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## Medicine consumptions and occupational road risk

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### What is new in the paper/what are the policy implications of the paper

It is the first study which focus on the association between exposure to ten classes of medicines and the risk of being responsible for a road traffic crash according to the type of journey (private, commuting or mission) in France.

Medicines exposure levels were generally lower for drivers during occupational journeys.

The risk of being responsible for a road traffic crash was higher on commuting or mission journeys than on private journeys for antiepileptics, psycholeptics, psychoanaleptics and other nervous system drugs.

The implementation of preventive measures about some treatments and diseases in the context of occupational journeys should be developed.

1 **Abstract**

2

3 **Background:** Whereas an increased risk of road traffic crashes has been highlighted as linked  
4 to some medicine consumptions, there is no available data on this risk according to the type  
5 of journey (private, commuting or mission). Drivers on occupational journey (commuting or  
6 mission) are likely to have different coping behaviors related to the use of medicines than  
7 drivers on private journey.

8 The aim of our study was to investigate the association between exposure to ten classes of  
9 medicines and the risk of being responsible for a road traffic crash according to the type of  
10 journey (private, commuting or mission).

11

12 **Methods:** The data used came from three French national databases: the national police  
13 database of injurious crashes, the police reports and the national health care insurance  
14 database. A total of 179,269 drivers aged between 18 and 65 years old involved in an  
15 injurious crash in France between July 2005 and December 2015 were included in the  
16 analyses. Logistic regression models stratified by journey were used to estimate the Odds  
17 Ratios (OR) and 95% confidence intervals (95% CI), adjusted for potential confounding  
18 factors.

19

20 **Results:**

21 Medicines exposure levels were generally lower for drivers during occupational journeys, the  
22 risk of being responsible for a road traffic crash seems to be higher on commuting or mission  
23 journeys than on private journeys for four medicines.

24 Indeed, for antiepileptics the OR was 1.59 [1.01-2.51] for mission journeys, 1.63 [1.24-2.15]  
25 for commuting journeys, and 1.47 [1.25-1.73] for private journey. For psycholeptics the OR  
26 was 1.02 [0.80-1.28] for mission journey, 1.19 [1.03-1.39] for commuting and 1.17 [1.08-  
27 1.26] for private journey. For psychoanaleptics OR was 1.35 [1.02-1.78] for mission journeys,  
28 1.37 [1.17-1.60] for commuting journeys and 1.26 [1.14-1.40] for private journeys. Finally,  
29 for other nervous system drugs OR reached 2.04 [1.35-3.07] for mission journeys compared  
30 to 1.43 [1.21-1.70] for private journeys.

31

32 **Conclusion:** Our results encourage the implementation of preventive measures about some  
33 treatments and diseases in the context of occupational journeys.

34

35 **Keywords:** Road safety, responsibility analysis, road traffic crash, professional drivers,  
36 medicines

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## 48 **Introduction**

49

50 Several studies in France (1) and around the world have been carried out about the link  
51 between the consumption of several medicines and the risk of road traffic crash (2). Some  
52 drugs are identified as strongly associated to an increased risk of road crash, especially  
53 benzodiazepines which represent the most studied class in the literature (3–9).

54 Other drugs have been less studied, with sometimes inconsistent or contradictory results.  
55 This is the case, for example, with anti-epileptic drugs (10–12), analgesics (13,14),  
56 antidepressants (15–19), muscle relaxants (20) and antihistamines (21–25). In addition,  
57 there are several substances in some of these drugs classes that may have an impact on  
58 driving ability. This is the case of substances used as hypnotics or antiepileptics, which are  
59 likely to have a sedative effect; or some substances used for diabetes that can cause  
60 hypoglycemia (26).

61 Studies on the effects of medicines on the risk of road traffic crash are often focused on the  
62 elderly (14–16,21,27)). Studies that examined the relationship between drug use and the risk  
63 of work-related motor vehicle crashes are scarce, often inconsistent and mainly focused on  
64 truck drivers (27–29).

65 However, it can be argued that drivers on work-related journeys are more likely to have a  
66 different coping behavior due to many factors (30,31). For example, they may be more  
67 exposed to stress and fatigue because they are often required to move quickly and  
68 efficiently and because of the pressure that hierarchy can exert. This could lead to different  
69 medicine consumption behaviors compared to non-professional drivers.

70 On the other hand, there is reason to believe that some drivers on occupational journeys  
71 may have lower consumption prevalence than drivers on private journeys. Indeed, some of

72 them are subjects to specific regulations. Moreover, their journeys do not have the same  
73 stakes or objectives as drivers on private journeys, as driving may represent a (financial)  
74 livelihood.

75 To our knowledge, no study has compared the differences in consumption and road crash  
76 risk according to the type of journey, private or work-related (either commuting or mission).

77 The objective of this study was to determine whether the prevalence of drivers' medicines  
78 use differed between work-related journeys (commuting or mission) and non-work-related  
79 (private) for ten major classes of drugs and to describe the impact of these drugs on the risk  
80 of being responsible for a road crash according to the type of journey.

81

## 82 **Methods**

83

### 84 **Data sources**

85 The study is based on three French nationwide databases: police reports (PR), the national  
86 police database of injurious crashes (IC) and the national healthcare insurance database (HCI  
87 database).

88 The drivers were included in the study by their national ID number (NID, also called social  
89 security number) that was extracted from police reports (PRs) by an automatic procedure.

90 Next, drivers were linked to prescription medicines reimbursement data around the date of  
91 the crash by their NID. Then, PRs were linked to the National police database of injurious  
92 road traffic crashes (IC) records by a probabilistic linkage method (26).

93

94 *Police reports (PRs)*

95 In France, when a road crash with injuries occurs, police forces are called and have to file a  
96 report. This report contains general information about the crash. It is then scanned and  
97 stored as an image file by TransPv. Almost 70,000 reports are completed each year. The NID  
98 is sometimes recorded in the PR. It has been estimated, through manual assessment on a  
99 small sample in a previous study, that this NID could be found in 28 % of the drivers  
100 concerned (26).

101

### 102 *National police database of injurious road traffic crashes*

103 Details collected by police forces on each injurious crash are stored in the IC database  
104 (Bulletins d'Analyse des Accidents Corporels [BAAC]).

105 This standardized database is led by the National Interministerial Road Safety Observatory  
106 (Observatoire national interministériel de sécurité routière [ONISR]). It is filled after police  
107 reports.

108 This database contains details about injurious road traffic crashes like on the circumstances  
109 of the crash or the vehicles and persons involved.

110 It can contain the severity of the driver's injuries: unhurt, slightly injured, seriously injured  
111 (hospitalized for more than 24 hours) or killed (died within the 30 days following the crash)  
112 because the police may have to go to the hospital in order to carry out further  
113 investigations.

114 It also contains data on alcohol consumption. Indeed, police forces test every driver involved  
115 in an injurious crash for the presence of alcohol, using a breathalyzer. In the case where the  
116 test is positive ( $\geq 0.5$  g/l), the driver refuses or is incapable of doing the breath test, the blood  
117 alcohol level is measured.

118 When the breath test is negative, the driver is recorded as not being under the influence of  
119 alcohol.

120

121

122

### 123 **National health-care insurance database (HCI database)**

124 The HCI database (Système National d'Informations Inter Régimes de l'Assurance Maladie)  
125 covers the entire French population. Each time a medicine is delivered to an outpatient in a  
126 pharmacy, a record is added, containing different information like the NID, the day of  
127 dispensing and the seven-digit code that identifies the medicine prescription. The HCI  
128 database also records 30 long-term chronic diseases (for which patients' health care  
129 expenses are fully reimbursed) by their ICD-10 code (International Classification of Diseases,  
130 Tenth Revision) and by the dates of the beginning and the end of the disease.

131

### 132 **Participant inclusion**

133 In order to mitigate the impact of previous crashes on medicine exposure, drivers were  
134 censored at their first involvement in a road traffic crash if they were involved in more than  
135 one crash during the study period.

136 The drivers included in the study are those aged between 18 and 65 years old, who were  
137 involved in a road crash in France between July 2005 and December 2015. Subjects whose  
138 police reports did not contain their national ID or responsibility were not included.

139

### 140 **Medicines and exposure periods**

141 Daily exposure to drug prescription was estimated for ten medicines: drugs used in diabetes,  
142 antihypertensives, muscle relaxants, analgesics, antiepileptics, anti-parkinson drugs,  
143 psycholeptics (containing all benzodiazepines), psychoanaleptics, other nervous system  
144 drugs and antihistamines for systemic use.

145

146 Drivers for whom treatment had been delivered on the day of the accident were not  
147 considered to be exposed to this treatment because the prescription of this drug could be a  
148 consequence of the crash.

149

#### 150 **Concomitant medicine exposure**

151 In France, a four-level risk classification system of medicines affecting driving abilities is  
152 established, ranging from level 0 (no or negligible risk) to level 3 (major risk) (32,33).  
153 Comparisons were adjusted for exposure to other medicines classified in the highest risk  
154 levels (levels 2 and 3) used the day of the crash.

155

#### 156 **Determining driver crash responsibility**

157 A method adapted from Robertson and Drummer (34) was used to determine responsibility  
158 levels related to the crash.

159 This method is frequently used in the field of road safety. Six factors who are likely to reduce  
160 the responsibility of the driver were considered: road, vehicle and driving conditions, type of  
161 crash, traffic rule obedience, and difficulty of task involved. Each driver was then assigned a  
162 score for each of these factors. This score went from 1 (favorable for driving) to 4 (not  
163 favorable for driving). The scores were then added together to obtain a final score. If the

164 sum was between 8 and 15, the driver was considered to be responsible or partially  
165 responsible and if it was greater than or equal to 15 then he was considered not responsible.  
166 Then, the principle of responsibility analysis was to compare the probabilities of exposure on  
167 the day of the crash between non-responsible drivers and those deemed responsible for the  
168 crash. It allowed to include responsible and non-responsible drivers who were directly  
169 selected from the driver population.

## 170 **Statistical analysis**

171

### 172 *Descriptive analysis*

173 Drivers were classified according to the type of journey when the crash occurred (private,  
174 commuting, mission). Using proportions and Chi-2 squared tests, we compared age, gender,  
175 socioeconomic category, injury severity, responsibility, vehicle type, time of day, location,  
176 alcohol level, frequencies of exposure to medicines of interest and pictogram's levels.

177

### 178 *Responsibility analysis*

179 A cases-control study approach was developed, where cases were responsible drivers  
180 involved in road crashes and the controls were non-responsible drivers involved in road  
181 crashes with two assumptions: The first one is that non-responsible drivers are  
182 representative of the driving population (reference population). The second one is that  
183 responsible and non-responsible drivers were both driving a vehicle on the day of the crash  
184 so they had the same probability of being on the road at the same time (especially in the  
185 case where several vehicles were involved). It also allowed providing as much information on  
186 others exposures and risk factors for both categories.

187 The association between driver responsibility in the crash and exposure to drugs used in  
188 diabetes, antihypertensives, muscle relaxants, analgesics, antiepileptics, anti-parkinson  
189 drugs, psycholeptics, psychoanaleptics, other nervous system drugs (which include  
190 parasympathomimetics, drug used in addiction disorders, antivertigo preparations and  
191 other nervous system drugs) and antihistamines for systemic use by the type of journey was  
192 then investigated using univariate and multivariate logistic regression models with a  
193 stratification on the type of journey.

194 Interaction tests (likelihood ratio tests) were performed to determine if the type of journey  
195 did significantly modify the effect of medicines on responsibility.

196 Multivariate models included adjustment variables identified in the literature as potential  
197 risk or confounding factors: socio-economic characteristics (age, gender, socioeconomic  
198 category), health characteristics (exposure to another drug of level 2 or level 3 on the day of  
199 the crash), alcohol level and characteristics of the crash (year, month, day of week, time of  
200 day (daytime vs nighttime), location (urban area vs nonurban area), vehicle type, blood  
201 alcohol level, and injury severity).

202 An adjustment on the existence of the long-term chronic disease "epilepsy" was also  
203 performed for the model about antiepileptics use in order to look at the potential confusion  
204 effect of the disease. Indeed, epileptic seizures could be the triggering factor for the crash,  
205 independently of the effects of the drugs while antiepileptics are widely used for other  
206 indications as neuropathic pain, bipolar disorder or migraine. On private journeys, 1,644  
207 drivers were exposed to antiepileptic drugs. Among them, 138 had a long-term chronic  
208 disease related to epilepsy. It was the case for 43 drivers on commuting journeys (398  
209 drivers were exposed to antiepileptics) and 15 drivers on mission journeys (147 drivers were  
210 exposed to antiepileptics).

211 Missing data only concerned blood alcohol concentration (n = 22,225, 12.4 %). We estimated  
212 that it was not possible to make imputations on these missing values and consequently  
213 created a specific category “missing data”.

214 Data were analysed using R® statistical software package, version 3.2.3 and 3.5.0 (R  
215 foundation for statistical computing, Vienna, Austria).

216

#### 217 **Ethical statement**

218 Confidentiality was ensured by using the anonymization function of the Health Care  
219 Insurance system (35). The study was approved by the French data protection authority  
220 (Commission Nationale Informatique et Libertés).

221

222

## 223 **Results**

224

### 225 **Study population**

226 Police reports were available for 229,962 persons involved in road crashes with injuries  
227 during the study period. Among them, 22,196 were excluded because they were under 18  
228 years of age or over 65 years of age and 28,465 NIDs were excluded because they were  
229 pedestrians or passengers. 179,301 drivers were then included.

230 Responsibility in the crash was established for 179,269 drivers: 85,684 were identified as  
231 responsible and 93,585 as non-responsible (figure 1).

232 Drivers aged between 35 and 45 years were more represented among drivers on commuting  
233 (25.5%) or mission (27.8 %) journeys compared to drivers on private journeys (21.7 %).

234 The proportion of men was significantly higher among drivers on mission journeys (84.3 %)  
235 than among drivers on commuting (66.1%) or private journeys (67.4 %) (table 1).

236

### 237 **Exposure to Medicines**

238 Fourteen percent of the drivers included in the study (n = 25,466) were exposed to at least  
239 one prescription medicine on the day of the crash.

240 This proportion was about fifteen percent (n = 17,746) for private journeys, about thirteen  
241 percent (n = 5,400) for commuting journeys and about eleven percent for mission journeys  
242 (n = 2,320).

243 Standardized incidences on sex and age groups were also different depending on the type of  
244 journey with an incidence higher for private journeys (15,942 for 100,000 road crashes) than  
245 for commuting (12,963 for 100,000 road crashes) or mission (11,636 for 100,000 road  
246 crashes) journeys.

247 Drivers on private journeys had consumption prevalences twice as high as drivers on mission  
248 journeys for four classes of medicines: antiepileptics (1.4 % on private journeys and 0.7 % on  
249 mission journeys), psycholeptics (6.4 % on private journeys and 2.8 % on mission journeys),  
250 psychoanaleptics (4.8 % on private journeys and 2.2 % on mission journeys) and other  
251 nervous system drugs (1.3 % on private journeys and 0.7 % on mission journeys).

252 Consumption prevalences were similar among drivers regardless the type of journey for five  
253 medicines: antihypertensives, muscle relaxants, analgesics, anti-parkinson drugs and  
254 antihistamines (table 2).

255 Almost sixty-four percent (n = 16,775) of drivers exposed to one of the tenth medicines  
256 studied on the day of the crash were exposed to a level 2 treatment and more than five  
257 percent (n = 1,412) to a level 3 treatment (table 3).

258 After adjusting for risk factors identified from the literature (age, gender, socioeconomic  
259 category, blood alcohol concentration, year, month, day of the week and time of day of the  
260 crash, localization, vehicle type and injury severity) and for exposure to other level 2 or 3  
261 drugs on the day of the crash, the risk of being responsible for a road traffic crash was  
262 significantly increased for drivers on private journeys for four medicines: antiepileptics  
263 (N03), psycholeptics (N05), psychoanaleptics (N06) and other nervous system drugs (N07).

264 For drivers on commuting journeys positive associations were found for three medicines:  
265 antiepileptics (N03), psycholeptics (N05) and psychoanaleptics (N06) and for drivers on  
266 mission journeys for three treatments: antiepileptics (N03), psychoanaleptics (N06) and other  
267 nervous system drugs (N07) (table 4).

268 After taking account of the existence of a long-term chronic disease for epilepsy, the  
269 association of the responsibility and the exposure to antiepileptics were lower but still  
270 significant for private journeys (OR=1.39 [1.17-1.64]) and for commuting journeys (OR=1.43

271 [1.08-1.89]) whereas the association was no more significant for mission journeys (OR= 1.31  
272 [0.81-2.11]). In the same time, the association with the existence of a long-term chronic  
273 disease for epilepsy were significant (OR= 1.54 [1.15-2.06] for private journeys, OR= 2.94  
274 [1.73-4.99] for commuting journeys and OR= 3.49 [1.43-8.52] for mission journeys).

275 The results of the responsibility and interaction tests analysis revealed a significantly higher  
276 risk for drivers on commuting and mission journeys than for drivers on private journeys for  
277 four medicines: antiepileptics, psycholeptics and psychoanaleptics for drivers on commuting  
278 journeys and antiepileptics, psychoanaleptics and other nervous system drugs for drivers on  
279 mission journeys.

280 Indeed, for antiepileptics, the risk was 1.47 [1.25-1.73] for drivers who were on private  
281 journeys, 1.63 [1.24-2.15] for drivers who were on commuting journeys and 1.59 [1.01-2.51]  
282 for drivers who were on mission journeys.

283 For psycholeptics low differences were observed between private and commuting journeys.  
284 The risk reached 1.17 [1.08-1.26] on private journeys and 1.19 [1.03-1.39] on commuting  
285 journeys. The association was not significant for drivers on mission journeys.

286 For psychoanaleptics, the risk was lower for drivers on private journeys, 1.26 [1.14-1.40]  
287 journeys, and similar among drivers on commuting (OR = 1.37 [1.17-1.60]) and mission (OR =  
288 1.35 [1.02-1.78]) journeys.

289 Surprisingly, for private journeys, drivers exposed to antihistamines were less likely to be  
290 responsible for a road crash than unexposed drivers (OR = 0.89 [0.81-0.97]). Exposures to  
291 drugs used in the treatment of diabetes or hypertension, muscle relaxants, analgesics or  
292 anti-parkinson drugs were not significantly associated with an increase or a decrease in the  
293 risk of being responsible for a road crash, regardless of the type of journey performed.

294

## 295 **Discussion**

296

297 Lower medicines consumption prevalences were identified for drivers who were on  
298 commuting or mission journeys. On the other hand, slightly higher risks of being responsible  
299 for the crash were observed for drivers who were on commuting or mission journeys for four  
300 medicines: antiepileptics, psycholeptics (only for commuting journeys, not significant for  
301 mission journeys), psychoanaleptics and other nervous system drugs (only for mission  
302 journeys, not significant for commuting journeys). These differences may be explained by  
303 several factors.

304 First, it is possible that the effects highlighted for some medicines, particularly antiepileptic  
305 drugs, are more related to the expression of the pathology itself (epileptic seizures) than to  
306 the treatment taken. As shown before, results of responsibility analysis did suggest a  
307 confusion effect of epilepsy after adjusting on the existence of a long-term chronic disease  
308 (epilepsy) for drivers. Nevertheless, these results are based on low numbers (196 drivers  
309 under anti-epileptics were identified as having a long-term chronic disease related to  
310 epilepsy (138 on private journeys, 43 on commuting and 15 on mission).

311 Epilepsy is one of the pathologies that can contraindicate driving vehicles. These findings  
312 may suggest that it is probably not antiepileptics but the disease itself or related seizures  
313 that are likely to represent a risk factor for a car crash. Furthermore, it can possibly be  
314 because of the use of antiepileptics for other diseases than epilepsy (36). Further studies  
315 should be made in order to investigate this hypothesis.

316 Anyhow, the risk found in our study for antiepileptics is partially consistent with other  
317 studies. Indeed, one previous study performed within the framework of CESIR project (10)  
318 found a positive and significant association between the exposure to antiepileptics and the

319 risk of road crash (OR = 1.74 [1.29-2.34]) whereas other studies did not find any significant  
320 association (11,12).

321 The slightly higher increase in risk for crashes in mission and commuting may reflect the fact  
322 that there may be more drivers with severe epileptic conditions driving for professional sake.  
323 Drivers with a higher risk of seizure could be more easily be deterred to drive for private  
324 reasons than when facing the need to exercise a professional activity in order to have an  
325 income.

326 In this study, the most important association on mission journeys has been highlighted for  
327 other nervous system drugs (OR = 2.04 [1.35-3.07] on mission journeys against 1.43 [1.21-  
328 1.70] on private journeys and 1.33 [0.99-1.77] on commuting journeys). 87,5% of these  
329 drivers were males, 35,6% were between 25 and 34, 32,7% between 35 and 44 and 20,2%  
330 between 45 and 54. 31,7% were professional drivers. 26,9% drove a car, 22,1% a commercial  
331 vehicle and 17,3% a truck. Other nervous system drugs contain parasympathomimetics,  
332 drug used in addiction disorders, antivertigo preparations and other nervous system drugs.  
333 Those treatments are used in order to treat specific pathologies so we can make the  
334 assumption that the risk of being responsible for a car crash is, like for antiepileptics, maybe  
335 linked to the pathology itself more than to the treatment.

336 Medicine exposure was ascertained from computerized records of reimbursed prescriptions  
337 filled at the pharmacy. It allowed to have data that was not subject to underreporting, which  
338 is a real problem often encountered when people self-report medicine exposure  
339 information.

340 On the other hand, the HCl database does not provide information about compliance or self-  
341 medication. Non-compliance can sometimes induce exposure misclassification that would  
342 lead to underestimate the risk. Another limitation with this database is that real

343 consumption dates were not available and we had to impute them from dispensing dates.  
344 Our exposure measure should therefore be considered as a surrogate for actual  
345 consumption.

346 The responsibility analysis is a real strength of the study because it allowed using non-  
347 responsible drivers, who are sharing common characteristics with responsible drivers as  
348 control group (being a driver, road type, hour of the day...). Furthermore, the responsibility  
349 analysis is based on two main assumptions. The first one is that non-responsible drivers are  
350 representative of the driving population. **The second one is that responsible and non-**  
351 **responsible drivers were both driving a vehicle on the day of the crash so it also allowed**  
352 **providing the same information on other exposures for both categories (especially for**  
353 **accidents where several vehicles were involved). This would not have been the case in a**  
354 **case-control study where controls were only selected from medical or from driver's license**  
355 **databases.**

356 Finally, it is a method frequently used in the field of road traffic safety. This method has been  
357 approved by an independent expert evaluation of responsibility in a previous study (37)  
358 performed on the impact of illegal drug consumption, using this method and the same  
359 national database (but limited to fatal crashes). However, this method does not capture the  
360 risk, for non-responsible drivers, of being unable to avoid a crash that could be related to  
361 medicine use. This would lead to risk under-estimation.

362 **However, as responsibility studies typically report the increased odds of responsibility**  
363 **associated with some factor and as non-responsible drivers are considered to be comparable**  
364 **to non-accidentated drivers, this study design could lead to interpretational bias and over**  
365 **estimation of the odds ratio when the responsibility odds ratio are considered as direct road**  
366 **crash odds ratio (38).**

367 Seriously injured drivers were more likely to be taken to the hospital and so to have their  
368 national id number registered in police reports. Consequently, there was an association  
369 between injury severity and being part of the study and drivers who were more seriously  
370 injured and implicated in more serious traffic crashes were slightly over-represented in our  
371 sample. Killed or uninjured drivers had lower inclusion rates than severely injured driver.

372

373 In addition, the databases used for this study only include drivers involved in road crashes  
374 resulting in personal injury (to the driver or to someone else). Drivers who were involved in  
375 non-injury road crashes are not included. It could have led to a selection bias.

376 Other studies used the responsibility analysis approach in order to look at the relation  
377 between the exposure to some medicines classes and the risk of being responsible for a road  
378 crash (24,39,40). Nevertheless, to our knowledge, no study assessed the consumptions and  
379 risks differences between drivers on private journeys and drivers on professional journeys.

380 However, several studies assessed the consumptions and risks differences between  
381 professional and nonprofessional drivers. We found no association between the exposure to  
382 antihistamines during occupational journeys and the risk of being responsible for a road  
383 traffic crash unlike a previous study conducted among professional drivers (OR = 3.44 [1.06-  
384 11.16]). However, this latter study included truck drivers only.

385 The risks identified in our study for psycholeptics and psychoanaleptics are consistent with  
386 other previous studies not conducted but no data have been so far published on professional  
387 drivers in particular (19,21,41).

388

## 389 **Conclusion**

390

391 This study brings original results about the problematic of medicines consumptions and  
392 driving for purposes of work. Firstly, in terms of the prevalence of the exposure that is higher  
393 for drivers on private journeys. Then, in terms of the risk of being responsible for a road  
394 traffic crash linked to those consumptions, with a risk higher for drivers on commuting or  
395 mission journeys compared to private journeys for four medicines: antiepileptics,  
396 psycholeptics (only for commuting journeys, not significant for mission journeys),  
397 psychoanaleptics and other nervous system drugs (only for mission journeys, not significant  
398 for commuting journeys).

399

400 This study brings new information to health professionals (general practitioners,  
401 occupational practitioners and practitioners approved for driving licenses), especially about  
402 antiepileptics, psycholeptics, psychoanaleptics and other nervous system drugs  
403 consumptions. For those four medicines, an increased-risk was observed for drivers on  
404 commuting or mission journeys.

405 Preventive measures could be implemented in order to make occupational practitioners and  
406 employees aware of the occupational road risks associated with the use of some  
407 medications.

408 Further studies to confirm these results would be useful, including studies on the time to  
409 onset of work-related road crashes after the start of a drug prescription. This would clarify  
410 the impact of drugs and improve prevention and recommendations currently implemented  
411 by, for example, adjusting the time to return to driving.

412

413

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415

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417

418 **References**

- 419 1. Hours M, Fort E, Charnay P, Bernard M, Martin JLL, Boisson D, et al. Diseases,  
420 consumption of medicines and responsibility for a road crash: a case-control study.  
421 *Accid Anal Prev* [Internet] . 2008;40(5):1789–96. Available from:  
422 [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Ci](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18760109)  
423 [tation&list\\_uids=18760109](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18760109)
- 424 2. Elvik R. Risk of road accident associated with the use of drugs: A systematic review  
425 and meta-analysis of evidence from epidemiological studies. *Accid. Anal. Prev.* . 2013;
- 426 3. Orriols L, Philip P, Moore N, Castot A, Gadegbeku B, Delorme B, et al. Benzodiazepine-  
427 like hypnotics and the associated risk of road traffic accidents. *Clin. Pharmacol. Ther.*  
428 [Internet] . 2011;89(4):595–601. Available from:  
429 <http://www.ncbi.nlm.nih.gov/pubmed/21368756>
- 430 4. Orriols L, Gbaguidi GN, Contrand B, Gadegbeku B, Lagarde E. Trends in benzodiazepine  
431 anxiolytics and z-hypnotics use among French drivers involved in road traffic crashes  
432 from 2005 to 2015: a responsibility case-control study. *Inj. Epidemiol.* [Internet] .  
433 2019;6:32. Available from: [http://files/385/Orriols et al. - 2019 - Trends in](http://files/385/Orriols et al. - 2019 - Trends in benzodiazepine anxiolytics and z-hypnoti.pdf)  
434 [benzodiazepine anxiolytics and z-hypnoti.pdf](http://files/385/Orriols et al. - 2019 - Trends in benzodiazepine anxiolytics and z-hypnoti.pdf)
- 435 5. Nevriana A, Möller J, Laflamme L, Monárrez-Espino J. New, Occasional, and Frequent  
436 Use of Zolpidem or Zopiclone (Alone and in Combination) and the Risk of Injurious  
437 Road Traffic Crashes in Older Adult Drivers: A Population-Based Case-Control and  
438 Case-Crossover Study. *CNS Drugs* [Internet] . 2017;31(8):711–22. Available from:  
439 [http://files/388/Nevriana et al. - 2017 - New, Occasional, and Frequent Use of](http://files/388/Nevriana et al. - 2017 - New, Occasional, and Frequent Use of Zolpidem or Zopiclone.pdf)  
440 [Zolpidem or Zopiclone.pdf](http://files/388/Nevriana et al. - 2017 - New, Occasional, and Frequent Use of Zolpidem or Zopiclone.pdf)
- 441 6. Engeland A, Skurtveit S, Mørland J. Risk of road traffic accidents associated with the

- 442 prescription of drugs: a registry-based cohort study. *Ann. Epidemiol.* [Internet] .  
443 2007;17(8):597–602. Available from:  
444 <http://www.ncbi.nlm.nih.gov/pubmed/17574863>
- 445 7. Lai M-M, Lin C-C, Lin C-C, Liu C-S, Li T-C, Kao C-H. Long-term use of zolpidem increases  
446 the risk of major injury: a population-based cohort study. *Mayo Clin. Proc.* [Internet] .  
447 2014;89(5):589–94. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24684782>
- 448 8. Drummer OH, Gerostamoulos D, Di Rago M, Woodford NW, Morris C, Frederiksen T,  
449 et al. Odds of culpability associated with use of impairing drugs in injured drivers in  
450 Victoria, Australia. *Accid. Anal. Prev.* . 2020;
- 451 9. Gjerde H, Normann PT, Christophersen AS, Samuelsen SO, Mørland J. Alcohol,  
452 psychoactive drugs and fatal road traffic accidents in Norway: A case-control study.  
453 *Accid. Anal. Prev.* . 2011;
- 454 10. Orriols L, Foubert-Samier A, Gadegbeku B, Delorme B, Tricotel A, Philip P, et al.  
455 Prescription of antiepileptics and the risk of road traffic crash. *J. Clin. Pharmacol.*  
456 [Internet] . 2013;53(3):339–44. Available from: [http://files/391/Orriols et al. - 2013 -  
457 Prescription of antiepileptics and the risk of roa.pdf](http://files/391/Orriols et al. - 2013 - Prescription of antiepileptics and the risk of roa.pdf)
- 458 11. Sundelin HEK, Chang Z, Larsson H, Lichtenstein P, Almqvist C, Tomson T, et al.  
459 Epilepsy, antiepileptic drugs, and serious transport accidents: A nationwide cohort  
460 study. *Neurology* [Internet] . 2018;90(13):e1111–8. Available from:  
461 [http://files/394/Sundelin et al. - 2018 - Epilepsy, antiepileptic drugs, and serious  
462 transpo.pdf](http://files/394/Sundelin et al. - 2018 - Epilepsy, antiepileptic drugs, and serious transpo.pdf)
- 463 12. Bramness JG, Skurtveit S, Neutel CI, Mørland J, Engeland A. An increased risk of road  
464 traffic accidents after prescriptions of lithium or valproate? *Pharmacoepidemiol. Drug  
465 Saf.* [Internet] . 2009;18(6):492–6. Available from:

- 466 <http://www.ncbi.nlm.nih.gov/pubmed/19326366>
- 467 13. Wickens CM, Mann RE, Brands B, Ialomiteanu AR, Fischer B, Watson TM, et al. Driving  
468 under the influence of prescription opioids: Self-reported prevalence and association  
469 with collision risk in a large Canadian jurisdiction. *Accid. Anal. Prev.* . 2018;
- 470 14. Monárrez-Espino J, Möller J, Berg HY, Kalani M, Laflamme L. Analgesics and road  
471 traffic crashes in senior drivers: An epidemiological review and explorative meta-  
472 analysis on opioids. *Accid. Anal. Prev.* . 2013;
- 473 15. McGwin Jr. G, Sims R V, Pulley LV, Roseman JM, McGwin G, Sims R V, et al. Relations  
474 among Chronic Medical Conditions, Medications, and Automobile Crashes in the  
475 Elderly: A Population-based Cas-Control Study. *Am. J. Epidemiol.* [Internet] .  
476 Department of Epidemiology and International Health, School of Public Health,  
477 University of Alabama at Birmingham, 35294-0009, USA. [mcgwin@eyes.uab.edu](mailto:mcgwin@eyes.uab.edu);  
478 2000;152:424–31. Available from:  
479 <http://aje.oxfordjournals.org/cgi/reprint/152/5/424> LB - Manu 102
- 480 16. Meuleners LB, Duke J, Lee AH, Palamara P, Hildebrand J, Ng JQ. Psychoactive  
481 medications and crash involvement requiring hospitalization for older drivers: a  
482 population-based study. *J. Am. Geriatr. Soc.* [Internet] . 2011;59(9):1575–80. Available  
483 from: <http://www.ncbi.nlm.nih.gov/pubmed/21883110>
- 484 17. Orriols L, Queinec R, Philip P, Gadegbeku B, Delorme B, Moore N, et al. Risk of  
485 injurious road traffic crash after prescription of antidepressants. *J. Clin. Psychiatry*  
486 [Internet] . 2012 Feb 3;73(8):1088–94. Available from:  
487 <http://www.ncbi.nlm.nih.gov/pubmed/22967773>
- 488 18. Chang C-M, Wu EC-H, Chen C-Y, Wu K-Y, Liang H-Y, Chau Y-L, et al. Psychotropic drugs  
489 and risk of motor vehicle accidents: a population-based case-control study. *Br. J. Clin.*

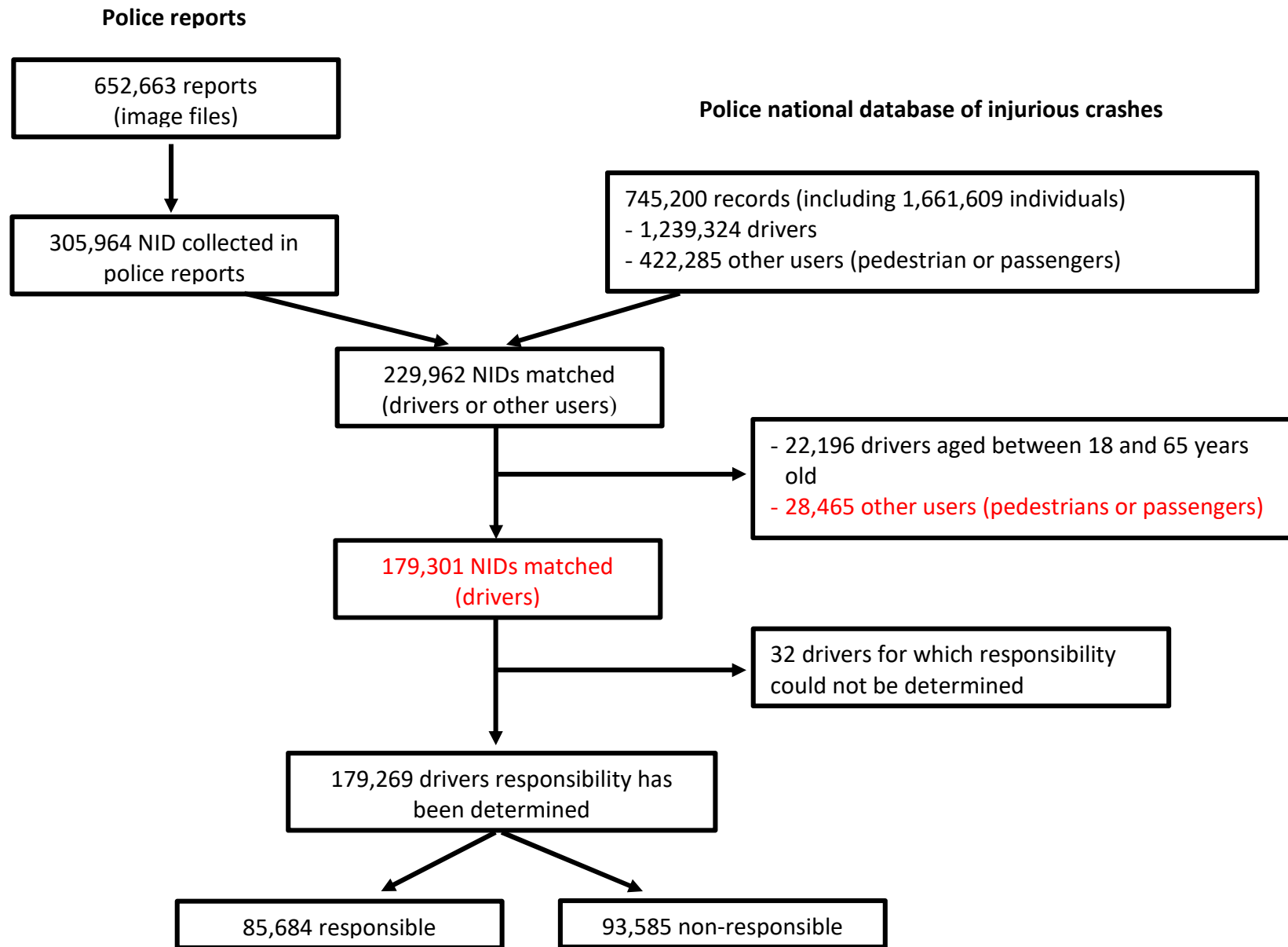
- 490 Pharmacol. [Internet] . 2013;75(4):1125–33. Available from: <http://files/399/Chang et>  
491 [al. - 2013 - Psychotropic drugs and risk of motor vehicle accid.pdf](#)
- 492 19. Leveille S, Buchner D, Koepsell T, McCloskey L, Wolf M, Wagner E. Psychoactive  
493 medications and injurious motor vehicle collisions involving older drivers. *Am. J.*  
494 *Epidemiol.* . 1994;5:591–8.
- 495 20. Bramness JG, Skurtveit S, Mørland J, Engeland A. The risk of traffic accidents after  
496 prescriptions of carisoprodol. *Accid. Anal. Prev.* . 2007;
- 497 21. Ray W, Fought R, Decker M. Psychoactive drugs and the risk of injurious motor vehicle  
498 crashes in elderly drivers. *Am. J. Epidemiol.* . 1992;136:873–83.
- 499 22. Howard ME, Desai A V, Grunstein RR, Hukins C, Armstrong JG, Joffe D, et al.  
500 Sleepiness, sleep-disordered breathing and accident risk factors in commercial vehicle  
501 drivers. *Am. J. Respir. Crit. Care Med.* [Internet] . 2004;170:1014–21. Available from:  
502 <http://ajrccm.atsjournals.org/cgi/reprint/170/9/1014?maxtoshow=&HITS=10&hits=10>  
503 [&RESULTFORMAT=&author1=howard&searchid=1&FIRSTINDEX=0&fdate=1/1/2004&t](#)  
504 [date=12/31/2004&resourcetype=HWCIT LB - Manu 122](#)
- 505 23. Verster JC, Volkerts ER. Antihistamines and driving ability: evidence from on-the-road  
506 driving studies during normal traffic. *Ann. Allergy, Asthma Immunol. Off. Publ. Am.*  
507 *Coll. Allergy, Asthma, Immunol.* [Internet] . 2004;92(3):294-305,355. Available from:  
508 <http://files/411/Verster et Volkerts - 2004 - Antihistamines and driving ability>  
509 [evidence from .pdf](#)
- 510 24. Orriols L, Luxcey A, Contrand B, Bénard-Larivière A, Pariente A, Gadegbeku B, et al.  
511 Road traffic crash risk associated with prescription of hydroxyzine and other sedating  
512 H1-antihistamines: A responsibility and case-crossover study. *Accid. Anal. Prev.* . 2017;
- 513 25. Woratanarat P, Ingsathit A, Suriyawongpaisal P, Rattanasiri S, Chatchaipun P,

- 514 Wattayakorn K, et al. Alcohol, illicit and non-illicit psychoactive drug use and road  
515 traffic injury in Thailand: a case-control study. *Accid. Anal. Prev.* [Internet] .  
516 2009;41(3):651–7. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/19393818>
- 517 26. Orriols L, Delorme B, Gadegbeku B, Tricotel A, Laumon B, Salmi L-R, et al. Prescription  
518 Medicines and the Risk of Road Traffic Crashes: A French Registry-Based Study.  
519 Pirmohamed M, editor. *PLoS Med.* [Internet] . 2010 Feb 3;7(11):e1000366. Available  
520 from: <https://dx.plos.org/10.1371/journal.pmed.1000366>
- 521 27. Labat L, Fontaine B, Delzenne C, Doublet A, Marek MC, Tellier D, et al. Prevalence of  
522 psychoactive substances in truck drivers in the Nord-Pas-de-Calais region (France).  
523 *Forensic Sci. Int.* [Internet] . Laboratoire Toxicologie et Genopathies, CHRU de Lille, Av.  
524 Professeur J. Leclercq, 59037 Lille Cedex, France. [l.labat@chru-lille.fr](mailto:l.labat@chru-lille.fr); 2008;174:90–4.  
525 Available from:  
526 [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Ci](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17418990)  
527 [tation&list\\_uids=17418990](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17418990)
- 528 28. Khoshakhlagh AH, Yazdanirad S, Laal F, Sarsangi V. The relationship between illnesses  
529 and medical drug consumption with the occurrence of traffic accidents among truck  
530 and bus drivers in Tehran, Iran. *Chinese J. Traumatol. = Zhonghua Chuang Shang Za Zhi*  
531 [Internet] . 2019;22(3):142–7. Available from: [http://files/422/Khoshakhlagh et al. -](http://files/422/Khoshakhlagh%20et%20al.%20-%202019%20-%20The%20relationship%20between%20illnesses%20and%20medical%20dru.pdf)  
532 [2019 - The relationship between illnesses and medical dru.pdf](http://files/422/Khoshakhlagh%20et%20al.%20-%202019%20-%20The%20relationship%20between%20illnesses%20and%20medical%20dru.pdf)
- 533 29. Giroto E, Guidoni CM, González AD, Mesas AE, Andrade SM de. Continued use of  
534 drugs and working conditions among truck drivers. *Cien. Saude Colet.* [Internet] .  
535 2016;21(12):3769–76. Available from: [http://files/425/Giroto et al. - 2016 -](http://files/425/Giroto%20et%20al.%20-%202016%20-%20Continued%20use%20of%20drugs%20and%20working%20conditions%20amon.pdf)  
536 [Continued use of drugs and working conditions amon.pdf](http://files/425/Giroto%20et%20al.%20-%202016%20-%20Continued%20use%20of%20drugs%20and%20working%20conditions%20amon.pdf)
- 537 30. Fort E, Pourcel L, Davezies P, Renaux C, Chiron M, Charbotel B. Road accidents, an

- 538 occupational risk. *Saf. Sci.* . 2010;48(10):1412–20.
- 539 31. Fort E, Gadegbeku B, Gat E, Pelissier C, Hours M, Charbotel B. Working conditions and  
540 risk exposure of employees whose occupations require driving on public roads –  
541 Factorial analysis and classification. *Accid. Anal. Prev.* [Internet] . 2019 Oct;131:254–  
542 67. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S000145751830705X>
- 543 32. Arrêté du 8 août 2008 pris pour l’application de l’article R. 5121-139 du code de la  
544 santé publique et relatif à l’apposition d’un pictogramme sur le conditionnement  
545 extérieur de certains médicaments et produits [Internet]. May 17, 2020. Available  
546 from: <https://www.legifrance.gouv.fr/eli/arrete/2005/7/18/SANP0522726A/jo>
- 547 33. Arrêté du 18 juillet 2005 pris pour l’application de l’article R. 5121-139 du code de la  
548 santé publique et relatif à l’apposition d’un pictogramme sur le conditionnement  
549 extérieur de certains médicaments et produits | Legifrance [Internet]. 2020. Available  
550 from: <https://www.legifrance.gouv.fr/eli/arrete/2005/7/18/SANP0522726A/jo>
- 551 34. Robertson MD, Drummer OH. Responsibility analysis : A Methodology to Study the  
552 Effects of Drugs in Driving. *Accid. Anal. Prev.* . 1994;26:243–7.
- 553 35. Trouessin G, Allaert FA. FOIN: A nominative information occultation function. *Stud.*  
554 *Health Technol. Inform.* . 1997.
- 555 36. Molero Y, Larsson H, D’Onofrio BM, Sharp DJ, Fazel S. Associations between  
556 gabapentinoids and suicidal behaviour, unintentional overdoses, injuries, road traffic  
557 incidents, and violent crime: Population based cohort study in Sweden. *BMJ* . 2019;
- 558 37. Laumon B, Gadegbeku B, Martin J-L, Biecheler MB, the Sam Group. Cannabis  
559 intoxication and fatal road crashes in France: population based case-control study. *Br.*  
560 *Med. J.* [Internet] . 2005; Available from:  
561 <http://www.bmj.com/cgi/reprint/331/7529/1371?maxtoshow=&HITS=10&hits=10&R>

- 562 ESULTFORMAT=&fulltext=laumon&searchid=1&FIRSTINDEX=0&resourcetype=HWCIT
- 563 LB - Manu 62
- 564 38. Rogeberg O. A meta-analysis of the crash risk of cannabis-positive drivers in culpability  
565 studies—Avoiding interpretational bias. *Accid. Anal. Prev.* . Elsevier Ltd; 2019 Feb  
566 1;123:69–78.
- 567 39. Barbone F, McMahon AD, Davey PG, Morris AD, Reid IC, McDevitt DG, et al.  
568 Association of road-traffic accidents with benzodiazepine use. *Lancet* (London,  
569 England) [Internet] . 1998;352(9137):1331–6. Available from:  
570 <http://www.ncbi.nlm.nih.gov/pubmed/9802269>
- 571 40. Lowenstein SR, Koziol-McLain J. Drugs and traffic crash responsibility: A study of  
572 injured motorists in Colorado. *J. Trauma - Inj. Infect. Crit. Care* . 2001;
- 573 41. Bramness JG, Skurtveit S, Neutel CI, Mørland J, Engeland A. Minor increase in risk of  
574 road traffic accidents after prescriptions of antidepressants: A study of population  
575 registry data in Norway. *J. Clin. Psychiatry* . 2008;

Figure 1: Flowchart of the inclusion procedure.



**Table 1: Baseline characteristics according to the type of journey, N = 179,269.**

	Private N = 114,767 (64%)		Commuting N = 43,012 (24%)		Mission N = 21,490 (12%)	
	n	%	n	%	n	%
<b>Age (years) **</b>						
[18-25[	27,423	23.9	7,964	18.5	2,580	12.0
[25-35[	28,262	24.6	12,253	28.5	5,828	27.1
[35-45[	24,941	21.7	10,984	25.5	5,971	27.8
[45-55[	20,145	17.6	8,622	20.0	4,999	23.3
[55-65]	13,996	12.2	3,189	7.5	2,112	9.8
<b>Sex**</b>						
Men	77,342	67.4	28,451	66.1	18,115	84.3
Women	37,425	32.6	14,561	33.9	3,375	15.7
<b>Socioeconomic category **</b>						
Professionnal driver	1,579	1.4	757	1.8	4,513	21.0
Farmer	580	0.5	243	0.6	372	1.7
Craftsman, trader, intermediate profession	4,189	3.7	1,969	4.6	1,729	8.0
Higher managerial and professional occupations	4,613	4.0	3,118	7.2	1,465	6.8
Intermediate occupations	28,958	25.2	19,161	44.5	7,489	34.8
Workers	16,903	14.7	9,349	21.7	3,306	15.4
Retired	5,938	5.2	65	0.2	50	0.2
Unemployed	8,504	7.4	187	0.4	71	0.3
Toher/missing	33,465	29.2	6,888	16.0	2,266	10.5
Student	10,038	8.7	1,275	3.0	229	1.1
<b>Long-term chronic disease**</b>						
Yes	10,177	8.9	2,605	6.1	1,380	6.4
No	104,590	91.1	40,407	93.9	20,110	93.6
<b>Injury severity**</b>						
Unhurt	32,530	28.4	10,515	24.5	10,183	47.4
Slightly injured	40,672	35.4	18,042	41.9	7,294	33.9
Seriously injured	39,689	34.6	13,839	32.2	3,794	17.7
Killed	1,876	1.6	616	1.4	219	1.0
<b>Responsibility**</b>						
Non-responsible	57,608	50.2	24,122	56.1	11,855	55.2
Responsible or partially responsible	57,159	49.8	18,890	43.9	9,635	44.8
<b>Pictogram levels **</b>						
Level 0	73,841	64.3	28,272	65.7	12,625	58.7
Level 1	6,632	5.8	2,779	6.5	1,629	7.6
Level 2	3,471	3.0	1,338	3.1	670	3.1
Level 3	61	0.1	24	0.1	29	0.1
NI	30,762	26.8	10,599	24.6	6,537	30.5

(Continuation of table 1)

	Private		Commuting		Mission	
	N = 114,767 (64%)		N = 43,012 (24%)		N = 21,490 (12%)	
	n	%	n	%	n	%
<b>Vehicle type**</b>						
Bicycle	6,105	5.4	2,180	5.1	296	1.4
Scooter	11,044	9.6	3,855	9.0	1,189	5.5
Motorbike	21,129	18.4	10,364	24.1	2,225	10.4
Light vehicle	72,235	62.9	24,211	56.2	7,623	35.5
Commercial vehicle	2,994	2.6	1,872	4.3	3,915	18.2
Heavy goods vehicle	470	0.4	282	0.7	3,018	14.0
Other	790	0.7	248	0.6	3,224	15.0
<b>Time of the day**</b>						
Day [7h-20h]	94,786	82.6	37,899	88.1	19,177	89.2
Night [21h-6h]	19,981	17.4	5,113	11.9	2,313	10.8
<b>Alcohol (g/L) **</b>						
Not applicable, rate of 0	90,163	78.5	36,657	85.2	18,889	87.9
<0,5	1,025	0.9	134	0.3	52	0.2
[0,5 – 0,8[	1,775	1.5	130	0.3	41	0.2
[0,8-1,2[	4,122	3.6	294	0.7	94	0.4
[1,2-2,0[	3,389	3.0	214	0.5	65	0.3
NI	14,293	12.5	5,583	13.0	2,349	10.9
<b>Localisation**</b>						
Urban areas	64,945	56.6	23,519	54.7	9,916	46.1
Suburban areas	49,822	43.4	19,493	45.3	11,574	53.9
<b>Exposure to a level 2 medicine**</b>	12,187	10.6	3,277	7.6	1,311	6.1
<b>Exposure to a level 3 medicine**</b>	1,066	0.9	250	0.6	96	0.4

\*\*p<0,001 (Chi-2 square test). NI : No Information

**Table 2: Numbers and proportions of exposed drivers on the crash day by classification of medicines used (overall and according to the type of journey), N = 179,269.**

	Full population N = 179,269		Private N = 114,767		Commuting N = 43,012		Mission N = 21,490	
	n	%	n	%	n	%	n	%
Drug used in diabetes (A10)	2,689	1.5	1,837	1.6	502	1.2	350	1.6
Antihypertensives (C02)	316	0.2	220	0.2	56	0.1	40	0.2
Muscle relaxants (M03)	715	0.4	485	0.4	174	0.4	56	0.3
Analgesics (N02) <sup>a</sup>	9,527	5.3	6,546	5.7	2,064	4.8	917	4.3
Antiepileptics (N03)	2,189	1.2	1,644	1.4	398	0.9	147	0.7
Anti-Parkinson drugs (N04)	294	0.2	233	0.2	45	0.1	16	0.1
Psycholeptics (N05) <sup>b</sup>	9,525	5.3	7,342	6.4	1,583	3.7	600	2.8
Psychoanaleptics (N06) <sup>c</sup>	7,415	4.1	5,491	4.8	1,443	3.4	481	2.2
Other nervous system drugs (N07) <sup>d</sup>	1,983	1.1	1,486	1.3	340	0.8	157	0.7
Antihistamines for systemic use (R06)	4,462	2.5	2,949	2.6	1,064	2.5	449	2.1

a Including opioids (n= 4,288), other analgesics and antipyretics (n= 4,448) and antimigraine preparations (n= 791)

b Including antipsychotics (n= 1,833), anxiolytics (n= 6,195) and hypnotics and other sedatives (n= 1,497)

c Including antidepressants (n= 7,256), psychostimulants (n= 66) and antidementia drugs (n= 93)

d Including parasympathomimetics (n = 17), drug used in addiction disorders (n= 1,634), antivertigo preparations (n= 303) and other nervous system drugs (n= 29)

**Table 3: Exposure prevalence (overall and by type of medicines) to at least another medicine of level 2 or level 3, N = 179,269.**

	N global* = 25,466		Drugs used in diabetes N = 2,689		Anti-hypertensives N = 316		Muscle relaxants N = 715		Analgesics N = 9,527		Anti-epileptics N = 2,189		Anti-parkinson drugs N = 294		Psycho-leptics N = 9,525		Psycho-analeptics N = 7,415		Other nervous system drugs N = 1,983		Anti-histamines for systemic use N = 4,462	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Exposure to at least another treatment of level 2	16,775	63.8	732	27.2	129	40.8	369	51.6	2,706	28.4	1,228	56.1	218	74.1	5,632	59.1	4,571	61.6	997	50.3	1,092	24.5
Exposure to at least another treatment of level 3	1,412	5.4	97	3.6	19	6.0	28	3.9	361	3.8	104	4.8	7	2.4	0	0	400	5.4	90	4.5	111	2.5

\*drivers under one of the ten medicines studied on the day of the crash

**Table 4: Associations between the exposition to ten medicines and the risk of being responsible for a road traffic accident according to the type of journey (private, commuting, mission). Multivariate logistic regression, N = 179,269.**

Medicines (yes/no)	Private N = 114,767			Commuting N = 43,012			Mission N = 21,490		
	n Responsible/ Non- responsible	% Responsible/ Non- responsible	adjusted OR [95% IC] <sup>a</sup>	n Responsible/ Non- responsible	% Responsible/ Non- responsible	Adjusted OR [95% IC] <sup>a</sup>	n Responsible/ Non- responsible	% Responsible/ Non- responsible	Adjusted OR [95% CI] <sup>a</sup>
Drugs used in diabetes (A10)	909 / 928	1.6 / 1.6	1.05 [0.93-1.18]	219 / 283	1.2 / 1.2	1.07 [0.87-1.31]	167 / 183	1.7 / 1.5	1.13 [0.89-1.43]
Antihypertensives (C02)	92 / 122	0.2 / 0.2	0.83 [0.58-1.20]	26 / 30	0.1 / 0.1	0.95 [0.47-1.91]	18 / 22	0.2 / 0.2	1.09 [0.53-2.24]
Muscle relaxants (M03)	219 / 266	0.4 / 0.5	0.75 [0.56-1.00]	75 / 99	0.4 / 0.4	0.99 [0.65-1.49]	19 / 37	0.2 / 0.3	0.77 [0.35-1.70]
Analgesics (N02) <sup>b</sup>	3,232 / 3,314	5.7 / 5.8	0.95 [0.90-1.02]	890 / 1 174	4.7 / 4.9	0.99 [0.89-1.10]	398 / 519	4.1 / 4.4	0.91 [0.78-1.06]
Antiepileptics (N03)	983 / 661	1.7 / 1.1	1.47 [1.25-1.73]**	202 / 196	1.1 / 0.8	1.63 [1.24-2.15]**	86 / 61	0.9 / 0.5	1.59 [1.01-2.51]*
Anti-parkinson drugs (N04)	125 / 108	0.2 / 0.2	1.25 [0.74-2.10]	18 / 27	0.1 / 0.1	0.80 [0.20-3.24]	7 / 9	0.1 / 0.1	0.62 [0.14-2.64]
Psycholeptics (N05) <sup>c</sup>	4,265 / 3,077	7.5 / 5.3	1.17 [1.08-1.26]**	767 / 816	4.1 / 3.4	1.19 [1.03-1.39]*	297 / 303	3.1 / 2.6	1.02 [0.80-1.28]
Psychoanaleptics (N06) <sup>d</sup>	3,192 / 2,299	5.6 / 4.0	1.26 [1.14-1.40]**	681 / 762	3.6 / 3.2	1.37 [1.17-1.60]**	247 / 234	2.6 / 2.0	1.35 [1.02-1.78]*
Other nervous system drugs (N07) <sup>e</sup>	997 / 489	1.7 / 0.8	1.43 [1.21-1.70]**	188 / 152	1.0 / 0.6	1.33 [0.99-1.77]	104 / 53	1.1 / 0.4	2.04 [1.35-3.07]**
Antihistamines for systemic use (R06)	1,346 / 1,603	2.4 / 2.8	0.89 [0.81-0.97]*	460 / 604	2.4 / 2.5	0.99 [0.87-1.14]	199 / 250	2.1 / 2.1	1.03 [0.83-1.27]

a ORs adjusted for age, gender, socioeconomic category, blood alcohol concentration (g/L), year, month, day of the week and time of the day (day/night), localisation (urban/nonurban area),

vehicle type, injury severity and other medicines of level 2 or level 3

b Including opioids (n= 4,288), other analgesics and antipyretics (n= 4,448) and antimigraine preparations (n= 791)

c Including antipsychotics (n= 1,833), anxiolytics (n= 6,195) and hypnotics and other sedatives (n= 1,497)

d Including antidepressants (n= 7,256), psychostimulants (n= 66) and antidementia drugs (n= 93)

e Including parasympathomimetics (n = 17), drug used in addiction disorders (n= 1,634), antivertigo preparations (n= 303) and other nervous system drugs (n= 29)

\*p<0.05 \*\*p<0.001