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Prescribed anti-glaucoma medication consumption and road traffic crash

Li Lu[1,2,3] | Benjamin Contrand[2,3] | Cedric Schweitzer[4,5] | Blandine Gadegbeku[6] | Cécile Delcourt[5] | Emmanuel Lagarde[2,3]

[1]Health Management and Policy Institute, School of Public Policy and Administration, Xi'an Jiaotong University, Xi'an, China

[2]Institut de Santé Publique, d'Epidémiologie et de Développement (ISPED), Université de Bordeaux, Bordeaux, France

[3]Université de Bordeaux, INSERM, Bordeaux Population Health Research Center, team IETO, UMR1219, Bordeaux, France

[4]CHU Bordeaux, Department of Ophthalmology, F-33000, Bordeaux, France

[5]Univ. Bordeaux, INSERM, Bordeaux Population Health Research Center, team LEHA, UMR1219, Bordeaux, France

[6]Univ Lyon, Univ Gustave Eiffel, IFSTTAR, UMRESTTE UMR_T9405, F-69675, Lyon, France

Correspondence
Dr. Li Lu, Xi'an Jiaotong University, China & Université de Bordeaux, Bordeaux, France.
Email: liser@outlook.com

Dr. Emmanuel Lagarde, Universit´e de Bordeaux, Bordeaux, France.
Email: emmanuel.lagarde@u-bordeaux.fr

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Abstract

Background: Glaucoma is one of the leading causes of visual impairment worldwide. Influence of visual defects associated with this condition, as well as potential side effects of anti-glaucoma medications on driving may be a relevant traffic safety concern. This study therefore aimed to investigate whether and/or to what extent prescribed anti-glaucoma medicine consumption is associated with increased likelihood of crash risk, and traffic crash responsibility among drivers involved in road traffic crashes.

Methods: Data from three French national databases were extracted and matched as part of the CESIR (a combination of studies on health and road safety) project. The sample included 201 497 drivers involved in an injurious road crash in France from July 1, 2005 to December 31, 2015, and an age- and sex-matched control group (113 357 drivers) that was randomly drawn from the general population. Exposure to anti-glaucoma medications were compared between responsible and non-responsible drivers involved in a crash and between drivers involved in a crash and people from the control group.

Results: The proportion of drivers with prescribed anti-glaucoma medicine markedly increased with age. One type (OR = 0.79, 95% CI: 0.72–0.86) and two or more types (OR = 0.82, 95% CI: 0.68–0.98) anti-glaucoma medicine prescriptions were less frequent in crash-involved drivers than in controls. One type (OR = 0.99, 95% CI: 0.88–1.12) and two or more types (OR = 1.04, 95% CI: 0.82–1.33) anti-glaucoma medicine prescriptions were not associated with crash responsibility.

Conclusion: Our findings are reassuring as regard to existing guidelines for safe driving for individuals using anti-glaucoma medications. Our results also suggest that driving behavior adaptation is effective mitigating potential traffic crash risks for people diagnosed with glaucoma.

KEYWORDS
drivers, prescription anti-glaucoma medication, road traffic crash

Key Points

- Prescribed anti-glaucoma medicine was negatively associated with road traffic crash.
- No relationship was found between anti-glaucoma medicine use and traffic crash responsibility among crash-involved drivers.
- Existing guidelines for safe driving for individuals using anti-glaucoma medications are reassuring.
- Our results also strongly suggest that driving behavior adaptation is effective mitigating potential traffic crash risks for people diagnosed with glaucoma.

Plain Language Summary

Glaucoma is one of the leading causes of visual impairment worldwide. Influence of visual defects associated with this condition, as well as potential side effects of anti-glaucoma medications on driving may be a relevant traffic safety concern. This study used data from three French national databases that were extracted and matched as part of the CESIR (a combination of studies on health and road safety) project. The sample included 201 497 drivers involved in an injurious road crash in France from July 1, 2005 to December 31, 2015, and an age- and sex-matched control group (113 357 drivers) that was randomly drawn from the general population. The results showed that the proportion of drivers with prescribed anti-glaucoma medicine markedly increased with age. One type and two or more types anti-glaucoma medicine prescriptions were less frequent in crash-involved drivers than in controls. While one type and two or more types anti-glaucoma medicine prescriptions were not associated with crash responsibility. Our findings are reassuring as regard to existing guidelines for safe driving for individuals using anti-glaucoma medications. Our results also suggest that driving behavior adaptation is effective mitigating potential traffic crash risks for people diagnosed with glaucoma.

1 | INTRODUCTION

People aged 65 or over represented 9.1% (703 million) of the worldwide population in 2019; the corresponding figure in France was 20.4% (13 million).[1] The current growth of the elderly population is paralleled by a growth in the population of active older drivers, which has led to a rise in their contribution to the road safety toll. The age-related cognitive and physiological decline is a matter of concern for road safety and led to guidelines and restrictions for older drivers.[2] These restrictions must be supported by the results of studies that seek to identify the pathologies and handicaps that are effectively linked to the greater vulnerability of this population. These studies must, however, take into account the fact that stopping driving for an elderly person may increase their dependence and precipitate a state of vulnerability both physically and psychologically.[3] Driving continues to be the key to independence for many individuals, particularly older drivers who live in an area where public transportation is limited or nonexistent.[4] Driving cessation not only affects an individual's independence and freedom, but may also influence self-esteem and perceived locus of control.[5] The balance between safety aspects and the independence of drivers with visual defects is therefore important.[6]

Driving is a complex activity requiring a high level of motor and sensory integrity[7] and a highly visual task.[8] The risk of unsafe driving varies greatly across medical conditions.[4] It has been reported that cognitive and visual factors can explain 83%–95% of age-related variance in the capacity to drive safely.[9] However, the relationship between visual function and driving is not straightforward.[10,11]

Glaucoma is the leading cause of irreversible blindness and one of the leading causes of visual impairment worldwide, and is characterized by optic nerve damage and associated visual field defects.[10,12–14] Evidence from a laboratory-based assessment showed that compared to older drivers without glaucoma, those with glaucoma had delayed hazard response times, with associated changes in eye movement patterns.[15] The relationship between glaucoma and traffic crashes is widely documented in many studies based both on lab-based simulator systems (simulated glaucomatous visual field loss or other vision impairment, or simulated driving systems, etc.) and on real-world road traffic crashes. The designs of these studies, however, vary significantly, thus impeding the generation of consensus recommendations.[13,16–18] Both findings from the real-world and simulation studies yield conflicts. For example, one French cohort study indicated that glaucoma did not increase crash risk,[19] whereas other studies reported drivers with glaucoma are more prone to traffic crash involvement than those without glaucoma in both the real-world and simulation studies.[13,18,20–22] The areas and degrees of visual field impairment probably play a key role here but no study was able so far to characterize it. For example, the simulation study including participants underwent testing in a novel driving simulator (DS) system[22] was conducted only among patients with advanced visual field damage.

It should be noted that a consistency observed among most studies is that individuals with glaucoma are more likely to self-regulate and restrict their driving, especially in highly demanding situations.[6,17,19,23] However, the simulation studies were not capable of reflecting the self-regulation behaviors on driving that people imposed.

With regard to prescribed anti-glaucoma medications, their side effects have been categorized as ocular and systemic, and they potentially interact with other systemic drugs.[24] For example, it was stated that long-term applications of topical antiglaucoma medications damage the ocular surface.[25] Apart from the treatment benefits, the influence of the side effects of anti-glaucoma medications on driving may therefore be a relevant traffic safety concern. On the other hand, taking antiglaucoma medications can be probably regarded as a fairly good surrogate for glaucoma diagnoses when relevant studies are conducted. In addition, approximately 80% of people who holds a driver's license were aware of the effects of pharmaceutical drugs on driving ability when they took prescribed medication,[26] which may lead them changing or limiting driving behavior. The arguments stated above lead us to speculate that the use of anti-glaucoma medications could be related to road traffic crashes.

We used data extracted and matched from three French national databases to investigate: (1) whether and to what extent glaucoma and/or prescribed anti-glaucoma medicine use are associated with increased likelihood of crash risk; (2) whether there is a relationship between prescribed anti-glaucoma medicine consumption and traffic crash responsibility among drivers involved in road traffic crashes.

2 | METHODS

The data collection methodology of the CESIR (a combination of studies on health and road safety) project has been described elsewhere.[27] We extracted and matched the data from three French national databases: police reports, the national police database of injurious crashes (ICs) and the national health care insurance (HCI) database.

2.1 | Data sources

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.[27] 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 forces and stored in a national database (Bulletins d'Analyse d'Accident Corporel) administered by ONISR (Onservatoire National interministériel de Sécurité Routière). 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 occupation of the drivers, vehicle type, blood alcohol concentration (g/L) and severity of injury. All drivers involved in a road traffic crash with injuries 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. In France, patients are fully reimbursed for health care expenses related to 30 recognized long-term chronic diseases (the most common being cancers, severe arterial hypertension, long-term psychiatric disorder and coronary diseases); it should be noted that glaucoma does not belong to the list.[28,29] 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.

2.1.4 | NID extraction and matching procedures

The data matching procedures has been described in previous work in detail.[27] Drivers involved in an injurious crash in France, between July 2005 and December 2015, were included through their national ID, gender, and date of birth, as extracted from police reports by an automatic procedure. The NID number was used to link drivers to prescription drug reimbursement data around the date of the crash. The PRs were linked to the IC database records by a probabilistic linkage method.[30]

2.2 | Case group: drivers involved in a crash

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 documented in the police reports. A driver was excluded if 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 | Anti-glaucoma medication exposure

The use of prescribed anti-glaucoma medicine was estimated using prescription data recorded in the health care insurance database with the Anatomical Therapeutic Chemical (ATC) Classification System code: S01E (anti-glaucoma preparations and

miotics), which include six types, i.e., sympathomimetics in glaucoma therapy (S01EA), parasympathomimetics (S01EB), carbonic anhydrase inhibitors (S01EC), Beta blocking agents (S01ED), Prostaglandin analogues (S01EE), Other antiglaucoma preparations (S01EX). Consumption of anti-glaucoma medication 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 prescriptions (EPPM).[31] 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 | Determining crash responsibility

Crash responsibility levels were determined based on a standardized method adapted from Robertson and Drummer,[32] factors possibly mitigating drivers' responsibility in each accident were identified and scored. If a sufficient number of mitigating factors were identified a driver would be found to be either partly or totally exonerated from blameworthiness and scored either as a contributory or nonculpable driver.[32] The methodology was described in more detail in our previous work.[27,33] The principle of responsibility analysis is to compare the probabilities of exposure on the day of the crash between the drivers deemed responsible for the crash and those non-responsible.[29] This determination method was validated in France using the national police database of fatal crashes (kappa =0.71),[34] 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. A score is assigned to each driver for each of these factors from 1 (favorable to driving) to 4 (not favorable to driving). The higher the sum of the scores, the less favorable 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 | Control group: individuals from the general population

To estimate the level of exposure to anti-glaucoma medications, an age- and sex-matched control group was randomly derived from the entire HCI database, that is, population based controls. The control group was built in order to have the same distribution of age and sex as individuals involved in a crash of the case group using the incidence density control sampling method. An index date equal to the matched case's crash date was attributed to each control and medicine exposure was estimated around this date. The control sample therefore comprised individuals from the general population, not selected as being involved in a road traffic crash. It is, however, possible that a very small proportion of them

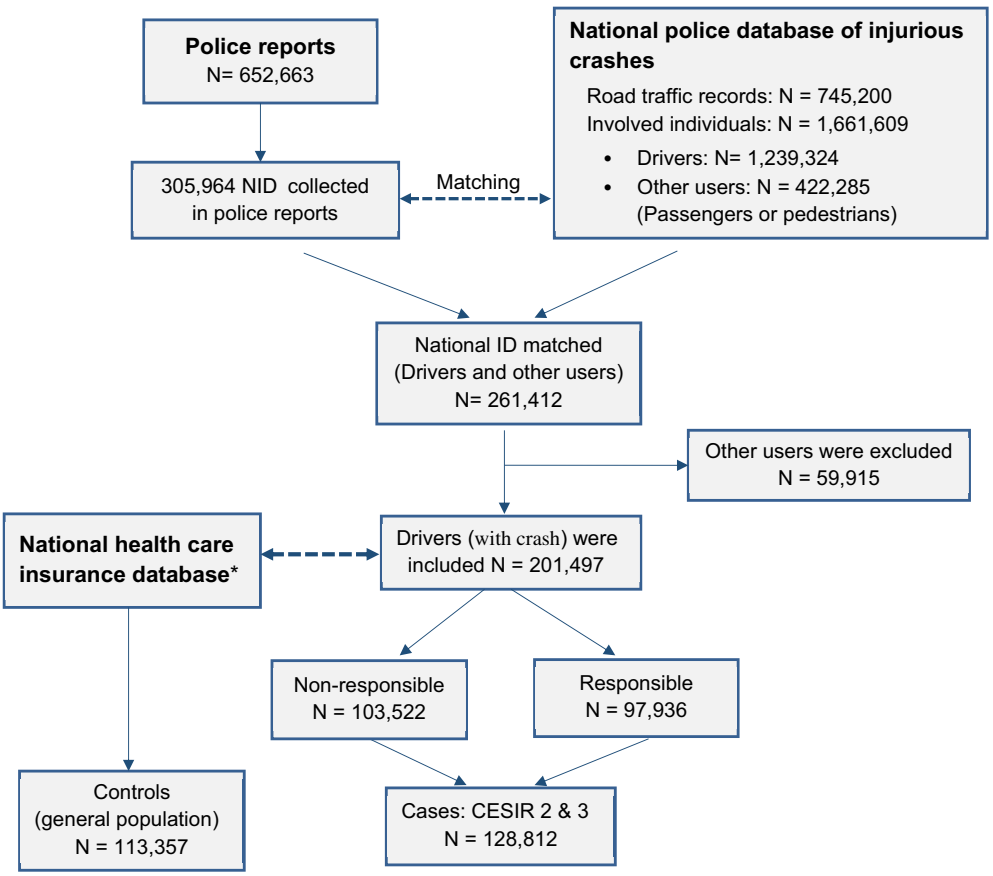

FIGURE 1 Flowchart of the inclusion procedure. *A random sample from the national health care insurance database was selected, matched on the age and sex distribution of the cases. This was done only for wave 2 and 3

TABLE 1 Basic characteristics of the included sample

	Drivers with crash ($N = 201\,458$)					
	Non-responsible ($n = 103\,522$)		Responsible ($n = 97\,936$)		Control group ($N = 113\,357$)	
Variables	***n***	**%**	***n***	**%**	***n***	**%**
Anti-glaucoma medicine use						
No use	102 767	99.3	97 185	99.2	111, 729	98.6
One type	613	0.6	592	0.6	1315	1.16
≥2 types	142	0.1	159	0.2	313	0.28
Age group (years)						
≤24	19 651	19.0	25 421	26.0	14 001	12.4
25–44	47 060	45.5	41 179	42.0	46 685	41.2
45–64	30 055	29.0	23 008	23.5	37 456	33.0
≥65	6756	6.5	8328	8.5	15 215	13.4
Sex						
Male	70 039	67.7	70 004	71.5	66 172	58.4
Female	33 483	32.3	27 932	28.5	47 185	41.6
Long-term chronic condition						
No	94 161	91.0	87 627	89.5	94 781	83.6
Yes	9361	9.0	10 309	10.5	18 576	16.4
Occupation						
Professional driver	3773	3.6	3178	3.2		
Farmer	656	0.6	583	0.6		
Craftsman, shopkeeper, independent profession	4208	4.1	3848	3.9		
Higher managerial and professional occupations	5342	5.2	3984	4.1		
Middle manager, employee	32 156	31.1	23 787	24.3		
Workers	13 853	13.4	16 269	16.6		
Retired	9286	9.0	10 206	10.4		
Unemployed	3597	3.5	5265	5.4		
Student	23 208	22.4	21 719	22.2		
Other	7443	7.2	9097	9.3		
Vehicle type						
Light vehicle	57 974	56.0	58 440	59.7		
Bicycle	7492	7.2	3483	3.6		
Scooter and motorcycle	29 079	28.1	27 391	28.0		
Commercial vehicle	4505	4.4	4809	4.9		
Heavy goods vehicle	2094	2.0	1743	1.8		
Other	2378	2.3	2070	2.1		
Blood alcohol concentration (BAC, g/L)						
<0.5	89 146	86.1	75 736	77.3		
0.5 ≤ BAC < 0.8	296	0.3	1004	1.0		
0.8 ≤ BAC < 1.2	275	0.3	1767	1.8		
1.2 ≤ BAC < 2.0	451	0.4	4223	4.3		
≥2.0	301	0.3	3455	3.5		
Missing	13 053	12.6	11 751	12.0		
Severity of injury						
Unhurt	29 659	28.6	29 364	30.0		
Slightly injured	44 041	42.5	28 406	29.0		

(Continues)

TABLE 1 (Continued)

	Drivers with crash ($N = 201\ 458$)					
	Non-responsible ($n = 103\ 522$)		Responsible ($n = 97\ 936$)		Control group ($N = 113\ 357$)	
Variables	***n***	**%**	***n***	**%**	***n***	**%**
Seriously injured	29 011	28.0	37 783	38.6		
Killed	811	0.8	2383	2.4		
CESIR (year)						
2005–2008	37 789	36.5	34 896	35.6		
2009–2011	35 582	34.4	34 457	35.2	55 342	48.8
2012–2015	30 151	29.1	28 583	29.2	58 015	51.2

Note: There were 39 cases that lacked information on responsibility.

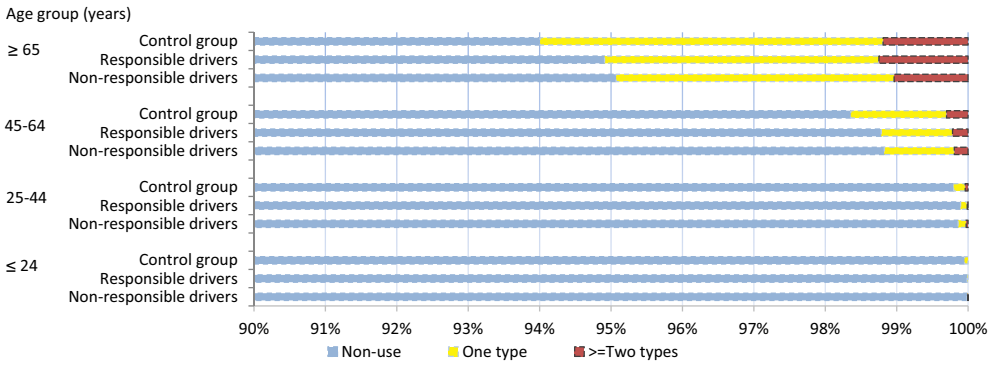

FIGURE 2 The distribution of anti-glaucoma medicine use in the sample by age group. The *X* axes has been adjusted and started with 90%

were indeed involved in a crash during the study period. This sample was only available in the last two time periods of the study (cases in CESIR 2 (2009–2011) and 3 (2012–2015) were matched), since data from earlier periods had already been archived.[35]

2.6 | Statistical analyses

Two comparisons were performed in this study. The first one compares use of anti-glaucoma medication between individuals involved in a crash (drivers in CESIR 2 and 3) and people with the same age and sex randomly drawn from the general population. The difference examined here is the result both of the potential impact of the medicine on crash risk and of potentially differential driving behaviors between those who used the medication and those who did not. The second is a responsibility comparison between responsible and non-responsible drivers. The non-responsible group is used as a proxy of people driving vehicles but having no crash. The differences in the level of anti-glaucoma medication use observed here are more likely to be related to the impact of the medicine consumption, or the severity of the condition itself on the risk of crash.

The selection of potential covariates and effect modifiers was conducted reviewing the existing related literatures[27,36] and univariate analyses (Table S1), then was incorporated into a directed acyclic graph (Figure S1) that was used to guide the modeling strategy. Logistic regression models were adjusted for age and sex and the presence of at least one type of long-term chronic conditions, and for the responsibility comparison supplemented with occupation, vehicle type, blood alcohol concentration (g/L) and severity of injury among drivers with road traffic crashes. Although this variable is the result of the crash itself, it was selected as an adjustment variable because of the strong relationship observed between the severity of injuries and the likelihood of being in the study sample. Sensitivity analyses regarding the first comparison were further conducted by restricting study samples to specific groups. The adjusted odds ratio (OR) and 95% confidence interval (95% CI) were used to express the potential associations. Data analyses were performed using R Studio software, version 1.2.1335, ©2009–2019 RStudio, Inc.

2.7 | Patient and public involvement

Patients and/or the public were not involved in the design, conduct, reporting or dissemination of this research. Confidentiality was ensured by using the personal information anonymization function of the health care insurance system.[37] The study was approved by the French Data Protection Authority (CNIL 906030).

TABLE 2 Odds ratio of prescribed anti-glaucoma medicine use for road traffic crashes

	Overall ($N = 242\ 169$)	Control group ($n = 113\ 357$)	Drivers involved in a crash ($n = 128\ 812$)		
Anti-glaucoma medicine use	***n* (%)**	***n* (%)**	***n* (%)**	**OR**	**95% CI**
No use	239 501 (98.9)	111 729 (98.6)	127 772 (99.2)	1.0	-
One type	2153 (0.9)	1315 (1.2)	838 (0.7)	0.79	0.72–0.86***
≥2 types	515 (0.2)	313 (0.3)	202 (0.2)	0.82	0.68–0.98*

Note: Adjusted for age group, sex and long-term chronic condition.
*$p < 0.05$. ***$p < 0.001$.

TABLE 3 Odds ratio of prescribed anti-glaucoma medicine use in crash responsibility among drivers with road traffic crashes ($N = 201\ 458$)

	Responsible ($n = 97\ 936$)	
Variables	**OR**	**95% CI**
Anti-glaucoma medicine use		
No use	1	-
One type	0.99	0.88–1.12
≥Two types	1.04	0.82–1.33

Note: Adjusted for age group, sex and long-term chronic condition, occupation, vehicle type, blood alcohol concentration and severity of injury.

3 | RESULTS

Figure 1 shows the results of the extraction and matching procedures. 201 497 drivers who were involved in road traffic crashes were analyzed in this study and 48.6% ($n = 97\ 936$) were considered responsible for the crashes. After matching age and sex as drivers in the period of CESIR 2 and 3 ($n = 128\ 812$), 113 357 individuals from the general population in the control group were included.

The basic characteristics among drivers involved in traffic crashes and controls are presented in Table 1. The proportion of at least one type of prescribed anti-glaucoma medicine use in the drivers with road traffic crashes was 0.75% ($n = 1506$); the figure for the control group was 1.44% ($n = 1628$). Figure 2 shows the distribution of anti-glaucoma medicine use in the sample by age group. As expected, the proportion of use of one or more types of prescribed anti-glaucoma medicine was higher in the elderly, and it was higher in the control group in each of the age categories.

After adjusting for age group, sex and long-term chronic conditions, logistic regression identified that use of one type (OR = 0.79, 95% CI: 0.72–0.86) and two or more types (OR = 0.82, 95% CI: 0.68–0.98) of prescribed anti-glaucoma medicine was less frequent in crash-involved drivers than in controls (Table 2). By fitting the model in two separate age groups and among females and males separately, it showed similar associations between prescribed anti-glaucoma medicine consumption and crash involvement (Tables S2 and S3). Notably the younger group (individuals were less than 45 years) showed smaller estimate parameters.

Responsibility analysis controlled for age, sex, the presence of long-term chronic conditions, occupation, vehicle type, blood alcohol concentration (g/L) and severity of injury. There were no associations between one type (OR = 0.99, 95% CI: 0.88–1.12) and two or more types (OR = 1.04, 95% CI: 0.82–1.33) of prescribed anti-glaucoma medicine use and crash responsibility among drivers with road traffic crashes (Table 3).

4 | DISCUSSION

Using French national datasets, our study indicated there is a negative association between prescribed anti-glaucoma medicine consumption and road traffic crash involvement. Another finding is that, among crash-involved drivers, there was no significant association between prescribed anti-glaucoma medicine use and responsibility. Our findings provide clues concerning establishment of guidelines for safe driving and crash avoidance.

It is documented that the history of glaucoma among older male drivers is a significant predictor of crash involvement,[38] and that older adults with glaucoma and limited useful visual field are more likely to be involved in an injurious crash.[39] Both real-world and simulation studies including simulated glaucomatous visual field loss or other vision impairment, or simulated driving systems, etc., have found that drivers with glaucoma are more prone to traffic crash involvement than those without glaucoma.[13,18,20–22] Compared to glaucoma patients with no visual field impairment in the worse functioning eye, those with moderate or severe field defects are at increased likelihood of being involved in a vehicle crash.[40] In our study however, we identified a negative association between prescribed anti-glaucoma medicine consumption and traffic crash involvement. This is surprising as one could have expected biotherapy to ascertain an actual glaucoma. Another possible interpretation is that the anti-glaucoma medications are keeping the disease from progressing to a more severe stage which could be dangerous for driving, and thus anti-glaucoma medications are in that sense protective against crashes. Besides, our results also strongly suggest that driving behavior adaptation is effective mitigating potential traffic crash risks for people diagnosed with glaucoma.

Vision impairment among older drivers, such as impaired useful visual field,[41] severe contrast sensitivity impairment due to cataract[42] and glaucoma with severe pattern deviation field defects in the

binocular field[43] can elevate at-fault crash risk. Older drivers with glaucoma are also more likely to have a history of at-fault motor vehicle collision involvement than those without glaucoma.[13] Nevertheless, we did not identify the association between prescribed anti-glaucoma medicine use and being responsible for road traffic crash among drivers involved in a crash.

Older drivers with glaucoma are less confident on roads and modify their driving habits.[17] One cohort study in the United States demonstrated that older drivers with diagnosed glaucoma drove at least as safely as their peers without glaucoma and showed no greater crash risks.[23] A Japanese study found that older glaucoma patients show greater driving self-restriction.[44] A great array of studies has also documented that in older drivers glaucoma is associated with driving avoidance, lower density driving and driving mileage, and less driving in challenging situations (such as at night, on the highway, etc.).[6,19,23] Reduced driving exposure and increased apparent self-regulatory practices were also exhibited by the elderly with vision deficits, such as older drivers aged 70 years or over with contrast sensitivity impairment.[45] Since driving self-restriction was associated with a reduced prevalence of vehicle collision in male drivers with glaucoma,[44] individuals with glaucoma should be aware of their medical conditions and self-regulate in driving to mitigate potential traffic crash risks.

Finally, as expected, we found that the elderly had a greater prevalence of prescribed anti-glaucoma medicine use than other age groups. It is a fact that the elderly are more likely to have cognitive, motor and sensory defects, to suffer from chronic diseases, such as eye diseases, and thus to use medication that could unfavorably influence their driving performance.[38] However, although older groups had poorer driving-related skills than younger groups, a previous study using an interactive driving simulator failed to discover significantly higher on-road accident rates among older than younger drivers.[46] In the present study, drivers older than 65 years had a lower risk of being responsible for the crash than drivers younger than 25 years, although they had a somewhat increased risk by comparison with middle-aged drivers.

The merits of our study were that we relied on documented governmental data rather than self-reports, which tend to be less reliable, and crash responsibility was determined by a standardized method that could therefore alleviate potential deviations due to self-estimation. However, several limitations should be noted. First, we were unable to access the clinically ophthalmic diagnoses or field loss of the drivers, which made it difficult to document the relationship between disease-related effects and crash risk. In particular, many of the subjects using anti-glaucoma medications do not exhibit significant visual impairment and this may be another reason for the lack of association of crash responsibility. Conversely, one cohort French study showed that about 38% of people with glaucoma were undiagnosed.[47] Second, we just took age, sex and long-term chronic conditions into account and adjusted for in the model. Third, a very small proportion of individuals from the general population (0.1%) were likely to have been involved in a crash during the study period. It is therefore unlikely that this would lead to a significant bias in the relationship between anti-glaucoma medication use and crash risk. As the matching process relied on the availability of NID, individual without NID were not included, which could lead to another possible systematic bias. Because NID were more often missing for the less severe cases, we considered severity in the models. In addition, 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.[27] 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, in our study, only drivers' NID that could be matched between databases were included. The most injured drivers were more likely to be admitted to hospitals, so their NID were more likely to be noted in the police reports[27,48] and they were consequently more likely to be part of our sample. This selection bias could lead to slight overrepresentation of drivers with more severe crashes in our sample, which may in part affect the results.

5 | CONCLUSION

In conclusion, prescribed anti-glaucoma medicine consumption was negatively associated with road traffic crash involvement and there was no evidence for a relationship between prescribed anti-glaucoma medicine use and traffic crash responsibility among crash-involved drivers. Our findings are reassuring as regard to existing guidelines for safe driving for individuals using anti-glaucoma medications.

AUTHOR CONTRIBUTIONS

Li Lu, Cécile Delcourt, Emmanuel Lagarde: Study design. **Li Lu, Benjamin Contrand, Emmanuel Lagarde:** Data collection and analysis. **Li Lu, Cécile Delcourt, Emmanuel Lagarde:** Data interpretation. **Li Lu, Cedric Schweitzer, Blandine Gadegbeku, Cécile Delcourt, Emmanuel Lagarde:** Manuscript draft. All authors approved the final version for publication.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Access to the French national healthcare insurance database, the police reports and the national police database of injurious crash have

been respectively provided by the French National Health Insurance (CNAMTS), Agira-TransPV and the National Interministerial Road Safety Observatory (ONISR). Access to the national healthcare insurance database and matching with other datasources requires the authorization of the Health Data Institute (Institut des donneÂes de Santé [IDS]) and the French Data Protection Authority (Commission nationale de l'informatique et des libertés [CNIL]). More information can be found at http://www.institut-des-donnees-de-sante.fr/etudes-recherches or email to: emmanuel.lagarde@u-bordeaux.fr.

ETHICS STATEMENT

Confidentiality was ensured by using the personal information anonymization function of the health care insurance system. The study was approved by the French Data Protection Authority.

ORCID

Li Lu https://orcid.org/0000-0002-0060-1725
Benjamin Contrand https://orcid.org/0000-0002-2012-2676

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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