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Emmanuel Lagarde

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Road traffic crash characteristics of drivers who take prescription medicines that carry a risk to driving

Running head: Crash characteristics among drivers with medications consumption

Li Lu ^{1,2}, Benjamin Contrand ^{1,2}, Blandine Gadegbeku ^{3,4,5}, Louis-Rachid Salmi ^{1,2,6}, Emmanuel Lagarde ^{1,2}

1. Institut de Santé Publique, d'Epidémiologie et de Développement (ISPED), Université de Bordeaux, Bordeaux, France
2. Team IETO, Bordeaux Population Health Research Center, UMR U1219, INSERM, Université de Bordeaux, Bordeaux, France
3. Université de Lyon, Lyon, France
4. UMRESTTE, UMR T9405, l'Institut Français des Sciences et Technologies des Transports, de l'Aménagement et des Réseaux (IFSTTAR), Bron, France
5. UMRESTTE, Université Lyon 1, Lyon, France
6. Service d'Information Médicale, Pôle de Santé Publique, Centre Hospitalier Universitaire de Bordeaux, Bordeaux, France

Correspondence: Dr. Emmanuel Lagarde, Université de Bordeaux, Bordeaux, France; Email address: emmanuel.lagarde@u-bordeaux.fr; or Dr. Li Lu, Université de Bordeaux, Bordeaux, France; Email address: liser@outlook.com

ABSTRACT

Background: The specific features of crashes involving an alcohol-intoxicated driver have been extensively characterized, but no such data are available for crashes involving a driver who has used a prescription medicine, which could help to plan and target prevention and control initiatives. This study aimed to describe the characteristics of crashes involving drivers under the influence of prescription medicines.

Methods: We took advantage of CESIR, a French record linkage study for which data were extracted and matched from three French national databases: police reports, the national police database of injurious crashes and the national health care insurance database (HCI database). The drivers included in the study were those involved in an injurious road crash in France from July 1, 2005 to December 31, 2015, whose national identity number, date of birth and sex allowed matching. Prescription medicines considered were those with the two highest levels of warning.

Results: Similar crash profiles were found when drivers used alcohol or medicines, particularly with respect to injury severity, type of vehicle, type of collision, type of road and cross-track profile. Alcohol-related crashes were over-represented during weekends and in low-density areas and medicine-related crashes were over-represented during weekdays and in cities of fewer than 300 000 inhabitants. While a much higher strength of association with responsibility was found for alcohol than for medicines, the proportion of crashes with drivers using medicines was twice as high as crashes with drivers using alcohol.

Conclusion: The lower risk carried by medicines is therefore in part compensated by a higher prevalence of use, making medicines one of the hidden factors of road risk. Characterizing these crashes will therefore be useful to better focus road safety intervention on the prevention of driving under the influence of psychotropic medicines.

Key words: Road traffic crash characteristics; drivers; prescription medication; alcohol

1. INTRODUCTION

Psychotropic substances have the potential to increase the risk of road traffic crashes. This has been known for a long time for alcohol (Cameron, 1940) and more recently for cannabis (Laumon, Gadegbeku, Martin, & Biecheler, 2005) and psychotropic medicines (Barbone et al., 1998; Orriols et al., 2010). The consumption of medicines, and especially anxiolytics and hypnotics, can interfere with factors that are essential for driving, including perception, attention, coordination, and reaction time. Medication can be the direct cause of blurred vision, seizures, drowsiness, altered motor coordination and skills, and has repeatedly been reported to be associated with an increased risk of road traffic crashes in most studies (Barbone et al., 1998; Brubacher et al., 2018; Caputo, Trevisani, & Bernardi, 2007; Engeland, Skurtveit, & Morland, 2007; Gjerde, Normann, Christophersen, Samuelsen, & Morland, 2011; Hemmelgarn, Suissa, Huang, Boivin, & Pinard, 1997; Odero, Garner, & Zwi, 1997; Orriols et al., 2010; Orriols et al., 2016; Ray, Fought, & Decker, 1992; Smink, Egberts, Lusthof, Uges, & De Gier, 2010). In France, an estimated 3.3% of road traffic crashes are attributable to prescription medicines (Orriols et al., 2010).

In order to provide patients and health care professionals with sufficient information on the influences of medicines on driving performance, a multidisciplinary group of experts was appointed by the French National Agency for Medicines and Health Products Safety to classify all medicines according to a four-level risk classification system with regard to their effects on driving performance (Castot & Delorme, 2009). Pharmaceutical companies gradually implemented this policy from 2005 to 2008 and now all outer packaging of medicines must be labeled with the appropriate pictogram (level 1: Be careful. Read the patient leaflet carefully before driving; level 2: Be very careful. Take advice from a physician or a pharmacist before driving; level 3: Danger: do not drive. Seek medical advice before driving again).

Several studies have described the specific features of crashes involving an alcohol-intoxicated driver: they lead to more severe injuries (Caputo et al., 2007; Rosman, Ferrante, & Marom, 2001), occur more often at night-time and during weekends (Gusfield, 1985; Voas, Wells, Lestina, Williams, & Greene,

1998), on two-way roads and roads with curves (Akepati & Dissanayake, 2011; Maistros, Schneider, & Savolainen, 2014), are much less frequent for professional road use (Nordfjærn, Jørgensen, & Rundmo, 2012) and more frequent in areas of lower population density (Meliker et al., 2004). Alcohol-intoxicated drivers are also younger and more likely to belong to underprivileged populations (Karjalainen, Blencowe, & Lillsunde, 2012; Males, 2009). These data proved to be of interest for at least three reasons: (i) they are needed to help to plan roadside blood alcohol testing; (ii) knowledge of the circumstances of these accidents is also useful for better targeting of prevention initiatives; (iii) finally, the crash characteristics of intoxicated drivers help us to understand why alcohol is associated with such a massive increase in road crash risk.

The same considerations apply to medicines consumption and no published study has yet reported such information. To address this gap, we took advantage of CESIR, a French record linkage study that matched police crash report databases with national health insurance data on medicines delivery. The objective was to build on this work to describe the characteristics of crashes involving drivers under the influence of prescription medicines. In practice, we compared crash characteristics between drivers who used medicine, alcohol and other non-user drivers.

2. METHODS

The data collection methodology of the CESIR project has been described in detail elsewhere (Orriols et al., 2010). We provide here a summary of its main features.

2.1 Data sources

Data were extracted and matched from three French national databases: police reports, the national police database of injurious crashes and the national health care insurance (HCI) database. An injurious crash was defined as a crash occurring in a road open to public circulation with at least one vehicle involved and leading to at least one victim needing medical care or being killed (Nee et al., 2017).

2.1.1 Police reports (PRs)

French police officers are required to fill out a police report for each injurious crash occurring in the country (about 70,000 reports each year). A previous validation study showed that the national healthcare ID (NID) number was recorded for 28% of the drivers involved (Orriols et al., 2010). Police reports available from July 1, 2005 to December 31, 2015 were collected and matched to the HCI database.

2.1.2 National police database of injurious crashes (ICs)

Details of each injurious road traffic crash are collected by the police and stored in the national police database (Bulletins d'Analyse d'Accident Corporel). This standardized injurious crash database contains related information on the crash, vehicles and persons involved. The crash characteristics used in this study included: age, sex and socioeconomic category of the drivers, vehicle type, severity of injury with four levels, time of day, day of week, season, manoeuvre prior to the accident, collision direction, type of road, traffic separation, curve of road, population density of the crash location, and presumed responsibility for the crash as assessed by police officers. All drivers involved in a road traffic crash are supposed to be tested for the presence of alcohol using a breath test. If this test is positive (≥ 0.5 g/L), the driver refuses to take the test, or the severity of the crash makes the test impossible, then the blood alcohol concentration is measured.

2.1.3 Health care insurance database (HCI)

The HCI database (Système National d'Informations Inter Régimes de l'Assurance Maladie) covers the entire French population. When a reimbursed prescription medicine is dispensed to an outpatient in a pharmacy, a record that includes the NID number, the date of dispensing and the 7-digit code which identifies the prescription medicine is added to the database.

2.2 Inclusion and exclusion criteria

The drivers included in the study were those involved in an injurious road crash in France from July 1, 2005 to December 31, 2015 and whose NID number, date of birth and sex were correctly entered in the police reports.

They were excluded when the police report data extraction process failed or when the connection between the police report database and the injurious crash database could not be established.

2.3 Prescription medicines exposure

For the present study, medicine users were defined as drivers who used prescription medicines with the two highest levels of warning as those were found to be associated with crash risk in previous studies (Nee et al., 2017; Orriols et al., 2010). Prescription medicine exposure was considered to start on the day after dispensing day. Exposure duration was estimated from median values reported in France in a survey of medicine prescription (EPPM) (IMS Health, 2005). To ensure that prescribed medicines were not a result of the crash, medications dispensed on the crash day were not included in the analysis.

2.4 Determination of crash responsibility

Crash responsibility was determined by a standardized method adapted from Robertson and Drummer (Robertson & Drummer, 1994) and described in previous work (Orriols et al., 2017). This determination method was validated among France population using the national police database of fatal crashes, by considering various factors likely to reduce driver responsibility: road, vehicle and driving conditions, type of accident, traffic rule obedience and difficulty of the task involved (Laumon et al., 2005). A score is assigned to each driver for each of these factors from 1 (favourable to driving) to 4 (not favourable to driving). The higher the sum of the scores, the less favourable the driving conditions, and consequently the more likely the driver will be considered not responsible for the crash. Drivers were further grouped into two levels of crash responsibility: responsible (score < 15) or non-responsible (score ≥ 15).

2.5 Statistical analyses

The "nnet" R package (Venables & Ripley, 2002) was used to fit multinomial regression models adjusted for age and sex, with each crash characteristic as

the dependent variable and medicine use and alcohol use as the independent variable within the same model. The adjusted odds ratio (OR) and 95% confidence interval (95% CI) were used to express the potential correlations. For a given model examining one given crash characteristic, the ORs for association between alcohol use on one hand and medicine use on the another hand are presented separately in Figure 3 and 4, respectively. Data analyses were performed using the R Studio software, version 1.2.1335, ©2009-2019 RStudio, Inc.

2.6 Ethics statement

Confidentiality was ensured by using the personal information anonymization function of the health care insurance system (Trouessin & Allaert, 1997). The study was approved by the French Data Protection Authority (CNIL 906030).

3. RESULTS

The results of the extraction and matching procedures are shown in Figure 1. A total of 16.3% (201,497) of the drivers of the injurious crash database were included in this study, among which 48.6% (n=97,936) were classified as responsible for the crashes. Mean age was 39.2 (SD=15.98) years and males accounted for 69.5% of drivers. A total of 72.0% (145,041) of the drivers neither used alcohol nor medications, 0.93% (1,877) of the drivers were combined users of alcohol and prescribed medicine, 9.9% (19,877) were prescribed medicine users only and 4.9% (9,896) were alcohol users only. Figure 2 provides details concerning categories of medications with the two highest level of warning.

Table 1 compares the drivers' characteristics in the two groups of crashes with a driver using either medicine (12.2% of drivers) or alcohol (5.8% of drivers). As compared to other drivers, medicine users are older, more likely to be retired, female, and less likely to be scooter and motorcycle users.

The associations between alcohol use and medicine use and each crash characteristic after adjusting for age and sex are shown in Figure 3 and Figure 4, respectively. As expected, the use of medicine and use of alcohol were

associated with the risk of being responsible for the crash (ORs were 1.3 and 9.5 respectively).

Crashes with alcohol intake and crashes with medicine consumption shared many common features: lower socioeconomic status, lighter vehicles, more severe injuries, direction change prior to the crash, more collision-free crashes, more frequent on two-way roads and roads with curves. The strength of the association proved, however, to be systematically much greater for alcohol than for medicine.

Conversely, a small number of features differed between alcohol and medicine: crashes with alcohol were more frequent at night-time and during weekends, while crashes with medicines were more frequent in the morning and on weekdays. Finally, the occurrence of crashes with alcohol decreased with population density, while it was maximum in cities with populations of 50,000-300,000 for crashes involving a driver using medicine.

4. DISCUSSION

This study, based on a sample of 201,497 drivers involved in traffic crashes from July 2005 to December 2015, allowed a comparison of crash profiles associated with alcohol consumption and the consumption of risky medications. The latter shared several crash profiles in common with crashes involving alcohol consumption, but with lower strength of association. However, and contrary to what is observed for crashes involving alcohol, medicine crashes were over-represented during weekdays and in cities of fewer than 300,000 inhabitants.

Our data were consistent with both a strong association of alcohol use and a moderate association of psychotropic medicines use with responsibility in the crash. In spite of this much lower association with crash risk, medicine use accounts for a non-negligible proportion of all traffic crashes. We previously estimated this attributable fraction to be 3.3% (Orriols et al., 2010). A recent study conducted among 4,443 Italian drivers involved in road traffic crashes (Favretto et al., 2018) found that 23.7% and 19.9% of drivers were positive for alcohol (>0.1 g/L) and psychoactive drugs, respectively, while the same proportions in our study were 5.8% (≥ 0.5 g/L) and 12.2%. This discrepancy

could be partly attributed to the standards used to assess alcohol (>0.1 g/L vs. ≥ 0.5 g/L) and the use of laboratory examination of venous blood samples to ascertain medicine consumption, while our data were derived from the health care insurance reimbursement database which cannot capture the use of over-the-counter medicines.

The time pattern observed for alcohol consumption was expected, with consumption opportunities at the weekend and at night. Other studies already identified a higher proportion of drunk drivers during the night (Gusfield, 1985; Voas et al., 1998). Medicine users, as opposed to alcohol users, were more likely to be involved in crashes during the daytime and on weekdays. Some medicines taken during the night, such as sleep medication, could have residual effects on the body and driving performance during the following morning (Leufkens, Lund, & Vermeeren, 2009; Vermeeren et al., 2002; Verster, Veldhuijzen, & Volkerts, 2004). Medicine use was also more frequently observed in crashes on weekdays, perhaps because individuals who used medicine during weekends may choose to stay at home or decrease their driving exposure, while there is no such choice for those who work during the week. Probably for similar reasons, mileage has been reported to be lowest on the weekend among drivers with Parkinson's disease (Crizzle & Myers, 2013). These contrasting temporalities of crashes between alcohol and medicine consumers have implications in terms of planning potential roadside checks. In practice, should checks on the use of some medicines be decided, specific time slots for police checks should be added to those used for illegal drugs and alcohol.

Another difference between crashes involving a driver who uses alcohol and a driver who takes medicines was the population density of the crash area. Economic and behavioural factors (such as lower rates of seat belt use and more frequent drinking behaviour) and road design elements (non-existing road shoulders and lack of night lighting, etc.) could all play a part in the negative association between alcohol-related crashes and population density (Meliker et al., 2004; Muelleman & Mueller, 1996). In addition, the larger likelihood of medicine-related crashes in smaller communities probably results

from the fact that seniors are both more likely to live in those communities and to use medicines.

The positive associations between alcohol-related crashes and lower socioeconomic status (such as unemployed individuals) were also previously documented (Asgarian, Namdari, & Soori, 2019; Karjalainen et al., 2012). Even when adjusted for age, crashes with medicines appeared to be more frequent among retirees, which is consistent with the fact that retirement has been shown to be associated with poorer health (Pit, Shrestha, Schofield, & Passey, 2010). A similar point could be made for unemployed drivers, but the strong association with medicines-related crashes could also be related to poor mental condition associated with psychotropic medicine consumption. One Australian study among outpatients who drive regularly, found no significant difference regarding work status between drivers who took medication with different warning levels (Smyth, Sheehan, & Siskind, 2011), which is not consistent with our results. This study however did not specifically consider drivers involved in crashes.

As we observe in this study, less risky behaviours have been noted among professional drivers (Mirzaei et al., 2014; Nordfjærn et al., 2012), for whom professional ethics, internal regulations and management procedures are efficient ways of preventing drinking and driving. This is probably less the case for medication, which is less of a focus for the world of work and occupational preventive medicine. However, the likelihood of being employed as a professional driver is certainly lower for those in poor health, thereby reducing drug use in this population.

The positive relationship between alcohol and trauma severity in road crashes has been fully described (Caputo et al., 2007; Gjerde et al., 2011; Rosman et al., 2001; Vaez & Laflamme, 2005; World Health Organization, 2018). We found the same association with medicines consumption, but at a much lower magnitude. The most injured drivers were, however, more likely to be admitted to hospital, so their NIDs were more likely to be noted in the police reports (Nee et al., 2017; Orriols et al., 2010) and they were consequently more likely to be part of our sample. This is explaining higher rates of inclusion for bicycle and scooter drivers and drivers involved in

nonurban accidents, all of whom have been consistently documented in the literature to be more seriously injured. The inclusion rate was slightly lower for responsible drivers than for nonresponsible drivers (Orriols et al., 2010). In addition, the study was based on a large sample size (N=201,497), which represented, however, only 16.3% of the drivers in the injurious crash database. A more complete filling of forms by police authorities would have allowed for a much more powerful analysis and lessen the impact of potential selection biases.

With regards to the crash characteristics and environment, the same pattern was found for alcohol and medicines (manoeuvre prior to the crash, collision direction, type of road, regime of road and curve of road). This may reflect the fact that medicines and alcohol are all psychotropic substances that similarly affect the cognitive ability to drive. There was, however, a very large difference in amplitude, alcohol being correlated to various crash patterns with greater association strengths than medicine.

Among study limitations, it is important to note that the data regarding personal driving abilities and exposures, which could be potential confounding factors, were not accessible. Secondly, self-medication and the use of over-the-counter medicines were not captured in our study. About 15% of medicines sold in France correspond to non-reimbursable medicines, but most of these products have either no or a negligible influence on driving ability (Orriols et al., 2010). We also did not know whether the medicines reported as delivered in our database were actually ingested or not. Non-compliance would result in exposure misclassification that would deserve further study. Lastly, information such as therapeutic levels of medication and repeat prescription were not available, which could have affected crash profiles. This should be considered and explored in further research.

Even though alcohol use has a greater magnitude of risk than medicine use, medicines appear to lead to the same kind of crashes, albeit at a much smaller magnitude and greater frequency during the daytime and on weekdays, as opposed to night-time and weekends for alcohol use. The lower risk carried by medicines is in part compensated by a higher prevalence of use, making medicines one of the hidden factors of road risk. Further studies should also

determine whether medication compliance, therapeutic levels and health condition affect crash profiles. Our study provides a comprehensive description of the associations between medicine use and alcohol use and various road traffic crash characteristics, which could help to describe the two exposed populations better and focus road safety intervention on the prevention of driving under the influence of psychotropic medicines.

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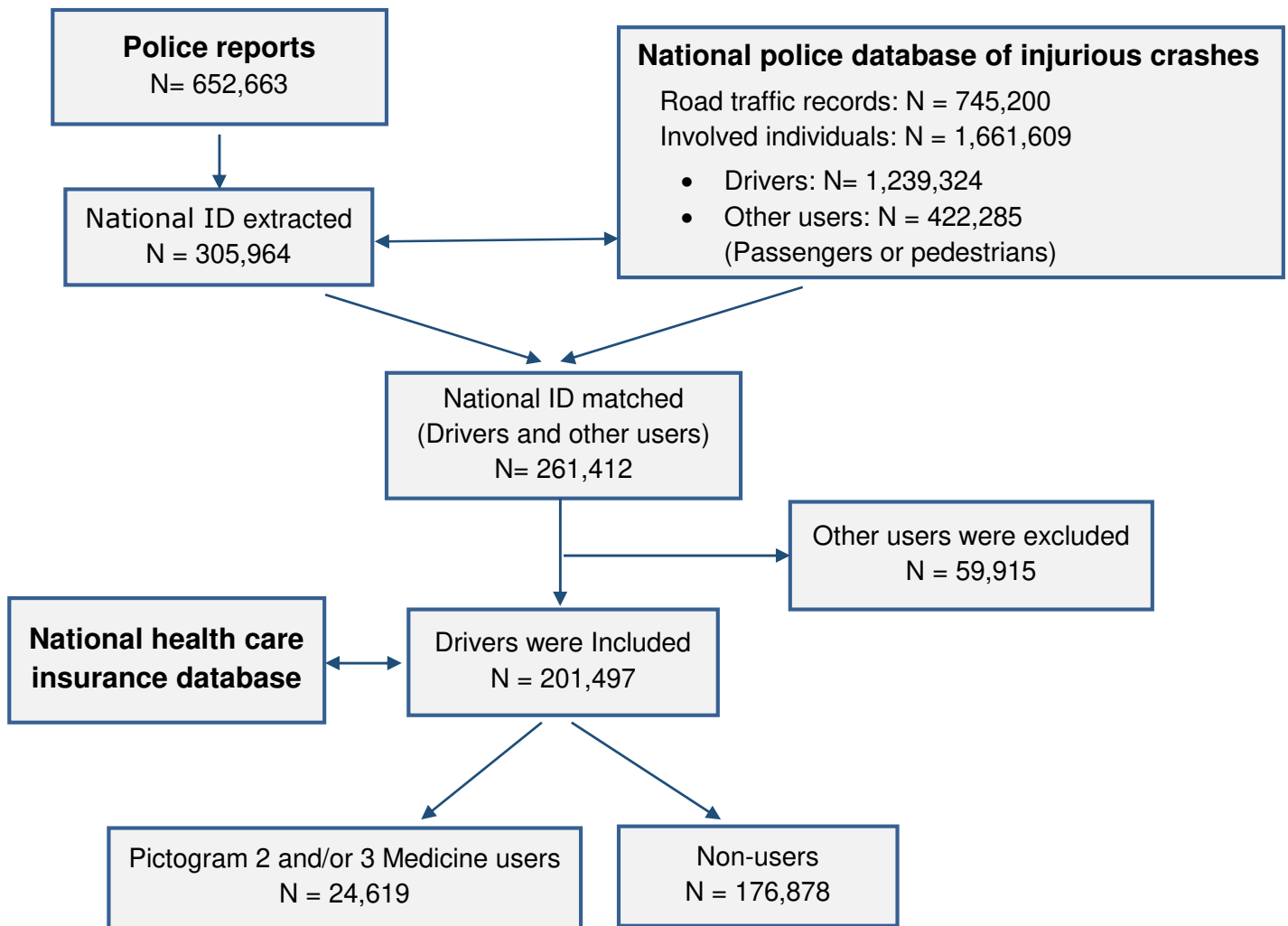


Figure 1 Flowchart of the inclusion procedure

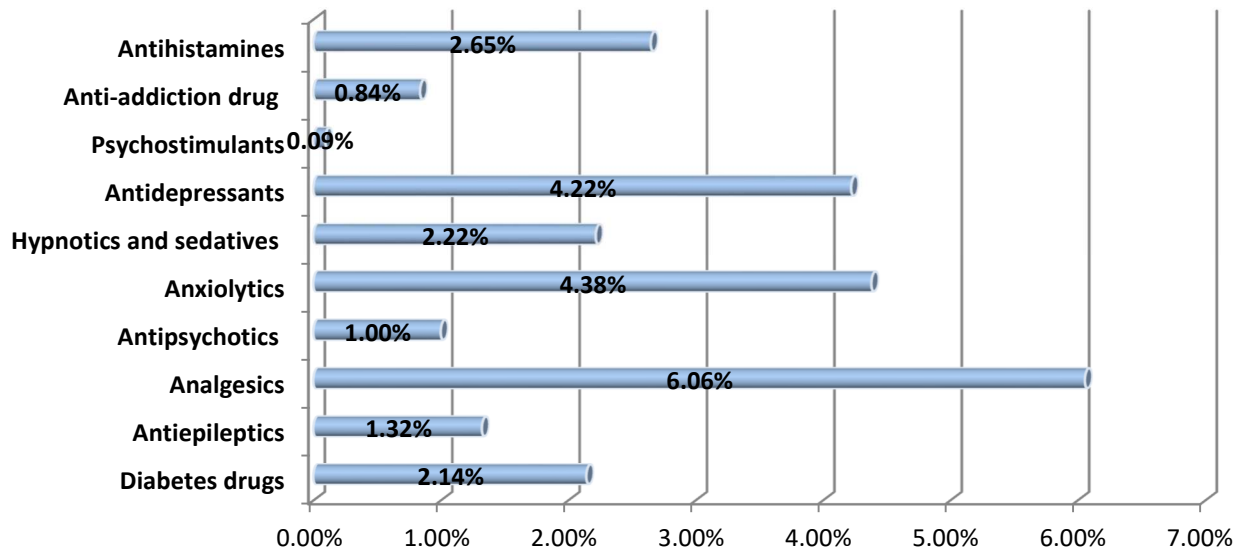


Figure 2. Prevalence of prescription medications use with level 2 and/or 3 of warning among drivers involved in a crash (N=201,497)

Table 1 Comparisons of driver characteristics between medicine users, alcohol users and non-users

Variables	Medicine use (n=24,619)		Alcohol use (n=11,773)		Overall (n=201,497)	
	n	%	n	%	n	%
Age (years)						
<18	100	0.4	147	1.2	7,107	3.5
18–24	1,532	6.2	2,600	22.1	37,974	18.8
25–34	3,721	15.1	3,264	27.7	46,356	23.0
35–44	5,247	21.3	2,801	23.8	41,898	20.8
45–54	5,561	22.6	1,909	16.2	33,772	16.8
55–64	4,071	16.5	762	6.5	19,302	9.6
65–74	2,405	9.8	226	1.9	8,812	4.4
≥ 75	1,982	8.1	64	0.5	6,276	3.1
Sex						
Male	14,719	59.8	10,299	87.5	140,072	69.5
Female	9,900	40.2	1,474	12.5	61,425	30.5
Socioeconomic category						
Professional driver	601	2.4	238	2.0	6,951	3.4
Farmer	103	0.4	71	0.6	1,239	0.6
Craftsman, shopkeeper, independent profession	714	2.9	491	4.2	8,056	4.0
Higher managerial and professional occupations	947	3.8	258	2.2	9,328	4.6
Middle manager, employee	6,012	24.4	2,112	17.9	55,958	27.8
Workers	2,913	11.8	3,065	26.0	30,127	15.0
Retired	5,463	22.2	504	4.3	19,498	9.7
Unemployed	1,478	6.0	1,462	12.4	8,864	4.4
Student	704	2.9	518	4.4	16,544	8.2
Other	5,684	23.1	3,054	25.9	44,932	22.3
Vehicle type						
Light vehicle	17,037	69.2	7,772	66	116,434	57.8
Bicycle	1,159	4.7	181	1.5	10,978	5.4
Scooter & motorcycle	4,804	19.5	3,145	26.7	56,484	28.0
Commercial vehicle	883	3.6	483	4.1	9,316	4.6
Heavy-goods vehicle	322	1.3	67	0.6	3,837	1.9
Other	414	1.7	125	1.1	4,448	2.2
Blood alcohol concentration (BAC, g/L)						
< 0.5	19,877	80.7	0	0	164,918	81.8
0.5 ≤ BAC < 0.8	170	0.7	1,300	11.0	1,300	0.6
0.8 ≤ BAC < 1.2	284	1.2	2,042	17.3	2,042	1
1.2 ≤ BAC < 2.0	709	2.9	4,675	39.7	4,675	2.3
≥ 2.0	714	2.9	3,756	31.9	3,756	1.9
Missing	2,865	11.6	0	0	24,806	12.3
Pictogram risk level of medicine used*						
Level 0	16,630	67.5	2,037	17.3	45,467	22.6
Level 1	8,427	34.2	833	7.1	21,496	10.7
Level 2	23,156	94.1	1,743	14.8	23,156	11.5
Level 3	5,759	23.4	763	6.5	5,759	2.9
Severity of injury						
Unhurt	6,809	27.7	1,918	16.3	59,038	29.3
Slightly injured	8,770	35.6	2,662	22.6	72,459	36.0
Seriously injured	8,526	34.6	6,517	55.4	66,806	33.2
Killed	514	2.1	676	5.7	3,194	1.6
Time of day						
05:00 - 10:59	5,507	22.4	1,881	16.0	47,658	23.7
11:00 - 13:59	4,462	18.1	530	4.5	31,407	15.6
14:00 - 19:59	11,503	46.7	3,685	31.3	91,013	45.2
20:00 - 22:59	1,925	7.8	2,312	19.6	18,605	9.2
23:00 - 01:59	818	3.3	1,838	15.6	8,025	4.0
02:00 - 04:59	404	1.6	1,527	13.0	4,789	2.4
Day of week						

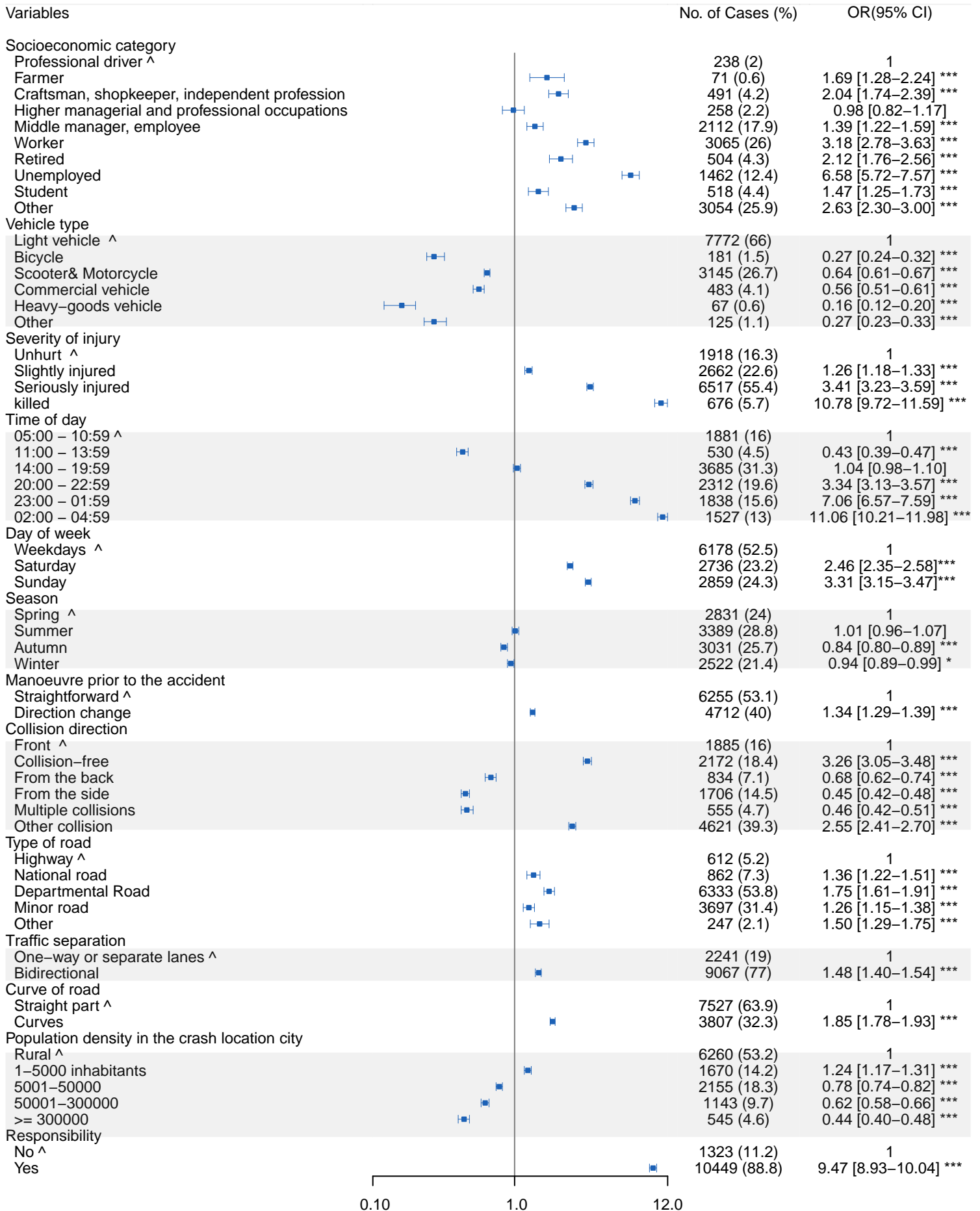
Weekdays	18,696	75.9	6,178	52.5	150,679	74.8
Saturday	3,287	13.4	2,736	23.2	28,243	14.0
Sunday	2,636	10.7	2,859	24.3	22,575	11.2
Season						
Spring	5,679	23.1	2,831	24.0	45,894	22.8
Summer	6,240	25.3	3,389	28.8	53,796	26.7
Autumn	7,016	28.5	3,031	25.7	58,211	28.9
Winter	5,684	23.1	2,522	21.4	43,596	21.6
Manoeuvre prior to the accident						
Same direction	14,169	57.6	6,255	53.1	120,047	59.6
Turning	9,169	37.2	4,712	40.0	71,258	35.4
Missing	1,281	5.2	806	6.8	10,192	5.1
Collision direction						
Front	4,248	17.3	1,885	16	34,409	17.1
Collision-free	1,800	7.3	2,172	18.4	23,061	11.4
From the back	2,897	11.8	834	7.1	70,078	34.8
From the side	7,941	32.3	1,706	14.5	9,565	4.7
Multiple collisions	2,612	10.6	555	4.7	12,826	6.4
Other collision	5,120	20.8	4,621	39.3	37,807	18.8
Missing	1	0	0	0	2	0
Type of road						
Highway	1,623	6.6	612	5.2	13,749	6.8
National road	1,854	7.5	862	7.3	15,089	7.5
Departmental road	11,042	44.9	6,333	53.8	88,033	43.7
Minor road	9,431	38.3	3,697	31.4	79,081	39.2
Other	527	2.1	247	2.1	4,342	2.2
Missing	142	0.6	22	0.2	1,203	0.6
Traffic separation						
One-way or separate lanes	6,057	24.6	2,241	19	52,385	26.0
Two-way	17,476	71	9,067	77	140,082	69.5
Missing	1,086	4.4	465	3.9	9,030	4.5
Curve of road						
Straight part	18,234	74.1	7,527	63.9	150,398	74.6
Curves	5,142	20.9	3,807	32.3	40,739	20.2
Missing	1,243	5.0	439	3.7	10,360	5.1
Population density of the crash location						
Rural	11,098	45.1	6,260	53.2	88,773	44.1
1-5000 inhabitants	2,581	10.5	1,670	14.2	20,522	10.2
5001-50000 inhabitants	5,419	22.0	2,155	18.3	43,319	21.5
50001-300000 inhabitants	3,606	14.6	1,143	9.7	28,953	14.4
≥ 300000	1,915	7.8	545	4.6	19,930	9.9
CESIR (year)						
2005-2008	8,735	35.5	4,284	36.4	72,685	36.1
2009-2011	8,768	35.6	4,235	36.0	70,078	34.8
2012-2015	7,116	28.9	3,254	27.6	58,734	29.1
Responsibility						
No	11,422	46.4	1,323	11.2	103,522	51.4
Yes	13,191	53.6	10,449	88.8	97,936	48.6
Missing	6	0	1	0.0	39	0

* Proportion does not add up to one hundred as several medicines could have been used.

Figure 3 Associations between crash characteristics and alcohol use.

Figure 4 Associations between crash characteristics and medicine use.

Alcohol use

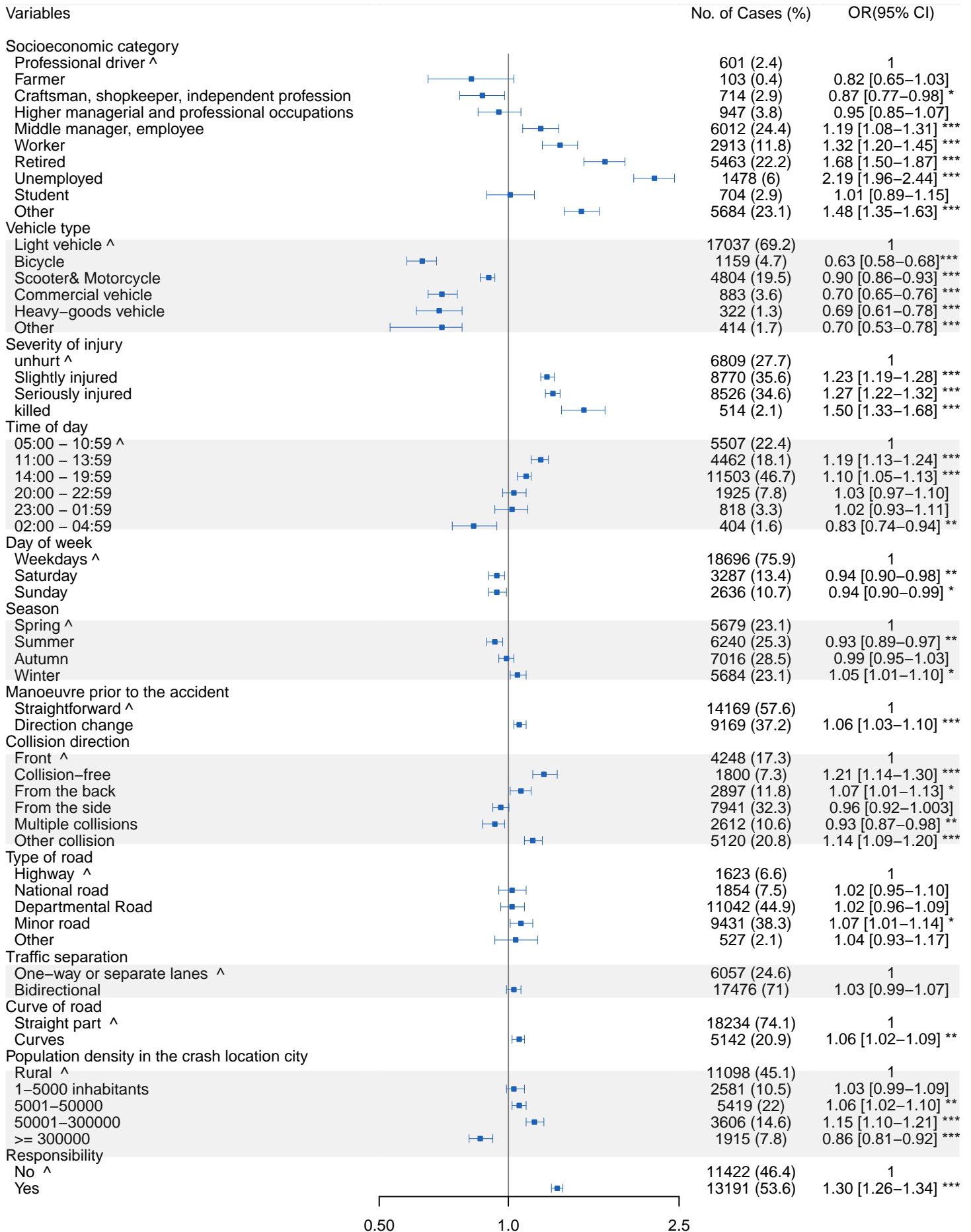


[^] Reference group.

p<0.05; ** p<0.01; *** p<0.001.

Odds ratios adjusted for age groups, sex and medicine use.

Medicine use



[^] Reference group.

p<0.05; ** p<0.01; *** p<0.001.

Odds ratios adjusted for age groups, sex and alcohol use.