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The use of electronic pharmacy data to investigate prescribed medications and fatal motor vehicle crashes in a military population, 2002–2006

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ABSTRACT

The authors examined the association between prescribed medications and fatal motor vehicle crashes (MVCs) in an active duty military population between 2002 and 2006. Using a case–control design, MVC deaths were ascertained using a military mortality registry, and an integrated health system database provided information on health system eligibility, pharmacy transactions, and medical encounters. Cases and controls were matched on comparable observation time outside periods of deployment. Among selected categories, only one, antidepressant medications, was an independent predictor of fatal MVC (odds ratio, 3.19; 95% confidence interval, 1.01–10.07). Male gender, Black race, enlisted rank, service branch (Navy and Marine Corps), and selected co-morbidities were also independent predictors. Unexpectedly, the odds of younger age quartiles (<27 years) and history of deployment were reduced for MVC cases. Although results need to be considered in the context of data limitations, the association between prescribed antidepressants and fatal MVC may reflect unmeasured co-morbidities, such as combined effects of prescribed and over-the-counter medications and/or alcohol or other substance abuse. Younger individuals, representing new military accessions in training or returning from deployment with serious injuries, may have fewer opportunities to operate vehicles, or targeted efforts to reduce MVC following deployment may be showing a positive effect.

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1. Introduction

Motor vehicle crashes (MVCs) continue to be a leading cause of death in the U.S. among individuals three to 33 years of age, accounting for over 43,500 traffic-related deaths in 2005 and representing 25.1% of all injury deaths (Kung et al., 2008; NHTSA, 2005). The cost to society in terms of property damage, injury and disability, and years of productive life lost remains high (NHTSA, 2005). Among U.S. military personnel, MVC injury and fatality rates declined from 1980 to 1995 (Jones, 1999) but remain an important cause of injury hospitalization for all service branches (Armed Forces Health Surveillance Center, 2007). Based on 2006 data from the Department of Defense (DoD) Medical Mortality Registry, MVCs are the second leading cause of death, following combat (unpublished data, LP).

Numerous MVC risk factors have been documented in the literature, including demographic characteristics (young males) (NHTSA, 2005; Tavris et al., 2001) and behavioral factors (speeding, non-use of occupant restraints and helmets, fatigue, distraction, cellular phone use, and alcohol consumption) (Bell et al., 2000; CDC, 1995; Connor et al., 2002; Kraus et al., 1995; Laberge-Nadeau et al., 2003; Lardelli-Claret et al., 2003; Stutts et al., 2001; Van Tuinen, 1994). Studies of MVC in military populations reflect the high proportion of young, single males at increased risk of MVC (Bell et al., 2000; Hooper et al., 2005, 2006; Krull et al., 2004; Lincoln et al., 2006). Increased fatal crash risk has previously been reported in the military following combat deployment (Hooper et al., 2006; Kang and Bullman, 2001; Lincoln et al., 2006). Proposed explanations have included the consequences of adverse psychological outcomes following deployment or coping mechanisms for war-related stresses and traumatic experiences (Bell et al., 2001).

Certain medical conditions have also been associated with increased risk of MVC in the general population through impairment of physical or cognitive functioning, including sleep disorders (Ellen et al., 2006; Howard et al., 2004; Sagberg, 2006; Teran-Santos et al., 1999), non-medicated diabetes (Sagberg, 2006), seizure disorders (Tomson et al., 2004), prior transient ischemic attack or stroke (McGwin et al., 2000; Sagberg, 2006; Sims et al., 2000), heart con-

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ditions (McGwin et al., 2000; Sagberg, 2006), arthritis (McGwin et al., 2000), mental disorders (including substance abuse) (Hooper et al., 2006), and prior MVC injury (Hooper et al., 2006; McGwin et al., 2000). Furthermore, therapeutic or side effects of medications prescribed for anxiety or depression (e.g., benzodiazepines (Barbone et al., 1998; Drummer et al., 2004; Movig et al., 2004; Mura et al., 2003; Ray et al., 1992; Thomas, 1998; Verster and Volkerts, 2004; Walsh et al., 2004) and anti-depressants (Mura et al., 2003; Sagberg, 2006; Walsh et al., 2004)), allergies (e.g., sleep-inducing antihistamines (Finkle et al., 2002)), and pain (e.g., opiates (Drummer et al., 2004; Leveille et al., 1994; Movig et al., 2004; Walsh et al., 2004)) have been implicated in increasing MVC risk. A recently published Norwegian cohort study examined the risk of road accidents associated with prescribed medications using three population-based registries (Engeland et al., 2007). Risk of an injury-producing MVC was significantly increased for drivers who were prescribed opiates and benzodiazepines.

Our study is the first to investigate prescribed medications and fatal motor vehicle crash risk in a large population of active duty U.S. military service members. Active duty personnel generally seek health care through the military health system, a single managed care system that captures all patient encounters electronically, including prescribed and dispensed medications. Using available electronic data, we evaluated selected prescription medications as predictors of fatal MVC in this occupational group.

2. Materials and methods

2.1. Data sources

We used a case–control study design to investigate the association between selected categories of prescription medications and fatal MVC in a population of active duty military personnel based on electronic data from the following sources: the DoD Medical Mortality Registry maintained by the Armed Forces Institute of Pathology, Rockville, Maryland, to ascertain deaths; the Contingency Tracking System maintained by the Defense Manpower Data Center, Seaside, California, for dates of deployment; and the Military Health System Data Management Analysis and Reporting Tool (M2) maintained by TRICARE Management Activity. M2 served as our integrated information source on health care eligibility, pharmacy transactions, and medical encounters, and its components include the Defense Enrollment Eligibility Reporting System (DEERS), Pharmacy Data Transaction Service (PDTS), Standard Ambulatory Data Record (SADR), Standard Inpatient Data Record (SIDR), and Health Care Service Record (HCSR) for care obtained outside the military health system but subsidized by DoD. The common matching variable used across all data systems was Social Security number (SSN). These data systems are regularly maintained and updated, making the probability of a false match very low.

2.2. Case identification

A case was defined as an active duty U.S. military service member who died as a result of a MVC occurring outside the Theater of Operations for the conflicts in Iraq and Afghanistan between fiscal years (FYs) 2002 and 2006 (October 1, 2001, to September 30, 2006). Cases were limited to drivers of privately owned motor vehicles on public roads, including motorcycles. We restricted our study outcome to MVC fatalities because non-fatal MVCs resulting in a health encounter were incompletely cause-coded for the period of our study. To ensure that automated prescription medication data would potentially be available for analysis, cases must have been eligible for military health care benefits by enrollment in DEERS. Reserve and National Guard members were not included in this study since they generally obtain health care outside the military health system when not on activated status.

A total of 1262 MVC deaths were identified through the DoD Medical Mortality Registry. Cause of death was based on the "underlying cause" field, derived from death certificates, medical records, autopsy reports, police reports, and/or investigative reports. Since the Registry captures all active duty deaths through direct connection with the Defense Casualty Information Processing System, death ascertainment for our active duty study population was considered to be complete and include accurate cause-of-death information.

Deaths due to MVC identified by the Medical Mortality Registry were linked to M2 data files using SSNs, with an exact match required. Enrollment in DEERS established military health care eligibility and, therefore, the potential for electronic prescription medication records. Decedents' SSNs were initially matched to DEERS data using the last month of each fiscal year because of the routine database archiving procedure that applied in FY 2002 (only the last month was accessible for FY 2002). Among the 1262 registry-based deaths, 824 were identified in DEERS. Of the remaining 438 MVC deaths, 204 were Reserve/Guard members and, therefore, excluded. Further examination of M2 files resulted in 168 additional deaths meeting the case definition based on the following circumstances: decedent was not in DEERS during the last month of FY 2002 because death occurred in the preceding 11 months, but medical encounter records were identified indicating health care eligibility; or DEERS enrollment and death both occurred during the first eleven months of any one fiscal year between 2003 and 2006. From the total of 992 cases meeting the case definition, 30 were subsequently excluded due to missing deployment end dates. Therefore, our final analysis data set included 962 fatal MVC cases. Fig. 1 illustrates the process of generating the case group.

2.3. Control selection

Our pool of potential controls consisted of active duty U.S. military personnel enrolled in DEERS between October 1, 2001, and September 30, 2006, and presumed alive as of September 30, 2006 (Fig. 1). M2 eligibility data (DEERS) were used to identify potential controls, whose SSNs were then matched to Medical Mortality Registry data to exclude decedents. From this pool ($n = 2{,}185{,}122$), controls were matched to cases by DEERS enrollment at the end of the FY of index case death and comparable observation time outside deployment periods and then randomly selected in a 3:1 ratio. The final study population thus consisted of 962 cases and 2886 controls.

Both DEERS enrollment and deployment start and end dates were used to establish observation periods for purposes of case–control matching. For all cases, we initially selected 120 days of observation time prior to the occurrence of a fatal MVC in order to allow a reasonable time interval for exposure to dispensed prescription medications and to also maximize our potential for stratification by possible medication exposure windows. We censored observation periods for controls to make them similar in length to matched index cases. Strict attention was paid to comparable health care eligibility periods falling outside deployments in order to ensure equal opportunity for controls to become a case, as well as for prescribed medications to be captured in the pharmacy database.

2.4. Primary predictor variables

Our primary predictor variables were medications dispensed within the military health system and captured in the automated PDTS database, which does not typically include prescriptions

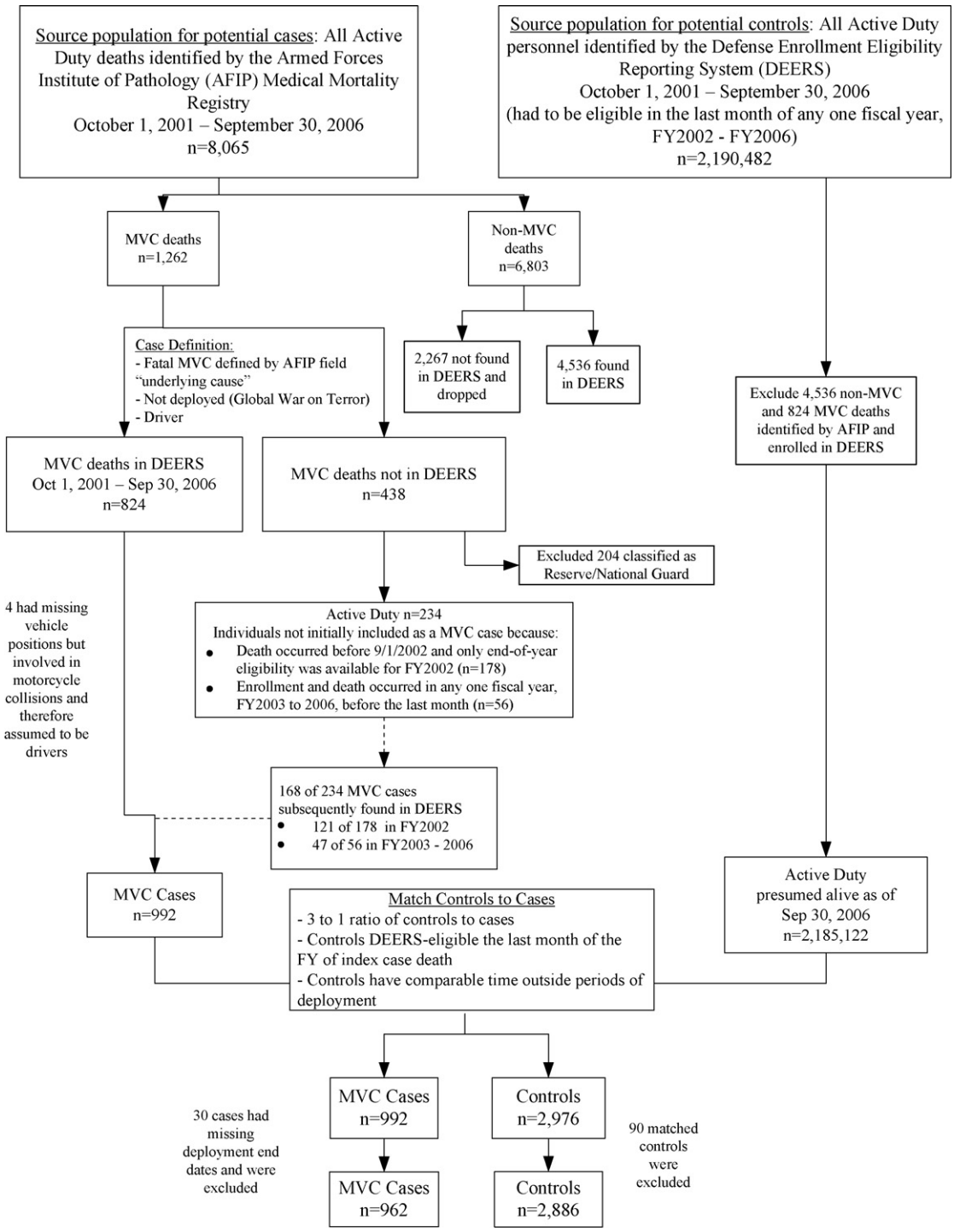

Fig. 1. Identification of fatal motor vehicle crash (MVC) cases and selection of matched controls among active duty military service members, FY 2002–2006.

dispensed during deployment. Each of the selected prescription medications was associated with MVC in the published literature and was initially grouped according to therapeutic purpose (antihistamines; analgesics and antipyretics; psychotherapeutic agents; anticonvulsants; and anxiolytics, sedatives, and hypnotics) and/or potential for side effects (barbiturates, benzodiazepines, opiate antagonists, serotonin agonists, and amphetamines). The variables for each medication category were dichotomized ('yes'/'no'), and we assumed that medications appearing in PDTS were consumed during associated medication exposure windows. Medications dispensed prior to the exposure window but in amounts that presupposed usage within that given time interval were also included. We explored three medication exposure windows: 0–14, 0–30, and 0–120 days. For cases, we examined selected medications captured in PDTS over these medication exposure windows up to the time of death. For matched controls, we examined PDTS medications over a comparable time period ending in the same fiscal year as the index case death. We conducted detailed exploratory analyses for each of the selected medication subcategories. Preliminary results directed additional analyses and, for multivariable modeling, collapsing of some groups and exclusion of others due to small cell sizes.

2.5. Covariates of interest

Several known risk factors for MVC and potential confounders were considered for inclusion in a multivariable model. These covariates included demographic and military service characteristics, selected medical co-morbidities, including prior MVC injury. Demographic and military service characteristics were obtained from DEERS at the time study eligibility was established and included the following variables: gender (male, female), age (based on quartiles: ≤20, 21–22, 23–26, ≥27 years), race (White, Black, other), and marital status (currently single, currently married). Data on ethnicity were incomplete and therefore not considered. Military service characteristics included branch of service (Army, Navy, Air Force, Marine Corps) and rank (enlisted, officer, cadet). Data on deployment start and end dates (more than one deployment possible) within the study period were used to assess available observation time for cases and controls; the deployment variable was dichotomized as 'yes'/'no' up to the time of index case death (for cases and matched controls). For fatal MVC cases missing demographic information in DEERS, we used data from the Medical Mortality Registry.

Medical co-morbidities were based on any primary or secondary diagnoses, using International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes, in medical encounter databases (SIDR, SADR, and HCSR) within the M2 system between FY 2002 and 2006, prior to the time of index case death (for cases and matched controls). We examined the following co-morbidities, selected *a priori*: organic sleep disorders; asthma; substance abuse; other mental disorders, excluding mental retardation; aneurysms; embolisms; diabetes mellitus; epilepsy and recurrent seizures; migraine; cataplexy and narcolepsy; ischemic heart disease; other forms of heart disease; diseases of the musculoskeletal system and connective tissue; and prior MVC injury. Prior MVC injury was defined as a medical encounter for non-fatal MVC for cases and controls based on ICD-9-CM injury codes combined with relevant NATO Standardization Agreement (STANAG) codes and/or External Cause Codes (E-Codes) related to MVC. Any medical encounter for MVC injury within 10 days of death was considered part of the fatal event.

2.6. Statistical analyses

Following data cleaning and validation procedures (including removal of any duplicate records), we performed univariate and bivariate analyses and calculated conditional crude odds ratios and 95% confidence intervals for our primary predictor variables and covariates of interest. We used conditional logistic regression in order to make comparisons of exposure to prescribed medications within matched sets of cases and controls. Our approach to multivariate modeling was a backwards stepwise elimination procedure resulting in a final reduced model to assess prescribed medications as independent predictors of fatal MVC, while adjusting for all other variables in the model. All analyses were performed using SAS V 9.1 (2004).

The study protocol was reviewed and approved by the Institutional Review Boards at the Uniformed Services University of the Health Sciences, the Centers for Disease Control and Prevention, the Armed Forces Institute of Pathology, and the TRICARE Management Activity, Office of the Assistant Secretary of Defense (Health Affairs).

3. Results

Table 1 presents a distribution of demographic and military service characteristics for our study population by case–control status. Cases were more likely to be men, in the oldest age quartile, categorized as Black race, married, enlisted, and not have a history of deployment to Iraq and Afghanistan. The 30 cases excluded from this study because of missing deployment end dates were dissimilar to remaining eligible cases in several ways: more likely to be younger (<21 years: 43.3% vs. 33.5%), single (70% vs. 61%), and in the Navy (36.7% vs. 24.6%).

Table 1
Demographic and military characteristics for active duty fatal motor vehicle crash cases[a] and controls, fiscal year 2002–2006.

Characteristics	Cases		Controls	
	n = 962	%	*n* = 2886	%
Gender				
Men	897	93.2	2420	83.9
Women	65	6.8	466	16.2
Age group based on quartiles				
≤20	208	21.6	1062	36.8
21–22	208	21.6	670	23.2
23–26	235	24.4	625	21.7
≥27	310	32.2	529	18.3
Missing	1	0.1		
Race				
White	638	66.3	2093	72.5
Black	224	23.3	440	15.3
Other[b]	91	9.5	251	8.7
Unknown/missing	9	0.9	102	3.5
Marital status				
Currently single	583	60.6	2101	72.8
Currently married	322	33.5	757	26.2
Unknown/missing	57	5.9	28	1.0
Branch of service				
Army	338	35.1	1199	41.6
Navy	237	24.6	616	21.3
Air Force	206	21.4	630	21.8
Marine Corps	181	18.8	441	15.3
Rank				
Enlisted	893	92.8	2567	89.0
Officer	63	6.6	246	8.5
Cadet	6	0.6	73	2.5
Deployment[c]				
No	613	63.7	1553	53.8
Yes	349	36.3	1333	46.2

[a] Cases are active duty driver deaths with a motor vehicle crash underlying cause in Department of Defense Medical Mortality Registry.
[b] Includes American Indian/Alaskan Native, Asian or Pacific Islander, and Hispanic.
[c] Iraq and Afghanistan Theater of Operations.

The frequency distribution of selected prescription medication groups was examined as cumulative totals within three possible medication exposure windows, 0–14, 0–30, and 0–120 days (data not shown). The greatest proportion of individuals by case–control status with records of prescribed medication were in the categories of analgesics and antipyretics (24.0% of cases vs. 15.1% of controls), which included non-steroidal anti-inflammatory drugs (NSAIDs) and opiate agonists, and antihistamines (7.0% of cases vs. 3.9% of controls). Other sub-categories of interest included benzodiazepines (1.7% of cases vs. 0.3% of controls) and antidepressants (3.9% of cases vs. 0.5% of controls). Individuals could be counted in more than one medication category within the 120-day exposure window. Overall, 281 of 962 cases (29.2%) had a medication prescribed in one or more of the initially selected categories compared with 482 of 2886 controls (16.7%).

Preliminary results led to adjustments to initial medication groups. Several categories (amphetamines, opiate antagonists, and serotonin agonists) were excluded due to small cell sizes. For antihistamines and NSAIDs, although bivariate analysis resulted in crude odds ratios that were statistically significantly elevated (odds ratio [OR] = 1.57, 95% confidence interval [CI]: 1.03, 2.38, for

Table 2
Number of cases and controls with selected co-morbid medical conditions[a] within the study period, fiscal year 2002–2006.

Medical condition (ICD-9-CM)	Cases $n = 962$		Controls $n = 2886$	
	n	%	n	%
Asthma (ICD-9-CM: 493)	19	2.0	13	0.5
Sleep Disorders (ICD-9-CM: 327)	1	0.1	0	0.0
Substance Abuse (ICD-9: 291, 292, 303, 304, 305.2–305.9)	92	9.6	42	1.5
Other Mental Disorders Excluding Mental Retardation (ICD-9-CM: 290, 293–302, 306–316)	94	9.8	53	1.8
Aneurysm (ICD-9-CM: 441–442)	3	0.3	0	0.0
Embolism (ICD-9-CM: 444–445)	3	0.3	0	0.0
Diabetes (ICD-9-CM: 250)	4	0.4	3	0.1
Epilepsy (ICD-9-CM: 345)	6	0.6	1	0.0
Narcolepsy (ICD-9-CM: 347)	0	0.0	0	0.0
Migraines (ICD-9-CM: 346)	17	1.8	9	0.3
Ischemic Heart Disease (ICD-9-CM: 410–414)	5	0.5	0	0.0
Other Forms of Heart Disease Excluding Cardiac Arrest (ICD-9-CM: 420–429)	47	4.9	7	0.2
Musculoskeletal Diseases (ICD-9-CM: 710–739)	379	39.4	314	10.9
Prior MVC Injury	27	2.8	5	0.2

ICD-9-CM: International Classification of Diseases, 9th Revision, Clinical Modification.
[a] Personnel could be counted in more than one co-morbid medical condition category.

antihistamines and OR = 1.43, 95% CI: 1.10, 1.87, for NSAIDs), no further analyses were conducted due to the expectation that PDTS data would provide an incomplete picture due to over-the-counter medication use. The following medication groups were considered for multivariable modeling: benzodiazepines, antidepressants, and opiate agonists. With respect to medication exposure intervals, we selected the 0–30 day window because adequate numbers were available for the assessment of potential short-term medication effects.

The co-morbidities presented in Table 2 were disproportionately distributed among cases compared with controls. Of the 962 cases, 469 (48.8%) had a history of one or more of the selected co-morbid conditions compared with only 366 out of 2886 controls (12.7%). After examining cell sizes, we retained for further analyses only substance abuse, other mental disorders, and musculoskeletal diseases, as well as prior MVC injury because of its importance as a predictor in previous studies.

Table 3 presents the results of conditional logistic regression for our reduced set of explanatory variables. Unadjusted measures suggest that cases were statistically significantly more likely than controls to be men (crude OR = 2.67, 95% CI: 2.04, 3.51), Black versus White race (crude OR = 1.67, 95% CI: 1.39, 2.02), Navy (crude OR = 1.38, 95% CI: 1.13, 1.68) or Marine Corps (crude OR = 1.48, 95% CI: 1.19, 1.83) versus Army, and enlisted (crude OR = 1.38, 95% CI: 1.03, 1.84) versus officer. Cases were significantly less likely to be single versus married (crude OR = 0.58, 95% CI: 0.49, 0.69), in younger age quartiles (≤20 years: crude OR = 0.32, 95% CI: 0.25, 0.39; 21–22 years: crude OR = 0.51, 95% CI: 0.41, 0.63; 23–26 years: crude OR = 0.62, 95% CI: 0.50, 0.77) versus the oldest quartile (≥27 years), and deployed (one or more times) during the study period (crude OR = 0.67, 95% CI: 0.58, 0.78).

Table 3 also shows that cases were statistically significantly more likely to have had a prescription for antidepressants (crude OR = 12.00, 95% CI: 4.91, 29.36), opiate agonists (crude OR = 1.62, 95% CI: 1.07, 2.46), or benzodiazepines (crude OR = 7.80, 95% CI: 2.78, 21.88), dispensed within a 30-day window, and a medical encounter with a diagnosis of substance abuse (crude OR = 7.37, 95% CI: 5.01, 10.85), other mental disorders (crude OR = 5.70, 95% CI: 4.02, 8.08), musculoskeletal diseases (crude OR = 5.69, 95% CI: 4.70, 6.88), and/or injury due to prior MVC (crude OR = 16.20, 95% CI: 6.24, 42.17).

Multivariable conditional logistic regression resulted in a more parsimonious model in which opiate agonists and benzodiazepines, as well as the marital status variable, were found not to be significant and removed. Antidepressant medication remained statistically significantly associated with fatal MVC, after adjustment for all other variables in the model (adjusted OR = 3.19, 95% CI: 1.01, 10.07). Age, history of deployment(s), gender, and race were also independent predictors of fatal MVC, with direction and magnitude of effect similar to crude associations. All co-morbidities retained in the multivariable model emerged as strong independent predictors. Cases were found to be statistically more likely to have a prior diagnosis of substance abuse (adjusted OR = 4.25, 95% CI: 2.57, 7.03), other mental disorders (adjusted OR = 2.28, 95% CI: 1.41, 3.70), diseases of the musculoskeletal system (adjusted OR = 4.66, 95% CI: 3.68, 5.90), and/or injury due to a prior MVC (adjusted OR = 9.34, 95% CI: 2.86, 30.53).

4. Discussion

4.1. Main findings

Our population-based study examined the association between MVCs and dispensed prescription medications in active duty service members over a five-year study period using available electronic databases. Among the medication groups analyzed, only one, antidepressant medication, remained significantly associated with fatal MVC after adjustment for covariates. This finding should be considered preliminary due to data limitations. Additionally, since fatal MVC is a rare event, small numbers precluded analysis of several medication categories of interest, as well as variables related to dosage, timing, and multi-drug use. Multi-drug use has frequently been detected among drivers suspected of driving under the influence of drugs (Weiler et al., 2000), and the combination of alcohol and drugs or use of multiple drugs increases MVC risk (CDC, 2006; Christophersen and Morland, 1997; Kelly et al., 2004; Movig et al., 2004). Also of note are the elevated adjusted odds ratios for co-morbid conditions, specifically substance abuse, other mental disorders, and musculoskeletal diseases. Further investigation of interaction between these co-morbidities and specific medications prescribed to treat them would be informative.

Consistent with previous studies in military populations, we found that enlisted males are at increased risk of MVC (Bell et al., 2000; Hooper et al., 2005; Krull et al., 2004). However, an unexpected finding was that individuals in younger age quartiles were less likely to be involved in a fatal MVC compared with those in the oldest quartile (in this population, ≥27 years). The reduced odds of being in younger age categories was also consistent with the unadjusted reduced odds of “currently single” marital status for MVC cases.

Table 3
Crude and adjusted odds ratios and 95% confidence intervals of selected characteristics for matched MVC cases[a] and controls, fiscal year 2002–2006.

Characteristics	Crude		Adjusted	
	Odds ratio	95% Confidence interval	Odds ratio	95% Confidence interval
Demographic and military characteristics				
Gender				
Men	2.67	2.04, 3.51	3.81	2.70, 5.38
Women	ref		ref	
Age group based on quartiles				
≤20	0.32	0.25, 0.39	0.31	0.23, 0.41
21–22	0.51	0.41, 0.63	0.48	0.36, 0.63
23–26	0.62	0.50, 0.77	0.58	0.44, 0.76
27+	ref		ref	
Missing				
Race				
White	ref		ref	
Black	1.67	1.39, 2.02	1.87	1.48, 2.37
Other[b]	1.19	0.92, 1.54	1.42	1.04, 1.96
Unknown/missing				
Marital status				
Currently single	0.58	0.49, 0.69		
Currently married	ref			
Unknown/missing				
Branch of service				
Army	ref		ref	
Navy	1.38	1.13, 1.68	1.45	1.13, 1.85
Air Force	1.16	0.95, 1.41	1.13	0.87, 1.47
Marine Corps	1.48	1.19, 1.83	2.02	1.53, 2.66
Rank				
Enlisted	1.38	1.03, 1.84	1.67	1.15, 2.43
Officer	ref		ref	
Cadet	0.32	0.14, 0.78	0.97	0.31, 3.04
Deployment[c]				
No	ref		ref	
Yes	0.67	0.58, 0.78	0.53	0.44, 0.64
Primary variables of interest				
Medication dispensed within 30 days				
Antidepressants	12.00	4.91, 29.36	3.19	1.01, 10.07
Opiates agonists	1.62	1.07, 2.46		
Benzodiazepines[d]	7.80	2.78, 21.88		
Selected co-morbidities				
Substance Abuse (ICD-9: 291, 292, 303, 304, 305.2–305.9)	7.37	5.01, 10.85	4.25	2.57, 7.03
Other Mental Disorder (ICD-9: 290, 293–302, 306–316)	5.70	4.02, 8.08	2.28	1.41, 3.70
Musculoskeletal Disease (ICD-9: 710–739)	5.69	4.70, 6.88	4.66	3.68, 5.90
Prior MVC Injury	16.20	6.24, 42.17	9.34	2.86, 30.53

ICD-9: International Classification of Disease, 9th Revision; MVC: motor vehicle crashes.
[a] Cases are active duty driver deaths with a motor vehicle crash underlying cause in the Department of Defense Medical Mortality Registry.
[b] Includes American Indian/Alaskan Native, Asian or Pacific Islander, and Hispanic.
[c] Iraq and Afghanistan Theater of Operations.
[d] Benzodiazepines include anticonvulsants and anxiolytics/hypnotics and sedatives.

In addition to younger age, deployment was associated with a reduced risk of fatal MVC, and this finding is not consistent with previous studies in military and veteran populations (Hooper et al., 2005, 2006; Kang and Bullman, 2001). One possible explanation for the apparent protective effect of both younger age and deployment is that the majority of new military accessions are in the youngest age categories, and these individuals have a high likelihood of deployment immediately following training and, therefore, reduced risk of MVC as defined in this study (outside theater of operations). Furthermore, deployments of long duration and often back-to-back, multiple deployments associated with the wars in Iraq and Afghanistan might also result in less opportunity to drive vehicles. It is also possible that the greatest risk takers or those in high-risk occupations were in the youngest age categories and disproportionately represented among those severely injured in combat or MVCs in theater, and, therefore, not at risk of MVC after return from deployment.

On the other hand, it is possible that older individuals (≥27 category included 27–54 years) with co-morbid conditions, who were less likely to be deployed, were more likely to die from a crash once it occurred compared with younger individuals with better overall health and fitness levels (Tavris et al., 2001). It should be noted that a larger proportion (50%) of the 30 excluded cases with missing deployment end dates were in the youngest age category (<21 years) compared with cases that were retained. One final consideration is that the collective effect of DoD safety and injury prevention initiatives in response to the previously identified post-deployment increase in fatal MVC risk is beginning to show positive results among those at highest risk (young males).

4.2. Study strengths and limitations

A number of study limitations, some previously discussed, should be mentioned. Small numbers did not allow stratified anal-

yses by dosage, duration of use, or other variables of interest. Moreover, the fact that prescription medications were dispensed does not guarantee consumption by the patient at therapeutic levels and within the putative exposure window. There was also no ability to capture information on medications acquired outside the military health system (over-the-counter or through other health systems). Some medication groups would be more subject to this bias, such as antihistamines and NSAIDs, which were excluded from the final analysis for this reason.

Using the Medical Mortality Registry, complete mortality ascertainment could only be assured for active duty personnel, thereby restricting this study to the active duty component of the military. However, a previous study in Gulf War era veterans reported that Reserve/National Guard status was not an independent predictor of fatal MVC (Hooper et al., 2006). Another limitation is that the source population for potential controls did not include individuals enrolled in DEERS in FY 2002 if they were not enrolled through the final month or those enrolled and disenrolled within any subsequent fiscal year prior to the final month, which differed from the process applied to identification of cases. Finally, we could not account for other influential predictors of MVC, such as actual miles driven, vehicle type, crash circumstances, or risk taking behaviors (e.g., alcohol use, speeding), some of which affect survivability once a crash has occurred.

Despite these limitations, our population-based study contributes to a better understanding of the multiple factors influencing this ongoing public health problem by investigating prescribed medications and co-morbid medical conditions in addition to other previously studied predictor variables. Our study population was a large U.S. occupational cohort, not limited geographically (e.g., regional trauma center or State) or restricted to a narrowly defined driver subset (e.g., teen drivers or elderly drivers). The Medical Mortality Registry provided complete and reliable death ascertainment for active duty military members, and the M2 integrated health system captured data on prescribed medications, as well as co-morbidities from both inpatient and outpatient medical encounters paid for by DoD. Active duty military personnel use the military health system for most of their health care needs, including prescription medications.

5. Conclusion

In conclusion, our preliminary findings suggest a need to further investigate MVC risks associated with prescription medication use because of the potential for increased crash risk due to therapeutic and/or side effects of certain medication groups. If our observation of an association between antidepressant medication and fatal MVC is supported by additional research, implications might include greater attention to proper prescribing practices for effective treatment of mood disorders (to prevent unintentional or intentional injury involving motor vehicles), closer monitoring of therapeutic or side effects that might affect driving ability in high risk groups, or clinical assessment of the existence of co-morbid conditions with potential for multiple drug interactions or the combined effects of alcohol, illicit drugs, and prescribed or over-the-counter medications that could increase MVC risk. Our specific recommendations for future research include assessment of non-fatal MVC data. Larger numbers may make subgroup analyses and investigation of interactions possible. Current DoD efforts to improve data collection and cause-coding should make such future analyses possible. A cohort study over a longer period of observation may highlight time trends superimposed on interventions or policy changes. Future research exploring causal pathways, that is, how symptoms, various coping mechanisms, or medication effects alone or in combination influence MVC risk, could inform targeted prevention strategies. Moreover, assessment of medication prescribing patterns for alcohol dependence or other substance abuse disorders may further efforts to promulgate evidence-based treatment guidelines with the potential added benefit of reducing MVC risk. Finally, groups at high risk for MVC may change over time, supporting the need for continued surveillance.

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