The prevalence and relative risk of drink and drug driving in the Netherlands: a case-control study in the Tilburg police district

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Research in the framework of the European research programme IMMORTAL

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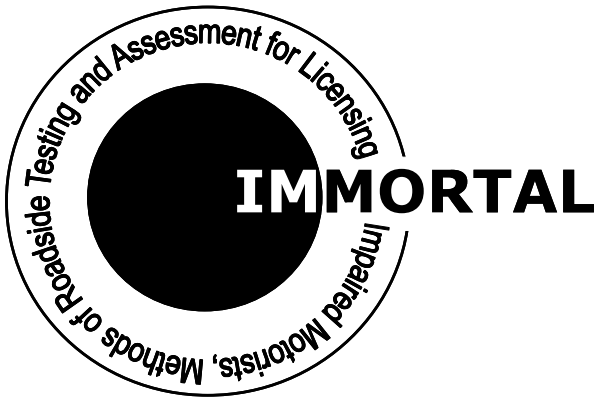

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Summary

The present study forms the Dutch part of a larger, EU-wide investigation into the impact of drugs, medications and medical conditions on road safety. This research programme, known as the IMMORTAL project (Impaired Motorists, Methods of Roadside Testing and Assessment for Licensing) investigated the accident and/or injury risk associated with different types of driver impairment and examined the implications for licensing assessment and roadside impairment testing (including drug screening).
Eight drug groups were included in the Tilburg study: benzodiazepines, tricyclic antidepressants, methadone, opiates, amphetamines, cannabis, cocaine and alcohol. The methodology used was that of a case-control study, where the prevalence of the substances among injured drivers (a hospital sample) was compared with the prevalence in the general driving population (a random roadside sample), and risk ratios were calculated.
Data on substance use by seriously injured drivers (in-patients) was collected in the St. Elisabeth Hospital in the city of Tilburg.
Data on substance use by the general driving population was collected in the Tilburg police district, which is the hospital's catchment area. A random roadside survey was conducted in close cooperation with the Tilburg police force. Among the general driving population, cannabis, benzodiazepines and alcohol were the prevailing substances. Out of the 3,799 stopped and tested drivers:

- 4.5% were positive for cannabis; 3.9% for cannabis only and 0.6% for cannabis in combination with other drugs and/or alcohol;
- 2.1% were positive for benzodiazepines; 2.0% for benzodiazepines only and 0.1% for benzodiazepines in combination with other drugs and/or alcohol;
- 2.1% were positive for alcohol (BAC $\geq$ 0.2 g/l); 1.8% for alcohol only and 0.3% for alcohol in combination with other psychoactive substances.

Drugs of abuse were strongly concentrated in male drivers aged 18-24. No less than 17.5% were positive for illegal drugs. Psychoactive prescription drugs were strongly concentrated in female drivers aged 50 and older: 11.3% were positive.

Comparison of the road and hospital samples showed that approx. 35% of serious injuries among drivers in the Tilburg police district were associated with self-administered alcohol and/or illegal drugs, and especially with drug-free BAC-levels $\geq$ 1.3 g/l, with drug/alcohol combinations at BAC-levels $\geq$ 0.8 g/l, and with drug/drug combinations. These three categories accounted for 12.7%, 8.3% and 7.2%, respectively, of the 184 seriously injured drivers included in the hospital sample. The corresponding odds ratios were 87, 179 and 24, respectively. In order to be effective, road safety policy should target these three categories with priority.
Considering the fact that in part of the alcohol and/or drug-related serious-injury crashes a sober driver was seriously injured, it can be assumed that alcohol and/or illegal drug use accounted for even more than 35% of serious road injuries in the Tilburg police district.
In addition to the case-control study, and combined with the roadside survey, an observational method of detecting drug impaired drivers was tested. The method consisted of a checklist of signs of impairment supplemented with

two questions about recent drug use. Specificity (98.6%) and negative predictive value (95.8%) of the method were satisfactory, whereas sensitivity (61.1%) and positive predictive value (82.9%) were rather low. It is recommended to try and improve the method in future trials, since large-scale random analytical drug-screening at the roadside will probably not be feasible in the years to come. This is due partly to the high cost of the screening devices and partly to the time-consuming procedure.

Contents

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1. Introduction

1.1. Background

In the last two decades, the number of drivers who drive while under the influence of illegal and impairing medicinal drugs has been increasing dramatically. A Dutch hospital study conducted by SWOV in the mid-1980s, found these substances among 8.5% of the injured drivers (Vis, 1988). A hospital survey conducted in 2000/2001 found these substances among 30% of the injured drivers (Mathijssen et al., 2002).
The present case-control study forms the Dutch part of a Europe-wide investigation of the influence of chronic and acute impairment factors on driving performance and accident risk. This research programme is known as the IMMORTAL project: Impaired Motorists, Methods Of Roadside Testing and Assessment for Licensing. The aim of IMMORTAL is "to provide evidence to propose intervention methods for driver impairment, and support the future development of European policy governing driver impairment legislation".
The intention of the case-control study was to determine relative risk factors associated with the use of eight different drug groups, including alcohol, by drivers. Similar studies were conducted in two other European countries, the United Kingdom (by TRL) and Norway (by TØI). In order to get comparable outcomes for the three countries, a common methodological approach was made.
The study described in this paper was jointly funded by the European Commission, the Dutch Ministry of Transport, Public Works and Water Management, and the Dutch Ministry of Health and Welfare.

1.2. Study objectives and research design

The present study's objective was to examine the relative accident risk associated with the use of one or more of eight defined drug groups by car drivers. The accident rate of users of these substances was related to the accident rate of drivers not using any of these substances.
The common research design across the three countries (Netherlands, United Kingdom and Norway) was that of a case-control study. In the Netherlands, cases were a sample of seriously injured drivers admitted to the hospital. Controls were a sample of drivers taken from the general driving population in the hospital's catchment area. The relative accident risk was determined by computing odds ratios.
The eight drug groups included in the study were: benzodiazepines, tricyclic antidepressants, methadone, opiates, amphetamines, cannabis, cocaine and alcohol. The opiates group was subdivided into morphine, heroin and codeine. The amphetamines group was subdivided into amphetamine, methamphetamine and ecstasy (MDMA, MDEA and MDA). Alcohol use was subdivided into four BAC-classes: 0.2-0.5 g/l, 0.5-0.8 g/l, 0.8-1.3 g/l and ≥ 1.3 g/l.

2. Methodology

The methodology used to estimate the relative risk of driving under the influence of one or more of the psychoactive substances under scrutiny, was that of a case-control study. Cases consisted of injured drivers admitted to the St. Elisabeth Hospital in the city of Tilburg. Controls consisted of a representative sample of the general driving population in the Tilburg police district, which covers the hospital's catchment area. Both cases and controls comprised drivers of passenger cars, small vans and minibuses.

2.1. Hospital survey (case sample)

Cases were seriously injured drivers, who were admitted to the St. Elisabeth Hospital. Body fluids were collected under the responsibility of the hospital's Department of Surgery. Blood or urine samples were taken on admission at the hospital's Emergency Department. Hospital and ambulance records were examined to control for medicinal drugs administered before a blood or urine sample was taken. The doctors at the Emergency Department completed a detailed questionnaire regarding the crash circumstances.
All patients, or their legal representatives, were asked for informed consent to be included in the study. All data was processed anonymously. The Medical Ethics Committee of the St. Elisabeth Hospital approved the study protocol.
The representativeness of the case sample was tested by comparing its distribution by gender with the official Road Accident Statistics' distribution.

2.2. Roadside survey (control sample)

2.2.1. *Research area and selection of research sites*

Control drivers were taken at random from moving traffic in the Tilburg police district, which covers the St. Elisabeth Hospital's catchment area. The police district consists of the city of Tilburg and 3 smaller municipalities, covering an area of 322 km^2 with a total population of approx. 260,000 inhabitants.
A total number of about 50 different research sites were selected, equally distributed over the whole police district. The main selection criteria were: traffic flow, (lack of) possibilities for drivers to avoid the research site, enough room for the research and police teams and their vehicles, safe working conditions. All sites except one were selected along main municipal and provincial roads. During the period 1999-2003, these road types accounted for 88% of serious injury crashes in the Netherlands.

2.2.2. *Research periods*

In order to be able to construct a representative control sample, the week was systematically divided into 28 consecutive 6-hour periods. Each of the roadside survey sessions that were conducted, covered one of these 6-hour periods. For the sake of statistical analysis, the original 28 6-hour periods were next aggregated into eight day/time categories, which were supposed to be more or less homogeneous with respect to traffic volume and substance use. The eight periods are listed in *Table 2.1*.

Days of the week	Times of the day
1. Monday to Friday	04:00 to 10:00 h
2. Monday to Friday	10:00 to 16:00 h
3. Monday to Thursday	16:00 to 22:00 h
4. Monday to Thursday	22:00 to 04:00 h
5. Saturday and Sunday	04:00 to 10:00 h
6. Saturday and Sunday	10:00 to 16:00 h
7. Friday to Sunday	16:00 to 22:00 h
8. Friday to Sunday	22:00 to 04:00 h

Table 2.1. *Sampling periods.*

In the framework of the IMMORTAL project, 36 roadside survey sessions were conducted between January 2002 and March 2004. But before the start of the project, SWOV had already conducted 25 roadside sessions, between May 2000 and December 2001, as part of a feasibility study, also including in-hospital data collection (Mathijssen et al., 2002).

In order to get an optimal geographical coverage of the police district as well as the various periods of the year, days of the week and times of the day, the results of all 61 sessions were aggregated for analysis.
During each 6-hour roadside session, four different research sites were visited, thus strongly diminishing the predictability of the test sites for (impaired) drivers.

2.2.3. *Driver selection and data collection procedure*

Drivers were stopped by the police at the request of the acting research coordinator. As soon as one of the two interviewers/nurses was ready for interviewing and urine/blood sampling a driver, the next car approaching the research site was stopped. The stopped drivers were asked to cooperate with the research team on a voluntary basis. Drivers who agreed to cooperate, were interviewed on their drug and medicine use. The results for each driver were entered on a uniquely numbered research form; see *Appendix A*. Subsequently, subjects were requested to produce a urine specimen. If they were not able or willing to do so, they were requested to deliver a blood specimen. A trained research nurse performed the venapuncture. Subjects who delivered a urine or blood specimen, received a € 5 reward. All specimens were numbered; the numbers corresponding with those of the subjects' research forms.
Interviewing and sampling of body fluids took place in a specially equipped mobile research unit with private toilet. After the interview and the urine or blood sampling, all subjects were breath-tested for alcohol by a police officer, using a *Dräger Alcotest 7410 Plus com* screening device. The breath test was compulsory for all stopped drivers. Breath test results were entered on the (anonymous) research form. Apart from self-reported drug use and time of administration, data collection also comprised date and time of selection, gender and age of the subject, and signs of impairment.

2.2.4. *Weighting procedure*

The unweighted control sample could not be considered to be representative of all drivers who participated in road traffic in the Tilburg police district at all days of the week and all times of the day, since the sample distribution over different times and days was not equal to the distribution of traffic volumes. The reason for this was the more or less constant sampling capacity of the research team, regardless of the traffic volumes that are strongly varying by day of the week (weekdays versus weekend) and by time of the day. Furthermore, the police had a quite understandable preference for enforcement activities during high-risk hours, i.e. the nighttime hours with low traffic volumes. So, in order to make the control sample representative of the whole week, it had to be weighted, based on traffic flow distribution over the various days of the week and times of the day.

2.3. **Analysis of body fluids**

2.3.1. *Blood analysis*

Serum specimens were analyzed by the Netherlands Forensic Institute (NFI) of the Ministry of Justice.
Screening for *opiates and cannabis* in serum was performed by Cozart® Enzyme ImmunoAssay (EIA), which is based on competition for drug antibody binding sites. After incubating and washing, a substrate was added. The absorbance was measured spectrophotometrically. The cut-offs used were 5 ng/ml for cannabis and 20 ng/ml for opiates.
Cannabis and opiate-positive screening results of injured drivers and opiate-positive screening results of control drivers were confirmed whenever that was possible, allowing for opiates to distinguish between codeine, (nor)morphine and heroin.
Confirmation of opiates was performed with GC/MS after solid phase extraction (SPE) and derivatisation with bis-trimethylsilyl-trifluoroacetamide (BSTFA). For quantification, deuterated analogues from codeine and morphine were used as internal standards.
Confirmation of cannabis was performed with GC/MS after SPE and derivatisation with methyl iodide. For quantification, deuterated analogues from THC, 11-OH-THC and THC-COOH were used as internal standards. Cannabis confirmation was based on Daldrup et al. (1995).
The applied confirmation cut-off levels were 2 ng/ml for cannabis and 20 ng/ml for opiates.
Cannabis-positive screening results of control drivers were only GC/MS-confirmed, if a driver's self-reported cannabis use was negative.
For the *other drugs* included in the study, toxicological serum analysis was performed by HPLC (high-performance liquid chromatography) after solid phase extraction. Positive results were not confirmed by GC-MS. HPLC-analysis was based on Gaillard & Pepin (1997). Analytical cut-offs (detection limits) were applied; see *Table 2.2*.

Component	Detection limit (ng/ml)
Cocaine:	
Cocaine	70
Benzoylecgonine	50
Methadone	100
Amphetamines:	
Amphetamine	50
Methamphetamine	70
MDMA	30
MDEA	30
MDA	20
Benzodiazepines:	
Alprazolam	30
Bromazepam	20
Brotizolam	50
Chlordiazepoxide	20
Clobazam	20
Dealkyl flurazepam	30
Desmethyl diazepam	?
Diazepam	50
Flunitrazepam	20
Loprazolam	10
Lorazepam	20
Lormetazepam	50
Midazolam	30
Nitrazepam	30
Oxazepam	50
Temazepam	20
Zolpidem	10
Zoplicon	30
Tricyclic antidepressants:	
Amitriptyline	30
Clomipramine	100
Dosulepine	?
Doxepine	?
Imipramine	?
Trimipramine	?
Desipramine	?
Maprotiline	?
Nortriptyline	?

Table 2.2. *Components and detection limits of HPLC serum analysis.*

2.3.2. *Urine analysis*

Urine specimens were analyzed by the Dutch Laboratory for Drugs and Doping, Tilburg.
Screening of the urine specimens was performed by Enzyme Multiplied Immunoassay Technique (EMIT® II Plus). Like EIA, this technique is based on competition for drug antibody binding sites.
For benzodiazepines a special high sensitivity protocol was used with on-line deglucuronidation.
EMIT® II Plus ethanol assay was used for injured drivers only (control drivers were breath-tested). This technique is based on oxidation of ethanol in presence of alcoholdehydrogenase (ADH) with NAD to acetaldehyde.
Generally, screening results were considered to be positive in accordance with the SAMHSA guidelines for drug of abuse testing (www.workplace.samhsa.gov). Only for opiates, a lower cut-off of 1,000 ng/ml was applied instead of the SAMHSA cut-off of 2,000 ng/ml. A SAMHSA guideline for tricyclic depressant cut-off levels does not exist. The applied cut-off level of 150 ng/ml was derived from a comparison between screening results and self-reported use of these medicines.
Amphetamine and opiate-positive screening results of injured drivers were confirmed by Gas Chromatography/Mass Spectrometry (GC/MS) whenever that was possible. GC/MS-confirmation of opiates allowed distinguishing between codeine, morphine and heroin. GC/MS-confirmation of amphetamines allowed to distinguish between amphetamine, methamphetamine, MDMA, MDEA and MDA.
Amphetamine and opiate-positive screening results of control drivers were only GC/MS-confirmed, if a driver's self-reported amphetamine or opiate use was negative.
Table 2.3 gives an overview of the applied cut-off levels for urine screening and confirmation.

Substance	Cut-off immunoassay	Cut-off GC/MS
Cannabis (THC-COOH)	50 ng/ml	15 ng/ml
Cocaine (benzoylecgonine)	300 ng/ml	150 ng/ml
Amphetamine	1000 ng/ml	500 ng/ml
Opiates	1000 ng/ml	2000 ng/ml
Heroin (6-MAM)	--	10 ng/ml
Benzodiazepines	300 ng/ml	300 ng/ml
Methadone	300 ng/ml	300 ng/ml
Tricycl. Antidepressants	150 ng/ml	Not applicable

Table 2.3. *Cut-off levels applied for urine screening and confirmation.*

2.4. **Statistical analysis**

In order to test if the *case sample* was representative of all seriously injured car drivers in the Tilburg police district, its distribution by gender was compared with the distribution according to official Road Accident Statistics. The variable gender was chosen because of its strong correlation with psychoactive substance use.

The *control sample* could not be considered to be representative of the general driving population in the Tilburg police district, since its distribution over different times and days was not equal to the traffic flow distribution. One reason for this was the more or less constant sampling capacity of the research team, regardless of the traffic flow, which was strongly varying by day of the week (weekdays versus weekend) and by time of the day. Furthermore, the police had a quite understandable preference for enforcement activities during high-risk hours, i.e. the nighttime hours with low traffic volumes. In order to make the control sample representative, it was weighted, based on trip data that was collected over 1999 and 2000 by the Dutch Central Bureau of Statistics (CBS).
The relative risk of drivers who used one or more of the psychoactive substances involved in the study, was determined by comparing the prevalence of these substances in the weighted case and control samples. Odds ratios were computed using the statistical package SAS, version 9.1.. Subjects who had used one particular substance or a combination of different substances were related to subjects who had used none of these substances. 95% confidence intervals were used for significance.

2.5. Field trial of an observational drug screening method

As part of the roadside survey, an observational method for detecting drug-impaired drivers by the police was tested. Drugs under scrutiny were cannabis, amphetamines, cocaine, opiates, methadone and benzodiazepines. The method consisted of a checklist of signs of impairment supplemented by two questions about recent drug use and a list of benzodiazepines that were available on prescription in the Netherlands (see *Appendix B*). The checklist was completed by the police officers that also carried out the breath test for alcohol. The checklist included only one physiological test, namely of pupil reaction to light, which had to be performed if dilated pupils were observed. Generally, completing the checklist took no more than one to two minutes. Training of the police officers took approx. three quarters of an hour: 30 minutes during the briefing and another 15 minutes at the roadside.
The method was meant to allow a quick scan of potential drug impairment, aimed at pre-selecting drivers suspected of impairing drug use other than alcohol. In everyday police enforcement of drug driving, some kind of pre-selection will be necessary for the time consuming and relatively expensive on-site screening of body fluids (urine or oral fluid). The validity of the observational screening method was assessed by comparing the police officer's final judgement with the results of urine and blood analysis or, when these results were absent, with self-reported drug use to the research team.

3. Results of the hospital survey

3.1. Sample size and non-response

During the whole 2000-2004 period, a total of 207 seriously injured drivers were included in the study. This number was smaller than expected, since 112 drivers were included during the one-year feasibility study alone. Hence, it was expected that it would be possible to include approx. 350-400 seriously injured drivers during the whole 2000-2004 period.
The main reasons for the relatively small sample size were the lack of a special trial nurse at the emergency department and the frequent change of the medical teams that manned the department. The surgeons who were in charge of the in-hospital data collection were often not able to immediately instruct new medical teams. During the feasibility study, a Ph.D. student assisted the surgeons in charge, thus relieving their self-imposed task. The in-hospital data collection was beyond direct control of the SWOV researchers. According to the surgeons in charge, the sample of included drivers was not in any way selective, however.
Out of the 207 included drivers, a total number of 23 drivers could not be evaluated. For two drivers, consent was denied; for another two, personal and crash data was missing. And for 19 drivers, blood or urine specimens were missing or containing insufficient material for toxicological analysis.
For the remaining 184 valid cases, 121 blood specimens (66%) and 63 urine specimens (34%) were available for toxicological analysis.
In order to test if the case sample was representative of all car and van drivers who were admitted to a hospital in the Tilburg police district, the distribution by gender was compared with the distribution according to the official Road Accident Statistics (RAS) of the Dutch Ministry of Transport, Public Works and Water Management. The results are shown in *Table 3.1*.

Sample	Distribution of seriously injured drivers by gender		
	Male	Female	Total
Tilburg case sample	76%	24%	100%
RAS sample	68%	32%	100%

Table 3.1. *Comparison of the Tilburg case sample and the Road Accident Statistics sample (2000-2003) of seriously injured drivers, by gender.*

76% of the Tilburg case sample consisted of men, versus only 68% of the RAS sample, both in the Tilburg police district and in the whole of the Netherlands. The case sample did not significantly differ from the RAS sample for the Tilburg police district (p = 0.083), but it did significantly differ from the national RAS sample (p = 0.032). The latter result makes it unlikely that the different sample distributions for the Tilburg police district were determined by chance. In order to make the case sample more representative, it was weighted by dividing RAS fractions for the Tilburg police district by case sample fractions.

3.2. Prevalence of psychoactive substances among seriously injured drivers

Table 3.2 gives a detailed picture of the prevalence of psychoactive substances in the seriously injured drivers who were admitted to the Tilburg St. Elisabeth Hospital. The table shows that 54.0% of male drivers and 24.4% of female drivers were positive for one or more of the psychoactive substances included in the study. When considering only illegal drugs and illegal BAC-levels, the difference between male and female drivers was even greater: 49.6% of male drivers and 15.6% of female drivers were positive. Among male injured drivers, no less than 26.6% had a BAC ≥ 1.3 g/l.

Psychoactive substance use	Distribution by gender		
	Male drivers	Female drivers	All drivers (weighted)
Negative	46.0%	75.6%	55.4%
Cannabis only	5.0%	--	3.4%
Amphetamine only	--	--	--
Ecstasy only	--	--	--
Cocaine only	--	--	--
Morphine/heroin only	0.7%	--	0.5%
Codeine only	1.4%	--	1.0%
Benzodiazepines only	2.2%	6.7%	3.6%
Tricyclic antidepres. only	--	--	--
Methadone only	--	--	--
Combination of drugs	6.5%	8.9%	7.2%
Alcohol* 0.2-0.5 BAC	0.7%	2.2%	1.2%
Alcohol* 0.5-0.8 BAC	2.2%	2.2%	2.2%
Alcohol* 0.8-1.3 BAC	3.6%	--	2.5%
Alcohol* ≥ 1.3 BAC	16.6%	4.4%	12.7%
Alcohol 0.2-0.5 + drug(s)	2.2%	--	1.5%
Alcohol 0.5-0.8 + drug(s)	0.7%	--	0.5%
Alcohol < 0.8 + drug(s)	*2.9%*	--	*2.0%*
Alcohol 0.8-1.3 + drug(s)	2.2%	--	1.5%
Alcohol ≥ 1.3 + drug(s)	10.1%	--	6.9%
Alcohol ≥ 0.8 + drug(s)	*12.2%*	--	*8.3%*
Total N	139	45	184
* alcohol only			

Table 3.2*. Weighted distribution of psychoactive substances among case drivers, by gender.*

A further subdivision of the prevalence of psychoactive substances among injured drivers, e.g. by gender *and* age, was considered as being not very useful because of the small numbers and the resulting influence of chance.

4. Results of the roadside survey

4.1. Sample size and non-response

In the framework of the IMMORTAL project, 36 roadside survey sessions were conducted between January 2002 and March 2004. During that period, a total number of 2,489 drivers were stopped by the police, only 10 (0.4%) of whom declined to cooperate with the researchers. But before the start of the IMMORTAL project, SWOV had already conducted 25 roadside sessions, between May 2000 and December 2001, as part of a feasibility study (Mathijssen et al., 2002). During the latter period, a total number of 1,362 drivers were stopped, 42 (3.1%) of whom declined their cooperation. These figures clearly reflect the effect of growing experience with the research team. With growing experience, the average number of drivers who were asked for informed consent to participate in the study increased from 53 to 69 per session, while the non-response rate decreased significantly.
In order to get an optimal geographical coverage of the Tilburg police district as well as the various periods of the year, days of the week and times of the day, the results of all 61 sessions were aggregated for analysis.
Table 4.1 gives an overview of the urine and blood specimens provided by the drivers who agreed to cooperate (consenting drivers). All of these drivers were interviewed by researchers and breath-tested by the police. Not all of them were willing or able to provide a urine or blood specimen, though.

Period		Urine samples	Blood samples	Missing samples	Total no. of consenting drivers
May '00-Dec. '01	N	944	164	212	1,320
	%	71.5%	12.4%	16.1%	100%
Jan. '02-March '04	N	1,929	337	213	2,479
	%	77.8%	13.6%	8.6%	100%
Total '00-'04 period	N	2,873	501	425	3,799
	%	75.6%	13.2%	11.2%	100%

Table 4.1. *Specimens of body fluids provided by consenting drivers.*

The figures in *Table 4.1*, too, reflect the effect of growing experience with the research team. During the pilot period, the percentage of missing specimens of body fluids was nearly twice as high as during the actual IMMORTAL survey period.
The number of drivers that declined any cooperation with the researchers was very small, totalling only 1.4% of all stopped drivers. Even if these drivers were a selective group with regard to drug use, their biasing effect would be negligible. A comparison between respondents and non-respondents showed no significant difference with regard to BAC: 5.3% and 3.8%, respectively, had a positive BAC (> 0.2 g/l); 2.7% and 1.9%, respectively, had an illegal BAC (> 0.5 g/l). Based on the BAC-distributions, it was assumed that there was no big difference between the two groups with regard to the use of psychoactive substances other than alcohol.

Among consenting drivers, 11.2% were not able or willing to provide a urine or blood sample. For these drivers, selectivity was examined with regard to gender, age, BAC and self-reported drug use.

Table 4.2 shows the missing specimen rates by gender and age. Among male drivers, this rate was slightly lower than among female drivers. Differences by age were much larger: the younger the driver, the higher the missing specimen rate. Among female drivers ageing 18-24, this rate was 2.4 times higher than among male drivers of 50 years and older.

Gender	Age				
	18-24	25-34	35-49	50+	Total
Male (N=2,682)	15.1%	13.2%	10.1%	6.5%	10.8%
Female (N=1,117)	15.5%	15.4%	10.7%	7.2%	12.1%
Total (N=3,799)	15.2%	13.9%	10.3%	6.7%	11.2%

Table 4.2. *Missing specimen rates, by gender and age.*

Table 4.3 shows the differences in psychoactive substance use between drivers who did, respectively did not, provide a urine or blood specimen. For drivers who did provide a specimen, drug and medicine use was based on toxicological analysis. For drivers who did not, it was based on self-reporting. Only drivers who-reported drug and medicine use less than one week before the interview, were considered to be positive. All drivers were breath-tested for alcohol.

Specimen	Psychoactive substance distribution					
	Negative	Illegal drugs	Medicinal drugs	BAC 0.2-0.5 g/l	BAC ≥ 0.5 g/l	BAC ≥ 0.2 g/l+drug(s)
Urine/blood*	86.2	6.2	2.5	2.4	2.0	0.7
Missing**	85.2	7.1	1.2	1.6	3.1	1.9
*drug use based on toxicological analysis **drug use based on self-reporting						

Table 4.3. *Psychoactive substance use by drivers who did/did not provide a specimen of body fluid.*

The figures of *Table 4.3* indicate that drivers with missing specimens had higher rates of illegal drug use, of illegal BAC-levels, and of combined alcohol and drug use. The actual differences regarding illegal drug use were possibly even somewhat larger than the figures in the table indicate. Out of the 3,374 drivers who provided a specimen, 6.1% reported they had used illegal drugs, but according to the results of toxicological analysis, 6.9% of the specimens were positive. This difference was not significant, however (p = 0.18).
Based on the above analyses, the conclusion is that missing specimens biased the sample of drivers who provided a urine or blood specimen. In order to minimize this bias, it was decided to consider the drivers with missing specimens as valid controls, using their self-reported drug use as an estimate of their actual drug use.

4.2. Weighting of the control sample

In order to make the control sample representative of the general driving population in the Tilburg police district, it had to be weighted (see *Section 2.4*). The weighting procedure was based on 1999-2000 trip data collected by the Dutch Central Bureau of Statistics (CBS). *Table 4.4* shows the control sample and trip distributions.

Day/time categories	Distribution of control sample	Distribution of trips
1	4.1%	15.0%
2	12.8%	25.7%
3	15.4%	19.3%
4	8.5%	3.2%
5	6.9%	4.8%
6	9.2%	12.8%
7	17.9%	16.6%
8	25.2%	2.6%

Table 4.4*. Comparison between day/time-distributions of the control sample of drivers and the CBS-sample of trips.*

The comparison shows that weekend nights and, to a lesser degree, weekday nights (categories 8 and 4, respectively) were strongly over-represented in the control sample. Drink driving is strongly concentrated in nighttime hours. As a consequence, drink driving was over represented in the unweighted control sample. Weighting the control sample solved this problem. Weight factors for each of the eight day/time categories were computed by dividing traffic flow (trip) fractions by control sample fractions.

4.3. Prevalence of psychoactive substances among control drivers

4.3.1. *The general picture*

Table 4.5 shows the prevalence of psychoactive substances among the general driving population of the Tilburg police district, by gender.
Among all drivers, 9.9% were positive for one or more of the psychoactive substances included in the study. There was, however, a significant difference between male and female drivers: 11.2% of males were positive versus 6.9% of females. When considering only illegal drugs and illegal BAC-levels, the difference between males and females even greater: 7.7% of males were positive versus 2.9% of females. Furthermore, male drivers had a 70% share in the traffic flow.

For drug/drug and alcohol/drug combinations, which were detected in 0.8% of the control drivers, the prevalence of the various separate drugs was determined; see *Table 4.6*.
Among the drug/drug and alcohol/drug combinations, cannabis prevailed (70%), followed by cocaine (44%) and ecstasy (36%). On the other hand, only 13% of the cannabis-positive drivers had also used one or more other drugs. Among the cocaine and ecstasy positive drivers, the corresponding shares of concomitant drug use were 52% and 46%, respectively.

Psychoactive substance use	Distribution by gender		
	Male drivers	Female drivers	All drivers
Negative	88.8%	93.1%	90.1%
Cannabis only	4.8%	1.5%	3.9%
Amphetamine only	<0.01%	--	<0.01%
Ecstasy only	0.4%	0.2%	0.3%
Cocaine only	0.4%	0.09%	0.3%
Morphine/heroin only	0.03%	--	0.02%
Codeine only	0.5%	0.6%	0.5%
Benzodiazepines only	1.6%	2.8%	2.0%
Tricyclic antidepres. only	0.2%	0.5%	0.3%
Methadone only	--	--	--
Combination of drugs	0.6%	0.3%	0.5%
Alcohol* 0.2-0.5 BAC	1.3%	0.1%	0.9%
Alcohol* 0.5-0.8 BAC	0.4%	0.4%	0.4%
Alcohol* 0.8-1.3 BAC	0.2%	0.2%	0.2%
Alcohol* ≥ 1.3 BAC	0.3%	0.1%	0.2%
Alcohol 0.2-0.5 + drug(s)	0.1%	0.01%	0.09%
Alcohol 0.5-0.8 + drug(s)	0.2%	0.01%	0.2%
Alcohol < 0.8 + drug(s)	*0.3%*	*0.02%*	*0.2%*
Alcohol 0.8-1.3 + drug(s)	0.06%	--	0.04%
Alcohol ≥ 1.3 + drug(s)	0.05%	--	0.03%
Alcohol ≥ 0.8 + drug(s)	*0.1%*	--	*0.08%*
Total N (weighted)	2,661	1.138	3,799
* alcohol only			

Table 4.5. *Weighted distribution of psychoactive substances among the general driving population, by gender.*

Substance	Prevalence		
	Alone	Combined with other drug(s)	Total
Cannabis	3.9%	0.6%	4.5%
Amphetamine	0.003%	0.03%	0.03%
Ecstasy	0.3%	0.3%	0.6%
Cocaine	0.3%	0.4%	0.7%
Morphine/heroin	0.02%	0.04%	0.06%
Codeine	0.5%	0.07%	0.6%
Benzodiazepines	2.0%	0.1%	2.1%
Tricycl. antidepressants	0.3%	0.04%	0.3%
Methadone	--	0.04%	0.04%
Alcohol (BAC ≥ 0.2 g/l)	1.8%	0.3%	2.1%
Total	9.1%	0.8%	9.9%

Table 4.6. *Weighted prevalence of separate drugs, taken alone and concomitantly, among the general driving population.*

4.3.2. *Psychoactive substance use by gender and age*

Table 4.7 displays the distribution of psychoactive substances by gender and age, allowing a more detailed insight into the correlation between demographical factors and the use of psychoactive substances.

Gender and age	Distribution of psychoactive substances							
	Negative	Single illegal drug	Single medicinal drug	Drug combi-nation	BAC 0.2-0.5 g/l	BAC ≥ 0.5 g/l	BAC 0.2-0.8 + drug(s)	BAC ≥ 0.8 + drug(s)
Male drivers								
18-24	79.5%	14.6%	1.2%	1.4%	0.9%	0.9%	1.0%	0.6%
25-34	85.5%	10.9%	0.5%	0.8%	1.0%	0.8%	0.4%	0.1%
35-49	91.6%	3.4%	2.2%	0.5%	1.3%	0.8%	0.2%	--
50+	92.1%	0.6%	4.2%	0.05%	1.6%	1.3%	0.2%	--
Total	88.8%	5.7%	2.3%	0.6%	1.3%	1.0%	0.3%	0.1%
Female drivers								
18-24	95.5%	2.3%	0.3%	--	0.6%	1.3%	--	--
25-34	94.5%	3.4%	1.1%	0.8%	0.04%	0.07%	0.04%	--
35-49	95.7%	1.7%	2.0%	0.03%	0.08%	0.5%	0.03%	--
50+	86.8%	0.04%	11.3%	0.5%	0.04%	1.4%	--	--
Total	93.1%	1.8%	3.9%	0.3%	0.1%	0.7%	0.02%	--

Table 4.7. *Weighted distribution of psychoactive substances among the general driving population, by gender and age.*

Among male drivers, 6.7% were positive for illegal drugs. By far the highest prevalence of illegal drugs was found among young males aged 18-24. No less than 17.6% of the young male drivers were positive: 14.6% for a single illegal drug, 1.4% for a combination of two or more illegal drugs and 1.6% for a combination of alcohol and one or more illegal drugs. On top of that, 0.9% had an illegal BAC without having used illegal drugs.
Among male drivers above the age of 24, 5.2% were positive for illegal drugs, and 1.0% had an illegal BAC without having used illegal drugs.
The highest prevalence of psychoactive prescription drugs among male drivers was found in the age group of 50 and older: 4.2%. Among all male drivers, 2.3% were positive.
Among female drivers, the rate of illegal drug use was significantly lower than among male drivers: 2.2% of the females were positive. The prevalence among females aged 18-24 was not significantly higher than among older females: 2.2% and 2.1%, respectively. None of females under the age of 25 were positive for a combination of two or more psychoactive substances, while such a combination was found among 0.4% of the older females. On the other hand, 1.3% of the young females had a (drug-free) illegal BAC, versus 0.6% of the age groups above 24.
Psychoactive prescription drug use was significantly higher among females than among males, 3.9% of the females being positive. The use of these medicines was strongly concentrated among females aged 50 and older, 11.3% of them being positive.

Table 4.8 shows the distribution of psychoactive substances by day of the week and time of the day, allowing a more detailed insight in high-prevalence days and times. The prevalence of illegal drugs and alcohol among drivers was strongly concentrated in the nighttime hours. The combined use of alcohol and illegal drugs was at a higher level during weekend nighttime hours than during weekday nighttime hours. The prevalence of prescription drugs, on the other hand, was lower during weekend nighttime hours than during the rest of the week. Significantly more drivers tested positive for illegal drugs (5.4%) than for alcohol (2.1%).

Day and time	Distribution of psychoactive substances							
	Nega-tive	Single illegal drug	Single medici-nal drug	Drug combi-nation	BAC 0.2-0.5 g/l	BAC ≥ 0.5 g/l	BAC 0.2-0.8 + drug(s)	BAC ≥ 0.8 + drug(s)
Mon-Sun 04-22 h	90.8%	4.4%	2.8%	0.4%	0.7%	0.7%	0.2%	0.06%
Mon-Thu 22-04 h	77.4%	8.4%	3.1%	0.9%	4.6%	4.3%	0.9%	0.3%
Fri-Sun 22-04 h	79.6%	6.1%	1.4%	1.5%	5.0%	4.5%	1.6%	0.4%
Whole week	90.1%	4.5%	2.8%	0.5%	0.9%	0.9%	0.2%	0.08%

Table 4.8. *Weighted distribution of psychoactive substances among the general driving population, by day of the week and time of the day.*

Table 4.9, finally, shows the development of psychoactive substance use between May 2000 and March 2004. Between 2000-01 and 2002-04, the prevalence of alcohol remained more or less stable (2.3% and 2.1% had a positive BAC, respectively), as did the prevalence of other drugs (8.1% in both periods). The combined use of alcohol plus drugs, however, doubled; from 0.2% to 0.4%. An increase of combined alcohol and drug use may be detrimental to road safety, but due to the very small numbers, the effect was not statistically significant.

Period	Distribution of psychoactive substances							
	Nega-tive	Single illegal drug	Single medici-nal drug	Drug combi-nation	BAC 0.2-0.5 g/l	BAC ≥ 0.5 g/l	BAC 0.2-0.8 + drug(s)	BAC ≥ 0.8 + drug(s)
2000-01	89.8%	5.6%	1.5%	0.8%	1.1%	1.0%	0.2%	0.01%
2002-04	90.2%	4.0%	3.4%	0.3%	0.8%	0.8%	0.3%	0.1%

Table 4.9. *Weighted distribution of psychoactive substances among the general driving population, by research period (May 2000-Dec. 2001 vs. Jan. 2002-March 2004).*

5. Relative risk calculations

The relative risk of using one or more of the psychoactive substances involved in the study was determined by comparing the prevalence of these substances among case and control drivers. Odds ratios were computed using the statistical package SAS. Subjects who used one particular substance or a combination of different substances were related to subjects who used none of these substances. An odds ratio of 1.0 was designated to the injury rate of 'negative' drivers (the reference group); 95% confidence intervals were used for statistical significance.
The results are shown in *Table 5.1*. A moderately increased risk of serious road *injury* was associated with a BAC-level between 0.5 and 0.8 g/l. At higher BAC-levels, the relative injury risk increased more or less exponentially. This result corresponds to the results of various earlier case-control studies that demonstrated an exponentially increasing *accident* risk at BAC levels above 0.8 g/l, e.g. the Grand Rapids Study by Borkenstein et al. (1974).
Strongly increased injury risks were also associated with the combined use of several drugs, and with the combination of drugs and a BAC between 0.2 and 0.8 g/l.

Psychoactive substances	Weighted distribution among cases and controls		Odds ratio	95% C.I.
	Cases (N=184)	Controls (N=3,799)		
Negative	55.4%	90.1%	1.00	
Cannabis only	3.4%	3.9%	1.45 (NS)	0.64-3.29
Amphetamine only	--	<0.01%	Undefined	--
Ecstasy only	--	0.3%	Undefined	--
Cocaine only	--	0.3%	Undefined	--
Morphine/heroin only	0.5%	0.02%	32.4 (NS)	1.78-592
Codeine only	1.0%	0.5%	3.04 (NS)	0.65-14.2
Benzodiazepines only	3.6%	2.0%	2.98	1.31-6.75
Tricyclic antidepr. only	--	0.3%	Undefined	--
Methadone only	--	--	Undefined	--
Combination of drugs	7.2%	0.5%	24.0	11.5-49.7
Alcohol* 0.2-0.5 BAC	1.2%	0.9%	2.12 (NS)	0.54-8.42
Alcohol* 0.5-0.8 BAC	2.2%	0.4%	8.28	2.73-25.2
Alcohol* 0.8-1.3 BAC	2.5%	0.2%	17.6	5.54-56.0
Alcohol*≥ 1.3 BAC	12.7%	0.2%	87.2	39.4-193
Alcohol < 0.8+drug(s)	2.0%	0.2%	12.9	3.78-44.2
Alcohol ≥ 0.8+drug(s)	8.3%	0.08%	179	49.9-638
* alcohol only				

Table 5.1. *Relative injury risk associated with the use of various psychoactive substances by car drivers.*

Extremely high relative risks were associated with the use of morphine/ heroin only and with the combination of drugs and BAC-levels above 0.8 g/l. Morphine/heroin, however, was hardly detected in controls, resulting in a much larger confidence interval than for drugs in combination with a BAC above 0.8 g/l.
Neither a positive BAC-level below 0.5 g/l nor the single use of most other drugs or medicines involved in the study were associated with a significantly increased injury risk. An exception was the use of benzodiazepines only, which was associated with an odds ratio of 2.98 (C.I. 1.31-6.75).
Appendix C gives an overview of all drug/drug and alcohol/drug combinations that were detected in cases and controls. *Appendix D* contains the odds ratio and confidence interval calculations.

6. Field trial of an observational roadside drug screening method

Together with the roadside survey, an observational method for detecting drug-impaired drivers by the police was tested, as Task 4.5 of the IMMORTAL project. The method consisted of a checklist of signs of impairment, supplemented with two questions about recent drug use (see *Appendix B*). The checklist was based on several existing checklists, e.g. one developed for the German police (Möller, 1998). It was completed by the police officers that also performed the breath test for alcohol. In most cases, completing the checklist took no more than one to two minutes. The method was meant to allow a quick scan of potential drug impairment, aimed at pre-selecting drivers for the time consuming and relatively expensive on-site screening of body fluids (urine or oral fluid). The validity of the method was determined by comparing the police officer's final judgement with the results of urine and blood analysis or, in the absence of these, with the self-reported drug use to the research team. Between February 2003 and March 2004, police officers screened 954 drivers.

Criteria for suspicion of impairing drug use were one or more of the listed signs of impairment and/or self-reported recent drug use. The validity of the screening method was expressed by sensitivity (SE), specificity (SP), positive predictive value (PPV) and negative predictive value (NPV). SE is defined by the percentage of positive screening results among positive drivers. A screening method with high sensitivity has few false negatives. SP is defined by the percentage of negative screening results among negative drivers. A screening method with high specificity has few false positives. PPV is defined by the percentage of true positive screening results among all positive screening results (true+false). PPV puts SP in the context of drug prevalence; lower prevalence results in lower PPV. NPV is defined by the percentage of true negative screening results among all negative screening results (true+false). PPV puts SE in the context of drug prevalence; lower prevalence results in higher NPV.

Table 6.1 shows the results for signs of impairment alone. Specificity and predictive values of drug detection based on signs of impairment alone were acceptable, but sensitivity was low. The 25.3% sensitivity means that three quarters of all drug users were not detected when using signs of impairment as the only selection criterion.

Screening result based on signs of impairment alone		Drug prevalence		
		Negative	Positive	Total
Negative	N	856	71	927
	Row %	92.3 (NPV)	7.7	
	Column %	99.7 (SP)	74.7	
Positive	N	3	24	27
	Row %	11.1	88.9 (PPV)	
	Column %	0.3	25.3 (SE)	
Total	N	859	95	954

Table 6.1. *Sensitivity (SE), specificity (SP), positive predictive value (PPV) and negative predictive value (NPV) of signs of impairment alone.*

Table 6.2 shows the results for self-reporting alone. Specificity and predictive values of self-reporting as the only selection criterion were not much different from signs of impairment alone, but sensitivity was significantly higher. However, the 56.8% sensitivity means that still 43.2% of all drug users were not detected.

Screening result based on self-reporting alone		Drug prevalence		
		Negative	Positive	Total
Negative	N	848	41	889
	Row %	95.4 (NPV)	4.6	
	Column %	98.7 (SP)	43.2	
Positive	N	11	54	65
	Row %	16.9	83.1 (PPV)	
	Column %	1.3	56.8 (SE)	
Total	N	859	95	954

Table 6.2*. Sensitivity (SE), specificity (SP), positive predictive value (PPV) and negative predictive value (NPV) of self-reporting alone.*

Table 6.3 shows the results for the combination of signs of impairment and self-reporting. The combination of these two elements produced the best results. Specifity and predictive values were more or less similar to those of the two separate elements, but sensitivity was significantly better: 61.1%. Nevertheless, using this combined screening method means that still 38.9% of all drug users would not be detected. On the other hand, random saliva testing of all stopped drivers would reduce the screening capacity of a police team by approx. a factor 5, on balance resulting in a 50-75% lower number of detected drug-positive drivers.

Screening result based on signs of impairment plus self-reporting		Drug prevalence		
		Negative	Positive	Total
Negative	N	847	37	884
	Row %	95.8 (NPV)	4.2	
	Column %	98.6 (SP)	38.9	
Positive	N	12	58	70
	Row %	17.1	82.9 (PPV)	
	Column %	1.4	61.1 (SE)	
Total	N	859	95	954

Table 6.3*. Sensitivity (SE), specificity (SP), positive predictive value (PPV) and negative predictive value (NPV) of signs of impairment plus self-reporting.*

The drawback of the relatively high proportion of false positive screening results (17.1% for the combined screening method; see *Table 6.3*) is of less importance if a positive screening result is followed by oral fluid testing than if it is followed by urine testing. Oral fluid sampling is far less invasive than

urine sampling, and it can easily be performed at the roadside. Urine sampling often requires that a suspect be arrested and transported to the police station.
Inter-rater reliability of the screening method could not be determined, since approx. 80% of the observations were performed by one and the same police officer, whereas the remaining 20% were performed by three different officers with varying (low) training levels.
The willingness of drivers to report drug use to the police was higher for cannabis and medicinal drugs than it was for other illegal drugs and for the combined use of two or more illegal drugs. Self-reporting rates were the following:

- 56% for cannabis only (27 out of 48);
- 54% for codeine or benzodiazepines only (14 out of 26);
- 30% for ecstasy or cocaine only (3 out of 10);
- 27% for a combination of two or more illegal drugs (3 out of 11);
- another 45% (5), however, reported the use of cannabis only.

In the Netherlands, there is no per se law for drug driving. In countries with per se laws, the willingness of drivers to self-report drug use to the police would probably be at a (much) lower level.
Summarizing, it can be concluded that specificity and negative predictive value of the observational drug detection method were satisfactory, whereas sensitivity and positive predictive value were rather low. It is recommended to try and improve the method in future trials, since large-scale random analytical drug screening at the roadside will probably not be feasible in the years to come.

7. Summary and discussion

The relative risk of road trauma associated with psychoactive substance use, was determined by comparing the prevalence of these substances between a sample of seriously injured drivers (cases) and a sample of the general driving population (controls). Both samples were taken in the same area, namely the Tilburg police district, in the south of the Netherlands. The samples have been weighted in order to make them representative.

7.1. Drug and alcohol use among the general driving population

Among the 3,799 drivers the control sample consisted of, cannabis, benzodiazepines and alcohol were the prevailing substances:
4.5% were positive for cannabis; 3.9% for cannabis-only and 0.6% for cannabis in combination with other drugs and/or alcohol.
2.1% were positive for benzodiazepines; 2.0% for benzodiazepines-only and 0.1% for benzodiazepines in combination with other drugs and/or alcohol.
2.1% were positive for alcohol (BAC ≥0.2 g/l); 1.8% for alcohol-only and 0.3% for alcohol in combination with other drugs; among the 1.8% being positive for alcohol-only, 0.8% had an illegal BAC (≥0.5 g/l).
Drugs of abuse were strongly concentrated in male drivers aged 18-24. No less than 17.5% were positive for illegal drugs: 14.6% for a single illegal drug, 1.4% for a combination of two or more illegal drugs, and 1.6% for a combination of alcohol and one or more illegal drugs. Among male drivers aged 25-34, 12.2% were positive for illegal drugs. Among all other gender/age categories, illegal drug use did not exceed 5%.
Psychoactive prescription drugs were strongly concentrated in female drivers aged 50 and older: 11.3% were positive, versus 2.8% of the total driving population.
Drink driving prevailed among males: 1.2% had an illegal BAC, versus 0.7% of female drivers.

7.2. Relative risk of drug and alcohol use

7.2.1. *Odds ratios*

Comparison of the road and hospital samples showed that serious road injuries were especially associated with drug-free BAC-levels ≥1.3 g/l, with combined alcohol and drug use at BAC-levels ≥0.8 g/l, and with combined use of two or more illegal drugs. These three categories accounted for 12.7%, 8.3% and 7.2%, respectively, of the 184 serious injuries included in the hospital sample. The corresponding odds ratios (OR) were 87 (C.I. 39-193) for drug-free BAC-levels ≥1.3 g/l, 179 (C.I. 53-2060) for combined alcohol and drug use at BAC-levels ≥0.8 g/l, and 24 (C.I. 12-50) for combined use of two or more illegal drugs.
Relatively high and statistically significant odds ratios were also computed for drug-free BAC-levels between 0.8 and 1.3 g/l (OR 18), for combined alcohol and drug use at positive BAC-levels below 0.8 g/l (OR 13), and for drug-free BAC-levels between 0.5 and 0.8 g/l (OR 8). Together, these categories accounted for 7.2% of the serious injuries.

For benzodiazepine-only users, a significantly but moderately increased injury risk was found (OR 3.0; C.I. 1.3-6.8). They accounted for 3.6% of all serious injuries. But it may be assumed that most, if not all of these drivers, used benzodiazepines on doctor's prescription. Without the use of their medicine, the relative injury risk of these drivers might have been higher than it was now, due to adverse effects of their diseases. This hypothesis is based on the results of experimental research by Schmitt et al. (2005) into the effects of depression and antidepressant treatment on driving ability. The study was conducted in the framework of the IMMORTAL study. Results showed that depression was associated with a significant and quite robust reduction of driving ability. Treatment with an SSRI-type antidepressant improved driving ability, although it was still worse than that of healthy subjects.
In the Tilburg study, no significantly increased injury risk was associated with the use of cannabis, amphetamine, ecstasy, cocaine, codeine or tricyclic antidepressants, when taken alone. Methadone alone was found neither in the road sample nor in the hospital sample (it was rarely found in both samples, though, in combination with morphine/heroin).

7.2.2. *Discussion of the odds ratio for cannabis*

With respect to cannabis, the most widely used illegal drug in Dutch and probably EU road traffic, the fact that no significantly increased risk was found might partly be due to the relatively small hospital sample. But it might also be due to the uneven distribution of blood and urine specimens over both samples. Among the hospital specimens, 66% consisted of blood and 34% of urine, whereas only 15% of the roadside specimens consisted of blood and 85% of urine. The detection window of the inactive THC-metabolite THC-COOH in blood is smaller than in urine. In blood, it can be found up to 2 days after cannabis use; in urine, up to 3 days and in chronic users even much longer. On the other hand, it can take up to 4 hours after smoking before THC-COOH reaches the cut-off level in urine, whereas in blood this takes only minutes. The potential biasing effect of the uneven distribution of blood and urine specimens over the hospital and road samples was tested by comparing positive test results for cannabis with regard to self-reported time of administration (see *Table 7.1*).
Among drivers with self-reported cannabis use more than 12 hours before specimen sampling, the proportion of positive blood specimens was 7.5% (4.4 percent points) lower than the proportion of positive urine specimens. This indicates that the biasing effect of the uneven distribution of blood and urine specimens over the hospital and road samples was minimal. Furthermore, this biasing effect was compensated for by the 21% under-reporting of cannabis use (for 10.6% of the road sample, drug-positives and negatives were based on self-reporting).

Positive specimen	Self-reported time of cannabis use (hours before sampling)					
	< 1 hr	1-4 hrs	4-12 hrs	12 hrs-1wk	> 1 wk/ not used	Total
Urine	6.1%	6.5%	28.6%	38.1%	20.7%	100%
Blood	5.6%	3.2%	36.8%	32.4%	22.0%	100%

Table 7.1. *Distribution of cannabis-positive blood and urine specimens by self-reported time of administration (road sample only).*

Finally, the odds ratio for cannabis might have been significantly increased, if only drivers were compared who were positive for THC and/or the psychoactive metabolite 11-OH-THC, and not drivers who were positive for THC and/*or* its metabolites, including the inactive metabolite THC-COOH (cf. Ramaekers et al., 2004). But then the proportion of serious road injuries associated with (recent) cannabis use would still have been relatively small. Approx. 65% of the cannabis-positive blood specimens from the hospital sample contained the parent drug THC and/or the psychoactive metabolite 11-OH-THC. So it can be estimated that the proportion of THC-*impaired* injured drivers was approx. 2.2%.

7.2.3. *Generalizability of the Tilburg results*

The risk of drink and drug driving as assessed in the Tilburg police district will probably not significantly differ from the risk in the Netherlands as a whole. In other EU countries, however, the risk may be different, e.g., due to different drug control legislation and enforcement. In how far the prevalence of alcohol and drugs among the general driving population of the Tilburg police district is representative of the Netherlands as a whole, is difficult to say. An indication with regard to the use of alcohol can be obtained by comparing the Tilburg and national BAC-distributions during weekend nights; see *Table 7.2*.

Area	BAC-distribution during weekend nights, 2000-2003				
	< 0.5 g/l	0.5-0.8 g/l	0.8-1.3 g/l	≥ 1.3 g/l	Total
Tilburg	94,3%	2.8%	1.6%	1.2%	100%
Netherlands	95,8%	2.3%	1.3%	0.6%	100%

Table 7.2*. BAC-distribution of drivers in the Tilburg police district and the Netherlands (AVV, 2002 and 2004), during weekend nights, 2000-2003.*

During the 2000-2003 period, drink-driving levels in the Tilburg police district were somewhat higher than in the Netherlands as a whole. This may be due, at least partly, to the meticulous selection of research sites in the Tilburg police district and the experienced police teams that made it very difficult for (drinking) drivers to avoid being tested. However, since comparable national data on the prevalence of alcohol is not available, generalization of the Tilburg data to the Netherlands as a whole lacks a solid basis. With respect to the prevalence of impairing drugs, comparable national data is also not available.

7.2.4. *Implications for drug driving policy and research*

Based on prevalence and corresponding odds ratios among seriously injured drivers (see *Table 5.1*), it can be concluded that 35% of serious injuries were associated with self-administered alcohol and/or illegal drugs: 17% were associated with illegal BAC-levels without drugs of abuse being involved; 10% with alcohol/drug combinations; and 8% with drugs of abuse without alcohol being involved. Considering the fact that in part of the alcohol and/or drug-related serious-injury crashes a sober driver was seriously injured, it

can be assumed that alcohol and/or illegal drug use accounted for even more than 35% of serious injuries among drivers in the Tilburg police district. In order to be effective, road safety policy in the Netherlands and possibly the whole EU should mainly target high BAC-levels (>1.3 g/l), alcohol/drug and drug/drug combinations. Almost 30% of serious injuries in the Tilburg police district were associated with these three categories of self-administered psychoactive substances.
The effect of alcohol/drug and drug/drug combinations on road safety is so detrimental, that effective legislation and enforcement are urgently needed. For most alcohol/drug and drug/drug combinations, a legal zero-tolerance limit for each of the substances involved seems to be appropriate. An exception might be made for ecstacy in combination with alcohol. Among the hospital sample no injured drivers were found who were ecstasy-positive and had a positive BAC below 0.8 g/l, whereas the (unweighted) control sample contained 6 drivers with this alcohol/drug combination (see *Appendix C*). This remarkable finding from the case-control study seems to be supported by the results of an experimental study into the effects of combined alcohol and ecstasy use on driving performance (Ramaekers et al., 2005). Results showed that driving impairment caused by a BAC of 0.5 g/l was slightly diminished by the additional administration of ecstasy. It is to early, though, to draw a final conclusion based on these limited study results.
In addition to legislation, further EU-wide experimental and epidemiological studies into the impairing and risk-increasing effects of poly-drug use are needed.
For illegal drugs, when taken alone, and with the exception of heroin, zero-tolerance legislation would seem to produce a massive overkill, however, resulting in very high cost and hardly any road safety benefits. This can be illustrated by taking cannabis use as an example: 87% of all cannabis users among the Tilburg control sample were positive for cannabis alone, which did not result in a significantly increased injury risk. (This does not mean that cannabis use is not detrimental to road safety, since the remaining 13% of cannabis-positive control drivers constituted 70% of the high-risk group of poly-drug users.)
In order to establish realistic, risk-related legal limits for single-used illegal drugs, especially case-control studies on an EU-wide scale are needed. For most medicinal drugs, like antidepressants, benzodiazepines, codeine, barbiturates and even morphine, therapeutic levels may be adequate as legal limits, at least for the time being.
The feasibility and success of EU-wide epidemiological and experimental studies will be greatly dependent on the co-operation of medical ethics committees, hospital staff and the police.

7.3. Field trial of an observational drug screening method

With regard to the field trial of an observational drug detection method, which also comprised self-reporting, it can be concluded that specificity (98.6%) and negative predictive value (95.8%) were satisfactory, whereas sensitivity (61.1%) and positive predictive value (82.9%) were rather low. Furthermore, sensitivity would have been only 25.1%, if exclusively based on observed signs of impairment. The actual sensitivity of the method was mainly resulting from the willingness of drivers to self-report psychoactive substance use to the police. In countries with per se laws, unlike the Netherlands, their willingness to self-report drug use would probably be at a

much lower level. Nevertheless, it is recommendable to further improve and test observational detection methods, since large-scale random body fluid screening is very expensive and time-consuming. It might even be counterproductive, if drug-driving enforcement would result in reduced drink-driving enforcement.

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Appendix 1 Roadside research form

PART A: TO BE COMPLETED BY SUPERVISOR (8-12 USUALLY BY INTERVIEWER)

1. *Police team:* Tilburg, City Centre

2. *Date, day and starting time:* 030511 (Sunday), 22.00 h.

3. *Time of random stopping of subject:* ..... h.

4. *Gender of subject:* **O** male **O** female

5. *Willing to co-operate:* **O** yes (accompany subject to interviewer)

O no (complete questions 6-12)

Complete questions 6 and 7 only in case of refusal to co-operate

6. *Reason of refusal:*
O does not have time
O does not feel like it
O other, namely: .....
O no reason given

Observation: passenger(s) in car: **O** yes **O** no

7. *Age:*
O reported by subject: ..... years
O if not reported, estimate by supervisor: ..... years

---

8. *Time of breath test for alcohol:* ..... hrs.

9. *Signs of impairment/intoxication:* **O** yes, namely:
O unsteady on one's feet
O uncontrolled movements
O drowsy appearance
O hyperactive/aggressive
O bloodshot eyes
O dilated pupils (in daylight)
O constricted pupils (at night)
O thick, slurred speech
O grinding teeth
O other,namely .....
O no

10. *Result of breath test for alcohol:* ..... g/l BAC (result to be noted in two decimals)

11. *Consequence of breath test:*
O subject may proceed; END OF QUESTIONNAIRE
O subject is arrested; COMPLETE QUESTION 12

12. *Activities following arrest:*
O evidential breath test; result: ..... µg/l BrAC
O evidential blood test
O refusal of evidential test

PART B: TO BE COMPLETED BY INTERVIEWER (NAME: .....)

1. *What is your age?* ..... years

2. *Have you used any medicines during the last two weeks?*
O no (proceed to question 4)

	3. *When for the last time?*				
O yes, namely:	<1hr	<4hrs	<12hrs	<1wk	>1wk
O	**O**	**O**	**O**	**O**	**O**
O	**O**	**O**	**O**	**O**	**O**
O	**O**	**O**	**O**	**O**	**O**
O	**O**	**O**	**O**	**O**	**O**
O	**O**	**O**	**O**	**O**	**O**
If name of medicine is unknown:					
O strong analgesic (opioid)	**O**	**O**	**O**	**O**	**O**
O hypnotic	**O**	**O**	**O**	**O**	**O**
O tranquillizer, anxiolytic	**O**	**O**	**O**	**O**	**O**
O antipsychotic	**O**	**O**	**O**	**O**	**O**
O antidepressant	**O**	**O**	**O**	**O**	**O**
O medicine against epilepsy	**O**	**O**	**O**	**O**	**O**
O medicine against coughing (codeine)	**O**	**O**	**O**	**O**	**O**
O other, namely	**O**	**O**	**O**	**O**	**O**

4. *Have you used cannabis or other illegal drugs during the last two weeks?*
O no (proceed to 6)

	5. *When for the last time?*				
O yes, namely:	<1hr	<4hrs	<12hrs	<1wk	>1wk
O cannabis	**O**	**O**	**O**	**O**	**O**
O cocaine	**O**	**O**	**O**	**O**	**O**
O heroin	**O**	**O**	**O**	**O**	**O**
O morphine	**O**	**O**	**O**	**O**	**O**
O ecstasy	**O**	**O**	**O**	**O**	**O**
O amphetamine	**O**	**O**	**O**	**O**	**O**
O GHB	**O**	**O**	**O**	**O**	**O**
O smart drugs	**O**	**O**	**O**	**O**	**O**
O other, namely	**O**	**O**	**O**	**O**	**O**

6. *Accompany subject to the bathroom for urine sampling. Stick label with form number (check carefully!) on filled urine pot and place it in refrigerator*.

Result: **O** urine specimen was obtained

O no urine specimen was obtained; reason: **O** subject was unwilling
O subject could not produce

7. *If no urine specimen was obtained, accompany subject to nurse for blood sampling. Stick label with form number (check!) on filled blood tube*.

Result: **O** blood specimen was obtained

O no blood specimen was obtained; reason: **O** subject was unwilling
O blood sampling failed

Accompany subject to the police for alcohol test; complete questions 8-12 of part A.

Appendix 2 Checklist observational drug detection method

1. Signs of impairment

Observation at some distance, when subject approaches and leaves research unit:

- **O** unsteady on one's feet, swaggering (benzodiazepines, opiates, GHB)
- **O** uncontrolled movements (benzodiazepines, GHB)
- **O** euphoria (opiates, XTC, amphetamine, cocaine)
- **O** not understanding instructions (GHB, opiates)
- **O** chattering (XTC, amphetamine, cocaine)
- **O** excited, aggressive behaviour (amphetamine, cocaine)

Observation at close range before and during breath test for alcohol:

- **O** drowsy, sleepy appearance (benzodiazepines, opiates)
- **O** slurred speech (THC, benzodiazepines)
- **O** bloodshot eyes (THC, XTC, amphetamine, cocaine)
- **O** red nostrils (cocaine)
- **O** trembling eyelids (XTC, amphetamine, cocaine)
- **O** sniffing (cocaine)
- **O** incoherent speech (GHB)
- **O** undue perspiring (GHB)
- **O** swallowing (THC, opiates, XTC, amphetamine, cocaine)
- **O** trembling (XTC, amphetamine, cocaine, GHB)
- **O** smell of hash (THC)
- **O** low, rasping voice (opiates)
- **O** scratching one's face (opiates)
- **O** pinpoint pupils: < 3.0 mm (opiates)

- **O dilated pupils: > 6.5 mm** (XTC, amphetamine, cocaine, sometimes THC)

2. Breath test for alcohol; result:..... g/l BAC (in **two** decimals)

3. Question to driver (while waiting for breath test result):

Did you, during the past 24 hours, use sleeping pills, tranquillizers, anxiolytics, anti-epileptics, strong painkillers, codeine, hash, weed or other illegal drugs?

- **O** no
- **O** yes, namely.: .....…….

Name of medicine, if used: ...……..…..…….....…...(checklist benzos!)

4. Pupil reaction to light (only if pupils are dilated and BAC is below 0.2 g/l):

- **O** normal reaction
- **O** slowed reaction (XTC, amphetamine, cocaine, THC)

5. Police officer's final judgement about the use of impairing drugs

- **O** not used
- **O** used, namely: …….....……

SEE OVERLEAF FOR SOME IMPORTANT REMARKS

SOME IMPORTANT REMARKS

Most of the listed signs of impairment may also be caused by other chronic or acute factors than impairing drug use, e.g. alcohol use, physical or mental disability, illness, sleeplessness, fatigue, climatological circumstances, light conditions, etc.
The following signs are nearly always associated with impairing drug use:

a. smell of hash
b. pinpoint pupils, especially under adverse daylight conditions
c. slowed reaction of dilated pupils to light.

Therefore, these signs deserve special attention of the observer!
Only medical drugs belonging to the group of benzodiazepines or opiates (codeine, morphine) are considered to be impairing and should be entered under question 6 of the checklist (see the alphabetical list of benzodiazepines).

ALPHABETICAL LIST OF BENZODIAZEPINES

A **a**lprazolam (anxiolytic, antipsychotic)
B **b**romazepam (anxiolytic)
brotizolam (hypnotic)
C **C**almday = nordazepam (anxiolytic)
chloordiazepoxide (anxiolytic)
clobazam (anxiolytic)
clonazepam (anxiolytic, antipsychotic, anti-epileptic)
Clorazepaat = clorazepinezuur (anxiolytic)
clorazepinezuur (anxiolytic)
D **D**almadorm = flurazepam (hypnotic)
Diazemuls = diazepam (anxiolytic, antipsychotic)
diazepam (anxiolytic, antipsychotic)
Dormicum = midazolam (hypnotic)
Dormonoct = loprazolam (hypnotic)
E **E**uhypnos = temazepam (hypnotic)
F **f**lunitrazepam (hypnotic)
flurazepam (hypnotic)
Frisium = clobazam (anxiolytic)
H **H**alcion = triazolam (hypnotic)
I **I**movane = zoplicon (hypnotic)
K **k**etazolam (anxiolytic)
L **L**endormin = brotizolam (hypnotic)
Lexotanil = bromazepam (anxiolytic)
Librium = chloordiazepoxide (anxiolytic)
loprazolam (hypnotic)
Loramet = lormetazepam (hypnotic)
lorazepam (hypnotic, anxiolytic)
Loridem = lorazepam (hypnotic, anxiolytic)
lormetazepam (hypnotic)
M **m**edazepam (anxiolytic)
midazolam (hypnotic)
Mogadon = nitrazepam (hypnotic)
N **n**itrazepam (hypnotic)
Nobrium = medazepam (anxiolytic)
Noctamid = lormetazepam (hypnotic)
nordazepam (anxiolytic)
Normison = temazepam (hypnotic)
Normitab = temazepam (hypnotic)
O **o**xazepam (anxiolytic)
P **p**razepam (anxiolytic)
R **R**eapam = prazepam (anxiolytic)
Rivotril = clonazepam (anxiolytic, antipsychotic, anti-epileptic)
Rohypnol = flunitrazepam (hypnotic)
S **S**eresta = oxazepam (anxiolytic)
Stesolid = diazepam (anxiolytic, antipsychotic)
Stilnoct = zolpidem (hypnotic)
T **t**emazepam (hypnotic)
Temesta = lorazepam (hypnotic, anxiolytic)
Tranxène = clorazepinezuur (anxiolytic)
triazolam (hypnotic)
U **U**nakalm = ketazolam (anxiolytic)
Urbadan = clobazam (anxiolytic)
V **V**alium = diazepam (anxiolytic, antipsychotic)
X **X**anax = alprazolam (anxiolytic, antipsychotic)
Z **z**olpidem (hypnotic)
zoplicon (hypnotic)

Appendix 3 Drug combinations among cases and controls

Drug/drug and alcohol/drug combinations detected among case drivers

Subject number	*Specimen*	*Substances**
23	blood	THC+XTC
31	urine	XTC+BZO
47	urine	THC+BZO+MOR+MTD+ETH3
49	urine	COC+XTC
60	urine	THC+COC+XTC
62	blood	THC+BAR
65	blood	THC+XTC+BZO
74	blood	XTC+BZO
83	urine	THC+COC+MOR
86	urine	THC+MOR
138	urine	BZO+MOR
155	blood	THC+XTC
157	blood	THC+COD
78	blood	ETH1+THC
79	blood	ETH1THC
107	urine	ETH1+COC+BZO
58	urine	ETH2+THC
38	blood	ETH3+THC+BZO+MOR+MTD
51	blood	ETH3+MOR
88	blood	ETH3+XTC
3	blood	ETH4+COC
4	urine	ETH4+COC+BZO
20	blood	ETH4+COC
21	urine	ETH4+COC+BZO
26	urine	ETH4+TCA
57	urine	ETH4+THC+COC
110	blood	ETH4+BZO
177	blood	ETH4+COC
178	urine	ETH4+COC+MOR
179	blood	ETH4+XTC
180	blood	ETH4+COC
181	urine	ETH4+COC
183	blood	ETH4+BZO
184	urine	ETH4+COC+MOR

*ETH1 = BAC 0.2-0.5 g/l; ETH2 = BAC 0.5-0.8 g/l; ETH3 = BAC 0.8-1.3 g/l; ETH4 = BAC ≥1.3 g/l

Drug/drug and alcohol/drug combinations detected among control drivers

Subject number	*Specimen*	*Substances**
733	urine	THC+COC
917	urine	THC+AMP
1134	urine	THC+COC+XTC
1414	blood	THC+COC+HER+MTD
1425	urine	COC+XTC
1613	urine	THC+COC+HER
1625	urine	THC+COC
1640	urine	COC+XTC
1747	urine	THC+COC
1945	none (self-rep.)	THC+COC+COD
2030	urine	THC+COC+BZO
2159	urine	THC+COC
2218	urine	THC+COD
2333	urine	THC+COC
2353	urine	COC+XTC
3108	blood	THC+COC
3414	urine	THC+XTC+BZO
3417	urine	THC+XTC
3538	urine	THC+COC+AMP+XTC
3858	urine	COC+XTC
4068	urine	BZO+TCA
4316	urine	THC+COC
4541	urine	THC+COC
4745	blood	THC+AMP
4855	urine	THC+XTC
5444	urine	THC+COC+XTC
5452	urine	THC+COC+XTC
5469	blood	THC+BZO
5643	urine	THC+AMP
5803	urine	THC+COC
5806	urine	THC+COC
2743	urine	ETH1+BZO
3405	blood	ETH1+THC
3525	blood	ETH1+THC
3550	none (self-rep.)	ETH1+THC
4356	urine	ETH1+THC+COC+XTC
4367	none (self-rep.)	ETH1+THC
4812	urine	ETH1+XTC
5212	urine	ETH1+THC
5459	urine	ETH1+COC
5675	urine	ETH1+THC
5945	urine	ETH1+COD
1530	urine	ETH2+XTC
1844	none (self-rep.)	ETH2+THC
2320	urine	ETH2+XTC
2366	urine	ETH2+THC+COC+XTC

Drug/drug and alcohol/drug combinations detected among control drivers *(continued)*

Subject number	*Specimen*	*Substances**
3539	urine	ETH2+COC
4342	blood	ETH2+THC
4349	urine	ETH2+THC
4852	urine	ETH2+XTC
4854	urine	ETH2+XTC
5216	urine	ETH2+THC+XTC
5254	none (self-rep.)	ETH2+THC
5661	urine	ETH2+THC
5673	none (self-rep.)	ETH2+THC+COC
5947	none (self-rep.)	ETH2+BZO
1644	urine	ETH3+THC
2755	none (self-rep.)	ETH3+THC
3413	urine	ETH3+THC
5512	urine	ETH3+THC+COC+XTC
2758	none (self-rep.)	ETH4+THC+COC
3422	urine	ETH4+THC
4778	blood	ETH4+THC
4817	urine	ETH4+THC

*ETH1 = BAC 0.2-0.5 g/l; ETH2 = BAC 0.5-0.8 g/l; ETH3 = BAC 0.8-1.3 g/l; ETH4 = BAC ≥1.3 g/l

Appendix 4 Odds Ratios and Confidence Intervals

1. Odds Ratio and 95% Confidence Interval for cannabis alone

Table of casecontrol by substance

casecontrol	substance		
Frequency Percent Row Pct Col Pct	Neg	THC	Total
controls	3420 93.07 95.90 97.10	146.22 3.98 4.10 95.86	3566.3 97.05
cases	102.01 2.78 94.17 2.90	6.32 0.17 5.83 4.14	108.33 2.95
Total	3522.04 95.85	152.54 4.15	3674.58 100.00

Estimates of the Relative Risk (Row1/Row2)

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	1.4491	0.6380	3.2911

Sample Size = 3674.58

Summary Statistics for casecontrol by substance

Cochran-Mantel-Haenszel Statistics (Based on Table Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	0.7942	0.3728
2	Row Mean Scores Differ	1	0.7942	0.3728
3	General Association	1	0.7942	0.3728

Estimates of the Common Relative Risk (Row1/Row2)

Type of Study	Method	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	Mantel-Haenszel	1.4491	0.6380	3.2911
	Logit	1.4491	0.6380	3.2911

2. Odds Ratio and 95% Confidence Interval for morphine/heroin alone

Table of casecontrol by substance

casecontrol substance

Frequency / Percent / Row Pct / Col Pct	Neg	MOR	Total
controls	3420	0.93	3421
	97.05	0.03	97.08
	99.97	0.03	
	97.10	50.82	
cases	102.01	0.9	102.91
	2.89	0.03	2.92
	99.13	0.87	
	2.90	49.18	
Total	3522.04	1.83	3523.87
	99.95	0.05	100.00

Estimates of the Relative Risk (Row1/Row2)

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	32.4449	1.7767	592.4761

Sample Size = 3523.87

Summary Statistics for casecontrol by substance

Cochran-Mantel-Haenszel Statistics (Based on Table Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	13.8165	0.0002
2	Row Mean Scores Differ	1	13.8165	0.0002
3	General Association	1	13.8165	0.0002

Estimates of the Common Relative Risk (Row1/Row2)

Type of Study	Method	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	Mantel-Haenszel	32.4449	1.7767	592.4761
	Logit	32.4449	1.7767	592.4761

3. Odds Ratio and 95% Confidence Interval for codeine alone

Table of casecontrol by substance

casecontrol substance

Frequency / Percent / Row Pct / Col Pct	Neg	COD	Total
controls	3420	19.85	3439.9
	96.51	0.56	97.07
	99.42	0.58	
	97.10	91.69	
cases	102.01	1.8	103.81
	2.88	0.05	2.93
	98.27	1.73	
	2.90	8.31	
Total	3522.04	21.65	3543.69
	99.39	0.61	100.00

Estimates of the Relative Risk (Row1/Row2)

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	3.0402	0.6528	14.1575

Sample Size = 3543.69

Summary Statistics for casecontrol by substance

Cochran-Mantel-Haenszel Statistics (Based on Table Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	2.2205	0.1362
2	Row Mean Scores Differ	1	2.2205	0.1362
3	General Association	1	2.2205	0.1362

Estimates of the Common Relative Risk (Row1/Row2)

Type of Study	Method	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	Mantel-Haenszel	3.0402	0.6528	14.1575
	Logit	3.0402	0.6528	14.1575

4. Odds Ratio and 95% Confidence Interval for benzodiazepines alone

Table of casecontrol by substance

casecontrol substance

Frequency / Percent / Row Pct / Col Pct	Neg	BZO	Total
controls	3420	74.46	3494.5
	94.92	2.07	96.99
	97.87	2.13	
	97.10	91.85	
cases	102.01	6.61	108.62
	2.83	0.18	3.01
	93.91	6.09	
	2.90	8.15	
Total	3522.04	81.07	3603.11
	97.75	2.25	100.00

Estimates of the Relative Risk (Row1/Row2)

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	2.9762	1.3115	6.7539

Sample Size = 3603.11

Summary Statistics for casecontrol by substance

Cochran-Mantel-Haenszel Statistics (Based on Table Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	7.4888	0.0062
2	Row Mean Scores Differ	1	7.4888	0.0062
3	General Association	1	7.4888	0.0062

Estimates of the Common Relative Risk (Row1/Row2)

Type of Study	Method	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	Mantel-Haenszel	2.9762	1.3115	6.7539
	Logit	2.9762	1.3115	6.7539

5. Odds Ratio and 95% Confidence Interval for drug/drug combinations

Table of casecontrol by substance

casecontrol substance

Frequency Percent Row Pct Col Pct	Neg	Combidrg	Total
controls	3420 96.23 99.46 97.10	18.65 0.52 0.54 58.32	3438.7 96.75
cases	102.01 2.87 88.44 2.90	13.33 0.38 11.56 41.68	115.34 3.25
Total	3522.04 99.10	31.98 0.90	3554.02 100.00

Estimates of the Relative Risk (Row1/Row2)

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	23.9629	11.5476	49.7262

Sample Size = 3554.02

Summary Statistics for casecontrol by substance

Cochran-Mantel-Haenszel Statistics (Based on Table Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	151.7917	<.0001
2	Row Mean Scores Differ	1	151.7917	<.0001
3	General Association	1	151.7917	<.0001

Estimates of the Common Relative Risk (Row1/Row2)

Type of Study	Method	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	Mantel-Haenszel	23.9629	11.5476	49.7262
	Logit	23.9629	11.5476	49.7262

6. Odds Ratio and 95% Confidence Interval for alcohol alone, BAC 0.2-0.5 g/l

Table of casecontrol by substance

casecontrol substance

Frequency Percent Row Pct Col Pct	Neg	ETH1	Total
controls	3420 96.10 99.00 97.10	34.72 0.98 1.00 94.04	3454.8 97.07
cases	102.01 2.87 97.89 2.90	2.2 0.06 2.11 5.96	104.21 2.93
Total	3522.04 98.96	36.92 1.04	3558.96 100.00

Estimates of the Relative Risk (Row1/Row2)

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	2.1244	0.5362	8.4171

Sample Size = 3558.96

Summary Statistics for casecontrol by substance

Cochran-Mantel-Haenszel Statistics (Based on Table Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	1.2053	0.2723
2	Row Mean Scores Differ	1	1.2053	0.2723
3	General Association	1	1.2053	0.2723

Estimates of the Common Relative Risk (Row1/Row2)

Type of Study	Method	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	Mantel-Haenszel	2.1244	0.5362	8.4171
	Logit	2.1244	0.5362	8.4171

7. Odds Ratio and 95% Confidence Interval for alcohol alone, BAC 0.5-0.8g/l

Table of casecontrol by substance

casecontrol substance

Frequency Percent Row Pct Col Pct	Neg	ETH2	Total
controls	3420 96.55 99.53 97.10	16.23 0.46 0.47 80.19	3436.3 97.01
cases	102.01 2.88 96.22 2.90	4.01 0.11 3.78 19.81	106.02 2.99
Total	3522.04 99.43	20.24 0.57	3542.28 100.00

Estimates of the Relative Risk (Row1/Row2)

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	8.2835	2.7283	25.1502

Sample Size = 3542.28

Summary Statistics for casecontrol by substance

Cochran-Mantel-Haenszel Statistics (Based on Table Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	19.8282	<.0001
2	Row Mean Scores Differ	1	19.8282	<.0001
3	General Association	1	19.8282	<.0001

Estimates of the Common Relative Risk (Row1/Row2)

Type of Study	Method	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	Mantel-Haenszel	8.2835	2.7283	25.1502
	Logit	8.2835	2.7283	25.1502

8. Odds Ratio and 95% Confidence Interval for alcohol alone, BAC 0.8-1.3 g/l

Table of casecontrol by substance

casecontrol substance

Frequency / Percent / Row Pct / Col Pct	Neg	ETH3	Total
controls	3420	8.59	3428.6
	96.74	0.24	96.99
	99.75	0.25	
	97.10	65.57	
cases	102.01	4.51	106.52
	2.89	0.13	3.01
	95.77	4.23	
	2.90	34.43	
Total	3522.04	13.1	3535.14
	99.63	0.37	100.00

Estimates of the Relative Risk (Row1/Row2)

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	17.6023	5.5368	55.9603

Sample Size = 3535.14

Summary Statistics for casecontrol by substance

Cochran-Mantel-Haenszel Statistics (Based on Table Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	44.3893	<.0001
2	Row Mean Scores Differ	1	44.3893	<.0001
3	General Association	1	44.3893	<.0001

Estimates of the Common Relative Risk (Row1/Row2)

Type of Study	Method	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	Mantel-Haenszel	17.6023	5.5368	55.9603
	Logit	17.6023	5.5368	55.9603

9. Odds Ratio and 95% Confidence Interval for alcohol alone, BAC ≥ 1.3 g/l

Table of casecontrol by substance

casecontrol substance

Frequency / Percent / Row Pct / Col Pct	Neg	ETH4	Total
controls	3420	8.98	3429
	96.22	0.25	96.47
	99.74	0.26	
	97.10	27.78	
cases	102.01	23.35	125.36
	2.87	0.66	3.53
	81.37	18.63	
	2.90	72.22	
Total	3522.04	32.33	3554.37
	99.09	0.91	100.00

Estimates of the Relative Risk (Row1/Row2)

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	87.1762	39.3906	192.9313

Sample Size = 3554.37

Summary Statistics for casecontrol by substance

Cochran-Mantel-Haenszel Statistics (Based on Table Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	452.4026	<.0001
2	Row Mean Scores Differ	1	452.4026	<.0001
3	General Association	1	452.4026	<.0001

Estimates of the Common Relative Risk (Row1/Row2)

Type of Study	Method	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	Mantel-Haenszel	87.1762	39.3906	192.9313
	Logit	87.1762	39.3906	192.9313

10. Odds Ratio and 95% Confidence Interval for drug(s) + alcohol, BAC 0.2-0.8 g/l

Table of casecontrol by substance

casecontrol substance

Frequency Percent Row Pct Col Pct	Neg	ETHa+drg	Total
controls	3420 96.75 99.73 97.10	9.36 0.26 0.27 72.17	3429.4 97.01
cases	102.01 2.89 96.58 2.90	3.61 0.10 3.42 27.83	105.62 2.99
Total	3522.04 99.63	12.97 0.37	3535.01 100.00

Estimates of the Relative Risk (Row1/Row2)

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	12.9306	3.7789	44.2459

Sample Size = 3535.01

Summary Statistics for casecontrol by substance

Cochran-Mantel-Haenszel Statistics (Based on Table Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	27.7161	<.0001
2	Row Mean Scores Differ	1	27.7161	<.0001
3	General Association	1	27.7161	<.0001

Estimates of the Common Relative Risk (Row1/Row2)

Type of Study	Method	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	Mantel-Haenszel	12.9306	3.7789	44.2459
	Logit	12.9306	3.7789	44.2459

11. Odds Ratio and 95% Confidence Interval for drug(s) + alcohol, BAC ≥ 0.8 g/l

Table of casecontrol by substance

casecontrol	substance		
Frequency Percent Row Pct Col Pct	Neg	ETHb+drg	Total
controls	3420 96.60 99.92 97.10	2.88 0.08 0.08 15.81	3422.9 96.69
cases	102.01 2.88 86.93 2.90	15.34 0.43 13.07 84.19	117.35 3.31
Total	3522.04 99.49	18.22 0.51	3540.26 100.00

Estimates of the Relative Risk (Row1/Row2)

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	178.5747	49.9499	638.4184

Sample Size = 3540.26

Summary Statistics for casecontrol by substance

Cochran-Mantel-Haenszel Statistics (Based on Table Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	373.7009	<.0001
2	Row Mean Scores Differ	1	373.7009	<.0001
3	General Association	1	373.7009	<.0001

Estimates of the Common Relative Risk (Row1/Row2)

Type of Study	Method	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	Mantel-Haenszel	178.5747	49.9499	638.4184
	Logit	178.5747	49.9499	638.4184