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Alcohol, psychoactive drugs and fatal road traffic accidents in Norway: A case–control study

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ABSTRACT

A case–control study was conducted on 204 drivers fatally injured in road traffic accidents in south-eastern Norway during the period 2003–2008. Cases from single vehicle accidents ($N = 68$) were assessed separately. As controls, 10 540 drivers selected in a roadside survey in the same geographical area during 2005–2006 were used. Blood samples were collected from the cases and oral fluid (saliva) samples from the controls. Samples were analysed for alcohol, amphetamines, cannabis, cocaine, opioid analgesics, hypnotics, sedatives and a muscle relaxant; altogether 22 psychoactive substances. Equivalent cutoff concentrations for blood and oral fluid were used. The risk for fatal injury in a road traffic accident was estimated using logistic regression adjusting for gender, age, season of the year, and time of the week. The odds for involvement in fatal road traffic accidents for different substances or combination of substances were in increasing order: single drug < multiple drugs < alcohol only < alcohol + drugs. For single substance use: medicinal drug or THC < amphetamine/methamphetamine < alcohol. For most substances, higher ORs were found when studying drivers involved in single vehicle accidents than for those involved in multiple vehicle accidents, but confidence intervals were wider.

1. Introduction

Traffic accidents are often related to the use of alcohol, illegal drugs or psychoactive medicinal drugs (Kelly et al., 2004; Raes et al., 2008; Walsh et al., 2004). Case–control-studies represent one of the best methodological approaches to determine crash risks associated with the use of different psychoactive substances (Berghaus et al., 2007). Such studies have clearly demonstrated the relationship between blood alcohol concentration and traffic accident risk (Blomberg et al., 2009; Borkenstein et al., 1974). Similar studies have also been performed for some psychoactive drugs (Assum et al., 2005; Brault et al., 2004; Drummer et al., 2004; Laumon et al., 2005; Movig et al., 2004; Mura et al., 2003; Woratanarat et al., 2009). The risk of traffic accident has been found to be increased after use of benzodiazepines, opiates, cannabis, amphetamines, cocaine and PCP in one or more of those studies. In general, the odds for accident involvements were higher after multiple drug use than single drug use.

Problems observed in some studies of this type include the analysis of a small selection of drugs which does not enable the detection of all relevant impairing substances or multi-drug use, analysis of inactive drug metabolite instead of the active drugs, non-representative selection of controls (e.g., patient groups), the use of non-equivalent biological samples for cases and controls (blood and urine), and inability to distinguish between drivers to blame for the accident and innocent drivers who were injured or killed in collisions.

In cases of fatally injured drivers, blood samples are often collected and analysed for alcohol and drugs as part of police investigations. The results of those samples may be used for research purposes. In cases of injured drivers admitted to hospital for treatment, blood samples may also be obtained after informed consent, but the refusal rate might be significant. For controls, which in an ideal situation should be random drivers in normal traffic, it is difficult to obtain reliable data on blood drug concentrations. An American study showed an unacceptably high refusal rate of 60.9% if collecting blood samples from random drivers, even when 50 US$ was offered as incentive for providing a sample (Lacey et al., 2009a). This is also likely to be the case in Norway.

Samples of oral fluid can be used instead of blood to detect and monitor alcohol and drug use (Caplan and Goldberger, 2001; Choo and Huestis, 2004; Cone, 2001; Spiehler, 2004). Oral fluid can be taken without the intrusion of privacy, and reflects better than urine whether a person has a drug present in the blood (Samyn et al., 1999). The distribution of drug concentrations in oral fluid reflects the distribution of drug concentrations in blood in a popu-

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lation of drug users if the population is large, and it may therefore be possible to estimate the prevalence of blood drug concentrations above a selected cutoff concentration by analysing oral fluid samples (Gjerde and Verstraete, 2010). Therefore, the collection and analysis of oral fluid may be a useful tool for obtaining data on drug use among random drivers in case–control-studies.

The incidence of alcohol or drug related road accidents varies from one country to another, and may be related to the incidence of drunken and drugged driving, the incidence of risk-taking behaviour among drivers, the state of roads and motor vehicles, as well as other factors. Norway has a relatively low number of fatal road traffic accidents compared to most other countries: 4.9 per 100 000 inhabitants in 2007 or 0.7 per 10 000 motor vehicles (IRTAD, 2009). The prevalence of drunken driving is also fairly low in Norway. A study organised by the European Traffic Police Network showed that 0.2% of drivers in Norway and 2–4% of drivers in most other European countries had breath alcohol levels above the national legal limits (TISPOL, 2009). In the USA, 2.3% of nighttime drivers had breath alcohol levels above 0.05 g/dL in the 2007 roadside survey (Lacey et al., 2009b). The incidence of drunken driving is in some countries higher; studies have shown that as much as 7–8% of the drivers in some African countries were driving under influence (Mock et al., 2001; Odero and Zwi, 1997).

Illegal drugs or psychoactive medicinal drugs were more frequently found than alcohol in samples of oral fluid from random drivers in a recent Norwegian roadside survey; illegal and psychoactive medicinal drugs were found in 1.0% and 3.4% of the samples, respectively (Gjerde et al., 2008). In a study of drivers killed in road accidents in Norway during 1989–1990, alcohol and/or psychoactive drugs were found in blood samples from 37.1% of the drivers; alcohol in 28.3% and drugs in 16.4% (Gjerde et al., 1993a). In a later study performed in 2001–2002, alcohol and/or psychoactive drugs were found in blood samples from 42.4% of killed drivers; alcohol in 21.8% and drugs in 29.6% (Christophersen et al., 2005). Alcohol and/or psychoactive drugs were found in blood samples from 54.4% and 60.9% of the drivers killed in single vehicle accidents in the first and second study, respectively; alcohol in 41.8% and 40.2%, and drugs in 21.5% and 37.0%. There was thus an increase in drug findings in the second study. The reported prevalence of psychoactive substances in blood samples from killed drivers from other countries have varied a lot, and were for alcohol 12.5–63.2%, cannabis 1.2–28.9%, cocaine 0.0–8.3%, opiates 0.7–3.5%, and amphetamines 0.0–7.5 (Gonzalez-Wilhelm, 2007; Odero et al., 1997).

The aim of this investigation was to compare the prevalence of alcohol and drugs in samples from drivers killed in traffic accidents in south-eastern Norway with random drivers, and to calculate the odds ratio (OR) for fatal injury in a road accident after using alcohol or drugs. In order to better distinguish between single and multiple substance use, samples were analysed for 21 of the active psychoactive substances that are most frequently found in samples from arrested drugged drivers in addition to alcohol. Blood samples were obtained from the cases, and oral fluid samples from the controls in order to get a high participation rate.

2. Materials and methods

2.1. Selection of cases

Data on persons injured or killed in road traffic accidents in Norway are submitted by the police to Statistics Norway on a regular basis. These data are entered into the Norwegian Road Accident Registry. The recorded data include the national identification number of the drivers in addition to information about the accidents.

Data on blood samples submitted for forensic toxicological analysis of alcohol or drugs at the Norwegian Institute of Public Health (NIPH) are recorded in NIPH's forensic toxicology database. This database contains the drivers' national identification numbers, information on gender and age, and analytical results of samples taken in police investigations from the whole country in addition to samples taken from legal autopsies from all regions of the country except two counties in middle Norway.

By coupling those two databases we selected drivers of car and vans who had been killed in road traffic accidents in south-eastern Norway from January 2003 to December 2008, and of whom blood samples were submitted for analysis of alcohol or drugs. The coupling was performed by Statistics Norway, and an additional control was performed by the NIPH investigators to ensure that date for blood sampling or date of death matched the date of the accident. Recorded data included age, gender, date of accident, time of accident, date of sampling, time of sampling (when available), date of death, autopsy sample (yes/no), type of vehicle, single vehicle accident (yes/no), and police district.

Samples of venous blood were taken from drivers who were alive at the time of blood sampling using 5 ml Vacutainer® tubes containing sodium fluoride and heparin (BD Vacutainer Systems, Belliver Industrial Estate, Plymouth, UK). In some cases, blood samples were taken shortly after death using the same type of vials. For legal autopsy samples, blood was transferred to Sterilin tubes (Bibby Sterilin, Staffordshire, UK) containing potassium fluoride. Samples were preferably taken from the femoral vein, alternatively from the heart. Blood samples were kept at 2–8 °C until the analyses had been performed, normally within 4 weeks, and thereafter frozen at about −20 °C. In cases where incomplete testing was performed initially, samples were thawed and analysed for remaining drugs listed in Table 1. The blood samples were handled using normal routine procedures for forensic toxicology analysis.

Cases were excluded if the time lapse between accident and death was more than one day. In some cases, drivers died after emergency treatment. Drug findings as a result of reported (4 cases) or likely (2 cases) emergency drug treatment cases were omitted from the evaluation; these included administration of morphine or diazepam.

2.2. Selection of controls

As controls, car and van drivers included in a roadside survey of alcohol and drugs among random drivers performed in south-eastern Norway from April 2005 to March 2006 were used. Details on the study design and prevalence of alcohol and drugs have been published previously (Gjerde et al., 2008).

2.3. Analysis of alcohol and drugs

Blood samples from the cases were screened for alcohol by using an enzymatic method (Kristoffersen and Smith-Kielland, 2005), and if alcohol was found, the concentration was quantified using gas chromatography (Kristoffersen et al., 2006). Blood samples were screened for amphetamines, cannabinoids, cocaine metabolites, and opiates by an immunological method (Gjerde et al., 1990). Screening for other drugs was performed using high-performance liquid chromatography with mass spectroscopy detection (LC–MS) (Christophersen et al., 2001). Drug findings were confirmed and quantified using gas chromatography with mass spectroscopy detection (GC–MS) or LC–MS (Christophersen, 1986; Christophersen et al., 2001; Gjerde et al., 1991, 1993b). The laboratory was accredited according to ISO 17025 for performing the confirmation and quantification methods for forensic toxicology purposes by the Norwegian body for accreditation of laboratories (Norsk Akkreditering, Kjeller, Norway).

Table 1
Cut-off limits for alcohol (mg/ml) and drugs (ng/ml) in blood and oral fluid, and oral fluid/blood (OF/B) concentration ratios employed.

Substance	Description	Blood	OF/B ratio	Oral fluid
Alcohol (ethanol)		0.1	1.02[a]	0.1
Alprazolam	Benzodiazepine; anxiolytic	10	0.36[b]	3.6
Amphetamine	Stimulant; mostly used illegally in Norway. Used to treat ADHD, narcolepsy, chronic fatigue syndrome	20	7.2[b]	144
Carisoprodol	Muscle relaxant	500	0.1[b]	50
Clonazepam	Benzodiazepine; anxiolytic, anticonvulstant	10	0.19[b]	2
Cocaine	Stimulant, illegal	30	30[c]	900
Codeine	Opioid analgesic, antitussive	10	10[c]	100
Diazepam	Benzodiazepine; anxiolytic, sedative, anticonvulsant, skeletal muscle relaxant	28	0.04[c]	1
Flunitrazepam	Benzodiazepine; hypnotic	1.3	0.23[b]	0.3
Methadone	Opioid analgesic, treatment of heroin addiction	31	2.2[b]	68
Methamphetamine	Stimulant. Only used illegally in Norway	22	4.5[b]	100
Morphine	Opioid analgesic. Also metabolite of codeine and heroin	10	2.8[c]	28
Nordiazepam	Psychoactive metabolite of diazepam	27	0.05[c]	1
Nitrazepam	Benzodiazepine; hypnotic	7	0.087[b]	0.6
Oxazepam	Benzodiazepine; anxiolytic, anticonvulsant, sedative, skeletal muscle relaxant	140	0.07[c]	10
Tetrahydrocannabinol	Cannabis (THC)	0.6	8.2[b]	5
Zolpidem	Short-acting non-benzodiazepine hypnotic	20	<1[d]	10
Zopiclone	Short-acting non-benzodiazepine hypnotic	10	3.8[e]	38
3,4-Methylenedioxy-N-methylamphetamine	Illegal psychedelic hallucinogenic drug (MDMA, Ecstacy)	29	10[c]	290

[a] An OF/B ratio of 1.077 (Jones, 1979) multiplied with a recovery of 94.9% for the Intercept device (Langel et al., 2008).
[b] Gjerde et al. (2010a).
[c] Wille et al. (2009).
[d] Kintz et al. (2004).
[e] Gjerde et al. (2010a,b) excluding outliers.

Oral fluid samples (mixed saliva) from the controls were analysed for alcohol by an enzymatic method (Kristoffersen and Smith-Kielland, 2005) and for drugs by liquid chromatography–tandem mass spectroscopy (Øiestad et al., 2007).

Cut-off limits for alcohol and drugs found are presented in Table 1. The cut-off limits for drug concentrations in oral fluid were calculated by multiplying the cut-off limits for drugs in blood with drug concentration ratios between oral fluid and blood (OF/B ratios) to obtain comparable detection times. The following drugs were analysed but not found: phenazepam, meprobamate, and 3,4-methylenedioxy-N-ethylamphetamine.

2.4. Statistical analysis

Adjusted ORs with 95% confidence intervals (95% CI) were calculated using multivariate unconditional logistic regression using SPSS 14.0 statistical software (SPSS Inc., Chicago, IL, USA). The following covariates were entered in the logistic model: gender, age, season of the year, and eight time periods of the week as previously used by the Immortal Project (Assum et al., 2005); 1: Mon to Fri 04:00–09:59; 2: Mon to Fri 10:00–15:59; 3: Mon to Thu 16:00–21:59; 4: Mon to Thu 22:00–23:59 and Tue to Fri 00:00 to 03:59; 5: Sat to Sun 04:00–09:59; 6: Sat to Sun 10:00–15:59; 7: Fri to Sun 16:00–21:59; 8: Fri to Sun 22:00–23:59 and Sat to Mon 00:00 to 03:59. The stratified sampling of controls was handled by including the stratification variables for time period and season of the year in the logistic regression models. A statistically significant association between a substance and fatal accident is indicated by a 95% CI that does not include 1.00.

3. Results

During the period 2003–2008, 333 drivers of cars and vans were killed in road traffic accidents in south-eastern Norway. Blood samples from 204 (61%) of these drivers were submitted for alcohol and drug analysis at the Norwegian Institute of Public Health, 68 were killed in single vehicle accidents. All drivers from whom blood samples had been submitted for analytical testing at our institute were selected for the study. Samples from nine killed drivers were only analysed for alcohol because small volumes of blood were submitted for analytical testing. Additional twelve samples were analysed for a limited number of drugs because insufficient volumes of blood were available, or because the blood samples were unsuitable for analysis of certain drugs. Thus, 90% of the selected blood samples were analysed for alcohol and all drugs.

Controls were selected in a roadside survey of alcohol drugs and driving. About 12 000 drivers were asked to participate, and 10 835 drivers (88%) gave an informed consent. After excluding samples from drivers of motorcycles, trucks and busses, and samples with insufficient volume for analytical testing, 10 540 drivers were used as controls.

In a few cases, corresponding to a maximum of 0.1% of the drivers, the police officer responsible for stopping random drivers did not refer clearly drunken drivers to sampling of oral fluid. These individuals were taken directly to the police station for evidential breath testing or blood sampling, and the project team has no access to the results of those tests; those drunken drivers are therefore missing among the controls. For this reason, the calculated OR alcohol is somewhat over-estimated (see also the discussion of OR calculations later in this paper). We decided not to calculate the OR for different blood alcohol concentration intervals. Samples of oral fluid from all selected controls were analysed for alcohol and drugs.

Characteristics of cases and controls and analytical results for alcohol and drugs in blood (cases) or controls (controls) are presented in Table 2. The table shows that male drivers and drivers below 25 years of age were over-represented among killed drivers compared to the controls. A large proportion of the accidents occurred at night-time. Alcohol and/or drugs were found in blood samples from 35.2% of killed drivers; in 54.4% of drivers killed in single vehicle road accidents and 25.7% of the drivers killed in multiple vehicle accidents.

Table 2
Characteristics of cases and controls. Data are presented as number of subjects and percent.

Characteristics	Cases		Controls
	Total $N = 204$	Single vehicle $N = 68$	$N = 10\,540$
Gender			
Male	161 (78.9)	59 (86.8)	7324 (69.5)
Female	43 (21.1)	9 (13.2)	3214 (30.5)
Age groups			
<25	39 (19.1)	21 (30.9)	980 (9.3)
25–34	43 (21.1)	12 (17.6)	1809 (17.2)
35–44	38 (18.6)	14 (20.6)	2443 (23.2)
45–54	25 (12.3)	6 (8.8)	2365 (22.4)
55–64	24 (11.8)	7 (10.3)	1940 (18.4)
>64	35 (17.2)	8 (11.8)	1001 (9.5)
Season			
Spring (March–May)	31 (15.2)	11 (16.2)	2988 (28.3)
Summer (June–August)	49 (24.0)	18 (26.5)	2559 (24.3)
Autumn (September–November)	64 (31.4)	25 (36.8)	2490 (23.6)
Winter (December–February)	60 (29.4)	14 (20.6)	2503 (23.7)
Time of the week			
Working day	136 (66.7)	36 (52.9)	6541 (62.1)
Weekend	68 (33.3)	32 (47.1)	3999 (37.9)
Time of day			
04.00–09.59	37 (18.1)	14 (20.6)	1797 (17.0)
10.00–15.59	69 (33.8)	15 (22.1)	3961 (37.6)
16.00–21.59	65 (31.9)	16 (23.5)	4328 (41.1)
22.00–03.59	33 (16.2)	23 (33.8)	454 (4.3)
Alcohol and/or drugs[a]			
Alcohol and/or drugs	72 (35.2)	37 (54.4)	310 (2.9)
Alcohol >0.2 g/l	43 (21.1)	31 (45.6)	31 (0.3)
Psychoactive medicinal drugs	27 (13.2)	9 (13.2)	239 (2.3)
Illegal drugs	24 (11.8)	10 (14.7)	53 (0.5)

[a] Samples from 21 killed drivers were not analysed for all types of substances due to small amounts of material submitted for testing.

Alcohol and/or drugs were detected in 2.9% of the oral fluid samples from random drivers when using the cut-off limits presented in Table 1. In the calculation of relative risks for accidents, it would be impossible to take drug concentrations into concern, because drug concentrations in oral fluid cannot be used to accurately estimate drug concentrations in blood for individual drivers (Gjerde et al., 2010a; Wille et al., 2009). It may also be difficult to use drug concentrations from autopsy samples to estimate impairment because of post-mortal changes in drug concentrations (Drummer, 2004; Hilberg et al., 1999).

Crude and adjusted ORs for fatal road traffic accidents associated with alcohol and drug use are presented in Table 3, and ORs for fatal single vehicle accidents are presented in Table 4. Results for the total amount of killed drivers (Table 3) are presented to enable comparisons with studies from other countries. However, the results for drivers killed in singe vehicle accidents reflect better the actual ORs for fatal accident, because drivers who are not to blame for the accidents are not included among those ones.

The highest odds ratios were found for the combination of alcohol and drugs. When adjusting for gender, age group, time of the week and season, the OR was 352.9 (95% CI 70.7–1762.2) for fatal accidents in total, 766.6 (95% CI 119.1–5064.3) for single vehicle accidents. The OR for alcohol was also high. The combination of two or more medicinal drugs or illegal drugs gave also high adjusted ORs of 17.1 and 49.7, respectively, for fatal accidents in total. None of the drivers killed in single vehicle accidents had such combinations. After single use of one medicinal drug the ORs were low, and not statistically significant. The adjusted OR after using THC was in general high, 8.6 (95% CI 3.9–19.3) for fatal accidents in total, and 9.0 (95% CI 2.7–30.3) for single vehicle accidents. However, the OR for only use of THC was low and not statistically significant. The use of amphetamine or methamphetamine was associated with high adjusted ORs: 57.1 (95% CI 27.3–119.5) and 49.2 (16.5–146.9) for fatal accidents in total and single vehicle accidents, respectively. The lower OR for single vehicle accidents was unexpected and was probably related to a fairly low number of cases. Single use of amphetamine or methamphetamine produced also high and statistically significant ORs: 20.9 (95% CI 7.3–60.0) and 10.8 (95% CI 1.3–93.5) for total and single vehicle accidents, respectively.

The ORs for fatal road traffic accidents for drivers having used alcohol and/or drugs was larger for those below 45 years was than for those aged ≥45 years; the adjusted ORs were 33.3 (95% CI 21.5–51.7) and 7.1 (95% CI 4.1–12.2), respectively (results not shown).

4. Discussion

The main strength of this study was the comprehensive testing of a fairly large number of substances; we were thus able to better distinguish between single and multiple substance use than in some of the previous studies of alcohol, drugs and traffic accidents. Secondly, the use of a large number of controls in a population with low prevalence of alcohol or drugs strengthened the study of ORs for drugs that are infrequently used.

The main weakness was that the police requested blood sampling and analysis of alcohol and drugs for only 61% of the killed drivers; this may have introduced a significant sampling bias. We expect that sampling was not performed if the police considered that the probability of finding alcohol or drugs was low, but other practical matters as economy and transportation over long distances to obtain an autopsy might also have contributed. Secondly, a limited number of cases were included and the time span for the selection was wide. Thirdly, we expect that a few of the fatal road traffic accidents were suicides, but we have not been able to identify those cases. Finally, the use of illegal drugs, the abuse of psychoactive medicinal drugs, binge drinking of alcohol can all be related

Table 3
Crude and adjusted odds ratios for fatally injured driver associated with alcohol or drug use.

Factors	Crude OR	95% CI	Adj. OR[b]	95% CI
Alcohol and/or drugs	18.0	13.2–24.5	16.9	12.2–23.4
Alcohol >0.2 g/l	90.5	55.6–147.4	114.4	64.6–202.5
Alcohol only, >0.2 g/l	55.3	32.1–95.3	68.6	36.5–129.0
Alcohol and drugs	329.3	73.2–1481.4	352.9	70.7–1762.2
Two or more substances	38.6	22.8–65.3	47.0	26.2–84.4
Psychoactive medicinal drugs	7.4	4.8–11.3	8.1	5.1–12.8
Two or more medicinal drugs[a]	8.8	3.0–25.5	17.1	5.7–51.9
Only a single medicinal drug[a]	1.8	0.8–3.9	1.7	0.8–3.8
Benzodiazepines	10.3	6.2–16.9	11.4	6.7–19.3
Only benzodiazepines[a]	1.6	0.5–4.9	1.6	0.5–5.2
Diazepam	9.8	5.1–18.8	11.0	5.5–22.0
Only diazepam[a]	1.0	0.1–7.4	0.9	0.1–7.0
Opioids	4.1	1.5–11.5	5.7	2.0–16.2
Codeine	2.3	0.5–9.4	3.0	0.7–12.6
Only codeine[a]	NC			
Zopiclone	5.3	2.4–11.6	5.4	2.3–12.6
Only zopiclone[a]	3.2	1.2–8.9	2.6	0.9–7.6
Illegal drug(s)	29.5	17.8–49.0	21.9	12.5–38.3
Two or more illegal drugs[a]	104.3	9.4–1155.4	49.7	4.4–561.6
Only a single illegal drug[a]	9.3	4.1–21.2	6.1	2.5–14.5
THC	13.9	6.6–29.2	8.6	3.9–19.3
Only THC[a]	1.9	0.3–13.7	0.9	0.1–7.3
Amphetamine/methamph.	68.4	34.9–133.8	57.1	27.3–119.5
Only amphetamine/metamph[a]	26.7	9.9–71.9	20.9	7.3–60.0

OR, odds ratio; CI, confidence interval; NC, no cases.
[a] No other drugs or alcohol.
[b] Adjusted for time period, season, gender, and age group.

to risk taking behaviour, and subsequently careless or aggressive driving. This may have been a significant confounding factor that cannot be adjusted for in the calculations.

We used different sample types for cases and controls. The collection of oral fluid from controls gave a high participation rate compared to what we would expect to get if collecting blood samples, but the comparison of analytical results was more difficult. Analysis of oral fluid with appropriate cutoff thresholds reflects better than urine any alcohol and drug presence in blood (Samyn et al., 1999). We have used equivalent cutoff thresholds for blood and oral fluid obtained by multiplying the cutoff concentration in blood with the average OF/B concentration ratio after excluding outliers. Thus, a blood sample and an oral fluid sample will, on average, be positive for a drug for the same length of time after intake, and the prevalence of positive drug findings in samples of oral fluid will reflect the prevalence of positive drug findings in blood samples taken at the same time. We have previously found that this procedure gave acceptable results for amphetamine and THC (Gjerde and

Table 4
Crude and adjusted odds ratios for fatally injured driver in single vehicle accident associated with alcohol or drug use.

Factors	Crude OR	95% CI	Adj. OR[b]	95% CI
Alcohol and/or drugs	39.4	24.1–64.3	37.5	21.9–64.2
Alcohol >0.2 g/l	284.0	156.9–514.1	414.4	181.5–946.5
Alcohol only	130.5	68.1–250.1	185.2	76.4–449.1
Alcohol and drugs	803.7	170.0–3799.7	766.6	119.1–5064.3
Two or more substances	59.2	29.4–119.3	64.8	27.4–153.4
Psychoactive medicinal drugs	7.8	3.8–16.0	9.6	4.4–21.2
Two or more medicinal drugs[a]	NC			
Only a single medicinal drug[a]	0.8	0.1–5.5	1.0	0.1–7.1
Benzodiazepines	13.2	6.2–28.5	16.5	7.1–38.6
Only benzodiazepines[a]	NC			
Diazepam	14.2	5.5–36.5	19.1	6.7–55.0
Only diazepam[a]	NC			
Opioids	NC			
Codeine	NC			
Only codeine[a]	NC			
Zopiclone	2.3	0.3–17.1	3.1	0.4–24.7
Only zopiclone[a]	2.4	0.3–17.6	2.8	0.3–21.9
Illegal drug(s)	38.1	18.4–78.9	21.4	9.1–50.5
Two or more illegal drugs[a]	NC			
Only a single illegal drug[a]	4.0	0.5–29.4	2.0	0.2–16.0
THC	18.9	6.5–54.6	9.0	2.7–30.3
Only THC[a]	NC			
Amphetamine/methamph.	76.0	30.4–190.3	49.2	16.5–146.9
Only amphetamine/metamph[a]	13.3	1.7–103.7	10.8	1.3–93.5

OR, odds ratio; CI, confidence interval; NC, no cases.
[a] No other drugs or alcohol.
[b] Adjusted for time period, season, gender, and age group.

Verstraete, 2010). In cases where the average OF/B ratios are based on few determinations, an inaccuracy in the calculations may have occurred.

A possible calculation of ORs for high dose drug use would probably have given higher values than those presented. The use of oral fluid and autopsy samples made such calculations unreliable (see our comment under results) and was therefore not performed.

The drug findings in blood samples from fatally injured drivers are similar to the results found in our previous study performed in 2001–2002 (Christophersen et al., 2005). In that study, which comprised fatally injured drivers from all parts of Norway, alcohol and/or psychoactive drugs were found in blood samples from 60.9% and 31.1% of drivers fatally injured in single vehicle accidents and collisions with other vehicles, respectively. In the latter type of cases, the killed driver might not be the one to blame for the accident, therefore the prevalence of alcohol and/or drugs was lower.

The inclusion rate was 61% for cases as compared to an 88% participation rate for controls. We have no information about the use of alcohol or drugs by killed drivers from whom blood samples were not taken as part of police investigations; the use of alcohol or drugs may be less likely in those cases. Similarly, some random drivers who had recently used psychoactive drugs may have refused to give a sample of oral fluid for testing. Therefore, the ORs presented in Table 3 are probably over-estimated.

The crude (unadjusted) OR is calculated as follows: $OR = (Positive\ Cases \times Negative\ Controls)/(Positive\ Controls \times Negative\ Cases)$; *Cases* are drivers killed in a traffic accident, *Controls* are random drivers in normal road traffic, and *Positive* means that a substance is found in blood or oral fluid with concentration above the cutoff. The OR for involvement in a fatal accident after using alcohol or drugs thus also depends on the risk for fatal accident among drivers who have not used such substances, reflected as *Negative Cases* in the OR calculation formula. In Norway, this risk is among the lowest in the world; therefore, the increased risk for involvement in fatal road traffic accident after using alcohol or drugs (calculated as OR) is expected to be higher in Norway than in most other countries. The prevalence among controls of low alcohol or drug concentrations that do not increase the accident risk will also affect the OR.

Very high ORs were found for the involvement in single vehicle accidents after using alcohol: the crude OR was 284.0 (31 Positive Cases, 37 Negative Cases, 31 Positive Controls, 10 509 Negative Controls). This OR is an over-estimation because some alcohol-positive controls were missed (a maximum of 10 drivers had alcohol in breath without providing samples of oral fluid for our study), and among the missing fatally injured drivers a large proportion were probably sober based upon a simple extrapolation of the proportion of drivers who are involved in fatal accidents that are not impaired (see Table 2). If adding 10 *Positive Controls*, and assuming that all cases that were not subject to blood sampling were negative, thus adding 32 *Negative Cases*, the crude OR would be 115.0, which is still a high number. If 4% of the controls were positive for alcohol, the crude OR would be 20.0, and if also assuming that all missing cases were negative for alcohol, the crude OR would have been 10.8 (adjusted ORs cannot be calculated without information about the covariates). As a comparison, alcohol was found in samples from 17% of injured drivers and 5% or controls in a French study of injured drivers, giving an OR of 3.8 (Mura et al., 2003). In a previous Norwegian study, the estimated relative risk for fatal injury among drunken drivers compared to sober drivers was found to be 160 (Glad, 1985).

High ORs were found for total use of medicinal drugs or illegal drugs. The OR after using a single medicinal drug was low, suggesting that the use of a single psychoactive medicinal drug does not increase the fatal accident risk dramatically in most cases. The OR after using two or more substances was high, especially if alcohol was involved.

No significant association between the use of cannabis only and fatal road accidents was observed. This does not indicate that the use of cannabis before driving is safe; a number of studies have shown that cannabis affects psychomotor abilities associated with safe driving (Bedard et al., 2007; Blows et al., 2005; Drummer et al., 2004; Kelly et al., 2004; Laumon et al., 2005; Ramaekers et al., 2004). Very few fatally injured drivers included in our study had been using cannabis only; the vast majority had also been using other drugs or alcohol. The combination of THC with other psychoactive substances gave a high OR.

Previous studies have also shown significant increased odds for traffic accidents after using alcohol or drugs (Assum et al., 2005; Blomberg et al., 2009; Borkenstein et al., 1974; Brault et al., 2004; Drummer et al., 2004; Kelly et al., 2004; Laumon et al., 2005; Movig et al., 2004; Mura et al., 2003; Woratanarat et al., 2009). Those studies showed higher odds after combining alcohol with illegal or psychoactive medicinal drugs than alcohol alone. Our study confirms those findings.

The ORs found in our study for the use of alcohol and drugs, benzodiazepines, and THC were somewhat higher than those found in previous studies (Brault et al., 2004; Movig et al., 2004). The OR was very much higher for amphetamines. Amphetamine and methamphetamine are in Norway mostly used by injecting drug users to obtain euphoria and to a small extent to combat sleepiness or exhaustion. The pattern of use might therefore be different in Norway than in many other countries, and might contribute to a higher OR finding.

In a previous study of seriously injured and killed drivers in Norway, 87 cases and 410 controls were studied (Assum et al., 2005). None of the controls had alcohol concentrations above the cutoff, so an OR could not be calculated. ORs were calculated for cannabis alone, opiates alone and benzodiazepines alone, and were found to be 3.4 (95% CI: 0.3–38.5), 13.8 (95% CI: 1.2–154.2) and 20.6 (95% CI: 2.1–201.8), respectively. The OR associated with a positive drug finding was 48.2 (95% CI: 16.3–142.2). These ORs were higher than found in our study, but the confidence intervals were wide. We included a total of 225 cases and 10 540 controls in our study, and were then able to provide more accurate estimated for the ORs associated with drug use.

To conclude, we found in our study that the odds for involvement in fatal road traffic accidents for different substances or combination of substances were in increasing order: single drug < multiple drug < alcohol only < alcohol+drugs. For single substance use: medicinal drug or THC < amphetamine/methamphetamine < alcohol.

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