Benzodiazepine use and motor vehicle accidents

Systematic review of reported association

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ABSTRACT

OBJECTIVE To examine the relationship between benzodiazepine (BZD) use and motor vehicle accidents (MVAs).

DATA SOURCES MEDLINE was searched from 1980 to 1997 using the key words traffic accidents or motor vehicle accidents and benzodiazepines (and alternative terms and outcomes) in English, German, French, or Italian.

STUDY SELECTION Case-control studies of BZDs and MVAs; police or emergency studies of BZD use among travelers; driving tests with subjects taking BZDs. Outcomes were impaired driving, accidents; mortality; postaccident medical attention, emergency ward care, or hospitalization. Quality criteria were whether all driving BZD users and non-users had an equal chance of entering the study; whether medication dosage and timing were ascertained; whether all kilometres driven by BZD users and non-users were studied; whether all types of accidents were ascertained; and whether medical conditions were controlled for.

SYNTHESIS In case-control studies, the odds ratios for mortality and emergency medical treatment ranged from 1.45 to 2.4 in relation to time of use and quantity of drug taken. In police and emergency ward studies, BZD use was a factor in 1% to 65% of accidents (usually 5% to 10%). In two studies where subjects had blood alcohol concentrations less than the legal limit, BZDs were found in 43% and 65% of subjects. In one study with controls, 5% of drivers and 2% of controls in accidents had used BZDs.

CONCLUSIONS Case-control studies suggest using BZDs approximately doubles the risk of motor vehicle accidents. The risk for drivers older than 65 of being involved in reported motor vehicle collisions is higher when they take longer-acting and larger quantities of BZDs.

RÉSUMÉ

OBJECTIF Examiner la relation entre l'usage de la benzodiazépine et les accidents de la route.

DEVIS Recherche dans MEDLINE sur des données de 1980 à 1997 à l'aide des mots clés « accidents de la route ou accidents d'automobile et benzodiazépines » (et d'autres mots et résultats connexes) en anglais, en allemand, en français et en italien.

MILIEU Études cas témoins de personnes prenant de la benzodiazépine et d'accidentés de la route; des rapports de police ou des services d'urgence sur l'usage de la benzodiazépine chez les automobilistes; des épreuves de conduite par des sujets prenant de la benzodiazépine. Les résultats cherchés étaient les facultés affaiblies, les accidents, la mortalité, les soins médicaux à la suite d'un accident, les soins à l'urgence ou l'hospitalisation. Les critères de qualité étaient la possibilité égale pour les personnes prenant de la benzodiazépine et celles n'en consommant pas de faire l'objet de l'étude; l'assurance de données exactes sur la posologie et la durée de la médication; la certitude que le kilométrage parcouru par les usagers du médicament et les autres personnes avait été étudié; l'existence d'une classification selon les différents types d'accidents; et la prise en compte des états pathologiques.

SYNTHÈSE Dans les analyses cas témoins, les risques relatifs de mortalité et de soins médicaux à l'urgence variaient de 1,45 à 2,4 selon la durée d'utilisation et la quantité de médicaments prise. Dans les rapports de police et des services d'urgence, l'usage de la benzodiazépine était un facteur de cause dans 1% à 65% des accidents (habituellement de 5% à 10%). Dans deux études sur des sujets dont le taux d'alcoolémie était plus bas que la limite permise, respectivement 43% et 65% d'entre eux avaient pris de la benzodiazépine. Dans une étude avec dossiers de contrôle à l'appui, 5% des conducteurs et 2% des sujets dans les dossiers vérifiés, qui étaient impliqués dans des accidents, avaient fait usage de benzodiazépine.

CONCLUSIONS Les études cas témoins portent à croire que l'usage de la benzodiazépine augmente de près du double le risque d'accident de la route. Le risque pour les conducteurs de plus de 65 ans d'être impliqués dans un accident de la route rapporté à la police est plus élevé s'ils prennent des benzodiazépines à effet prolongé et en grandes quantités.

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Benzodiazepine use and motor vehicle accidents

Associations between benzodiazepines (BZDs), impaired driving, and motor vehicle accidents (MVAs) in case-control studies that linked government files of health care, emergency, hospital, and pharmacy use; MVAs and drivers' licence data; case series of MVAs in emergency departments; police case series on impaired drivers, accidents, or fatal MVAs; and driving tests involving BZDs were systematically reviewed.

Meta-analysis was not performed because the four types of studies do not yield outcomes that can be pooled; the case-control studies do not study the same BZDs, and only one states the percentages of BZDs; and the police and emergency studies are often incomplete.

Data sources and study selection

MEDLINE searches from 1980 to 1997 found five case-control, one family practice, seven emergency, 20 police, and nine driving test studies (**Table 1**).

Methods of critical appraisal

Five challenges to validity needed to be investigated.

- Did all driving BZD users and non-users have an equal chance of entering the study?
- Were medication dosage and timing ascertained?
- Were all kilometres driven by BZD users and non-users studied?
- Were all types of accidents ascertained (fatal crashes involve male, younger, and multiply intoxicated persons[1,2])?
- Were medical conditions controlled for?[3,4]

Study quality and results

Studies using government databases. The strengths of the five case-control studies (**Tables 2**[5-10] **and 3**[5-10]) are their large numbers; monitoring of data-entry quality; careful definition of cases, controls, exposure, and outcomes; post-hoc study decreased coding bias; and assessment of demographic and confounding factors.

Limitations of the studies are their lack of assessment of medication compliance; interval before driving; all accident outcomes; kilometres traveled by cases and controls; kilometres traveled accident-free by individuals taking BZDs; medical conditions and medications; and drug and alcohol use. None of the studies assessed the same BZDs or used the same time frame for medications and accidents. Some studied only drivers. Only one study[5] made a power computation (and had only 25% of the cases required for this).

Saskatchewan Health databases covered 98% of the Saskatchewan population, had regular checks on claimant eligibility, included pharmacy audits, and provided data from all general and out-of-province hospitals.[6] Data were limited by including only accidents severe enough to require hospitalization, patients older than 20, odds ratios (ORs) analyzed for 20-year age groupings, traffic accidents monitored for only 2 months after BZD prescription, and prescriptions for other drugs monitored for only 30 days.[6]

The Quebec study used provincial driver's licence files, police reports of injurious crashes linked with medication use from provincial health insurance records, and provincial hospital discharge summaries.[7] Limitations were data restricted to drivers 67 to 84 years; accidents with only property damage excluded; controls defined as no injurious crash for 1 year; 10 controls for each case drawn from a subcohort of 14000 among the 224734 drivers; some controls used twice; 378 cases also controls; and those hospitalized in the 60 days before the accident excluded.

The Seattle study obtained the state driving records of all subjects, collected medical and pharmacy records (which covered 99% of members), and estimated drug use three ways.[8] Limitations were inclusion only of those 65 and older and those who sought treatment within 7 days of the accident; 25% of eligible subjects and 31% of controls declining participation; 34% of medications lacking indications; and 42% of psychoactive medications being prescribed "as needed."

The strengths of the Massachusetts study were the large membership (one million) and BZD users (4554); ICD-9-CM coding by physicians; each case having three controls; all claims for 3 months before and 6 months after the BZD prescription being ascertained; and three care variables (medical encounters, emergency visits, and hospitalizations).[5,9] Limitations were restriction to those older than 65 and the power calculation requiring 16 000 cases, but having only 4554 available.

The strengths of the Tennessee study were the data on medications, emergency treatment, hospitalization, and nursing home visits; the register of licence revocations, suspensions, and cancellations and crashes; and the assessment of other medications. Limitations were excluding those younger than 65; the 30-day period after discharge from hospital;

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Table 1. Literature search results

FIRST SEARCH: Searches using the words traffic accidents or motor vehicle accidents; and then further searches using the alternative words traffic accidents, motor vehicle accidents, vehicle, motor, accidents, impairment, or traffic accidents prevention; AND the alternative words benzodiazepines, analgesics, opioids, analgesics, antianxiety agents, morphine, alcohol, substance dependence, substance use disorders complications; administration and dosage, adverse effects, arousal drug effects, memory drug effects, reaction time drug effects, recall drug effects, cognition drug effects, psychomotor performance drug effects, drug tolerance, or central nervous system drug effects; AND English, German, French, or Italian language yielded 986 articles. Review articles and editorials were also sought. The abstracts of each of these articles were read, and studies with more than 30 subjects of benzodiazepines and motor vehicle accidents were located:

TYPE OF STUDY	FIRST SEARCH (N)	FIRST AND SECOND SEARCHES COMBINED (N)
Case-control (large databases)	5	5
Case-control (family practice)	1	1
Emergency ward	7	7
Police	13	20
Driving test	8	9

SECOND SEARCH: With the help of a medical librarian (Jessie McGowan, Head Librarian, Ottawa General Hospital), a search of MEDLINE from 1993 through 1997 using these MeSH headings yielded:

HEADING	NO. OF ARTICLES
Traffic accidents	2759
Automobile driving	937
Motor vehicles	889
Automobiles or traffic or vehicles	11483
Highways or roads or streets	2282
Alprazolam (eg, Xanax) or chlordiazepoxide (eg, Librium)	281
Medazepam (not available in Canada) or clorazepate (eg, Tranxene)	47
Lorazepam (eg, Ativan) or nitrazepam (eg, Mogadon) or flurazepam (eg, Dalmane)	567
Oxazepam (eg, Serax)	908
Flunitrazepam (not available in Canada)	1225
Diazepam (eg, Valium)	2266
Bromazepam (eg, Lectopam) or clonazepam (eg, Rivotril)	450
Triazolam (eg, Halcion) or temazepam (eg, Restoril)	428
Midazolam (Versed)	1539
Benzodiazepinones	3914
Benzodiazepines	6217
Zopiclone (Imovane)	87
Hypnotics and sedatives	9073
Antianxiety agents	8424
Benzodiazepines AND anticonvulsants AND narcotics AND antianxiety agents or hypnotics AND all the traffic accident terms	109

Table 2. Case-control studies of traffic accidents and benzodiazepine prescriptions

LOCATION (AGES STUDIED) DEFINITION OF CASES; PERIOD OF OBSERVATION AFTER ACCIDENT OR PRESCRIPTION	CASES		CONTROLS	
	SAMPLE N	TOTAL N	SAMPLE N	TOTAL N
Saskatchewan[6] (20-65+) patients taking flurazepam or triazolam who were hospitalized after traffic accidents; 2 months after Rx	55	78 070	23	97 862
Saskatchewan[6] (20-65+) patients taking diazepam, lorazepam, or oxazepam; 2 months after Rx	77	147 726	23	97 862
Quebec[7] (67-84) patients taking any BZD; 1 year after Rx	6064			14 000
Seattle[8] (over 65) patients taking alprazolam, diazepam, chlordiazepoxide, flurazepam, or triazolam after traffic accidents; 7 days after accident	234			447
Massachusetts[5,9] (18-64) patients taking alprazolam, chlorazepate, chlordiazepoxide, diazepam, lorazepam or oxazepam during 6-month period; any medical encounter; any emergency care or hospitalization	4554			13 662
Tennessee[10] (65-84) patients taking benzodiazepines other than flurazepam and triazolam after traffic accident with injury, hospitalization, or death	495			16 262

flurazepam (eg, Dalmane) and triazolam (eg, Halcion); and non-injurious crashes.[10]

The ORs for four studies for BZDs and MVAs were 0.9 to 2.4; and for Saskatchewan 5.6 to 6.5 (with wide confidence intervals and no explanations for the higher ORs). Other evidence linking BZDs and accidents is the declining accident rate with time after a BZD prescription and the increase in traffic accidents among people with three or more BZD prescriptions.

Emergency room and police data. Problems with drawing conclusions from police and emergency ward studies were:

- only a few receive a toxicological workup;
- only two studies used controls;
- medical conditions are usually not assessed;
- kilometres driven under the influence of BZDs, medications, alcohol, and drugs not resulting in accidents are not assessed; and
- only two studies examined drivers with low blood alcohol concentrations to assess which drugs were then involved in impairment or accidents.

Only three studies cited either analytical lower limits for detecting BZDs or actual concentrations (**Table 4**).

Fatal accidents tend to involve high blood alcohol concentrations. The rates in which BZDs and other medications are found in travelers involved in accidents vary substantially from country to country. The highest percentage of BZDs in MVAs (65%) occurred in Denmark[11] among individuals with blood alcohol concentrations < 0.8 g/L, and the lowest in an early 1970s study of fatal accidents in California (1%)[12] (**Table 5**[2,11-37]). In the Paris study,[13] the OR of being judged by the police to be responsible for the accident increased from 2 for alcohol alone to 7 for alcohol and BZD use. Swiss studies with high alcohol levels attribute this to being in a wine-growing area.[14]

The only study of BZDs and accidents in general practice[15] recorded only MVAs that came to physicians' attention. For the 205 case-control pairs, the cases had eight more accidents than expected ($P<.05$).

Only one emergency study both assessed health conditions and used controls.[16] For the 201 cases, 325 controls were selected randomly at gas stations. Alcohol was detected in 15% of subjects and 1% of controls; diazepam (eg, Valium) was detected in 5% of patients and 2.5% of controls. The authors concluded that benzodiazepines could have contributed to causing 1% to 5% of the accidents.

A study in Paris assessed responsibility: those with blood alcohol concentrations of 0.2 to 0.8 g/L had an OR of 2 of being held responsible for the accident, but those with blood alcohol concentrations above 0.2 g/L and positive results for BZDs had an OR of 7.2 of being held responsible.[13] In two UK teaching hospitals, 94% of benzodiazepine users and 61% of alcohol users were held responsible among patients in whom drugs were found.[17]

Injured travelers using BZDs are likely to have higher blood alcohol concentrations. In the emergency department of Angers Regional Hospital, the mean blood alcohol concentration of those who had not taken psychotropic drugs was 0.4 g/L, and of those who had taken psychotropic medication (BZDs, zolpidem, barbiturates, hydroxyzine [eg, Atarax]) was 0.76 g/L.[18]

Two studies assessed accident victims with blood alcohol concentrations below the legal limit. In Norway, of those arrested with blood alcohol concentrations below 0.01%, 56% had used cannabis (and 82% of these also had used BZDs).[19] Among fatally injured drivers, alcohol above the legal limit for Norway of 0.5 g/L was found in 27% and drugs (benzodiazepines and tetrahydrocannabinol [Marinol]) were found in 16%.[20] In Denmark, in cases with blood alcohol concentrations below 0.8 g/L, 65% had taken benzodiazepines, 38% opiates, 3% tricyclics, and 3% neuroleptics. The police estimated that 72% of those who had taken drugs were impaired.[11]

Fatally injured drivers tend to have high blood alcohol concentrations, but those taking BZDs varied from 9% in Bern[21]; 5% in British Columbia[22]; 4% in Ontario[23]; and 2% to 3% in Alabama[24]; to undetected in Washington State,[25] Sydney, Australia,[26] and North Carolina[2]; and to not stated for fatal truck driver accidents.[27]

Among trauma patients BZDs ranged from 12% in Toronto,[28] 11% in Sweden,[29] 10% in 21 hospitals in France,[30] 7% in Geneva,[31] 4% to 10% in Marseille hospitals,[32] 6% in Denmark[33] and Finland,[34] to 4% in Seattle[35] and unstated for two US trauma centres.[36]

The percentage of impaired drivers in the 1970s using BZDs was as low as 1%.[12] A later Australian study had 50%, and even with low blood levels (0.2 mg/L) of oxazepam (eg, Serax), drivers drove on the wrong side, were unable to stand unassisted, were speeding and weaving in and out of traffic, and drove dangerously.[37] In Finland, BZDs in impaired drivers increased from 6% in 1979 to 23% in 1993.[34] Detection does not necessarily result in correction: in two US trauma centres, 46% of car and motorcycle

Table 3. Adjusted odds ratios for traffic accidents for patients who had filled prescriptions for benzodiazepines

STUDY OBSERVATION PERIOD AFTER PRESCRIPTION OR ACCIDENT	ODDS RATIO	95% CONFIDENCE INTERVAL
SASKATCHEWAN[6]		
Hypnotics		
• <2 weeks	6.5	1.9-22.4
• <4 weeks	3.9	1.9-8.3
Anxiolytics		
• <2 weeks	5.6	1.7-18.4
• <4 weeks	2.5	1.2-5.2
QUEBEC[7] (DRIVERS IN ACCIDENTS IN WHICH AT LEAST ONE PERSON WAS INJURED)		
Long half-life		
• 1-7 days	1.45	1.04-2.03
• 8-30 days	1.16	0.90-1.50
• 31-60 days	1.22	0.84-1.79
• 61-365 days	1.26	1.09-1.45
Short half-life		
• 1-7 days	1.04	0.81-1.34
• 8-30 days	1.06	0.90-1.26
• 31-60 days	0.99	0.77-1.28
• 61-365	0.91	0.82-1.01
SEATTLE[8] (ACCIDENT)		
Estimated consumption of benzodiazepines		
• Lowest tertile	0.90	0.30-2.30
• Middle tertile	0.90	0.40-2.20
• Highest tertile	1.50	0.60-3.80
Time of filling prescription for benzodiazepines		
• Prescription filled 60-180 days	1.20	0.50-2.70
• Prescription filled 0-59 days	0.90	0.40-2.00
MASSACHUSETTS[5,9]		
Any medical encounter	1.20	1.10-1.30
Any emergency care	2.10	1.30-3.40
Any hospitalization	1.30	0.80-1.90
TENNESSEE[10]		
All benzodiazepines other than flurazepam and triazolam	1.50	1.10-2.00
Diazepam ≤ 4 mg/d	1.10	0.50-2.20
Diazepam ≥ 20 mg/d	2.40	1.30-4.40

Table 4. Quantifying benzodiazepines: *Only the following studies gave either analytical lower limits for detecting BZDs or actual BZD concentrations.*

	LOWER LIMITS FOR DESIGNATING BZDS PRESENT		MEDIAN CONCENTRATIONS
DRUG	ULRICH ET AL[21]	STEENTOFT ET AL[33]	GJERDE ET AL[19,20]
Diazepam	25 ng/mL	0.2 μmol/kg	0.28 mg/L
Bromazepam	90 ng/mL		
Chlordiazepoxide	350 ng/mL		
Oxazepam	60 ng/mL		1.5 mg/L
Desalkylflurazepam	60 ng/mL		
Flunitrazepam (not available in Canada)	60 ng/mL		0.009 mg/L
Nitrazepam			0.08 mg/L

drivers were impaired, but only 17% received citations for impairment.[36]

Driving experiments. The causes of accidents are improper lookout, excessive speed, inattention, and improper evasive action. In alcohol-associated accidents, causes are excessive speed, running off the road, and going off curves.[38]

Real life might not be replicated in tests of driving because drivers use one lane at a set speed and a set distance from another car; do not deal with sudden activities by other drivers; do not drive at night or in inclement weather; require few maneuvers; have no urgent goal, do not select the route, and often use low drug doses[38]; do not drive enough to encounter a serious accident; and do not cross intersections (55% of accidents in one Ontario study[28]). O'Hanlon in the Netherlands, however, noted that only one in 100 drivers receiving placebo halted the test because he or she felt impaired, whereas 16 of 100 drivers receiving BZDs halted the test.[38]

Drivers receiving BZDs were less able to circle roundabouts; to adjust for passengers obstructing their view; to avoid cutting corners; to anticipate problems[39]; to maintain 58 mph, position in the slow lane over a 61-mile 4-lane highway circuit, and distance from another car[40]; to hold lane position on a 100-km highway course[41,42]; to brake[43]; to go around curves[44]; to steer[45]; to park[46]; and to accomplish emergency maneuvers (**Table 6**).[47]

Key points

Case-control studies suggest benzodiazepines approximately double the risk of motor vehicle accidents.

Benzodiazepine use is seen in about 10% of those who have ingested alcohol and are involved in motor vehicle accidents.

Conclusion

Case-control studies suggest BZDs increase the risk of accidents. Emergency and police studies show that the proportion of impaired, traumatized, and dead travelers taking BZDs varies widely by country, and among those who have taken alcohol is typically 10%. Blood alcohol concentrations in non-fatal crashes are usually higher for those receiving BZDs. Driving tests may not replicate real-life driving, but subjects show selective impairments in driving, and 16 of 100 receiving BZDs withdrew from tests in the Netherlands compared with one in 100 of those receiving placebo.

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Table 5. Case series of emergency department and police data

DESCRIPTION (N)	OUTCOME AND % WHO RECEIVED TOXICOLOGICAL ASSESSMENT	BENZODIAZEPINES (%)	OTHER MEDICATIONS	ALCOHOL
FAMILY PRACTICES (*P* <.05)				
Berwick MVA (n = 205)[15]				
• 18 accidents in BZD recipients				
• 10 accidents in controls				
EMERGENCY DEPARTMENT PATIENTS				
Toronto[28] (n = 854)	MVA 56%	12%	Cannabis 14% Cocaine 5%	36% Mean BAC = 1.452 g/L BAC at crash time = 1.81 g/L
Helsinki[16]* (n = 201) Controls = 325	Drivers in MVA 100%	Drivers 5% Controls 2%		BAC drivers • 2% 0.6-1.5 g/L • 13% ≥ 1.6 g/L
Paris[13] (n = 3147)	MVA 91%, 14 hospitals • 1626 drivers • 912 motorbike riders • 314 pedestrians	8%		BAC • 18% > 0.8 g/L • 3% 0.5-0.8 g/L
United Kingdom[17] (n = 229)	MVA, 2 teaching hospitals	11%		15% (BAC not stated)
Seattle[35] (n = 1314)	MVA 47% • 452 emergency • 160 autopsy	4%	Cannabis 23%	38% 30% BAC > 0.1 g/L
Angers[18] (n = 363)	MVA • 172 drivers • 169 passengers • 22 pedestrians	8%		If taking psychotropic medications, BAC = 0.76 g/L; if not taking psychotropic medications, BAC = 0.4 g/L
Marseilles[32] (n = 234)	MVA 100%	Immunochemistry assessment 4% Chromatography assessment 10%		
CASE SERIES OF POLICE DATA				
Ontario[23]* (n = 1031)	Fatal MVA Drivers and pedestrians n = 484 (47%)	Drivers 3.7% Pedestrians 4.8%	Cannabis • Drivers 12% • Pedestrians 13%	56% • BAC drivers = 1.63 g/L • BAC pedestrians = 1.45 g/L
North Carolina[2] (N = 854)	Fatal MVA 70% (n = 600)	Not tested	Cannabis 8% Methaqualone 6%	79% BAC > 1 g/L
Alabama[24] (N = 2189)	Fatal MVA • Drivers 69% • Passengers 22% • Pedestrians 9%	• Drivers 2% • Passengers 3% • Pedestrians 3%	Cannabis 17%	BAC > 0.5 g/L • Driv ers 57% • Passengers 36% • Pedestrians 52%
Geneva[31] (N = 4592)	MVA 11% • 260 property damage • 110 injured • 13 fatal	7%		60% of subjects tested had BAC > 0.8 g/L

Continued...

Table 5. *Continued...*

DESCRIPTION (N)	OUTCOME AND % WHO RECEIVED TOXICOLOGICAL ASSESSMENT	BENZODIAZEPINES (%)	OTHER MEDICATIONS	ALCOHOL
Norway[19,20] (N = 1223)	425 impaired drivers with BAC < 0.01%	43%	Cannabis 56%	
Denmark[11] (n = 461)	180 accidents 281 impaired drivers with driving charges	65%	Opiates 38% Tricyclics 3% Neuroleptics 3%	BAC < 0.8 g/L
Australia[37]* (n = 163)	Impaired drivers with driving charges	50%	Cannabis 56% Opiates 14% Barbiturates 11%	
California[12] (N = 71 937)	Impaired driving with driving charges	1%	Barbiturates 2% Methaqualone 0.7%	Negative 9% BAC < 0.1 g/L 13% BAC ≥ 0.1 g/L 78%
United States,[27] 8 states (n = 168)	Fatally injured truck drivers		Cannabis 13% Cocaine 8% Amphetamines 7% Ephedrine 7%	13%
United States,[36] two trauma centres (N = 634)	Injured car and motorcycle drivers		Cocaine 9%	BAC > 0.1 g/L 32%
Finland[34] (n = 630)	Impaired drivers	1979 6% 1993 23%		
Washington State[25]	Fatally injured drivers		Cannabis 11% Cocaine 3% Amphetamines 2%	
Sydney, Australia[26] (n = 164)	Car drivers seen at Liverpool Hospital		Cannabis 15%	Urine alcohol concentration > 0.08 g/dL 15%
British Columbia[22] (n = 227)	Fatal MVA	5%	Cannabis 13% Cocaine 4%	48% BAC 0.164 g/L
Vaud[14] (n = 641)	368 suspected impaired drivers 254 accidents	15%	Cannabis 57% Opiates 36% Cocaine 11% Methadone 10% Amphetamines 4%	36% BAC > 0.1 g/L
Denmark[33] (N = 26 000)	Impaired drivers (random sample of 1382 analyzed only for BZDs)	6%		
Bern[21] (n = 144)	Traffic victims	9%	42%	8% 0.1-0.79 g/L 22% 0.8-2.0 g/L 11% > 2.0 g/L
Bern[21] (n = 250)	Traffic offenders	5%	95%	9% 0.1-0.79 g/L 71% 0.8-2.0 g/L 15% > 2.0 g/L
France[30] (n = 826)	MVA 21 hospitals	10%	30%	BAC > 0.1 g/L
Sweden[29] (n = 1603)	Impaired drivers (random sample of 17 000 apprehended drivers)	11%		

BAC—mean blood alcohol concentration.
Benzodiazepine blood levels measured for each subject were in McLinden,[37] oxazepam 0.2-8 mg/L; in Honkanen et al,[16] diazepam 30-2030 mg/L; in Cimbura et al,[23] diazepam trace 0.4 mg/L, oxazepam 0.3 mg/L, chlordiazepoxide 1 mg/L.

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Table 6. Studies of the effect of benzodiazepines on driving

STUDY AND SUBJECTS	MEDICATION	TEST	OUTCOME (WORSENED PERFORMANCE)	P (COMPARED WITH PLACEBO)
Irving and Jones[44] 1992 (12 women aged 45-55)	L 0.5 mg L 1.25 mg	Road lateral deviation		NS NS
	L 0.5 mg L 1.25 mg	Following distance		NS NS
	L 0.5 mg L 1.25 mg	Curve following		NS .005
De Gier et al[39] 1981 (22 men)	D 10-20 mg	22-item driving test.	05	
O'Hanlon et al[40] 1995 (53 women, 37 men)	D 5 mg tid L 0.5 mg tid L 2 mg bid	100-km driving test	25.3 24.9 58.3	.000 .000 .000
O'Hanlon and Volkerts[41] 1986 (11 women)	T 20 mg N 10 mg	100-km driving test	3.6 8.5	.07 .02
Laurell and Toernros[47] 1986 (18 women, 18 men)	T 0.25 mg N 5 mg	Driving situation with emergency maneuver	2.0	NS
Van Laar et al[42] 1992 (6 women, 6 men)	D 5 mg tid	100-km driving test	First week.003 Second week.002 Third week.058	
Schmidt et al[45] 1986 (12 women, 20 men)	F 2 mg T 20 mg	25-km driving test	Steering activity T less N more	
Betts et al[46] 1986 (113 students)	C 10 mg x 5 over 36 hours	Tests in parking lot	Increased times • Men: reversing, total • Women: gap estimating	
Biehl[43] 1979 (24 male students)	D 10 mg in mornings x 3 d	Road test	Decreased readiness to brake	

C—*chlordiazepoxide*, D—*diazepam*, F—*flunitrazepam*, L—*lorazepam*, N—*nitrazepam*, T—*temazepam*.

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