., 2008; Engeland et al., 2007;

Leung, 2011; Orriols et al., 2009; Ramaekers, 2003; Rapoport et al., 2009; Smink et al., 2010; Walsh et al., 2004b). Evidence regarding the effects of stimulants on crash risk is inconsistent (Kelly et al., 2004; Engeland et al., 2007; Leung, 2011; Musshoff and Madea, 2012; Smink et al., 2010; Walsh et al., 2004a). While therapeutic use of stimulants does not appear to be related to crash risk, nonmedical use of stimulants, in high doses, or in combination with alcohol or other drugs or with lack of sleep, can pose a threat to driving safety (Bogstrand et al., 2012; Ramaekers et al., 2012; Walsh et al., 2004a). There is a paucity of empirical data about the effects of opioids on driving performance and crash risk despite the tripling of opioid prescriptions in the United States in the past two decades (NIDA, 2010a).

Previous research examining the role of drugs in motor vehicle crashes was limited primarily to case series analysis of toxicological testing data for fatally injured drivers and comparison between drivers involved in culpable crashes and those in non-culpable crashes. Although these studies could provide useful information about the prevalence of drugs in specific driver groups, they are descriptive in essence. To understand the causal role of drug use in motor vehicle crashes, empiric evidence from controlled epidemiological studies is imperative. The case-control design, which requires cases and controls to be selected through such a sampling scheme that they are representative of the respective injured and non-injured source populations (Li and Baker, 2012), has played an instrumental role in understanding the causal relationship between alcohol use and crash risk and in quantifying the dose-response

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effect of blood alcohol level on crash risk (McCarroll and Haddon, 1962; Zador, 1991). Using a case-control design and drug testing data from two national information systems, we assessed the association of driver drug use with the risk of fatal crash involvement and the interaction effect of drugs and alcohol on fatal crash risk.

## 2. Materials and methods

### 2.1. Data sources

Data for this study came from two sources: the Fatality Analysis Reporting System (FARS) and the 2007 National Roadside Survey of Alcohol and Drug Use by Drivers; both were sponsored by the National Highway Traffic Safety Administration. Incepted in 1975, FARS is a repository of investigation data for all crashes that resulted in at least one fatality within 30 days of the crash and that occurred on a public road within the United States (NHTSA, 2012). This data system contains detailed information about the crash circumstances as well as individuals and vehicles involved in the crash. Data are collected from police reports, medical records, driving records, death certificates, and other sources by trained personnel using standard forms and protocols. Data quality is ensured through specified quality control procedures, including standardized coding and validation instructions (NHTSA, 2010, 2012). Data items in the FARS include driver characteristics (e.g., age, sex, alcohol and drug test results, history of driving-while-intoxicated conviction in the past three years, and survival status), vehicle characteristics (e.g., vehicle make and model, body type, model year, gross vehicle weight rating, and vehicle configuration), and crash circumstances (e.g., crash location, date, time, roadway type, manner of collision, light conditions, and atmospheric conditions).

The 2007 National Roadside Survey of Alcohol and Drug Use by Drivers consisted of a sample of drivers of non-commercial vehicles representative of the contiguous states, selected by the multistage random sampling method (Lacey et al., 2009a). Briefly, the sampling scheme included random selections of study units on each of the four levels in a descending hierarchy: primary sampling units, police jurisdictions, survey locations, and passing-by drivers. Drivers at selected survey locations were stopped at random from the traffic and directed to a safe off-road area by uniformed police, and then were invited by trained research personnel to voluntarily participate in the survey. Verbally consented drivers were asked to answer a set of questions about their basic demographic characteristics, annual mileage of driving, origin and destination of the ongoing trip, and drinking behavior and then to provide a breath sample for alcohol testing and an oral-fluid sample for drug testing. A total of 10,909 eligible drivers were stopped and directed to the 300 study sites; of these eligible drivers, 7719 (70.8%) completed the interview and provided an oral fluid sample for drug testing. To increase the yield of positive testing results and ensure comparability with previous national roadside surveys, the 2007 survey was conducted from 10:00 PM to midnight and from 1:00 AM to 3:00 AM on Fridays and Saturdays, and 9:30 AM to 11:30 AM and 1:30 PM to 3:30 PM on Fridays during July 20 through December 1, 2007. The sampling method and the study protocol of the 2007 National Roadside Survey were described in detail elsewhere by Lacey and colleagues (2009a).

### 2.2. Study design

A population-based case-control design was used to assess the association of drug use with the risk of fatal crash involvement. Cases ( $n = 737$ ) were drivers who were involved in fatal crashes in the continental United States that occurred during the same time periods as the control drivers were interviewed (i.e., 10:00 PM to

midnight and 1:00 AM to 3 AM on Fridays and Saturdays, and 9:30 AM to 11:30 AM and 1:30 PM to 3:30 PM on Fridays between July 20 and December 1, 2007) and who were tested for drugs, selected from the FARS. Excluded from the primary analysis were 1336 (64.4%) eligible case drivers for whom drug testing results were unavailable. Controls ( $n = 7719$ ) were drivers who participated in the 2007 National Roadside Survey and who provided an oral fluid sample for drug testing.

### 2.3. Drug and alcohol data

Drug tests for cases were performed using blood and/or urine specimens through liquid/gas chromatography, mass spectrometry, and radioimmunoassay techniques (Kaplan et al., 2006; Li et al., 2011). Of the 737 cases, 93% had at least one drug test based on a blood specimen. The FARS records up to three non-alcohol drugs for each driver. If a driver tests positive for multiple drugs, the FARS records the detected drugs in the following priority order: narcotics, depressants, stimulants, marijuana, and other (Kaplan et al., 2006; NHTSA, 2010). In this study, drugs were grouped into five categories according to the FARS coding manual (NHTSA, 2010): (1) marijuana; (2) narcotics; (3) stimulants; (4) depressants (exclusive of alcohol); and (5) other, including hallucinogen, phencyclidine, anabolic steroid, inhalant, and medications that might or might not be detrimental to driving safety. If a drug and its metabolite were detected in a specimen, only the parent drug was recorded. Blood alcohol concentrations (BACs) were recorded separately from drugs. Being alcohol-positive was defined as a BAC  $\geq 0.01$  g/dL.

Drug tests for controls were based on oral liquid samples, which were first screened for drugs through the enzyme-linked immunosorbent assay and then analyzed for confirmation through chromatography and spectrometry techniques (Lacey et al., 2009a). The screening and confirmatory tests were performed to detect a list of specific drugs that could potentially impair driving safety, determined by an expert panel (Lacey et al., 2009a). These drugs include illicit substances as well as prescription and over-the-counter medications. Information about the drugs tested and the minimum detection concentrations, along with other methodological aspects of the 2007 National Roadside Survey of Alcohol and Drug Use by Drivers, was described in detail elsewhere (Lacey et al., 2009a).

Blood alcohol levels for controls were measured based on breath samples. Given that drivers with high BACs are known to be more likely to refuse the breath alcohol test, a passive alcohol sensor was used in the 2007 National Roadside Survey when the driver was first invited to participate in the study. The passive alcohol sensor provided a semi-quantitative estimate of the driver's BAC, which was used to adjust the prevalence of alcohol and drugs for bias toward underestimation resulting from refusals (Lacey et al., 2009a). Prevalence data on alcohol and drugs for controls used in the present study were corrected for nonparticipating drivers, as documented in the report of the 2007 National Roadside Survey (Lacey et al., 2009b).

### 2.4. Statistical analysis

The association of drug use with fatal crash involvement was assessed by estimating odds ratios (ORs) and 95% confidence intervals (CIs). Stratification analysis was performed to assess the association between drug use and fatal motor vehicle crashes according to drug categories, driver demographic characteristics, geographic region, and time of day. The possible interaction of drug and alcohol on fatal crash involvement was also examined. Because data for the controls were publicly available only on the aggregate level, it was not possible to estimate the odds ratios based on multivariable analysis.

**Table 1**

Crude Odds Ratios and 95% Confidence Intervals of fatal crash involvement according to driver age, sex, alcohol and drug testing results in the continental United States, selected time periods on Fridays and Saturdays, July 20 through December 1, 2007.

Characteristic	% of Cases <sup>a</sup> (n = 737)	% of Controls <sup>a</sup> (n = 7719)	Crude OR	95% CI
Age (years)				
16–20	12.9	13.9	1.14	0.86, 1.50
21–34	43.0	37.6	1.40	1.14, 1.73
35–44	17.8	18.6	1.18	0.92, 1.52
45–64	20.1	24.7	1.00	
≥65	6.2	5.2	1.49	1.04, 2.14
Sex				
Male	84.1	60.2	3.50	2.84, 4.31
Female	15.9	39.8	1.00	
Blood alcohol concentration (g/dL)				
0.00	43.0	91.2	1.00	
0.01–0.07	9.1	7.1	2.71	2.02, 3.62
≥0.08	47.9	1.7	61.69	48.54, 78.45
Drug testing result				
Negative	68.1	86.4	1.00	
Positive	31.9	13.6	2.98	2.51, 3.53

OR = Odds Ratio; CI = Confidence Interval;

<sup>a</sup> There were 29 cases with missing data on blood alcohol concentration. There were 93 controls with missing data on age, 21 controls with missing data on sex, and 7 controls with missing data on blood alcohol concentration.

The primary analysis was based on the 737 cases who had actual drug testing data. To assess the potential bias resulting from the low drug testing rate in feasible cases, the missing drug testing data and other variables were imputed using sequential regression multiple imputation (SRMI) method implemented in the SAS (SAS Institute Inc., Cary, NC) callable software IVEware (version 0.2 Build 2012.02, Survey Research Center, Institute for Social Research, University of Michigan, Ann Arbor, MI). SRMI is an iterative multiple imputation process, where at each step of the imputation the conditional distribution of each variable is modeled using an appropriate regression model given the other variables. The imputed values are obtained from the posterior predictive distribution of the missing values given the observed data (Raghunathan et al., 2001). Using FARS data for all 2073 drivers involved in fatal crashes during the specified time periods in the continental United States in 2007, drug testing results were imputed using a logistic regression model to predict drug involvement. The imputation model included the following driver characteristics: age, sex, time to death, previous driving while intoxicated conviction in the 3 years prior to crash, previous motor vehicle crash in the 3 years prior to the crash, and blood alcohol concentration, as well as the following crash characteristics, region, indicator of single vs. multiple vehicle crash, driver type (motor carrier driver vs. non motor carrier driver and time of crash (day vs. night). Ten imputations were generated for each driver. Multiple imputation inference was computed for the natural log of the odds ratio and the 95% confidence interval of the natural log of the odds ratio using Rubin's rules (Rubin, 1987). Once these estimates were combined, they were transformed back to the odds ratio scale. A sensitivity analysis was performed by comparing the estimated odds ratios based on the multiply imputed drug data with those based on actual drug testing data.

### 3. Results

Of the 2073 eligible cases, 1336 (64.4%) were excluded from the primary analysis due to unavailable drug testing data. Drivers included in the study as cases and those excluded differed significantly in demographic characteristics and driving records. Specifically, drivers included in the study were more likely than those excluded to be under 35 years (55.9% vs. 47.1%,  $P=0.01$ ), be male (84.1% vs. 74.6%,  $P<0.0001$ ), have been involved in a crash within the prior three years (15.8% vs. 11.7%,  $P=0.01$ ), have been convicted of driving-while-intoxicated (DWI) in the prior three

years (6.2% vs. 3.6%,  $P=0.009$ ), and be fatally injured in the crash (80.6% vs. 34.2%,  $P<0.0001$ ).

Overall, 31.9% of the 737 cases and 13.6% of the 7719 controls tested positive for at least one non-alcohol drug, yielding a crude odds ratio of 2.98 (95% CI: 2.51, 3.53). Elevated BACs were found in 57.0% of the cases and 8.8% of the controls; and the risk of fatal crash involvement increased exponentially as BACs rose (Table 1). As expected, male drivers and drivers aged 21 to 34 years or 65 years and older were at significantly increased risk of fatal crash involvement (Table 1).

The heightened risk of fatal crash involvement associated with drug use existed in each age group and in both sexes (Table 2). Although drivers aged 35–44 years and female drivers appeared to be at particularly excess risk, the estimated odds ratios of fatal crash involvement did not vary significantly with age and sex. The association between drug use and fatal crash involvement also held fairly steady when the data were stratified according to the time of day or geographic region (Table 2).

The prevalence of drugs detected in cases was higher than in controls across the drug categories (Table 3). Marijuana, narcotics,

**Table 2**

Estimated Odds Ratios and 95% Confidence Intervals of fatal crash involvement associated with drug use according to strata of driver age, sex, time of day, and geographic region, the continental United States, selected time periods on Fridays and Saturdays, July 20 through December 1, 2007.

Strata	Estimated OR <sup>a</sup>	95% CI
Age (years)		
16–20	2.84	1.73, 4.57
21–34	2.52	1.93, 3.27
35–44	4.11	2.75, 6.09
45–64	3.03	2.00, 4.54
≥65	2.95	0.91, 8.25
Sex		
Male	2.64	2.18, 3.19
Female	3.35	2.15, 5.12
Time of Day		
Daytime	2.60	1.78, 3.75
Night-time	3.12	2.57, 3.80
Geographic region		
Midwest	3.22	2.21, 4.63
Northwest	2.50	1.63, 3.76
South	2.65	1.97, 3.55
West	3.56	2.47, 5.08

OR = Odds Ratio; CI = Confidence Interval;

<sup>a</sup> Drivers who tested negative for drugs were used as the reference group.

**Table 3**

Prevalence of drugs detected and crude Odds Ratios and 95% Confidence Intervals of fatal crash involvement according to drug category, in the continental United States, selected time periods on Fridays and Saturdays, July 20 through December 1, 2007.

Drug Category	% of Cases (n = 737)	% of Controls (n = 7719)	Crude OR <sup>a</sup>	95% CI
Marijuana	9.8	5.6	1.83	1.39, 2.39
Narcotics	4.8	1.6	3.03	2.00, 4.48
Stimulants	9.4	2.8	3.57	2.63, 4.76
Depressants	5.2	1.1	4.83	3.18, 7.21
Polydrug <sup>b</sup>	7.1	2.2	3.41	2.43, 4.73

OR = Odds Ratio; CI = Confidence Interval;

<sup>a</sup> Drivers who tested negative for the specific drug category were used as the reference group;

<sup>b</sup> Two or more non-alcohol drugs.

**Table 4**

Estimated Odds Ratios and 95% Confidence Intervals of fatal crash involvement according to alcohol and drug testing results, the continental United States, selected time periods on Fridays and Saturdays, July 20 through December 1, 2007.

Testing Result		Estimated OR	95% CI
Alcohol	Drug		
Negative	Negative	1.00	Reference
Positive	Negative	13.64	11.12, 16.72
Negative	Positive	2.22	1.68, 2.92
Positive	Positive	23.24	17.79, 30.28

OR = Odds Ratio; CI = Confidence Interval;

stimulants, and depressants were each associated with a significantly increased risk of fatal crash involvement, with estimated odds ratios ranging from 1.83 for marijuana to 4.83 for depressants (Table 3). Polydrug use, defined as use of two or more non-alcohol drugs, was associated with a 3.4-fold increased risk of fatal crash involvement (Table 3).

About one-fifth (20.5%) of the cases tested positive for alcohol and one or more drugs, compared with 2.2% of the controls. Relative to drivers who tested positive for neither alcohol nor drugs, the estimated odds of fatal crash involvement increased over 13 folds for those who were alcohol-positive but drug-negative, more than two folds for those who were alcohol-negative but drug-positive, and 23 folds for those who were positive for both alcohol and drugs (Table 4).

Nearly two-thirds of the eligible cases were excluded from the primary analysis because of unavailable drug testing data. To assess the possible bias resulting from incomplete drug testing, the relationship between state-level prevalence of drugs in drivers who were involved in fatal crashes and who were tested for drugs and state-level drug testing rates was examined through the scatter plot and correlation analysis. There was no apparent pattern in the scatter plot (data not shown). Correlation analysis indicated that the prevalence of drugs was not linearly associated with the drug testing rate (Pearson correlation coefficient = 0.086;  $P = 0.57$ ). To further assess the robustness of the estimated odds ratio of fatal crash involvement associated with drug use, the missing drug testing data were multiply imputed based on the variables that were significantly associated with drug use or drug testing. The estimated odds ratio of fatal crash involvement associated with drug use based on the multiply imputed drug data was 2.82 (95% CI: 2.44, 4.64). Estimated odds ratios generated from multiply imputed drug data for different strata of age, sex, time of day and geographic region were also slightly lower than those derived from actual drug testing data.

#### 4. Discussion

Results of this case-control analysis indicate that use of drugs, such as marijuana, narcotics, stimulants, and depressants, may

more than double drivers' risk of being involved in fatal motor vehicle crashes, irrespective of age, sex, time of the day, and geographic region. The heightened crash risk, however, appears to be dependent on the type of drugs used, with depressants conferring the highest risk, followed by stimulants, narcotics, and marijuana. The risk of fatal crash involvement is especially high when drugs are used in combination with alcohol.

The estimated odds ratios of fatal motor vehicle crashes associated with different drugs reported in this population-based case-control analysis are generally consistent with previous studies (Bedard et al., 2007; Brault et al., 2004; Laumon et al., 2005; Mathijssen and Houwing, 2005; Movig et al., 2004; Mura et al., 2003). For instance, in a case-control study conducted in the Netherlands, Movig et al. (2004) found that 11.8% of the drivers who were seriously injured in crashes and 6.0% of the drivers who were not involved in crashes tested positive for marijuana, yielding an odds ratio of 2.1 (95% CI: 1.1, 4.0). A study of drivers aged 18 to 69 years of age in Norway revealed that the incidence of crashes was more than two times higher for individuals the week after benzodiazepine-like hypnotics were dispensed compared to unexposed person time (Gustavsen et al., 2008). A meta-analysis of epidemiological studies showed that motor vehicle crash risk for benzodiazepine users was 60–80% higher than for nonusers (Dassanayake et al., 2011). It is also evident that crash risk in drivers with depression is particularly high at the initiation of antidepressant treatment and when antidepressant treatment regimen changes (Orriols et al., 2012).

The present study adds valuable evidence to a growing body of research on narcotic drugs and driving safety. Heightened crash risk has been linked to several commonly used narcotic drugs, including morphine, cocaine, heroin, and opiates (Gjerde et al., 2011; Kuypers et al., 2012; Mathijssen and Houwing, 2005; Movig et al., 2004; Mura et al., 2003). A recent epidemiologic study suggests that female drivers receiving methadone maintenance therapy are not at an increased risk of being involved in motor vehicle crashes but male drivers are (Bramness et al., 2012). Similarly, therapeutic use of opioids appears to increase the risk of crash involvement in young drivers but not in older drivers (Dassanayake et al., 2011). One of the stimulant drugs, amphetamines can be extremely detrimental to driving safety, increasing the risk of driver fatality by over 25 fold (Hels et al., 2012).

The possible interaction of drugs in combination with alcohol on driving safety has long been a concern (Gjerde and Kinn, 1991; Stramer and Bird, 1984). Toxicological testing data indicate that about 25% of drivers injured in motor vehicle crashes are positive for two or more substances, with alcohol and cannabis being the most common combination (Brady and Li, 2013; Kaplan et al., 2006; Romano and Voas, 2011; Walsh et al., 2005). Few epidemiologic studies, however, have assessed the interaction effect of alcohol and drugs on crash risk, due in part to the large sample sizes and considerable costs required (Bates and Blakely, 1999; Kelly et al., 2004; Walsh et al., 2005). This case-control study provides valuable data for better understanding the joint effect of alcohol and drugs on driving safety. Our results suggest that, when alcohol and drugs are used together, there is a modest negative interaction effect on the risk of fatal crash involvement on the multiplicative scale; relative to drivers testing negative for both alcohol and drugs, the estimated odds ratios of fatal crash involvement were 13.6 for those testing positive for alcohol only, 2.2 for those testing positive for drugs only, and 23.2 for those testing positive for both alcohol and drugs. Similar findings have been reported by other researchers examining the effects of alcohol and marijuana on driving performance and crash risk (Brault et al., 2004; Downey et al., 2013; Gadegebeku et al., 2011).

Findings from this study should be interpreted with caution. First, the primary exposure measure in this study is drug use,



determined by laboratory tests of specimens. A positive test indicates that the driver had used the drug detected but does not necessarily mean that the driver was impaired by the drug at the time of crash or survey. Variations in individual tolerance and pharmacological characteristics of different drugs make it difficult to determine drug impairment (Alvarez and Del Rio, 2003; Goodnough and Zezima, 2010; Walsh et al., 2004a). There is no uniformly accepted definition of impairment for different drugs (Alvarez and Del Rio, 2003; Dupont, 2011; Dupont et al., 2012; Li et al., 2010; Ramaekers, 2003; The Walsh Group, 2002). Legal definitions of drug impairment differ from state to state. Some states have characterized impairment as substance use that reduces a driver's ability to operate a vehicle safely by diminishing motor skills and reaction time and altering perception (Kelly et al., 2004; NIDA, 2010b). Because of the difficulties in determining drug impairment, a zero-tolerance approach, such as per se laws under which any detectable level of an illicit drug is regarded as prima facie evidence of driving under the influence, has been increasingly called on to control the epidemic of drugged driving (Dupont et al., 2012; Reisfield et al., 2012; Voas et al., 2013).

Additional notable limitations of this study include lack of uniformity in drug testing methods for cases and controls, missing drug data for a large proportion of eligible study subjects due to incomplete testing or refusals, and select time windows studied. Drug testing was based on blood specimens for cases and oral fluid for controls. The difference in specimens between cases and controls is unlikely to pose a serious threat to the validity of our study given the well-established validity and reliability of drug testing by oral fluid (Lacey et al., 2011). Our study is also susceptible to selection bias resulting from incomplete drug testing. For controls, remedial measures were taken to adjust for biases due to missing data and refusals (Lacey et al., 2011); and for cases, sensitivity analysis based on multiply imputed drug testing results indicates that odds ratios based on actual drug testing data are slightly overestimated. The restricted time segments studied, primarily weekend nighttime driving when use of alcohol and drugs is most prevalent, may somewhat limit the generalizability of the study results. However, the impact on the estimated odds ratios of fatal crash involvement associated with drug use is likely small given that prevalence of non-alcohol drugs in drivers does not vary greatly with time of day and day of week (Brady and Li, 2013; Lacey et al., 2009b) because many commonly used drugs are detectable long after the last use (e.g., 24 h for opiates and three months for marijuana).

## 5. Conclusions

The results of our study indicate that driver drug use is associated with a significantly increased risk of fatal crash involvement. The heightened risk appears to be comparable across demographic groups and geographic regions, and is most pronounced when drugs are used in combination with alcohol. These findings are particularly salient in light of the increases in the availability of prescription stimulants and opioids over the past decade. To control drugged driving and reduce injury morbidity and mortality from motor vehicle crashes, expanding and strengthening drug testing programs in drivers is warranted.

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## References

- Alvarez, F.J., Del Rio, M.C., 2003. Response to Ramaekers: pitfalls in estimating drug-related crash risk. *Trends Pharmacol. Sci.* 24 (3), 115.
- Arria, A.M., Caldeira, K.M., Vincent, K.B., Garnier-Dykstra, L.M., O'Grady, K.E., 2011. Substance-related traffic-risk behaviors among college students. *Drug Alcohol Depend.* 118 (2–3), 306–312.
- Asbridge, M., Hayden, J.A., Cartwright, J.L., 2012. Acute cannabis consumption and motor vehicle collision risk: systematic review of observational studies and meta-analysis. *BMJ*, <http://dx.doi.org/10.1136/bmj.e536>.
- Bates, M.N., Blakely, T.A., 1999. Role of cannabis in motor vehicle crashes. *Epidemiol. Rev.* 21 (2), 222–232.
- Battistella, G., Fornari, E., Thomas, A., Mall, J.F., Chtioui, H., Appenzeller, M., Annoni, J.M., Favrat, B., Maeder, P., Giroud, C., 2013. Weed or wheel! fMRI, behavioral and toxicological investigations of how cannabis smoking affects skills necessary for driving. *PLoS ONE* 8, e52545.
- Bedard, M., Dubois, S., Weaver, B., 2007. The impact of cannabis on driving. *Can. J. Public Health* 98 (1), 6–11.
- Bogstrand, S.T., Gjerde, H., Normann, P.T., Rossow, I., Ekeberg, Ø., 2012. Alcohol, psychoactive substances and non-fatal road traffic accidents – a case-control study. *BMC Public Health* 12, 734, <http://dx.doi.org/10.1186/1471-2458-12-734>.
- Brady, J.E., Li, G., 2013. Prevalence of alcohol and other drugs in fatally injured drivers. *Addiction* 108 (1), 104–114.
- Bramness, J.G., Skurtveit, S., Mørland, J., Engeland, A., 2012. An increased risk of motor vehicle accidents after prescription of methadone. *Addiction* 107 (5), 967–972.
- Braut, M., Dussault, C., Bouchard, J., Lemire, A., 2004. The contribution of alcohol and other drugs among fatally injured drivers in Quebec: final results. In: 17th International Conference on Alcohol, Drugs and Traffic Safety, Glasgow, Glasgow, UK, August 8–13. ICADTS.
- Dassanayake, T., Michie, P., Carter, G., Jones, A., 2011. Effects of benzodiazepines, antidepressants and opioids on driving: a systematic review and meta-analysis of epidemiological and experimental evidence drug safety. *Drug Saf.* 34 (2), 125–156.
- Downey, L.A., King, R., Papafotiou, K., Swann, P., Ogden, E., Boorman, M., Stough, C., 2013. The effects of cannabis and alcohol on simulated driving: influences of dose and experience. *Accid. Anal. Prev.* 50, 879–886.
- Dubois, S., Bédard, M., Weaver, B., 2008. The impact of benzodiazepines on safe driving. *Traffic Inj. Prev.* 9 (5), 404–413.
- Dupont, R.L., 2011. Drugged Driving Research: A White Paper. National Institute on Drug Abuse, Bethesda, MD.
- Dupont, R.L., Voas, R.B., Walsh, J.M., Shea, C., Talpins, S.K., Neil, M.M., 2012. The need for drugged driving per se laws: a commentary. *Traffic Inj. Prev.* 13 (1), 31–42.
- Engeland, A., Skurtveit, S., Mørland, J., 2007. Risk of road traffic accidents associated with the prescription of drugs: a registry-based cohort study. *Ann. Epidemiol.* 17 (8), 597–602.
- Gadegbeku, B., Amoros, E., Laumon, B., 2011. Responsibility study: main illicit psychoactive substances among car drivers involved in fatal road crashes. *Ann. Adv. Automot. Med.* 55, 293–300.
- Gjerde, H., Kinn, G., 1991. Impairment of drivers due to cannabis in combination with other drugs. *Forensic Sci. Int.* 50 (1), 57–60.
- Gjerde, H., Normann, P.T., Christophersen, A.S., Samuelsen, S.O., Mørland, J., 2011. Alcohol, psychoactive drugs, and fatal road traffic accidents in Norway: a case-control study. *Accid. Anal. Prev.* 43 (3), 1197–1203.
- Goodnough, A., Zezima, K., 2010. Drivers on prescription drugs are hard to convict. *The New York Times*, A1.
- Gustavsen, I., Bramness, J.G., Skurtveit, S., Engeland, A., Neutel, I., Mørland, J., 2008. Road traffic accident risk related to prescriptions of the hypnotics zopiclone, zolpidem, flunitrazepam and nitrazepam. *Sleep Med* 9 (8), 818–822.
- Hartman, R.L., Huestis, M.A., 2013. Cannabis effects on driving skills. *Clin. Chem.* 59 (3), 478–492.
- Hels, T., Bernhoft, I.M., Lyckegaard, A., Houwing, S., Hagenzieker, M., Legrand, S.A., Isalberti, C., Van der Linden, T., Verstraete, A., 2012. Risk of Injury by Driving with Alcohol and Other Drugs. DRUID, Bergisch Gladbach, Germany (DRUID Deliverable D2.3.5).
- Jones, R.K., Shinar, D., Walsh, J.M., 2003. State of Knowledge of Drug-Impaired Driving. National Highway Traffic Safety Administration, Washington, DC (Report No. DOT HS 809 642).
- Kaplan, J., Kraner, J., Palozzi, L., 2006. Alcohol and other drug use among victims of motor-vehicle crashes – West Virginia, 2004–2005. *Morb. Mortal. Wkly. Rep.* 55, 1293–1296.
- Kelly, E., Darke, S., Ross, J., 2004. A review of drug use and driving: epidemiology, impairment, risk factors and risk perceptions. *Drug Alcohol Rev.* 23 (3), 319–344.
- Kuyppers, K.P., Legrand, S.A., Ramaekers, J.G., Verstraete, A.G., 2012. A case-control study estimating accident risk for alcohol, medicines and illegal drugs. *PLoS ONE* 7 (8), e43496.
- Lacey, J.H., Kelley-Baker, T., Furr-Holden, D., Voas, R., Moore, C., Brainard, K., Tippetts, A.S., Romano, E., Torres, P., Berning, A., 2009a. 2007 National Roadside Survey of Alcohol and Drug Use by Drivers: Methodology. National Highway Traffic Safety Administration, US Department of Transportation, Washington, DC (DOT HS 811 237).

- Lacey, J.H., Kelley-Baker, T., Furr-Holden, D., Voas, R.B., Romano, R., Ramirez, A., Brainard, K., Moore, C., Torres, P., Berning, A., 2009b. 2007 National Roadside Survey of Alcohol and Drug Use by Drivers: Drug Results. National Highway Traffic Safety Administration, US Department of Transportation, Washington, DC (DOT HS 811 249).
- Lacey, J.H., Kelley-Baker, T., Voas, R.B., Romano, E., Furr-Holden, C.D., Torres, P., Berning, A., 2011. Alcohol- and drug-involved driving in the United States: methodology for the 2007 National Roadside Survey. *Eval. Rev.* 35 (4), 319–353.
- Laumon, B., Gadegebeku, B., Martin, J.L., Biecheler, M.B., SAM Group, 2005. Cannabis intoxication and fatal road crashes in France: population based case-control study. *BMJ* 331 (7529), 1371.
- Legrand, S.A., Isalberti, C., der Linden, T.V., Bernhoft, I.M., Hels, T., Simonsen, K.W., Favretto, D., Ferrara, S.D., Caplinskiene, M., Minkuviene, Z., Pauliukevicius, A., Houwing, S., Mathijssen, R., Lillsunde, P., Langel, K., Blencowe, T., Verstraete, A.G., 2013. Alcohol and drugs in seriously injured drivers in six European countries. *Drug Test Anal.* 5 (3), 156–165.
- Leung, S.Y., 2011. Benzodiazepines, opioids and driving: an overview of the experimental research. *Drug Alcohol Rev.* 30 (3), 281–286.
- Li, G., Baker, S.P., 2012. Epidemiologic methods. In: Li, G., Baker, S.P. (Eds.), *Injury Research: Theories, Methods, and Approaches*. Springer, New York, NY, pp. 203–220.
- Li, G., Brady, J.E., DiMaggio, C., Baker, S.P., Rebok, G.W., 2010. Validity of suspected alcohol and drug violations in aviation employees. *Addiction* 105 (10), 1771–1775.
- Li, L., Zhang, X., Levine, B., Li, G., Zielke, H.R., Fowler, D.R., 2011. Trends and pattern of drug abuse deaths in Maryland teenagers. *J. Forensic Sci.* 56 (4), 1029–1033.
- Li, M.-C., Brady, J.E., DiMaggio, C.J., Lusardi, A.R., Tzong, K.Y., Li, G., 2012. Marijuana use and motor vehicle crashes. *Epidemiol. Rev.* 34 (1), 65–72.
- Mathijssen, R., Houwing, S., 2005. The Prevalence and Relative Risk of Drink and Drug Driving in the Netherlands: A Case-Control Study in the Tilburg Police District, 2nd ed. SWOV Institute for Road Safety Research, Leidschendam, The Netherlands (SWOV publication R-2005-9).
- McCarroll, J.R., Haddon Jr., W., 1962. A controlled study of fatal automobile accidents in New York City. *J. Chronic Dis.* 15 (6), 811–826.
- Movig, K.L., Mathijssen, M.P., Nagel, P.H., van Egmond, T., de Gier, J.J., Leufkens, H.G., Egberts, A.C., 2004. Psychoactive substance use and the risk of motor vehicle accidents. *Accid. Anal. Prev.* 36 (4), 631–636.
- Mura, P., Kintz, P., Ludes, B., Gaulier, J.M., Marquet, P., Martin-Dupont, S., Vincent, F., Kaddour, A., Goullé, J.P., Nouveau, J., Moulisma, M., Tilhet-Coartet, S., Pourrat, O., 2003. Comparison of the prevalence of alcohol, cannabis and other drugs between 900 injured drivers and 900 control subjects: results of a French collaborative study. *Forensic Sci. Int.* 133 (1–2), 79–85.
- Musshoff, F., Madea, B., 2012. Driving under the influence of amphetamine-like drugs. *J. Forensic Sci.* 57 (2), 413–419.
- National Highway Traffic Safety Administration (NHTSA), 2010. 2009 FARS Coding and Validation Manual. National Highway Traffic Safety Administration, US Department of Transportation, Washington, DC (DOT HS 811 353).
- National Highway Traffic Safety Administration (NHTSA), 2012. FARS Analytical User's Manual 1975–2011. National Highway Traffic Safety Administration, US Department of Transportation, Washington, DC (DOT HS 811 693).
- National Institute on Drug Abuse (NIDA), 2010a. Prescription Drug Abuse. National Institute on Drug Abuse, National Institutes of Health, Bethesda, MD.
- National Institute on Drug Abuse (NIDA), 2010b. InfoFacts: Drugged Driving. National Institute on Drug Abuse, National Institutes of Health, Bethesda, MD.
- Orriols, L., Queinac, R., Philip, P., Gadegebeku, B., Delorme, B., Moore, N., Suissa, S., Lagarde, E., CESIR Research Group, 2012. Risk of injurious road traffic crash after prescription of antidepressants. *J. Clin. Psychiatry* 73 (8), 1088–1094.
- Orriols, L., Salmi, L.R., Philip, P., Moore, N., Delorme, B., Castot, A., Lagarde, E., 2009. The impact of medicinal drugs on traffic safety: a systematic review of epidemiological studies. *Pharmacoepidemiol. Drug Saf.* 18 (8), 647–658.
- Raghunathan, T.E., Lepkowski, J.M., Van Hoewyk, J., Solenberger, P., 2001. A multivariate technique for multiply imputing missing values using a sequence of regression models. *Surv. Methodol.* 27 (1), 85–95.
- Ramaekers, J.G., 2003. Pitfalls in estimating drug-related crash risk. *Trends Pharmacol. Sci.* 24 (3), 114–115.
- Ramaekers, J.G., Kuypers, K.P.C., Bosker, W.M., Brookhuis, K.A., Veldstra, J.A., Simons, R., Martens, M., Hjalmdahl, M., Forsman, A., Knoche, A., 2012. Effects of stimulant drugs on actual and simulated driving: perspectives from four experimental studies conducted as part of the DRUID research consortium. *Psychopharmacol.* 222 (3), 413–418.
- Rapaport, M.J., Lanctôt, K.L., Streiner, D.L., Bédard, M., Vingilis, E., Murray, B., Schaffer, A., Shulman, K.I., Herrmann, N., 2009. Benzodiazepine use and driving: a meta-analysis. *J. Clin. Psychiatry* 70 (5), 663–673.
- Reisfield, G.M., Goldberger, B.A., Gold, M.S., DuPont, R.L., 2012. The mirage of impairing drug concentration thresholds: a rationale for zero tolerance per se driving under the influence of drugs laws. *J. Anal. Toxicol.* 36 (5), 353–356.
- Romano, E., Voas, R., 2011. Drug and alcohol involvement in four types of fatal crashes. *J. Stud. Alcohol Drug.* 72 (4), 567–576.
- Rubin, D.B., 1987. Multiple Imputation for Nonresponse in Survey. Wiley, New York, NY.
- Smink, B.E., Egberts, A.C., Lusthof, K.J., Uges, D.R., de Gier, J.J., 2010. The relationship between benzodiazepine use and traffic accidents: a systematic literature review. *CNS Drug.* 24 (8), 639–653.
- Stramer, G.A., Bird, K.D., 1984. Investigating drug-ethanol interactions. *Br. J. Clin. Pharmacol.* 18 (S1), 27–35.
- The Walsh Group, 2002. The Feasibility of per se Drugged Driving Legislation: Consensus Report. The Walsh Group, Bethesda, MD.
- Voas, R.B., Dupont, R.L., Shea, C.L., Talpins, S.K., 2013. Prescription drugs, drugged driving and per se laws. *Inj. Prev.* 19 (3), 218–221.
- Walsh, J.M., de Gier, J.J., Christopherson, A.S., Verstraete, A.G., 2004a. Drugs and driving. *Traffic Inj. Prev.* 5 (3), 241–253.
- Walsh, J.M., Flegel, R., Cangianelli, L.A., Atkins, R., Soderstrom, C.A., Kerns, T.J., 2004b. Epidemiology of alcohol and other drug use among motor vehicle crash victims admitted to a trauma center. *Traffic Inj. Prev.* 5 (3), 254–260.
- Walsh, J.M., Flegel, R., Atkins, R., 2005. Drug and alcohol use among drivers admitted to a level-1 trauma center. *Accid. Anal. Prev.* 37 (5), 894–901.
- Zador, P.L., 1991. Alcohol-related relative risk of fatal driver injuries in relation to driver age and sex. *J. Stud. Alcohol* 52 (4), 302–310.