



Main DRUID results to be communicated to different target groups

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DRUID

Driving under the Influence of Drugs, Alcohol and Medicines

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Deliverable 7.3.2

Main DRUID results to be communicated to different target groups

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Main DRUID results to be communicated to different target groups

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List of abbreviations

AT	Austria
ATC	Anatomical Therapeutic Chemical classification system
BAC	Blood alcohol concentration
BASt	Bundesanstalt für Straßenwesen (Federal Highway Research Institute), DE
BE	Belgium
BG	Bulgaria
BIVV	Belgisch Instituut voor de Verkeersveiligheid, vzw (Belgian Road Safety Institute), BE
BrAC	Breath alcohol concentration
CA	Canada
CBA	Cost-benefit-analysis
CH	Switzerland
CHMP	Committee for Medicinal Products for Human Use
CMD (h):	Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human
CSI	Clinical Signs of Impairment
CY	Cyprus
CZ	Czech Republic
DE	Germany; equivalent to GE
DG MOVE	Directorate-General for Mobility and Transport of the EC
DG SANCO	Directorate General for Health and Consumer Affairs of the EC
DI	Driver Improvement
DK	Denmark
DR	Driver Rehabilitation
DRET	Driver Rehabilitation Evaluation Tool
DRUID	Driving Under the Influence of Drugs, alcohol and medicines
DUI	Driving under influence of alcohol
DUID	Driving under influence of (illicit) drugs
DWI	Driving while impaired/intoxicated
e.g.	exempli gratia (Latin): for example
EC	European Commission
EE	Estonia
EL	Greece
EMA	European Medicines Agency
ES	Spain
et al.	et alii (Latin): and others
ETSC	European Transport Safety Council
EU	European Union
EUR	Euro
FI	Finland
FR	France
HU	Hungary
IAPO	International Alliance of Patients' Organisations
IBSR	Institut Belge pour la Sécurité Routière, asbl (Belgian Road Safety Institute), BE
ICADTS	International Council on Alcohol, Drugs & Traffic Safety
IE	Ireland
INRETS	Institut National de Recherche sur les Transports et leur Sécurité (National Institute for Transport and Safety Research), FR

IT	Italy
KfV	Kuratorium für Verkehrssicherheit (Austrian Road Safety Board), AT
LT	Lithuania
LU	Luxembourg
LV	Latvia
MT	Malta
NA	Not applicable
NL	Netherlands
NO	Norway
OR	Odds ratio
p.	Page
PhVWP	Pharmacovigilance Working Party
PIL	Patient Information Leaflet
PL	Poland
PT	Portugal
PURS	Police user requirements and specifications
RH	Rehabilitation
RUGPha	University of Groningen, Pharmacy, NL
SE	Sweden
SI	Slovenia
SK	Slovakia
SmPC	Summary of Product Characteristics
TEN_TEA	Trans-European Transport Network Executive Agency of the EC
THC	Delta-9-tetrahydrocannabinol
THCCOOH	11-nor-9-carboxy- 9-tetrahydrocannabinol
UK	United Kingdom
USA or US	United States of America
vs.	versus
WP	Work Package
Z-drugs	zolpidem and zopiclone

Executive summary

The objective of this deliverable is to summarize the main DRUID results and to extract relevant information for different target groups. Part I. discusses the theory of risk communication. Part II. summarizes the main DRUID results and Part III. presents the derived extraction per target group.

Part I. describes the theoretic frame of risk communication in a broader perspective (definitions and communication theory, risk communication and sources for patients, managing risk communication related to driving with impairing substances, risk management framework and risk acceptability). Furthermore, it tries to answer the question on how effective are pictograms in communicating risk to patients who drive under the influence of medicines? Two studies are presented which evaluated different pictograms for risk communication with patients (a triangle and a rating pictogram on medicines and driving, each one using 4 different categories, ranging from no or negligible influence to major influence on fitness to drive).

The results of these studies show that both pictograms were effective in communicating risk. Those who participated in the studies were able to recognize and understand the risk of driving under the influence of medicines and have shown their intention to change their driving behaviour by driving less frequently. In both studies, the rating pictogram was preferred over the triangle pictogram.

Part II. presents an overview of the main DRUID results derived from the available DRUID deliverables (status 07.09.2011). It is separated into two subchapters: problem situation (mainly DRUID WP1-2) and countermeasures (mainly DRUID WP3-7). Eight overview boxes were produced to summarize the most relevant information per topic:

- Alcohol;
- Illicit drugs;
- Psychoactive medicines;
- Enforcement
- Classification;
- Rehabilitation;
- Withdrawal (of driving license);
- Guidelines/risk communication).

Within Part III., the most relevant issues from Part I. and Part II. were extracted for each target group: (1) general public, (2) drivers as patients, (3) young drivers, (4) physicians and pharmacists and (5) policy makers on EU and national level.

The following part presents the extraction for policy makers on EU level. This extraction is chosen as example within this executive summary, not only because of its relevance but also because it gives a condensed overview of the main issues mentioned above (in particular the main DRUID results).

Extraction policy makers on EU level

Key elements risk communication

The aim of risk communication addressed to European policy makers is to (i) make them aware that the use of psychoactive substances (including some medicines) is not always compatible with car driving, (ii) support them to make their own problem definition, according to personal beliefs and professional responsibilities within the European context, (iii) provide them opportunities to use risk management tools (such as the risk management framework) in discussing risk control with relevant European stakeholders, (iii) allow them to decide how to contribute to the management of the risk in European society.

For addressing risk communication messages to *policy makers* on an EU level, the following issues need to be considered:

1. Policy makers need to be addressed with information on risk communication using the risk management framework (see table 1, p. 17). This will allow them to understand that DRUID outcomes describing the risk of driving under the influence of alcohol, illicit drugs or psychoactive medicines, can serve the purpose of discussing EU policy measures, e.g. EU risk control measures.

2. European stakeholders need to be involved in the development of a risk management framework for risk communication aiming at European bodies, such as:
- Directorate General for Health and Consumer Affairs of the EC (DG SANCO);
 - Directorate-General for Mobility and Transport of the EC (DG MOVE);
 - Trans-European Transport Network Executive Agency of the EC (TEN-T EA);
 - European Transport Safety Council (ETSC);
 - European Parliament;
 - European Commission;
 - European Medicines Agency (EMA);
 - European professional organisation of pharmacists, physicians, psychologists and other health professionals;
 - International Alliance of Patients' Organisations (IAPO);
 - European Association of Pharmaceutical Manufacturers;
 - other bodies...

Extraction of main DRUID results

Alcohol is the most serious problem compared to illicit drugs and psychoactive medicines in traffic in all investigated EU Member States (e.g. prevalence, risk estimates and cost-benefit-analysis of enforcement measures). Consequently, the first priority of countermeasures should always lie on alcohol; other psychoactive substances are second priority.

The results of the DRUID studies in regard to the problem situation can generally be used in selecting overall activities and target groups in the policy field of psychoactive substance use in traffic across Europe. However, the results indicate, that the prevalence of psychoactive substances by gender, age and time period varies largely per country. "Therefore, recommendations for national activities regarding, e.g., policy issues, enforcement, education or campaigns, should primarily be based on the results of the country reports, rather than on the general report" (D2.2.3, Part I p. 10).

Problem Situation (WP1/2)

Alcohol

- Alcohol ($\geq 0.1\text{g/L}$) is the most frequently detected psychoactive substance in the driving population (estimated EU mean 3.48%) (D2.2.3) as well as in the seriously injured (range 17.7-42.5%) and in killed drivers (range 19.0-44.9%) in Europe (D2.2.5; D2.2.4; D2.3.4).
- Alcohol was in the general driving population mainly detected among older male drivers, with lower BAC levels (D2.2.3).
- Within the accident involved drivers alcohol was mainly detected among younger male drivers with a high BAC level (D2.2.5).
- Alcohol has a negative impact on driving performance and highly increases accident risk (e.g. D1.1.2a, D2.3.2; D2.3.3; D2.3.4; D2.3.5 DRAFT).
- Based on case- control studies, the relative risk of serious injury or fatality for alcohol ($\geq 0.5\text{g/L}$) is estimated to be significantly increased compared to that of drivers below the DRUID cut-off for any substance (D2.3.5) The risk increases dramatically with the alcohol concentration.
- An increased risk was associated with high BAC level, young age and speed (D2.3.3).
- The risk multiplies with combined use (e.g. cannabis) (D2.3.2).
- For more details see overview box 1.

Illicit drugs

- All DRUID investigations (e.g. D2.2.3, D2.2.5, D2.3.4) show that the prevalence of illicit drugs in the driver population (estimated EU mean 1.90%) is lower than the alcohol prevalence (estimated EU mean 3.48%) (D2.2.3).
- Within the accident involved drivers, the majority of drugs appeared to be used in combination with other psychoactive substances (mainly alcohol) (D2.2.5).
- THC is generally the most frequently detected illicit drug, followed by cocaine, but the prevalence of the different illicit substances show high national variability (e.g. D2.2.3, D2.2.5, D2.3.4).
- Illicit drugs were in general mainly detected among young male drivers, during all times of the day but mainly at the weekend (D2.2.3).
- Combined use of alcohol and drugs (illicit drugs and/or psychoactive medicine) is in general often prevalent among young (<35 years) male drivers during night time hours (D2.2.3).

- Multiple drugs (illicit drugs and/or psychoactive medicines) use is in general most common in males (D2.2.3).
- Age groups and time periods vary considerably by country (D2.2.3).
- Based on case-control studies, the relative risk of serious injury or fatality for different illicit substances varies between the substances. For: THC about 1-3 times; benzoyllecgonine, cocaine and illicit opiates about 2-10 times; amphetamines about 5-30 times as high as that of drivers below the DRUID cut-off for any substance (D2.3.5 DRAFT; see also D1.1.2b, D1.2.1, D2.3.2). Some of the risk estimates for illicit drugs vary to a high degree among the single countries; others are based on few positive cases and/or controls which result in very wide confidence intervals. Therefore the estimates are uncertain.
- Experimental studies have shown that the dose equivalent for BAC 0.5g/L-3.7ng/mL THC (range 3.1-4.5ng/mL) for oral administration and 3.8 ng/mL (range 3.3-4.5ng/mL) for smoked administration (D1.1.2b, see also D1.4.2 for more information on cut-offs equivalent to BAC 0.5g/L).
- The risk multiplies with combined use (e.g. alcohol) (e.g. D2.3.2, D2.3.5).
- Experimental studies evaluating the effect of stimulants on driving (MDMA and dexamphetamine) did not reveal impairing effects on driving performance. However, the stimulant effects of MDMA and dexamphetamine are not sufficient to overcome or compensate driving impairments produced by concomitant of alcohol use or sleep deprivation (D1.1.2b, D1.2.1).
- For more details see overview box 2.

Medicines

- DRUID studies indicate that some selected psychoactive medicines (benzodiazepines, medicinal opiates and opioids and Z-drugs) are less prevalent in the driving population (estimated EU mean 1.4%) (D2.2.3) as well as is in seriously injured drivers (D2.2.5) compared to alcohol (estimated EU mean 3.48%) and illicit drugs (estimated EU mean 1.90%). Among the killed drivers the presence of benzodiazepines was the second most frequent toxicological finding after alcohol (D2.2.5). Psychoactive medicines, such as (frequently used) antidepressants, anti-epileptics and antipsychotics, were not included in the DRUID studies. Therefore an underestimation of prevalence should be considered.
- In most countries benzodiazepines were the most common psychoactive medicines in traffic but as for illicit drugs the prevalence of the different psychoactive medicines show high national variability (D2.2.3, D2.2.5).
- Epidemiological studies indicate a major increase in the consumption of antidepressants and drugs used in addictive disorders in the general population in Europe within the last years (D2.1.1).
- Psychoactive medicines were in general mainly detected among older female drivers during daytime hours (D2.2.3).
- Alcohol impaired driving is the main problem in traffic safety, but also psychoactive medicines can constitute a problem in traffic safety. Therefore, both health care providers and patients should be properly informed and aware of the potential risks associated with the use of psychoactive medicines (link WP4/7).
- Based on case-control studies, the relative risk of serious injury or fatality for benzodiazepines + Z-drugs and medicinal opioids is estimated to be about 2-10 times (medicinal opioids in the upper part of the interval; benzodiazepines + Z-drugs in the lower part of the interval) as high as that of drivers below the DRUID cut-off for any substance (D2.3.5).
- The risk of being involved in an accident for medicine users compared to non-users is highest for users of modern antidepressants (1.76, CI: 1.38-2.24), followed by patients who use combinations of psychoactive medicines (1.55, CI: 1.20-2.02), and patients using at least one psychoactive medication (1.28, CI: 1.12-1.46) (D2.3.1).
- For more details see overview box 3.

Countermeasures (WP3-7)

Countermeasures always have to be seen as a comprehensive countermeasure system.

Enforcement (WP3)

- DRUID provides guidelines for everyday policy enforcement and installs scientific demands for on-site drug screening (e.g. legal frame; basic standards of on-site screening procedure; basic standards for on-site screening detection devices).
- Cost benefit analyses have shown that first enforcement priority should lie on alcohol; other psychoactive substances are second priority.

- For more details see overview box 4. Furthermore, a detailed evaluation of legal countermeasures from the perspective of criminology can be found in D1.4.1

Classification (of driving impairing medicines) (WP4)

- DRUID WP4 proposed four level classification and a labelling system regarding the influence of medicines on driving performance, from category 0 (no or negligible influence on fitness to drive) to category 3 (major influence on fitness to drive). The DRUID WP4 categorization was in line with the recent approved SmPC guidelines adopted in September 2009 (which applies as from 1st of May 2010) by EMA.
- DRUID WP4 reviewed over 3000 medicines and over 1500 of them were categorized in regard to their influence on fitness to drive: Most of them were Category 0: 50.7%, while 6% were Category III (Major influence in fitness to drive). DRUID results are compatible with any existing national classification system (e.g. FR, ES) and could be integrated in them.
- Politicians should promote that the DRUID WP4 categorization and labelling be integrated in existing computerized prescribing and dispensing systems for physicians/pharmacists at the various EU member states.
- There is a need to improve information related to effects on driving, particularly in the Patient Information Leaflet (PIL). Information to patients who are advised to use medicines that may impair driving fitness needs to be improved by simple and patient-centred directions based on a clear categorisation system and reflected in the PIL.
- For more details see overview box 5.

Rehabilitation (WP5)

- It should be stated on EU level that Driver Rehabilitation should be an integrated part of a comprehensive countermeasure system.
- Main outlines of rehabilitation procedures should be formulated on EU level (guidelines for legal regulations and standardised procedure). DRUID WP5 developed Europe-wide standards and recommendations of good practice for DUI/DUID rehabilitation measures, which were couched into the form of a user friendly tool (Development of Driver Rehabilitation Evaluation Tool, DRET) for implementation, assessment or evaluation of existing or new DR systems or programmes. It can be the starting point of a European networking and documentation process of DR measures.
- For more details see overview box 6.

Withdrawal (of driving license) (WP6)

- Regulations in European countries regarding withdrawal and accompanying measures should be unified. So far, national strategies are very heterogeneous. Hence a clustering of strategies or countries is difficult.
- DRUID WP6 developed Europe-wide recommendations on withdrawal and conditional withdrawal for the general driving population and specific problem groups such as DUI/DUID drivers, patients in substitution or other long-term treatment with psychoactive medicines (see also D1.4.1).
- For more details see overview box 7.

Guidelines for health care professionals (WP7)

- Decision support at the start of a treatment is needed for selecting the least impairing medicines. Therefore, guidelines and standards for health care professionals pertaining to medicines and driving could be initiated on EU level (D7.2.1).
- Eight recommendations on improving the procedures for assessing fitness to drive within the framework of Council Directive 91/439/EEC (on driving licences) have been formulated within DRUID WP7. These suggestions should be discussed in working groups/expert rounds with physicians, pharmacists, driving licensing authorities and policy makers in order to reach a consensus at European level (D7.2.1).
- The implementation of existing protocols and guidelines into existing computer software used by health care professionals could be stimulated by e.g. incentives for organisations for maintaining databases and software companies.
- For more details see overview box 8.

Risk communication (WP7)

- The focus of campaigns (content, target group, media etc.) should be selected according to the specific characteristic of problem situation and risk group (D7.1.1, D7.3.1).
- Campaigns are more successful if they are targeted (specific issues, groups, etc.). Therefore, large campaigns should be designed as sets of a larger number of activities on a smaller scale (D7.1.1, D7.3.1).

- Campaigns should be evaluated (D7.1.1, D7.3.1). The EU project CAST provides guidelines in designing and evaluating campaigns (D7.1.1; D7.3.1).
- Risk communication pictograms on medicine boxes are effective in communicating risk to the patient (rating models are preferred over no rating indications) (study: ES NL) (D7.3.2).
- Prescribing and dispensing guidelines show a positive effect (e.g. reported behaviour, attitude) after training and implementation phase (study: BE, ES, NL). Health care professionals strongly prefer ICT supporting tools which are integrated in their daily dispensing/prescribing software packages (D7.4.2).
- The emphasis of risk communication towards young people should be given to drink driving prevention, targeting the age group 15-24 year. Preventive measures should be differentiated into general preventive approaches (e.g. campaigns) and special focussed preventive measures for certain smaller subgroups (lifestyle types e.g. personal communication). The effectiveness of approaches should be analyzed in-depth based on representative samples (according results for e.g. DE will be available at the end of the DRUID project) (D7.4.3Draft).
- For more details see overview box 8.

Part I: Risk communication in a broader perspective

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1 Introduction

Communication is crucial to the efforts by which governmental agencies, organisations or institutions aim to change human behaviour among target groups, such as individuals, communities, populations and societies. Efforts related to risk communication by governmental agencies concerning driving with impairing substances can have different purposes. The scope is mostly to reduce traffic fatalities and injuries caused by driving under the influence of alcohol or other psychoactive substances, whereas the assessment of driver fitness and prescribed use of driving impairing medication are considered as decisions to maintain mobility of road users with the least but acceptable risk concerning fitness to drive. At an individual level the scope is to address the risks and benefits from taking psychoactive substances, for example if drivers start to use prescribed medication or decide to use substances that might hold risks, e.g. of being impaired while driving. In this Chapter it will be described how communication at different levels will have an effect on outcomes of risk communication. It will give a broader risk communication perspective by discussing in short how communication theory can help to understand changing human behaviour, it will describe definitions and after some focus on the clinical context, more information will be presented to understand the management framework for stakeholders on how to develop optimal risk communication. Based on this framework risk management activities within DRUID will be illustrated and linked to the different sources developed within DRUID, which are available as Deliverables. Readers of this Chapter who are more interested to know how the management framework has been developed are directly referred to paragraph 4.1.

2 Definitions and communication theory

Communication is the production and exchange of information and meaning by use of signs and symbols. It involves encoding and sending messages, receiving and decoding them, and synthesizing information and meaning (Finnigan & Viswanath, 2011). Risk communication is defined as any two-way communication between stakeholders about the existence, nature, form, severity, or acceptability of risks (McCull, Hicks, Craig, & Shortreed, 2000). This definition clearly points out that stakeholders are involved in dialogues, but it also implies that those who are affected by decisions have to follow a decision-making process, based in their views and capabilities on the assessments of risk, public values, acquired knowledge and perceptions.

Communication theory is the basis for understanding human behaviour in the field of public health by using applied communication perspectives. Communication is key for developing health behaviour strategies which are based on theories of health behaviour change, such as the health belief model and the theories of reasoned action and planned behaviour. According to the health belief model, individuals will be likely to change their health-related behaviour if they judge a health risk as important, view themselves as susceptible to the risk and regard the benefit of changing their behaviour. In the theories of reasoned action and planned behaviour it is considered that behaviour is influenced by intentions to change. People's attitude towards a specific behaviour as well as their perceptions of what important referent groups think about the behaviour, will influence their intentions. The likelihood to change behaviour in these theories is determined by influencing the individual's perceptions.

For decades health behaviour change strategies have been focused on community-based public health interventions and campaigns, where changes in health behaviour (from the individual to the community level) are anticipated. Media communication in community-based campaigns, aims to achieve an impact on behavioural norms by promoting, discouraging or inhibiting healthy behaviours. Media campaigns are seldom effective, if not addressed to the target populations in the right way (CAST 2009). One important aspect of media communication is about creating the messages based on the definition of a public health problem. The latter will determine how target populations, in particular its individuals will be likely to affect the problem.

Research on the consequences of media exposure on individuals, groups, institutions and social systems has shown that the order of effects on knowledge, behaviour and attitudes depends on where individuals or groups are positioned with respect to a given outcome (Chaffee & Roser, 1986). The development of the appropriate messages is crucial and should be based on a thorough assessment of target group characteristics, social structure and needs. Knowledge and information about health issues are not equally distributed across populations. It is well known that people with more formal education learn and know more health issues than people with less formal education (Mosteller & Moynihan, 1972). As a consequence, groups with higher socioeconomic status are more likely to benefit from an increasing flow of information on many issues, including health issues. However, there are factors that could reduce the knowledge gap. For example, people might feel that health issues are more relevant to them than other issues, also certain groups could experience a greater impact of information due to the channel that was chosen, and used more frequently by them (e.g. internet applications, newsgroups). It is expected that users of ICT technologies will search the information “on demand”, allowing them to control the media technologies and attempts to change their behaviour. This, however, is also a risk for widening the knowledge gap, because access could be determined by socioeconomic status and necessary skills. Another factor is the ability to use multiple sources, if needed. It is suggested that the “power” of any single channel of communication (being mass media or interpersonal) may depend on the complexity of the behaviour change being sought. If the change is less complex, a single channel of communication may lead to development of the promoted behaviour. If, however, the behaviour change is more complex an individual will need the use of multiple sources of information and the application of multiple channels of communication (Bandura, 1994).

3 Risk communication and sources for patients

The definition of risk communication that can be adopted from a clinical context is: one-to-one communication in which the intervention includes a stimulus to patients to weigh the risks and benefits of a treatment choice or behavioural (risk reducing) change (Edwards & Elwyn, 1999b). The key outcomes after such an intervention are in general effects on patient knowledge, risk perception, anxiety or behavioural change. However, clinical research outcomes are shifting from traditional cognitive and behavioural research outcomes (patient knowledge, risk perception, and compliance) to more affective outcomes (assessment of the information provided, shared decision-making, certainty about the best option, patient satisfaction). This shift towards affective measures also reflects the changing characteristics of patient-provider relationships in health care. The need for this change is well illustrated by the fact that approximately 50% of patients in developed countries fail to take their medicines properly, despite information that is provided in patient information leaflets. This is partly due to a lack of comprehension and estimation of the risks of their medicines, and partly because they have no control over planning and conduct of their health care and related safety activities (lack of patient empowerment). Patients need a full set of information about anticipated benefits and risks as a prerequisite for shared decision making. They need clear guidance how to respond to impairing effects of substances by the provision of tailor-made information. Although physicians, pharmacists, nurses and pharmaceutical manufacturers play a role in providing comprehensive information to patients, sources of information are still unclear and better tools to help patients understand their treatment options and associated benefits and risks need to be developed (Ruland, 2004). In Deliverable 7.3.1. prototype documents have been developed that might give more information on what the messages should be in written and verbal risk communication, to be used by the public, patients, as drivers, health care professionals, young drivers and policy makers.

4 Managing risk communication related to driving with impairing substances

From a broader risk management perspective, it is clear that focus on risk communication is no longer limited to concern about how to inform the public about technical aspects, but more on how to start and maintain an on-going dialogue among stakeholders (e.g. breweries, drug manufacturers, consumers, patients, drivers, health care professionals, academics, traffic safety researchers, governmental agencies for road safety, health care and public health media, and policy makers). The most preferred way of managing the process of risk communication among all stakeholders is to develop a risk management framework to ensure that risk communication will be an integral part of all stages of the risk management process. In the next paragraph the risk management framework will be explained in more detail.

4.1 Risk management framework

A risk management process aims at defining all steps that need to be addressed in building good risk communication. By presenting these steps and describing the risk communication tasks for each step, a risk management framework will be developed for effective risk communication in DRUID. By showing the link to the various deliverables it will constitute a framework that allows referencing to background information as well as a reflection on weak and strong tasks for risk communication. It is recommended to address those reflections for improving the risk communication tasks needed to stimulate the dialogue among stakeholders. The overview of all necessary steps with risk communication tasks (derived after McColl et al., 2000) is presented in table 1.

Table 1: Risk communication tasks in the risk management process

Risk management step	Risk communication task	Sources in DRUID	Additional comments
Initiation	Identifying and consulting stakeholders, defining the scope	All DRUID partners represent some categories: academia (psychologists, toxicologists, physicians and pharmacists), police, traffic safety researchers, governmental agencies Task 4.2: regulatory agencies/ EMA, patient representatives (IAPQ), Task 7.2.2.: professional organisations of GPs and pharmacists in Europe Task 7.4.3.: young drivers who use drugs,	Groups that did not play a significant role in defining the scope are policy makers, pharmaceutical industry, public health authorities
Risk identification	Developing a stakeholder analysis	During developing tasks in various WPs analysis of needs, issues of concern, level of interest, knowledge gaps, trusted sources of information, and communication preferences were conducted.	A dialogue with the following stakeholders is recommended: policy makers, pharmaceutical industry, public health authorities
Risk estimation	Sources, communicating results with stakeholders, assess changes in knowledge and perceptions	WP 1 and 2 Deliverables	There will be a need to assess stakeholders' knowledge and perceptions based on new information before messages on risk communication can be developed.
Risk evaluation	Perception of risks and benefits, assess acceptability of risks	WP 1, Task 1.1 evaluated dose and blood concentrations related to accident risk (compared to a standard risk level of 0.5g/L blood alcohol concentration)	There will be a need to understand stakeholders' acceptability of risk resulting from stakeholders' perceptions
Risk control	Identifying and evaluating control options	WP 1 identified effective legal regulations for combating DUI and DUID. Deliverables: WP 3, 5 and 6 for controlling DUI drivers and WP 4 and 7 for controlling prescribing and dispensing of impairing medicines and controlling information to target groups	There will be a need to assess the stakeholders' acceptance about control options provided by various DRUID WPs
Implementation	Communication of risk control decisions and implementation strategies	WP 1 recommended how cut-off values in biological fluids could be defined for <i>per se</i> legislations WP 3,5 and 6 recommended procedures and activities for driver rehabilitation enforcement and withdrawal measures WP 4: medicines categorization system WP 7: prototype documents for target groups,	There will be a need to assess the stakeholders opportunities to communicate the risk control options, and possibilities to implement these control options.

		prescribing and dispensing information & pictogram evaluation, evaluation of DRUID materials in practice & patients responses, campaign design for young drivers who use drugs	
Monitoring	Ensure implementation of communication strategies, monitoring changes in needs and concerns of existing and new stakeholders	Recommendations in various Deliverables	There will be a need for continuous monitoring of changes in needs and concerns of (existing and new) stakeholders

Step 1: Initiation

During this step identification of stakeholders within DRUID was accomplished by inviting the DRUID partners representing academia (psychologists, toxicologists, physicians and pharmacists), police, traffic safety researchers, and governmental agencies. The appropriate level of stakeholder involvement is situation specific, and each stakeholder's perspective was described and all activities have been developed according to task development schemes with subsequent reporting in deliverables. However, some groups did not play a significant role in defining the scope such as policy makers, pharmaceutical industry, patient groups and public health authorities. It is recommended to involve these groups by informing them about the outcomes of DRUID before the final dissemination of the results at the closing of the project.

In various tasks stakeholders were involved who were not contributing as partners:

- Task 4.2: regulatory agencies (Pharmacovigilance Working Party of EMA), and patient representatives (IAPO);
- Task 7.2.2.: professional organisations of GPs and pharmacists in Europe;
- Task 7.4.3.: young drivers who use drugs.

Step 2: Risk identification

For each stakeholder group the following information was included in the stakeholder analysis: needs, perception and acceptability of risk, knowledge gaps, trusted information sources and communication preferences. Since a few stakeholder groups were not involved a dialogue with these groups is recommended before finalizing the risk communication messages. In particular verification with policy makers, pharmaceutical industry, public health authorities needs to provide the necessary update of their considerations in decision-making and communication processes.

Step 3: Risk estimation

Partners have contributed to determining the prevalence of substance use (alcohol, illicit drugs, psychoactive medicines), to describing characteristics of impaired drivers using those substances and the accident risk for driving. These results are presented in deliverables within WP 1 and 2 (see box 1-3). However, it is recommended to re-assess stakeholders' knowledge and perceptions based on new information before messages on risk communication can be developed.

Step 4: Risk evaluation

Discussions to determine stakeholder acceptability of the risk associated with DUI related problems have resulted in preliminary risk evaluation perspectives for cost and benefits. However, there will be a need to understand stakeholders' acceptability of risk resulting from stakeholders' perceptions in this risk evaluation step before messages on risk communication can be developed.

Step 5: Risk control

It is important to know stakeholders' acceptability of the residual risk after the implementation of proposed risk control options. Within DRUID priorities for police enforcement activities, characteristics of the problem situation at national levels, determination of the focus of enforcement, cost-benefits of increased drugs and driving enforcement, such as saliva screening in road side testing, and risks of cost cutting activities in drink-driving enforcement have been discussed. These results, as well as

recommendation of increasing the effectiveness of police enforcement are presented in deliverables within WP 3 (see also box 4).

Risk control can be achieved by implementing legal regulations for effective combating DUI and DUID. Identification of effective legal regulations is presented in WP1.

Another risk control focus has been given to driver rehabilitation activities. Recommendations on assignment to driver rehabilitation, the provision of different driver rehabilitation options according to offenders' needs, and quality related requirements are presented in deliverables within WP 5 (see also box 6). One important control option, alcohol ignition interlock programmes, has been recommended as effective measure for DUI offenders in combination with rehabilitation activities.

The risk focus for improving the control options in applying withdrawal measures for DUI(D) drivers, substitution therapy, conditional licensing based on fitness to drive examinations, is presented in deliverables within WP 6 (see also box 7).

A risk control focus related to medicines that can impair driving is presented by partners involved in developing a classification and labelling system. By improving the warnings for patients a better decision making process by patients is expected which will contribute a lower the risk of impaired driving under the influence of medicines. Recommendations are presented in deliverables within WP 4 (see also box 5).

A final focus on control options is given to recommendations for improving prescribing and dispensing practices of general practitioners and community pharmacist. In particular the application of Information and Communication Technology (ICT) in existing software packages has been emphasized for arriving at practical control options everyday medical and pharmaceutical practice. A specific control option has been developed in designing a communication pictogram which is linked to WP 4 labelling. Recommendations are presented in deliverables within WP 7 (see also box 8). Finally, recommendations for improving the procedures for assessing fitness to drive within the framework of Council Directive 91/439/EEC (on driving licences) have been developed and are presented in Deliverable 7.2.1. (p. 55-59).

There will be a need to assess the stakeholders' acceptance about control options provided by various DRUID WPs before communication messages can be developed.

Step 6: Implementation

This action step is associated with stakeholder outreach to communicate the risk control decision and its implementation involving all possible risk control options that various parties could apply in their standard (practice) procedures (see also Step 5).

There will be a need to assess the stakeholders' opportunities to communicate the risk control options, and possibilities to implement these control options before developing risk communication messages.

Step 7: Monitoring

Monitoring changes in needs and concerns of existing and new stakeholders will be needed as a continuous process for ensuring implementation of communication strategies. Recommendations in various deliverables are to be followed up in order to know the effects of risk management options on desired outcomes. This task will eventually be taken up by national organisations, institutions and governmental agencies.

The effects of new legislations in Member States based on DRUID results and/or developments in conjunction with the DRUID project need to be monitored, such as implementation of cut-off values in the Netherlands and Norway, as well as the effects of a new rehabilitation system in Slovenia.

However, there will be one specific task that needs consideration by the European Commission: the maintenance of WP 4 procedures to update the medicine lists with categorization, warnings and advices to patients, based on the criteria and the framework that has been presented in Deliverables 4.2. and 4.3.

Finally, in order to develop risk communication activities in the future, there will be a need for continuous monitoring of changes in needs and concerns of (existing and new) stakeholders.

In summary, risk communication tasks within DRUID have been developed with satisfactory results. However, the presentation of the risk communication tasks in the risk management process shows that there are various needs described for further review in order to be prepared for the development of a comprehensive risk communication strategy. In general it boils down to three activities:

1. Re-assessment of stakeholders' knowledge, perceptions and risk acceptability based on new information as presented in DRUID deliverables;
2. Assessment of stakeholders' acceptance of, and opportunities to communicate, the risk control options and possibilities to implement the various control options;

3. Identifying the (groups of) stakeholders who did not yet show any involvement in the development of risk communication tasks where the scope of the problem has been defined, e.g. policy makers, pharmaceutical industry and public health authorities.

It is recommended to pay attention to these activities in developing risk communication efforts. Stakeholders' participation remains the key issue in accepting risk management decision; they have been heard and are involved, and can better accept the decision even if they continue to dislike the decision itself.

4.2 Risk acceptability

In many considerations about risk control options, as described in the previous paragraph, risk acceptability is mentioned as key issue for developing a successful risk communication messages. It would be of interest to determine the acceptability of presenting substance dosages or substance blood concentrations which have the same risk of impairment as has been determined for alcohol at a blood alcohol concentration of 0.5g/L, which represents an accepted level of risk of impairment in road traffic in most countries.

It is important to realize that accepting risk is guiding people's behaviour. Several factors affect the acceptability of risk, often defined in a narrow technical perspective by experts and in a wider psychological, social and cultural perspective by the public. The following list shows some of the characteristics of factors that play a role in perceiving and accepting risk (derived after McColl et al., 2000):

- Voluntariness (voluntary risk, e.g. smoking is more acceptable than an involuntary risk, eg. air pollution);
- Control (risks not under personal control, e.g. passenger in a vehicle, are perceived more risky than those under one's own control, e.g. driving a car);
- Credibility (organization or individual: perceived caring and empathy are most important; competence and expertise only 15-20% of credibility. Academics are generally ranking higher in credibility than industry and governments);
- Familiarity (high/tech facilities provoke more outrage than familiar risks, e.g. risk at home, driving);
- Diffusion in space and time (rare events such as nuclear accidents are seen as far riskier than common ones, e.g. road traffic accidents);
- Trust (issue is important but organization or individual can not be trusted, feeling to be powerless);
- Morality (what is perceived as risky is seen as attacking core interests and values, e.g. children, health, security, the future, certainty).

For driving under the influence of psychoactive substances it seems obvious to address these factors carefully in defining messages of risk communication to drivers or patients who drive. A trusted organization, credible and with an eye on values and interests that drivers feel important can do a proper job in convincing them that, although DUI is a voluntary risk, it will not be completely controlled by the person due to the effects of psychoactive substances.

5 How effective are pictograms in communicating risk to patients who drive under the influence of medicines?

5.1 Abstract

Introduction: Risk communication is a two way exchange of information, leading to a better understanding of risk. Pictograms can be used to communicate risk, helping patients to make decisions about using their medicines while driving. Similar studies were conducted in the Netherlands and Spain. Despite having common aims, the results obtained in each country are presented separately.

Aim: To compare the effectiveness of two pictograms (rating model and triangle model pictograms) in communicating risk associated with driving impairing medicines to patients and to assess patients' level of understanding (and comprehensibility, in the Spanish study) and intention to change driving

behaviour when looking at various pictograms. The added-value of a explanatory side text was investigated as well.

Methods: Two studies using a 2x3 design were conducted. In the first study, the respondents (patients visiting a community pharmacy with a driving license) were exposed to a condition in which the pictogram (rating model or homologue triangle model pictogram) and the risk category (category 1, 2 or 3) were manipulated. In this study, both pictograms were accompanied by the same side-text (experiment 1). Additionally, the added value of the side-text was examined (experiment 2). Here, the respondents were exposed to the rating model pictogram with or without side-text and again one of the three risk categories.

Results:

The Netherlands – After observing both rating model and triangle model pictograms, respondents recognized the risk of driving while taking driving impairing medicines: 78.8% of the respondents were likely to change their behaviour and 36.3% said they would drive less frequently in the presence of a medicine with such pictograms. Patients showed preference for the 3 categories presented in the rating model pictogram.

Spain – The comprehensibility of the pictograms was good: 90.2% for the rating-model pictogram with side-text, 89.3% for the triangle-model pictogram, and 94.8% for the rating-model pictogram without side text. 77.7% of the respondents were likely to change their behaviour and 25.4% said they would not drive at all in the presence of a medicine with such pictograms. Overall, respondents preferred the rating-model pictogram over the triangle-model pictogram, as well as the rating-model pictogram with text rather than the same pictogram without text

Conclusion: In the two studies, both pictograms seem to be effective in communicating risk but the rating model pictogram was preferred over the triangle model one. In the Dutch study, for the rating model pictogram, a clear and direct correlation between the likelihood of changing driving behaviour and the level of impairment of a medicine has been observed: the higher the category, the more likely to change driving frequency (by driving less frequently).

5.2 Introduction

Pictograms for risk communication

Risk communication is central to effective decision making in modern healthcare (Davis et al., 2003; Edwards & Elwyn, 1999a; Edwards et al., 2003; Thomson, Edwards, & Grey, 2005) and constitutes the basis for informed patient consent (Gordon-Lubitz, 2003; Paling, 2003; Thomson et al., 2005). Risk communication can be defined as an interactive process of exchange of information about risk (R. Lofstedt, 2002; R. Lofstedt & Perri, 2008; R. Lofstedt, 2008a; R. Lofstedt, 2008b; R. E. Lofstedt, 2007), leading to a better understanding and better decisions about clinical management (Edwards, Elwyn, & Mulley, 2002; Edwards et al., 2003; Thomson et al., 2005). Risk communication stimulates patients to weigh the risks and benefits of a treatment choice or behavioural (risk reducing) change (Edwards & Elwyn, 1999a; Edwards et al., 2000). Visual displays of risk information, such as pictograms, are known to increase patient understanding of risk (Gordon-Lubitz, 2003; R. Lofstedt, 2008b; Paling, 2003). Non-verbal symbols, including pictograms, are increasingly being recommended and used to convey warnings and other safety-related information (Katz, Kripalani, & Weiss, 2006; Mansoor & Dowse, 2004) and are particularly useful to communicate information to patients with low literacy (Dowse & Ehlers, 2001; Dowse & Ehlers, 2005; Hill & Roslan, 2004; Houts, Doak, Doak, & Loscalzo, 2006; Mansoor & Dowse, 2004; Morrell, Park, & Poon, 1990; Ngoh & Shepherd, 1997).

Pictograms are known to enhance comprehension (Dowse & Ehlers, 2001; Dowse & Ehlers, 2005; Houts, Witmer, Egeth, Loscalzo, & Zabora, 2001; Houts et al., 2006; Katz et al., 2006; Mansoor & Dowse, 2004; Sorfleet, Vaillancourt, Grloves, & Dawson, 2009), recall of information (Dowse & Ehlers, 2001; Dowse & Ehlers, 2005; Hill & Roslan, 2004; Houts et al., 1998; Houts et al., 2006; Katz et al., 2006; Mansoor & Dowse, 2004; Sorfleet et al., 2009), adherence (Houts et al., 2006; Katz et al., 2006) and communication across language barriers (Lemmon & Hyman, 2006). In order to be effective, pictograms should consider the cultural background of the target population and make use of familiar objects and symbols (Dowse & Ehlers, 2001; Hill & Roslan, 2004; Ngoh & Shepherd, 1997). The design should be simple, realistic and with limited content (Hill & Roslan, 2004) and the pictogram should, at all times, be self-explanatory. If these requirements are not considered during the

development of pictograms, there is a higher chance that the message and/or concepts will be beyond patients' understanding.

Pictograms in traffic safety

The introduction of a compulsory and harmonised pictogram on the medicines' packaging, based on the European classification of drugs according to their effects, was suggested, in 2005, in the European Road Safety Action Programme as part of the "efforts to combat the scourge of drink-driving and find solutions to the issue of the use of drugs and medicines" (*European road safety action program for halving the number of road accident victims in the EU by 2010.*)

The development of such categorization system as well as a proposal to communicate the risk of driving under the influence of medicines to patients are part of the European DRUID (Driving under the influence of drugs, medicines and alcohol) project goals. Therefore, within DRUID, following the development of the categorization system (Task 4.3), the need to design appropriate pictograms to communicate risk arose (Task 7.3).

In some European Union countries, however, pictograms showing the potential risk of driving when taking medicines known to impair psychomotor performance have already been developed. In the Netherlands, psychoactive medicines have a yellow warning label that is affixed to the medicines' package (Wolf, Davis, Tilson, Bass, & Parker, 2006). The yellow sticker contains only written information that refers to the influence of that medicine in the ability to react adequately as well as the increased risk when combining the medicine with alcohol. Another country with warning labels related with medicines and driving is Spain, where a red triangle with a black car inside is printed in the box of medicines that influence driving ability (*Spanish royal decree 1345/2007 of October 11th*).

In France, a country where the categorization system was officially adopted, a graded pictogram was designed to be printed on the box of all category 1 to 3 medicines (Orriols et al., 2010) (figure 1).



Figure 1: Triangle model pictogram (French triangle on medicines and driving)

In Slovenia, medicines with major influence on driving fitness are labeled with a filled red triangle whereas medicines with minor to moderate influence are labeled with an empty triangle. In this case, three categories have been assigned to impairing medicines: cat. a) no or negligible influence; cat. b) minor or moderate influence; cat c) major influence on driving fitness. The symbols are printed on the medicine box, making all health care professionals aware of the warnings (Rules on Labelling of Medicinal Products and on the Packaging Leaflet (Official Journal of the Republic of Slovenia, no. 54/06 and the Medicinal Products Act (Official Journal of the Republic of Slovenia, no. 31/06).

The rating model pictogram

In the rating model pictogram, developed within DRUID (figure 2), the various possible risks of impairing driving ability are displayed, horizontally, in a bar. From left to right, categories range from 0 (no impairment) to 3 (severe impairment) and to each category a different colour was attributed. A traffic-light colour approach was followed, as people tend to associate the colour red to danger, the yellow to caution, and the green to safety (Veldhuijzen et al., 2006). Therefore, green, yellow, orange and red colours were chosen to represent each category of the medicine. Finally, the category attributed to a medicine is indicated by a triangle with a black car inside, as triangles are commonly associated to a warning message and the car is related with driving. A small text on the top of the pictogram saying "your risk in traffic" was added to avoid misunderstandings, allowing patients to associate the risk of taking a medicine and driving.

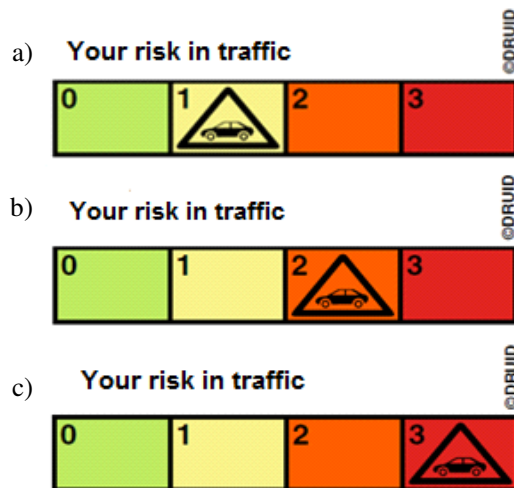


Figure 2: Rating model pictogram. a) category 1; b) category 2; c) category 3

Two studies were conducted in the Netherlands and Spain to evaluate the effectiveness of the two pictogram models, as shown above.

5.3 Dutch study

5.3.1 Aim

The primary aims of the present study was to evaluate i) the effectiveness of the rating and triangle model pictogram in communicating risk associated with driving impairing medicines to patients and ii) to assess patients' level of understanding and intention to change driving behaviour by looking at various pictograms. A comparison between triangle and rating model pictogram was carried out on these dimensions. Furthermore, participants were also asked about their preference for one of the two models of pictograms on medicines and driving.

A comparison with a similar and already existing (in France) pictogram (figure 1) was made (*triangle model pictogram*). The triangle model pictogram was selected for comparison due to the fact that these were the only existing pictograms in which a distinction between different categories or levels of impairment was made.

5.3.2 Methods

Design

This experimental study involved a 2 (rating model pictogram *versus* triangle model pictogram) X 3 (categories of impairment - category 1, 2 and 3) design. The size of the rating model pictogram was 17 x 46 mm. The pictograms were labelled on "fake" medicines' boxes created, on purpose, for the study. A comparison between the same category of the rating and the triangle pictorial models was conducted (experiment 1). The same participants were also asked their preference for one of the pictorial models (experiment 2).

In order to analyse the effectiveness of both pictograms and to investigate patients' level of understanding and intention to change behaviour by looking at various pictograms, 9 groups of 30 patients each, in a total of 270 participants, were created. The order in which the pictograms were shown to patients is relevant for the research question (especially in experiment 2) as it might constitute a bias. Therefore, 3 main groups of 90 participants (30 per category) were initially asked questions related with one category of the triangle model. During the course of the interview, the homologue category of the rating model pictogram (with side-text) was shown. Because the order was considered to be relevant, 3 other groups were shown pictograms in the reverse order. Three more groups were included and firstly shown the rating model (without side-text) and thereafter the triangle model. Table 2 gives a brief overview of the groups.

Table 2: Pictograms visualized by patients, at the start of the interview and thereafter

	Initial pictogram (experiment 1)	Comparison (experiment 2)
A) A1 – 30 patients A2 – 30 patients A3 – 30 patients	Triangle model Category 1 Category 2 Category 3	Rating model with side-text Category 1 Category 2 Category 3
B) B1 – 30 patients B2 – 30 patients B3 – 30 patients	Rating model with side-text Category 1 Category 2 Category 3	Triangle model Category 1 Category 2 Category 3
C) C1 – 30 patients C2 – 30 patients C3 – 30 patients	Rating model without side-text Category 1 Category 2 Category 3	Triangle model Category 1 Category 2 Category 3

Setting

A structured interview involving patients visiting a Dutch community pharmacy (location: Groningen) and actively participating in traffic with a motorized vehicles was carried out. Participants younger than 18 years old and those who could not speak nor read Dutch were considered not eligible for the interview and, as a consequence, were excluded.

Medical ethical approval

Since we only performed an interview about interpretation of pictograms among patients in a pharmacy (the results of which were anonymized) after explicitly asking their consent, no approval of a medical ethics committee was required.

More in detail: All health care professionals and patients were adequately informed about the nature of the study, participated voluntarily and their anonymity was preserved. Patients were interviewed in the waiting area of the pharmacy by a research associate who explained that that the interview was aimed at evaluating pictograms that could be used to warn patients about driving impairing side effects of certain medicines in the near future. Therefore, the therapeutic relationships with their pharmacist could not be influenced by the patients' responses to the interviewer.

Conflict of interests

The authors of the Dutch study declare there is no conflict of interests.

Acknowledgments

The authors of the Dutch study would like to thank the patients for their participation. We would also like to thank René Huiskes for interviewing the patients.

Experiment 1

In experiment 1, participants were exposed to a condition in which the pictogram (rating model pictogram, figure 2 or triangle model pictogram, figure 1) and the risk category (category 1, 2 or 3) were manipulated. Participants were always asked the same questions, regardless the pictogram, allowing comparisons between both pictograms (rating and triangle models).

Experiment 2

In experiment 2, the same group of patients were shown one category (1, 2 or 3, depending on the category group they were assigned to) presented by both pictorial models. Text that was part of the pictogram itself was not shown. Therefore, the rating model pictogram would not have the message "your risk in traffic" and the triangle model pictogram did not include side-text.

Patients were shown the side-text that belongs to one of the categories separately and they were asked which of the pictograms would better reflect the text (understandability) and which one would better show the levels of impairment. Figure 3 gives an example on how the pictograms (in this case it is exemplified category 1 medicines; the same was done for category 2 and 3 medicines) and the side-text were visualised for the patient.

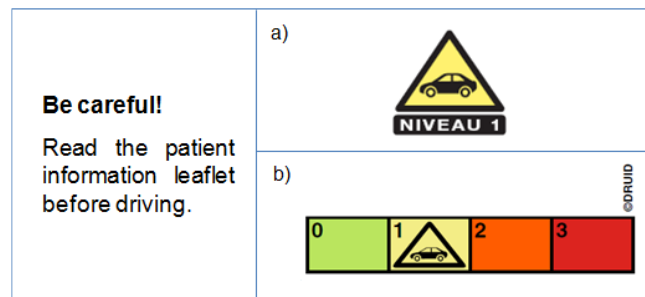


Figure 3: Presentation (as an example) in the experiment 2

Structured interview

The interview was carried out in Dutch. All responses were translated into English and transcribed for content analysis. The interview consisted of four distinct parts: 1) general knowledge about medicines and driving, 2) specific questions about the pictogram, 3) comparison between 2 pictograms, and 4) socio-demographic characteristics of the respondent. Below, it is described the questions that were asked in each section of the interview and the possible answers.

1. General knowledge about medicines and driving
 - a. Can medicines influence the ability to drive? (yes/no/don't know).
 - b. Did you know that certain medicines can influence driving ability? (yes/no/don't know).
 - c. Were you ever informed about the influence of medicines on driving ability? (yes/no). If yes, who provided you that information? (pharmacist, general practitioner, read it on the patient information leaflet)?
2. Specific questions about the pictogram – here, patients are shown the “fake” medicine’s box with the initial pictogram labelled (table 2). The questions in this section were used in Experiment 1.
 - a. What catches your attention? (open question)
 - b. What is your interpretation of the pictogram? (open question)
 - c. How likely would it be for you to change your driving behaviour if you would be taking a medicine with such a pictogram? (very unlikely (1), unlikely, neutral, likely, very likely (5)).
 - d. Suppose you are taking a medicine with this pictogram labelled on the box. How often you would drive? (equally (1), slightly less often, less often, much less often, not anymore (5)).
 - e. How would you rate the level of impairment on driving fitness of this medicine? (estimation level of danger: harmless (1), safe, not safe/not dangerous, dangerous, very dangerous (5))
 - f. How would you rate the pictogram in terms of:
 - i. Difficult / easy (7-point Likkert scale)
 - ii. Unclear / clear (7-point Likkert scale)
 - iii. Not informative / informative (7-point Likkert scale)
 - iv. Incomprehensible / Understandable (7-point Likkert scale)
 - v. Complex / not complex (7-point Likkert scale)
3. Comparison between 2 pictograms (in this section, patients were shown the homologue pictogram. The questions in this section were used in Experiment 2.
 - a. Which one of the pictograms helps you to better understand the text? (rating model or triangle model)
 - b. Which one the pictograms give you more insight about levels of impairment? (rating model or triangle model)

4. Socio-demographic characteristics and use of medicines
 - a. What is your gender? (male or female)
 - b. What is your age? (age in years).
 - c. What is your level of education? (not completed primary school, completed primary school, lower vocational training, intermediate vocational training, higher vocational training).

Dependent variable construction and statistical analysis

Descriptive analysis was conducted to analyse respondents' characteristics, such as gender, age and education level. For experiment 1, the intention to change behaviour, changes in driving frequency, estimation of level of danger and the evaluation of the pictograms was verified. For experiment 2, the preference for one of the pictogram models was analysed.

a) Intended change of behaviour

A 5-point Likert scale was used to analyse participants' intention to change their driving behaviour (1 = very unlikely to 5 = very likely). An ANOVA test was used to measure an interaction effect between the first presented model and the answers given by the respondents. A p-value < 0.05 (95% confidence interval) was considered significant. The same approach was carried out in order to investigate respondents' frequency of driving after looking at the pictogram.

b) Estimation of level of danger

The estimation of the level of danger represented by each category of the pictogram model was associated with a 5-point Likert scale (1 = harmless to 5 = very dangerous). Respondents could select one of the options given by the Likert scale. However, theoretically, the three categories of the pictogram models should be coupled to an answer from the Likert scale as follows:

Category 1: Likert scale option 3 = not dangerous / harmless;

Category 2: Likert scale option 4 = dangerous;

Category 3: Likert option 5 = very dangerous.

An independent T-test was executed to determine the correlation effect between the first presented pictogram model and the answers given by the respondents. A p-value < 0.05 was considered significant.

c) Evaluation of the pictograms

A 7-point Likert scale was used to evaluate the pictograms in six different parameters:

Clarity: 1 = unclear to 7 = clear;

Level of information: 1 = not informative to 7 = informative;

Understandability: 1 = not understandable to 7 = understandable;

Complexity: 1 = complex to 7 = not complex;

Level of difficulty: 1 = difficult to 7 = easy;

Level of ambiguity: 1 = ambiguous to 7 = unambiguous.

A p-value < 0.05 (95% confidence interval) was considered significant. The Cronbach's alpha value of 0.899 proves the reliability of the scale.

d) Pictograms preference (experiment 2)

To investigate respondents' preference for the pictogram that would better explain the side-text and the levels of impairment, a χ^2 – Test was performed in order to compare the differences between pictograms and between the categories of each pictogram. A p-value < 0.05 was considered significant.

5.3.3 Results

A total of 270 participants, assigned to 9 different groups, were interviewed. In order to reach the required number of participants, 360 patients were approached. Thirty-two participants (75% females) did not possess a driving license and, for that reason, could not be part of the study. Fifty-eight participants (62.1% females) did not want to take part of the study (non-respondents) for several reasons: no time (44.8%), no interest (29.3%), not feeling fit due to illness (12.1%), and other reasons (13.8%).

The relevant characteristics of the study population are summarised in table 3. The total study population (n = 270) was equally distributed in terms of gender (n=137; 50.7% males). The mean age

of the participants was 48.4 years-old and the majority of the respondents had a university degree (n = 123; 45.6%). No statistical significant differences were found between gender, age or education level between pictograms (rating model with and without side-text and triangle model).

Table 3: Characteristics of the respondents, stratified per pictogram

	Rating Model <u>without</u> side- text (n=90)		Rating Model <u>with</u> side-text (n=90)		Triangle Model <u>with</u> side-text (n=90)	
	N	%	N	%	N	%
Gender						
Male	45	50.0	50	55.6	42	46.7
Female	45	50.0	40	44.4	48	53.3
<i>For 'Gender' a χ^2 – Test was calculated: P-value=0.484</i>						
Age (in years)						
Mean	49.23		48.19		47.78	
Minimum	20		20		21	
Maximum	78		75		78	
<i>For 'Age' an ANOVA test was executed: P-value=0.785</i>						
Educational level:	N	%	N	%	N	%
Low	19	21.1	15	16.7	20	22.2
Intermediate	29	32.2	34	37.8	30	33.3
High	42	46.7	41	45.6	40	44.4
<i>For 'Education Level,' a χ^2 – Test was calculated: P-value=0.614</i>						

Almost all respondents were aware of the fact that some medicines can influence both reaction time (n = 261; 96.7%) and driving ability and (n = 264; 97.8%). Of the respondents, 48.5% received information about the influence of medicines on driving against 49.3% who did not. For those who received information, pharmacists were the preferable source of information (64.4%), followed by the patient information leaflet (12.1%). General practitioners were only mentioned by 7.6% of the respondents who received information about the influence of medicines on driving ability.

Experiment 1

The pictogram, with no distinction between the rating model and the triangle model, caught 84.8% of the respondents' attention right after looking at the medicines' boxes for the first time.

Respondents were asked to interpret the pictogram they were shown. Answers were divided in right or wrong. Those related to traffic without any reference to the category were still considered as correct answers. As illustrated in figure 4, 72.2% of the participants that were shown one of the triangle model pictograms (n = 90) did not make any reference to any category of impairment, against 46.7% and 36% of the respondents who looked at the rating model pictogram with and without side-text, respectively. With the rating model pictograms, more fully correct answers (traffic related with reference to categories of impairment) were obtained. Education level did not have a statistically significant influence in the correct interpretation of the pictograms. References to risk of driving under the influence of medicines were often made by participants who saw the rating model pictograms.

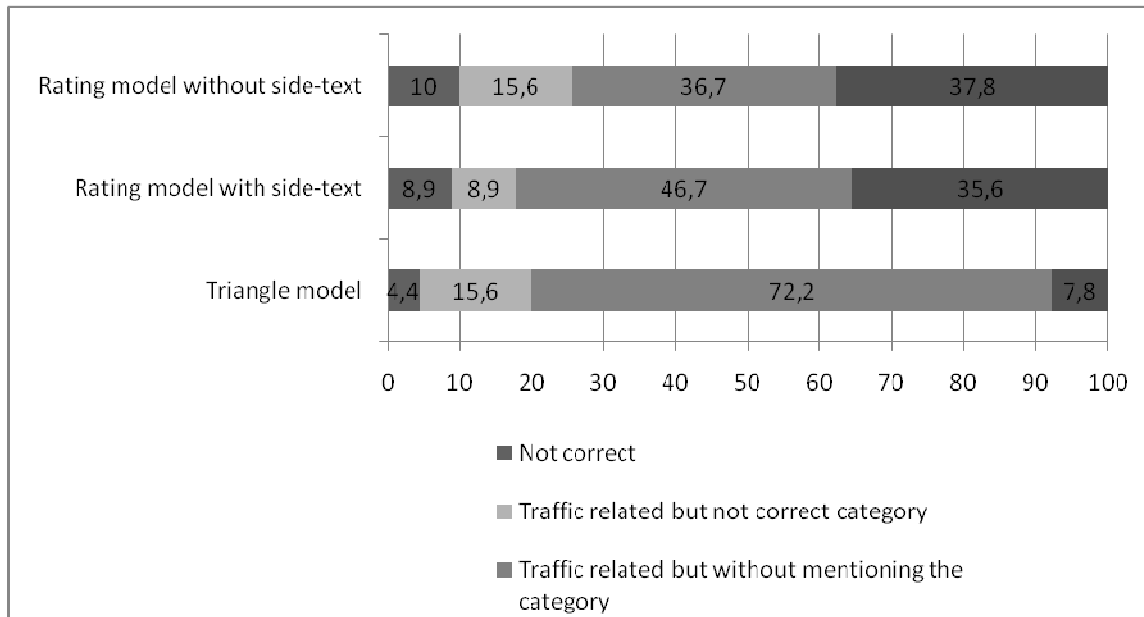


Figure 4: Respondents' interpretation of the starting pictogram (n=270; 90 respondents per pictogram group)

The estimated level of danger was assessed with a scale ranging from harmless to very dangerous. A significant difference (p-value = 0.033) between the rating model and the triangle model was found. A significant difference in category 1 pictograms was found as well (p-value = 0.027), meaning that, by looking at category 1 from the rating model, respondents think it is safer than the homologue category from the triangle model. According to participants' perspectives, categories 2 and 3 of the rating model were those associated, although not significantly, with more dangerous situations (figure 5).

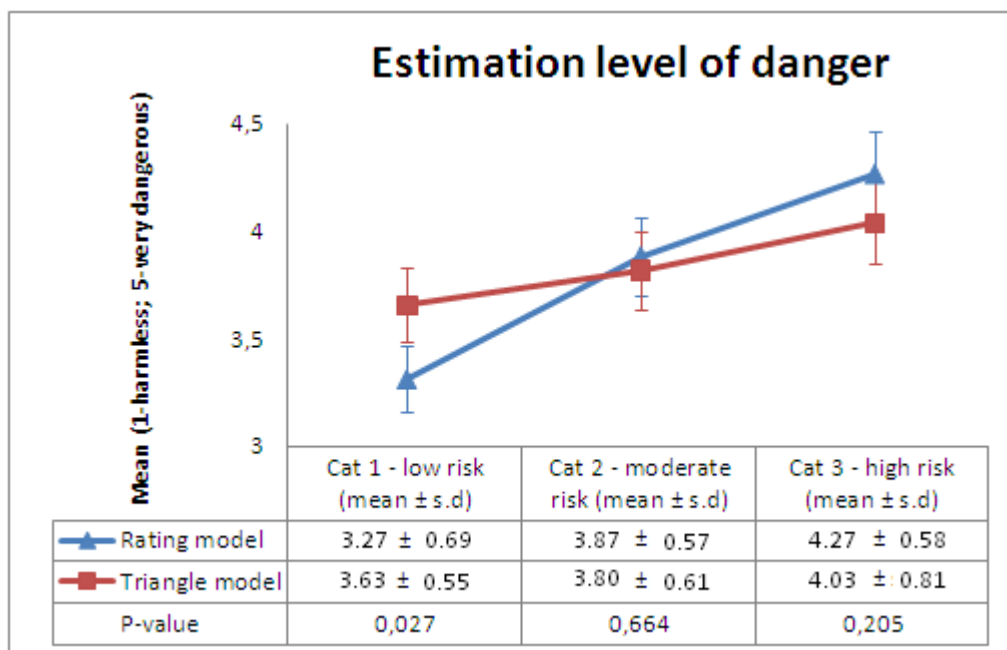


Figure 5: Estimation level of danger was assessed by asking the following question: "How would you rate the level of impairment on driving fitness of this medicine?" Every dot represents the mean estimation of risk value of 30 participants belonging to each category of the rating and triangle models pictogram

The estimation level of danger was assessed by asking the following question: "How would you rate the level of impairment on driving fitness of this medicine?". Every dot represents the mean estimation of risk value of 30 participants belonging to each category of the rating and triangle models pictogram.

The likelihood of changing driving behaviour by looking at pictograms was also investigated, by using a scale ranging from very unlikely to very likely. The likelihood to change driving behaviour is significantly higher (p-value = 0.022) with the rating model pictograms than with the triangle model. Figure 6 represents the likelihood to change driving behaviour according to the category of the pictogram. It is shown that, the higher the category (or risk level) the bigger the likelihood to change driving behaviour and that, respondents who saw category 1 pictograms are significantly more likely to change their behaviour with the triangle model than with the rating model (p-value = 0.004).

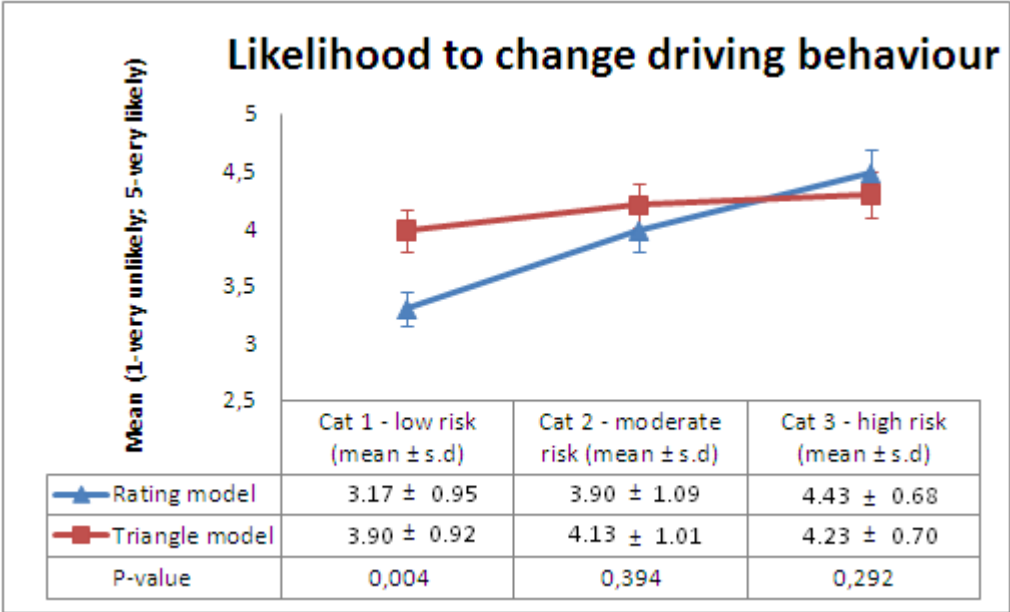


Figure 6: Respondents’ likelihood to change driving behaviour was assessed by asking the following question: “How likely would it be for you to change your driving behaviour if you would be taking a medicine with such a pictogram?” Every dot represents the mean likelihood value of 30 participants belonging to each category of the rating and triangle models pictogram

The respondents’ likelihood to change driving behaviour was assessed by asking the following question: “How likely would it be for you to change your driving behaviour if you would be taking a medicine with such a pictogram?” Every dot represents the mean likelihood value of 30 participants belonging to each category of the rating and triangle models pictogram.

Participants (36.3%; n = 270) stated they would be likely to change their driving behaviour by driving less frequently. No statistically significant differences (p-value = 0.100) were found between both types of models (figure 7). However, a statistically significant difference was found in category 1 pictograms (p-value = 0.037). Similarly to what was found with the likelihood to change behaviour, respondents who saw category 1 pictograms significantly drive less with the triangle model than with the rating model.

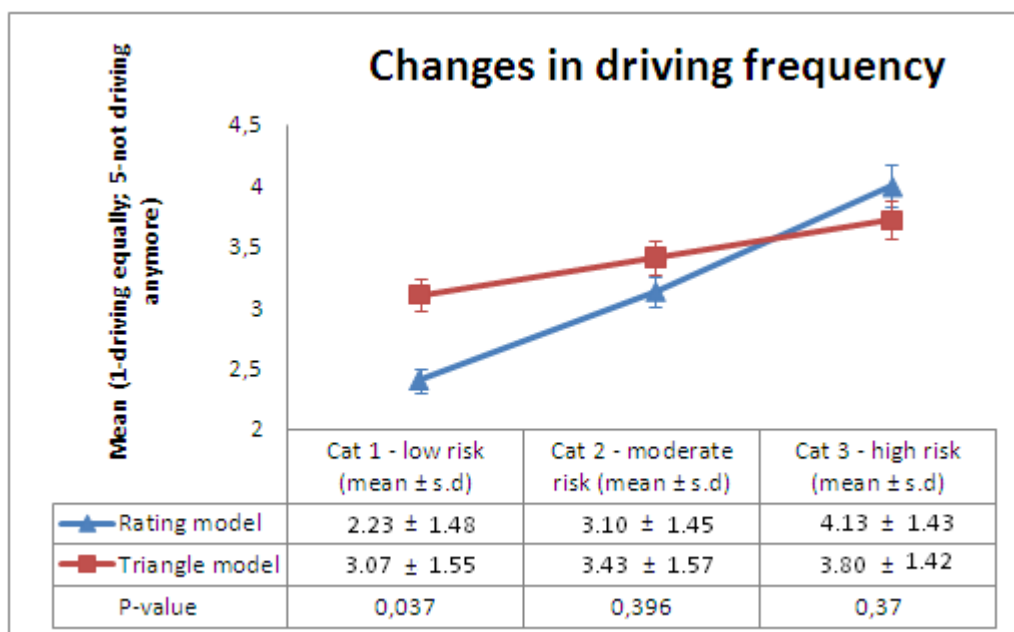


Figure 7: Respondents' changes in driving behaviour (frequency) was assessed by asking the following question: "Suppose you are taking a medicine with this pictogram labelled on the box. How often you would drive?". Every dot represents the mean change in driving behaviour value of 30 participants belonging to each category of the rating and triangle models pictogram

The respondents' changes in driving behaviour (frequency) were assessed by asking the following question: "Suppose you are taking a medicine with this pictogram labelled on the box. How often you would drive?". Every dot represents the mean change in driving behaviour value of 30 participants belonging to each category of the rating and triangle models pictogram.

40.7% of the respondents (n = 270), would change their driving behaviour by not driving anymore. Refrain from driving is advised whenever a category 3 medicine is prescribed. 60% (n = 90) of the respondents who first saw category 3 pictograms from the rating model would not drive anymore, against 43.3% of those who saw the homologue triangle model.

All pictograms (different categories from the two models) were found to be clear, informative, easy, understandable, not complex, and not ambiguous, as it is shown in table 4. For all deterrents, category 2 pictograms had lower mean scores than other categories. Education level did not influence respondents evaluation of the pictograms (p-value = 0.136).

Table 4: Mean scores (± standard deviation) for the evaluation of the pictograms. For each characteristic, a 7 point Likkert scale was used (1 – negative; 7 – positive).

	Rating model without side-text			Rating model with side-text			Triangle model with side-text		
	Cat 1	Cat 2	Cat3	Cat 1	Cat 2	Cat3	Cat 1	Cat 2	Cat3
Unclear - clear	5.73 (±1.55)	5.23 (±1.65)	6.37 (±1.22)	5.57 (±1.43)	5.13 (±1.55)	6.20 (±1.40)	4.83 (±1.82)	4.63 (±1.96)	5.37 (±1.52)
Not informative - informative	4.97 (±1.59)	5.13 (±1.57)	5.57 (±1.69)	5.27 (±1.62)	5.07 (±1.08)	6.07 (±1.28)	5.03 (±1.56)	4.77 (±1.87)	5.50 (±1.28)
Difficult - easy	5.77 (±1.38)	5.63 (±1.33)	6.10 (±1.49)	5.87 (±1.38)	5.87 (±1.07)	6.47 (±0.97)	5.83 (±1.17)	5.70 (±1.53)	5.97 (±1.22)
Not understandable - understandable	5.77 (±1.28)	6.13 (±0.94)	6.20 (±1.45)	5.87 (±1.31)	5.90 (±1.12)	6.40 (±1.04)	5.57 (±1.22)	5.57 (±1.32)	5.90 (±1.21)
Complex – not complex	5.93 (±1.23)	5.83 (±1.39)	6.30 (±1.42)	5.90 (±1.32)	5.77 (±1.22)	6.40 (±1.10)	5.93 (±0.98)	5.93 (±1.33)	6.13 (±1.11)
Ambiguous – Unambiguous	5.67 (±1.21)	5.27 (±1.80)	6.17 (±1.51)	5.53 (±1.59)	5.33 (±1.47)	5.83 (±1.58)	5.70 (±1.32)	5.70 (±1.73)	5.77 (±1.63)

Experiment 2

Respondents were asked which one of the models would better explain the side-text (that differs depending on the category) and which one of the pictograms would better show the levels of impairment. Table 5 illustrates participants' preferences, according to their age, gender, starting pictogram and education level.

Table 5: Participants pictogram preferences for explaining a side-text and levels of impairment

	Preference for understanding the warning in the side-text			Preference for showing the levels of impairment		
	Rating Model	Triangle Model	P-value	Rating Model	Triangle Model	P-value
<i>Category 1</i>	76.7%	23,3%	<0.001	86.7%	13.3%	<0.001
<i>Category 2</i>	81.1%	18.9%	<0.001	84.4%	15.6%	<0.001
<i>Category 3</i>	65.6%	34.4%	<0.001	76.7%	23.3%	<0.001
<i>Total</i>	74.1%	25.6%	<0.001	82.6%	17.4%	<0.001

A correlation between age and preference for one of the pictograms was found: older participants were more in favour of the triangle model than younger participants, who prefer the rating model (figure 8).

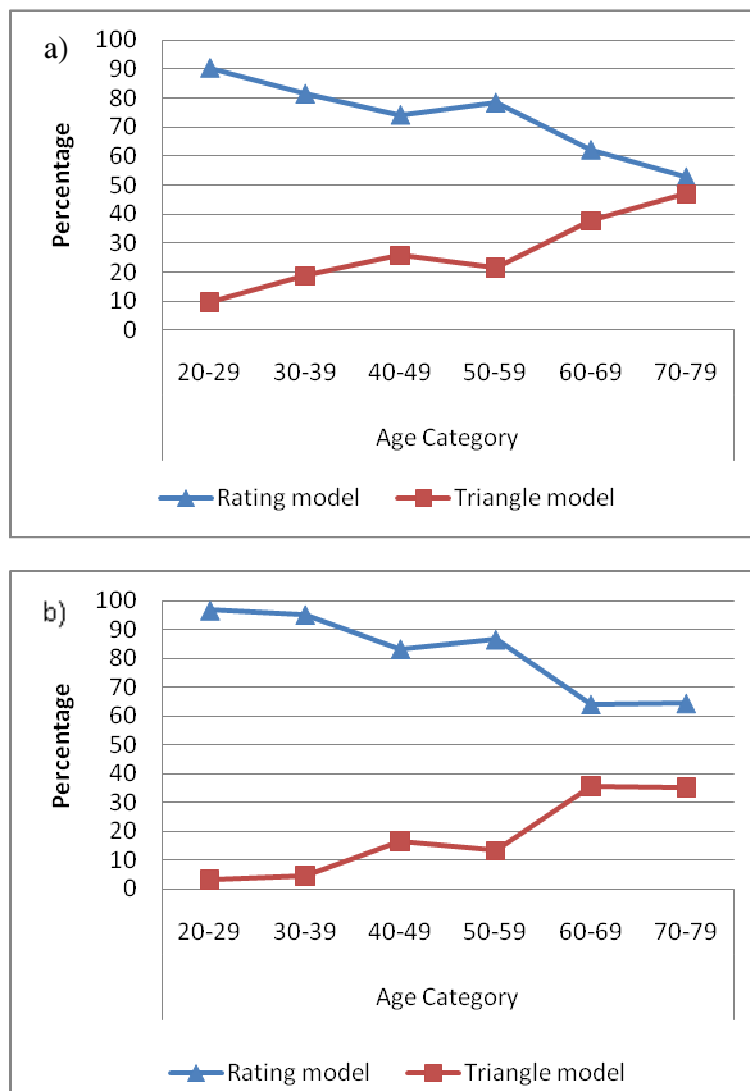


Figure 8: Participants' preference for a certain pictogram according to their age. a) Preferred pictogram for explaining better the side-text. b) Preferred pictogram to show better levels of impairment.

5.3.4 Discussion

The pictograms that were compared were effective in communicating risk. Respondents who participated in this study were able to recognize the risk of driving under the influence of medicines and showed their intention to change their driving behaviour by driving less frequently. For the rating model pictogram a direct correlation was shown between the likelihood of changing driving behaviour and the level of impairment of a medicine. The added value of the side-text was demonstrated.

Respondents had a high education level and were well aware of the fact that medicines can influence both reaction time and driving ability. Pharmacists were the preferable source of information in relation to receiving information about medicines.

Both pictograms, rating and triangle models, seemed to be eye-catching. This is an important factor because it is the first step to catch patients' attention which might stimulate patients to attend to the information that is on the pictogram (Davis et al., 2003). Respondents were able to interpret correctly the meaning of the pictogram, regardless of the category. It was considered that the correct interpretation needed to focus on risk in traffic (minor, moderate or severe risk). From the answers that were given, those who looked at the rating model pictograms gave more answers related to risk than those who looked at the triangle model. This could be due to the fact that the rating model has a small line of text stating "your risk in traffic". The authors believe that the sentence is of relevance to the correct interpretation of the pictogram. This line of text might also have contributed to the better estimation of danger that was associated with the rating model. Higher risk categories (category 2 and 3) were significantly more dangerous than the homologue from the triangle model. However, the lower category (category 1) of the triangle model had a higher mean score for the estimation of danger than the same category from the rating model. This could be due to the fact that the triangle model does not make any reference to the number of categories, which means that it is difficult to perceive the exact risk.

The risk message associated with both pictorial models (risk of driving) was well understood by the respondents as the intention to change driving behaviour, by driving less frequently, was mentioned by the majority of the respondents. A direct and significant correlation between likelihood to change driving behaviour and category was seen with the rating model: the higher the risk, the bigger the likelihood to change driving behaviour. As mentioned before this is believed to be due to the fact that the triangle model stands as a single pictogram, not giving the idea of the total range of categories and, therefore, missing the risk concept as a whole.

Respondents found both pictograms clear. However, for all three categories of risk, the rating model was found to be significantly clearer than the triangle model. The presence of all categories of risk that exist and the text "your risk in traffic" might be a reasonable explanation for this fact. In general, both pictograms were classified as informative, easy, understandable, not complex, and not ambiguous, meaning that pictograms were well designed. However, category 2 pictograms were not so well accepted, as category 2 pictograms had lower score rates. Considering that a great proportion of the medicines fell in this category, it is of great importance that category 2 pictograms have a message that leaves no doubt.

With no doubts, the rating model pictogram was, in respondents' opinion, the one explaining better the side-text that was shown as well as the levels of impairment. Despite the rating model was always preferred, the elderly respondents shown preference for the triangle model. It could be hypothesised that the triangle model has a more conservative design. A triangle with a car with a traffic-light-like colour system background seems to be enough to transmit the warning message to elderly patients.

The results of this study should be considered in the light of some strengths and limitations. The study population had a higher education level which could have contributed to the correct interpretation of the pictograms' message and to the relatively degree of acceptance. Pictograms are often used as a message vehicle for low literate populations. Therefore, it is important to make sure that patients with low education levels can understand the risk message. However, these pictograms are targeted to those who drive which certainly imply a certain level of education and literacy.

There are several studies that show the relevance of pictograms in health care (Dowse & Ehlers, 2001; Dowse & Ehlers, 2005; Hill & Roslan, 2004; Houts et al., 1998; Houts et al., 2001; Houts et al., 2006; Katz et al., 2006; Lemmon & Hyman, 2006; Mansoor & Dowse, 2004; Morrell et al., 1990; Ngoh & Shepherd, 1997; Sorfleet et al., 2009; Wolf et al., 2006). Still, not so much can be retrieved from the

field of medicines and driving (Veldhuijzen et al., 2006). For that reason, the DRUID partners believe in the novelty of the findings and are confident that the implementation of pictograms related with the influence of medicines on driving ability will be a substantial contribution to campaign development.

5.4 Spanish study

5.4.1 Aim

The aim of the Spanish study was to evaluate i) the comprehensibility of the triangle model and the rating model pictograms (with and without side-text) in communicating the risk associated with driving impairing medicines to patients; ii) the intention to change driving behaviour by looking at these pictograms; iii) to assess patients' preference: Comparison between the Rating model and the Triangle model, both with side-text (Study 1); Comparison between the Rating model with side-text and the Rating model without side-text (Study 2).

5.4.2 Methods

Target population

The target population was made up of "health service users". Throughout the current text, they shall be referred to as "patients". However, it should be taken into account that what we really mean by this term is people who come into contact with the National Health Service through Primary Care, Hospital-Specialized Attention or as consumers in pharmacies.

The "health service users" included in the study correspond to three different health service levels: i) Pharmacies; ii) Primary Care; iii) Hospital-Specialized Attention. The study was aimed at both patients with a driving license and those without.

Sample size

The study included a total of 736 patients. 541 patients were included in the Study 1, which compared the triangle-model pictogram and the rating-model pictogram. Study 2, which compared the rating-model pictogram, with and without text, included 195 patients.

Design

To evaluate "The comprehensibility of the triangle model and the rating pictogram (with and without side-text) in communicating the risk associated with driving impairing medicines to patients" and "The intention to change driving behaviour by looking at these pictograms" (first and second objectives), the answers about the first pictogram shown were used (annex 1, p. 129). Approximately one third of the sample was shown each one of the three DRUID categories (Categories I, II and III). This same proportion was maintained for each of the models of pictogram (triangle model with side-text and rating model pictogram with and without side-text). ISO 9186-1:2007 was the reference for testing the comprehensibility of the different pictogram models.

Both in Study 1 (Comparison between the Rating model and the Triangle model (both with side-text) and Study 2 (Comparison between the Rating model with side-text and the Rating model without side-text), on evaluating the preference for one model of pictogram or the other, the possible influence of the order in which they were shown was considered. In order to avoid this possible effect, the sample was stratified in such a way that, for each category and model of pictogram, half of those interviewed were first shown the category and model that was shown second to the other half.

Setting

- 2.
- 3.
- 4.

The study was carried out in different health care environments within the Province of Valladolid.

The patients were interviewed in:

1. Primary Care facilities by nursing staff,
2. In pharmacies by trained survey personnel,
3. In Specialist Attention (pre-anesthesia visits in the "Hospital Clínico" in Valladolid) by trained survey personnel.

Questionnaire

A questionnaire was created for this purpose, which can be seen in annex 1. It has been analysed as was agreed by the partners of task 7.4.

Medical Ethical approval

The study was approved by the Clinical Research Ethics Committee of the Faculty of Medicine at the University of Valladolid and by the Research Commission of the “Hospital Clínico Universitario” of Valladolid. All the health professionals and patients were adequately informed of the nature of the study, participated voluntarily and their anonymity was preserved.

Statistical analysis

The data gathered from the study have been recorded in a database of the statistical package PASW Statistics 18. The results are shown as mean \pm standard deviation and/or median for the quantitative variables and percentages for the categorical variables. Also, respectively, the T-test and the Squared Chi test have been used to analyze the results. Values of $P \leq 0.05$ were considered statistically significant.

Conflict of interests

The authors of the Spanish study declare there is no conflict of interests.

Acknowledgments

The authors of the Spanish study would like to thank the patients and health professionals (physicians, pharmacists and nursing staff) involved in the study for their participation. We would also like to thank the health authorities (“Junta de Castilla y León”, “Consejería de Sanidad”, “Sacyl”, “Ministerio de Sanidad y Consumo – Agencia Española de Medicamentos y Productos Sanitarios (AGEMED)”), the Primary Health Care Centers, the “Hospital Clínico Universitario” of Valladolid, the “Colegio Oficial de Farmacéuticos de Valladolid”, SEMT and SET for their collaboration at all times.

5.4.3 Results

The study included a total of 736 patients. Study 1, which compared the triangle-model pictogram and the rating-model pictogram included 541 patients. Study 2, which compared the rating-model pictogram, with and without text, included 195 patients.

Table 6 shows the distribution according to gender, educational level and mean age of the patients included in the study according to the pictogram they were shown first, independently of whether they were from study 1 or 2. As the Spanish study has included both drivers and non-drivers, table 6 shows the distribution according to whether or not they had a driving license.

Table 6: Characteristics of the respondents, stratified per pictogram

		Triangle Model (with side-text) N (%)	Rating Model (with side-text) N (%)	Rating Model (without side-text) N (%)
Gender	Male	140 (53.2)	177 (47.1)	48 (49.5)
	Female	123 (46.8)	199 (52.9)	49 (50.5)
Educational level	Did not finish primary school	4 (1.5)	13 (3.5)	1 (1.0)
	Finished primary school	79 (30.0)	139 (37.1)	36 (37.1)
	Finished secondary school	46 (17.5)	44 (11.7)	5 (5.2)
	Completed “A” level (age 18)	58 (22.1)	73 (19.5)	29 (29.9)
	University degree/diploma	76 (28.9)	106 (28.3)	26 (26.8)
Driver licence	Yes	240 (91.3)	324 (86.2)	79 (81.4)
	No	23 (8.7)	52 (13.8)	18 (18.6)
Age: Mean \pm SD (N)		49.03 \pm 14.20 (263)	49.85 \pm 14.64 (376)	50.04 \pm 13.88 (97)
Total		263 (100.0)	376 (100.0)	97 (100.0)

The meaning the pictogram on driving has for the patient

To analyse the meaning the patient gives to the pictogram on driving on the medicine packaging, all the patients were asked the following question: **In your opinion, what is the meaning for you of the pictogram on driving?**

The question was formulated openly and the answers were then codified into the 7 levels proposed in the norm ISO 9186:

- Level 1:** Correct understanding of the symbol is certain (estimated probability of correct understanding over 80%);
- Level 2:** Correct understanding of the symbol is very probable (estimated probability of correct understanding between 66% and 80%);
- Level 3:** Correct understanding of the symbol is very probable (estimated probability of correct understanding between 50% and 65%);
- Level 4:** The meaning which is stated is the opposite to that intended;
- Level 5:** Any other response;
- Level 6:** The response given is “Don’t know”;
- Level 7:** No response is given.

The criterion established for understanding was: “It may negatively affect driving or put the driver at risk” + “reference to the definition of each category”

The definition is different for each of the three categories, but the same for each of the three types of pictogram.

- Category I: “**Be careful:** Read carefully the patient leaflet before driving”;
- Category II: “**Be very careful:** Take advice from a physician or pharmacist before driving”;
- Category III: “**Danger: do not drive:** seek medical advice before driving again”.

Table 7 shows the answers obtained for each of the pictograms.

Table 7: The meaning the pictogram on driving has for the patient, according to pictogram type

	Triangle Model (with side-text) N (%)	Rating Model (with side-text) N (%)	Rating Model (without side-text) N (%)
Level 1: Correct understanding (p>80%)	13 (4.9)	23 (6.1)	0 (0.0)
Level 2: Correct understanding (66%<<80%)	139 (52.9)	192 (51.0)	80 (82.5)
Level 3: Correct understanding (50%<<65%)	74 (28.1)	118 (31.4)	12 (12.4)
Level 4: Opposite meaning	6 (2.3)	1 (0.3)	2 (2.1)
Level 5: Any other answer	18 (6.8)	18 (4.8)	1 (1.0)
Level 6: Don't know	3 (1.1)	17 (4.5)	2 (2.1)
Level 7: No response is given	10 (3.8)	7 (1.9)	0 (0.0)
Total	263 (100.0)	376 (100.0)	97 (100.0)

Percentages are calculated for all level except cases where no response is given. Figure 9 shows the distribution of responses by patients for the first 6 levels of the norm ISO 9186. As indicated in the norm ISO 9186, these percentages have been calculated excluding the no response cases (category 7).

Having grouped together the correct answers with a probability of above 50%, the comprehensibility of the three models of pictogram is Good: 90.2% in the group of the rating-model pictogram with text, 89.3% in the triangle-model pictogram, and 94.8% for the rating-model pictogram without side text.

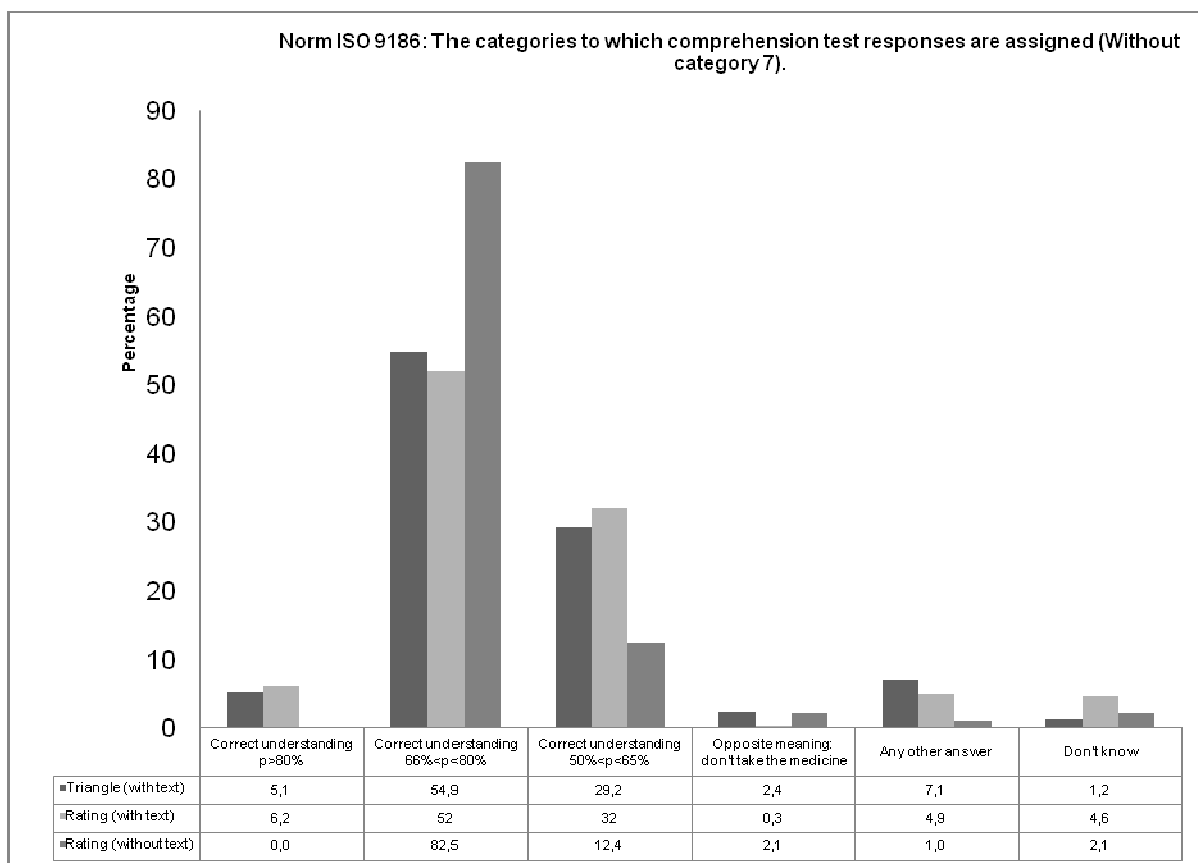


Figure 9: Norm ISO 9186: Comprehension test

Overall scores for each pictogram were obtained by weighting and summing the percentages of responses in the different categories. Weighting algorithm (Percentage X Weight):

- % Category 1 X 1.0
- % Category 2 X 0.75
- % Category 3 X 0.50
- % Opposite X -1.0
- % Wrong X 0.0

Table 8 shows comprehension scores for the three models of pictogram after summing weighting percentages to obtain comprehension score (the percentage of total comprehension).

Table 8: Comprehension scores for the three models of pictogram

	Weight	Triangle Model (with side-text)		Rating Model (with side-text)		Rating Model (without side-text)	
		%	% score	%	% score	%	% score
Correct understanding (p > 80 %)	1.00	5.1	5.1	6.2	6.2	0.0	0.0
Correct understanding (p: 66 %- 80 %)	0.75	54.9	41.2	52.0	39.0	82.5	61.9
Correct understanding (p: 50 %- 65 %)	0.50	29.2	14.6	32.0	16.0	12.4	6.2
Opposite meaning	-1.00	2.4	-2.4	0.3	-0.3	2.1	-2.1
Wrong	0.00	8.3	0.0	9.5	0.0	3.1	0.0
% Comprehension score			58.5		60.9		66.0

The International Organization for Standardization (norm ISO 9186) recommends a critical level of correct comprehension of at least 67% for signs and symbols. Thus, none of these three pictograms would pass the comprehensibility criterion, the rating-model without side text being the closest to this score (66.0%).

Estimation of the level of danger

The estimation of the level of danger represented by the pictogram model was studied by means of a 4 point Likert scale (0= very harmless to 3 = very dangerous). As shown in table 9 for each category (I to III), the mean scores do not differ within the three types of pictograms. In general, an increase in the risk perceived by the patients (increase in the average score) can be seen as the category of the medicine increases, for both the triangle-mode pictogram and the rating-model pictogram (either with or without side-text). However, as can be seen in figure 10, relatively higher scores tend to be given in categories I and II (average scores over 1.00 and 2.00 points respectively) and to underestimate the risk/danger in category III. Even with this effect, significantly different scores concerning the danger can be seen in all three models of pictogram between categories I and II. The same can be seen between categories II and III, except for the triangle–model pictogram, in which the average score given to the risk factor of categories II and III do not differ in any significant way (table 9).

Table 9: How would you evaluate the degree of influence of this medicine on driving, i.e., the risk you run using this medicine when driving?

	Category I		Category II		Category III		(cat I/II) T [95% IC]; p	
	N	Mean±SD	N	Mean±SD	N	Mean±SD	(cat II/III) T [95% IC]; p	
Triangle Model (with side-text)	81	1.88±0.75	84	2.54±0.65	80	2.69±0.57	-6.06 [-0.87,-0.44]; p<0.0001	
							1.60 [-0.34,0.04]; p>0.05	
Rating Model (with side-text)	130	1.78±0.77	111	2.35±0.63	107	2.77±0.52	-6.31 [-0.74,-0.39]; p<0.0001	
							-5.31 [-0.57,-0.26]; p<0.0001	
Rating Model (without side-text)	31	1.58±0.67	31	2.39±0.62	34	2.76±0.43	-4.93 [-1.13, -0.48]; p<0.0001	
							-2.84 [-0.64, -0.11]; p<0.01	
Total sample	242	1.79±0.75	226	2.42±0.64	221	2.74±0.53		
	F= 1.75; p>0.05		F= 2.09; p>0.05		F= 0.57; p>0.05			

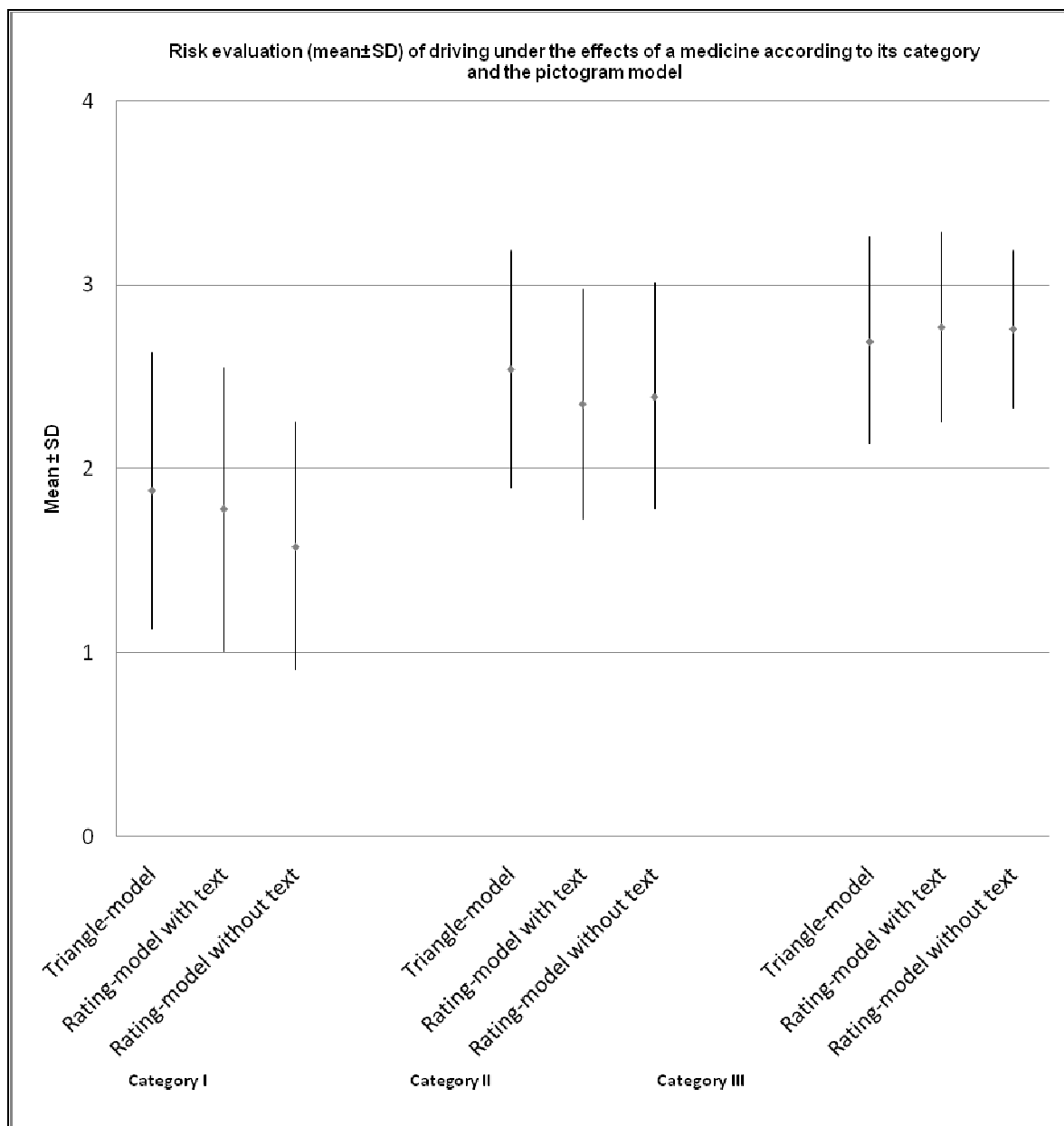


Figure 10: Risk of driving under the effects of a medicine (Mean±SD) according to its category.

Intended change of behaviour

Two questions in a 5 points Likert scale was used to analyse participants' intention to change their driving behaviour.

Question 1: "Supposing you were prescribed this medicine which has the pictogram concerning driving on the packaging. How frequently would you drive during the period in which you were taking the medicine?"

The interviewed patients were asked the following question: "Supposing you were prescribed this medicine which has the pictogram concerning driving on the packaging. How frequently would you drive during the period in which you were taking the medicine?" The question had 5 possible answers: the first answer would imply no change in attitude –"With the same frequency"- while the other four present a growing degree of change –"Less frequently"; "A lot less frequently"; "I would hardly drive at all" and "I would not drive at all".

There were significant differences in the answers concerning the change in frequency of driving depending on the different pictograms ($\chi^2_{(8)}=19.393$; $p<0.05$) (table 10, figure 11).

Comparing the answers given for each pictogram, significant differences can be seen between the triangle-model pictogram and the rating-model pictogram without text ($X^2_4=10.225$; $p<0.05$) and between the rating-model pictogram with and without text ($X^2_4=15.836$; $p<0.01$). However, no significant differences were found between the triangle-model pictogram and the rating-model pictogram with side-text ($X^2_4=3.596$; $p>0.05$). Thus, the triangle-model pictogram and the rating-model pictogram, both with side-text would have a similar influence at the time of deciding whether to reduce the frequency of driving while taking a medicine with one of these pictograms on the packaging; while the rating-model pictogram without side-text would, on the evidence of the results, have a significantly lower influence.

Table 10: Supposing you were prescribed this medicine which has the pictogram concerning driving on the packaging. How frequently would you drive during the period in which you were taking the medicine?

	With the same frequency N (%)	Less frequently N (%)	A lot less frequently N (%)	I would hardly drive at all N (%)	I would not drive at all N (%)
Triangle Model (with side-text)	34 (13.4)	62 (24.4)	39 (15.4)	60 (23.6)	59 (23.2)
Rating Model (with side-text)	45 (12.2)	88 (23.8)	61 (16.5)	70 (18.9)	106 (28.6)
Rating Model (without side-text)	26 (27.1)	24 (25.0)	10 (10.4)	18 (18.8)	18 (18.8)
Total	105 (14.6)	174 (24.2)	55 (7.5)	148 (20.6)	183 (25.4)
$X^2_8=19.393$; $p<0.05$					

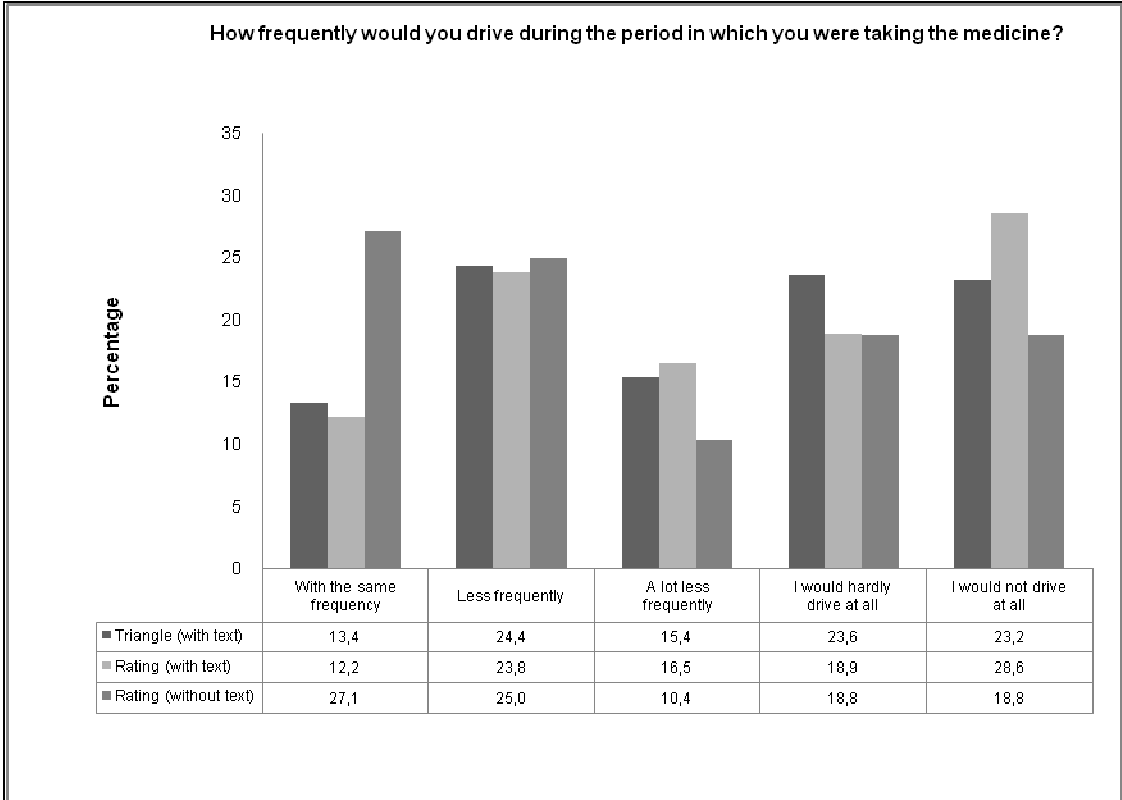


Figure 11: How frequently would you drive during the period in which you were taking the medicine?

Question 2: What are the probabilities that you would change your driving habits if you were prescribed or dispensed a medicine with this pictogram about medicines and driving on the packaging?

No significant differences were observed in the probability of changing driving habits when the interviewee was prescribed or dispensed a medicine with the pictogram, irrespective of the type of pictogram (table 11 and figure 12).

Table 11: What are the probabilities that you would change your driving habits if you were prescribed or dispensed a medicine with this pictogram about medicines and driving on the packaging?

	Very improbable N (%)	Improbable N (%)	Neither probable/nor improbable N (%)	Probable N (%)	Very probable N (%)
Triangle Model (with side-text)	12 (4.7)	23 (8.9)	16 (6.2)	88 (34.1)	119 (46.1)
Rating Model (with side-text)	15 (4.0)	19 (5.1)	31 (8.3)	148 (39.6)	161 (43.0)
Rating Model (without side-text)	2 (2.1)	9 (9.3)	8 (8.2)	37 (38.1)	41 (42.3)
Total	29 (4.0)	51 (7.0)	55 (7.5)	273 (37.4)	321 (44.0)
$\chi^2_{8}=7.826; p>0.05$					

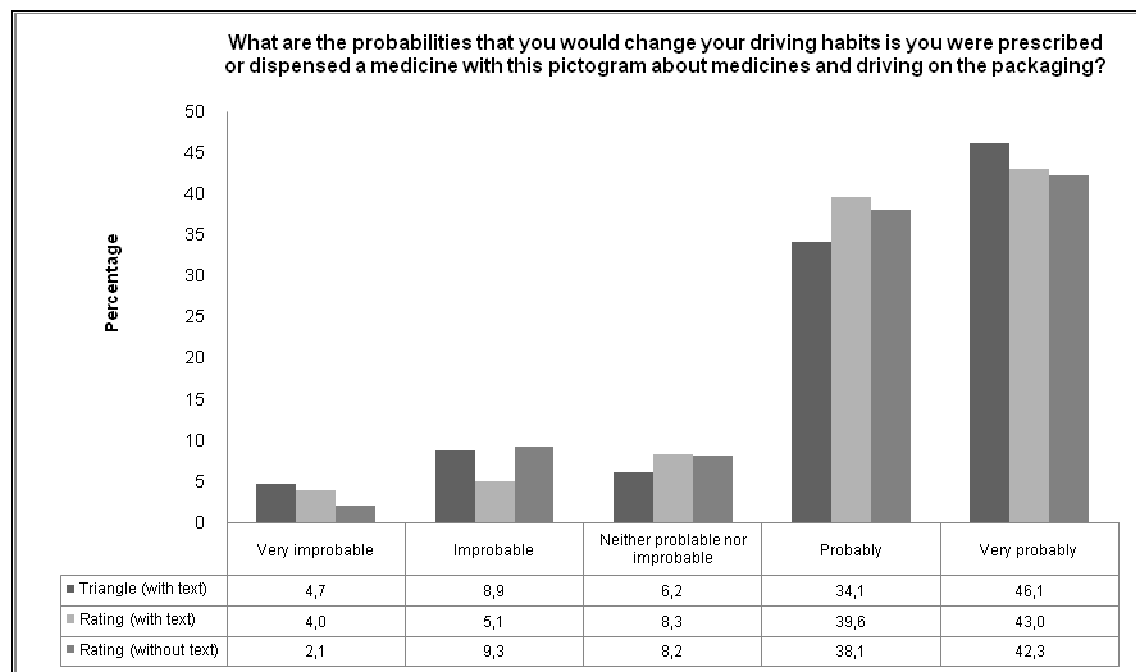


Figure 12: Probability of changing driving habits according to the type of pictogram on the prescribed/dispensed medicine

Evaluation of the pictograms

A 10-point scale was used to evaluate the pictograms in four parameters:

- Utility: 1 = unnecessary to 10 = useful;
- Level of information: 1 = not informative to 10 = informative;
- Understandability: 1 = not understandable to 10 = understandable;
- Complexity: 1 = complex to 10 = not complex.

Table 12 shows the mean scores (\pm SD) given to different aspects of the pictogram (utility, information, understandability and simplicity) for each of the types of pictogram. Of these characteristics, the best score was, in all three cases, for utility (8.37 ± 1.75 points for the triangle-model, 8.31 ± 1.74 for the rating-model with side-text and 7.75 ± 1.95 for the rating-model without side-text).

Table 12: Evaluation of the pictograms by pictogram type

	Triangle Model (with side-text)		Rating Model (with side-text)		Rating Model (without side-text)		F; p
	N	Mean±SD	N	Mean±SD	N	Mean±SD	
Utility	243	8.37±1.75	345	8.31±1.74	95	7.75±1.95	4.57; p<0.05
Information	241	8.11±1.84	346	8.10±1.82	95	7.40±2.00	5.94; p<0.005
Understandability	239	7.91±2.00	344	7.87±1.98	95	7.20±2.09	4.86; p<0.01
Simplicity	240	7.88±2.05	345	7.75±2.10	95	7.20±2.09	3.76; p<0.05

Comparing the replies given for each pictogram (Student's t test for independent samples), no significant differences were found between the average scores for any of the evaluated aspects of the triangle-model pictogram and the rating-model pictogram (both with side-text). Comparing the triangle-model pictogram and the rating-model pictogram without text, significant differences ($p<0.05$) were observed in the averages of all the scores; all of them being favorable (highest scores) to the triangle-model pictogram. Comparing the rating-model pictogram with and without text, significant differences ($p<0.05$) were found in the average scores given to utility and level of information; favorable to the rating-model pictogram with side-text. Therefore, it seems that it is the text rather than the design which increases the four scores significantly.

Pictograms preference

STUDY 1: Comparison between the Rating model (with side-text) and the Triangle model (with side-text)

A total of 541 questionnaires were done for this study. After the questions about the first pictogram, whose answers are shown in the previous paragraphs, the interviewee was shown a second pictogram and his/her preference for one or the other was analysed, taking into account two aspects, depending on their opinion:

- i) **Question 1:** Which of the two stickers helps you to understand the text better? and,
- ii) **Question 2:** Which of the two stickers gives you the best insight into the degree of impairment?

Question 1: For the question "Which of the two stickers helps you to understand the text better?" 517 replies were obtained. 63.4% of the answers ($n=328$) pointed to the rating-model (with side-text) sticker as the best option, while the remaining 36.6% ($n=189$) preferred the triangle model (with side-text) ($\chi^2=3.932$; $p<0.05$).

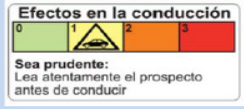

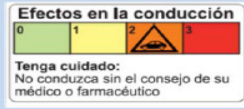

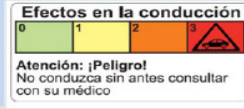
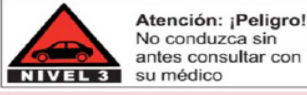

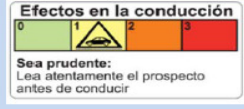




Which of the two stickers helps you to understand the text better?			
	First		Second
Group I (a) (N = 96)	 74,0% (N= 71)		 26,0% (N= 25)
Group II (a) (N = 79)	 57,0% (N=45)		 43,0% (N= 34)
Group III (a) (N = 88)	 45,5% (N= 40)		 54,5% (N= 48)
Group I (b) (N = 85)	 28,2% (N=24)		 71,8% (N=61)
Group II (b) (N = 85)	 45,9% (N= 39)		 54,1% (N= 46)
Group III (b) (N = 84)	 22,6% (N= 19)		 77,4% (N= 65)

Figure 13: “Which of the two stickers helps you to understand the text better?” Answer percentages

Question 2: For the question “Which of the two stickers gives you the best insight into the degree of impairment?” 511 replies were obtained, of which 69.1% (n= 353) pointed to the rating-model (with side-text) pictogram as the best option, while the remaining 30.9% (n=158) preferred the triangle model (with side-text) ($X^2=10.992$; $p<0.001$).










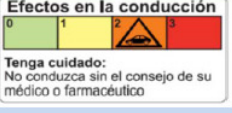

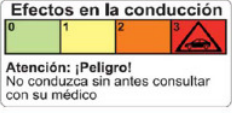
Which of the two stickers gives you the best insight into the degree of impairment?				
	First		Second	
Group I (a) (N = 98)		74,5% (N= 73)		25,5% (N= 25)
Group II (a) (N = 78)		61,5% (N=48)		38,5% (N= 30)
Group III (a) (N = 84)		48,8% (N= 41)		51,2% (N= 43)
Group I (b) (N = 84)		21,4% (N=18)		78,6% (N=66)
Group II (b) (N = 83)		36,1% (N= 30)		63,9% (N= 53)
Group III (b) (N = 84)		14,3% (N= 12)		85,7% (N= 72)

Figure 14: “Which of the two stickers gives you the best insight into the degree of impairment?” Answer percentages

We have performed logistic regression analysis to identify which of the sociodemographic characteristics of the patient (age, gender, educational level, and having a driving license or not) has an influence on the opinion given.

Regarding Question 1: Which of the two stickers helps you to understand the text better? Those who have a driving license were more likely (OR= 2.011, 95% IC 1.074-3.765] to select the rating-model pictogram.

Regarding Question 2: Which of the two stickers gives you the best insight into the degree of impairment?, those who have a driving license (OR= 2.682, 95% IC 1.405-2.704) and those with a higher educational level (OR= 1.288, 95% IC 1.090-1.523), were more likely to select the rating-model pictogram. Showing a pictogram in second place (irrespective of which one it was) increased the probability of its being chosen (OR= 1.816, 95% IC 1.219-2.704).

STUDY 2: Comparison between the Rating model (with side-text) and the Rating model (without side-text)

A total of 195 questionnaires were carried out for this study. As with Study 1, after the questions concerning the first pictogram shown, the interviewee was shown a second pictogram and his/her preference for the first or second one was analyzed, taking into account two aspects, according to his/her opinion (as in Study 1):

- i) **Question 1:** Which of the two stickers helps you to understand the text better? and,
- ii) **Question 2:** Which of the two stickers gives you the best insight into the degree of impairment?

Question 1: For the question “Which of the two stickers helps you to understand the text better?” 189 answers were obtained, of which 97.4% (n= 184) pointed to the rating-model (with side-text) sticker as the best option and only the remaining 2.6% (n=5) pointed to the rating-model (without side-text) sticker ($X^2=5.082$; $p<0.05$).




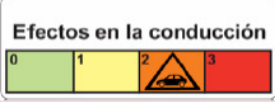
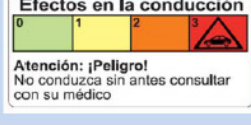
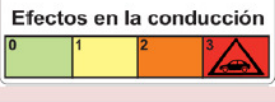
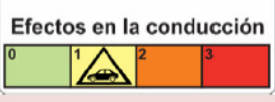
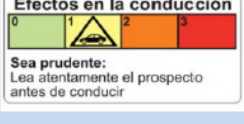
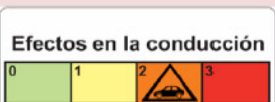
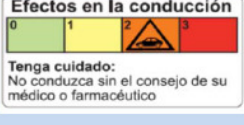
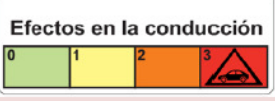

		Which of the two stickers helps you to understand the text better?		
		First	Second	
Group I (a) (N = 34)		100,0% (N= 34)		0,0% (N= 0)
Group II (a) (N = 30)		90,0% (N=27)		10,0% (N= 3)
Group III (a) (N = 31)		93,5% (N= 29)		6,5% (N= 2)
Group I (b) (N = 28)		0,0% (N= 0)		100,0% (N=28)
Group II (b) (N = 32)		0,0% (N= 0)		100,0% (N= 32)
Group III (b) (N = 34)		0,0% (N= 0)		100,0% (N= 34)

Figure 15: “Which of the two stickers helps you to understand the text better?” Answer percentages

Question 2: For the question “Which of the two stickers gives you the best insight into the degree of impairment?” 180 answers were obtained, of which 99.4% (n= 179) pointed to the rating-model (with side-text) pictogram as the best option and only the remaining 0.6% (n=1) pointed to the rating-model (without side-text) pictogram ($X^2=1.075$; $p>0.05$).

		Which of the two stickers gives you the best insight into the degree of impairment?		
		First	Second	
Group I (a) (N = 32)		96,9% (N= 31)		3,1% (N= 1)
Group II (a) (N = 27)		100,0% (N=27)		0,0% (N= 0)
Group III (a) (N = 28)		100,0% (N= 28)		0,0% (N= 0)
Group I (b) (N = 30)		0,0% (N=0)		100,0% (N=30)
Group II (b) (N = 31)		0,0% (N=0)		100,0% (N= 31)
Group III (b) (N = 32)		0,0% (N= 0)		100,0% (N= 32)

Figure 16: “Which of the two stickers gives you the best insight into the degree of impairment?” Answer percentages

5.4.4 Discussion

If we group together the replies considered correct (over 50% probability), the understandability of the three models of pictogram may seem to be good (for the rating-model pictogram with text: 90.2%, for the triangle-model pictogram: 89.3%, and for the rating-model pictogram without side text: 94.8%), in fact, none of them surpasses the understandability criteria of the Norm ISO 9186 (overall score >67%), the best option being the rating-model pictogram without side-text (overall score = 66%).

According to the scores given to the estimation of the level of danger of the pictograms, an increase in the risk perceived by the patients (increase in the mean scores) in line with the increase in the category of the medicine can be seen, both for the triangle-model pictogram and the rating-model pictogram (either with or without side-text). The triangle-model (with side-text) pictogram would be the least adequate for distinguishing between categories II and III (the mean score given to the risk of these categories does not differ significantly).

The triangle-model pictogram and the rating-model pictogram, both with side-text, would have a similar influence at the time the patient is deciding whether to reduce driving frequency while taking a medicine with one of these pictograms. On the other hand, the rating-model pictogram without side-text would, in view of the results, have significantly less influence

The rating-model pictogram and the triangle model pictogram did not differ regarding how patients evaluate the two pictograms with respect to Utility, Level of information, Understandability, and Complexity. However, both pictograms with text are better rated (have higher scores) by patients than the rating-model pictogram without text.

The studies on Pictograms preference showed that overall patients preferred the rating-model pictogram to the triangle-model pictogram, as well as the rating-model pictogram with text rather than this pictogram without text.

Having a driving license was associated with understandability of the text of the pictogram, while having a driving license, educational level and the order in which the pictograms are shown to the patients are associated with the reported insight of the patient's about the degree of impairment.

5.5 Overall conclusion

By carrying out these 2 separate studies with the same aims, it can be concluded that both the rating model and the triangle model were effective in communicating risk. Those who participated in the studies were able to recognize and understand the risk of driving under the influence of medicines and have shown their intention to change their driving behaviour by driving less frequently. The rating model pictogram showed a direct correlation between the likelihood of changing driving behaviour and the level of impairment of a medicine (category-related).

In both studies, the rating model pictogram was preferred over the triangle model pictogram.

Part II. Main DRUID results

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1 Introduction

The European Commission set up an ambitious target to increase road safety in the EU and to reduce road accidents fatalities by 50% by 2010 (White Paper). DRUID (Driving under the Influence of Drugs, Alcohol and Medicines) aimed to combat the problem of driving under the influence of psychoactive substances by providing a solid scientific base for European policy makers. It brought together experienced organisations in Europe to assemble a coordinated set of data resources and measures.

The DRUID consortium is composed of a total of 37 partners from 19 States (18 EC Member States and NO, see figure 17). As the majority of the participating institutions are members of FERSI they have a broad experience in road safety.

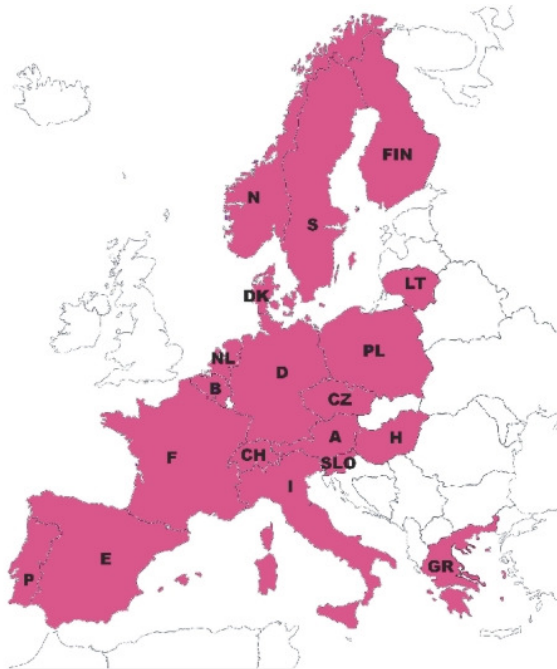


Figure 17: Geographic coverage of the EU project DRUID

DRUID is an integrated European research project which consisted of different sub-projects (Work Packages; see figure 18) that were aimed at different topics such as the prevalence and risk of psychoactive substances, enforcement, classification of medicines, rehabilitation of offenders and withdrawal of driving licenses (www.druid-project.eu) (D2.2.3 PART I p. 3).

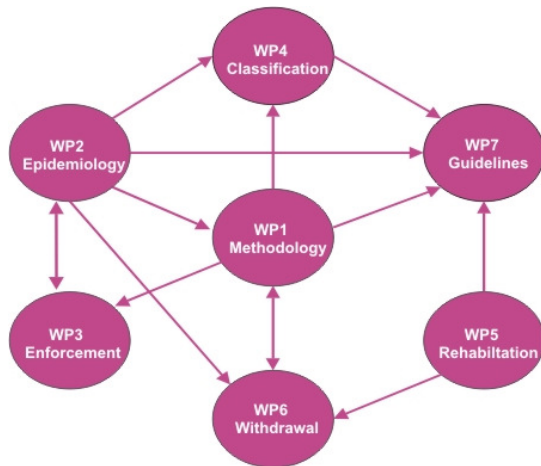


Figure 18: Overview of the different DRUID work packages

The objectives of the DRUID project are:

- “to conduct reference studies of the impact on fitness to drive for alcohol, illicit drugs and (psychoactive) medicines and give new insights to the real degree of impairment caused by psychoactive substances and their actual impact on road safety;
- to generate recommendations for the definition of analytical and risk thresholds;
- to analyse the prevalence of alcohol and other psychoactive substances in accidents and in general driving, set up a comprehensive and efficient epidemiological database;
- to evaluate "good practice" for detection and training measures for road traffic police allowing a legal monitoring of drivers;
- to establish an appropriate classification system of medicines affecting driving ability, give recommendations for its implementation and create a framework to position medicines according to a labelling system,
- to evaluate the efficiency of strategies of prevention, penalisation and rehabilitation, considering the difficulties of appropriate evaluation strategies for combined substance use and recommend "good practice";
- to define strategies of driving bans, combining the road safety objectives with the individual's need for mobility;
- to define the responsibility of health care professionals for patients consuming psychoactive substances and their impact on road safety, elaborate guidelines and make information available and applicable for all European countries” (DRUID TA p. 1f.).

2 Method

The summary of the main DRUID results is based on a review of the executive summaries and conclusion parts of finalized DRUID deliverables (WP1-7 until 07.09.2011) and the draft version of the DRUID case-control study (D2.3.5), presentations of the WP leaders at the DRUID general meeting (2010), input of the WP leaders to the coordinator for the annual periodic activity reports to the EC and the technical annex of the DRUID project. Outcomes in regard to legal limits (e.g. D1.4.2 “Methods of defining cut of values for zero tolerance”) could not be included in this report as these results will only be available at the end of the DRUID project (October 2011).

It was decided to separate the presentation of the main DRUID results into two main parts: (1) problem situation, which mainly focuses on input of WP1/2 and (2) countermeasures which is mainly summarizing results of WP3-7. Furthermore, a detailed evaluation of legal countermeasures from the perspective of criminology can be found in D1.4.1.

The authors of D7.3.2 provided a describing text and a summarizing overview table per WP. These texts and summaries were discussed in two rounds, first with the DRUID coordinator and WP7 partners (work sessions: 14.01.11 Madrid, 03.03.11 Brussels, 29.03.11 Thessaloniki, 23.05.11 Gent) and secondly with WP leaders and authors of main deliverables (via email until 07.09.11).

The reviewing WP leaders and main authors of the summarized WP texts were:

- Problem situation (WP1/2): Anja Knoche, Markus Schumacher (BAST); Inger Marie Bernhoft, Tove Hels (DTU), Sjoerd Houwing (SWOV), Kristin Thorsteinsdottir (LMU), Alain Verstraete and Sara-Ann Legrand (UGent);
- Enforcement (WP3): Sjoerd Houwing and Marjan Hagenzieker (SWOV);
- Classification (WP4): Javier Alvarez (UVa) and Han de Gier (RUGPha);
- Rehabilitation (WP5): Monika Pilgerstorfer (KfV), Sofie Boets and Uta Meesmann (IBSR);
- Withdrawal (WP6): Simone Klipp (BAST);
- Guidelines and risk communication (WP7): Han de Gier (RUGPha).

3 Problem situation and risk group characteristics (WP1/2)

The DRUID project (WP1/2) aimed at assessing the situation regarding the prevalence and risk of the use of alcohol, illicit drugs, and (psychoactive) medicines by drivers in Europe. Within WP2, two of the main investigations to obtain these insights were the DRUID roadside survey (D2.2.3) and the DRUID hospital study on seriously injured and killed drivers (D2.2.5) which were melded together in the DRUID case-control study (D2.3.5). These three investigations form the main base within this deliverable to scratch the problem situation (prevalence and risk) and risk group characteristics of driving under influence of alcohol (1), illicit drugs (2) psychoactive medicines (3).

This deliverable (D7.3.2) focuses on the general results assessing the situation in Europe, but since there is huge between-country variability in the results, any recommendation for national activities regarding, e.g., policy issues, enforcement, education or campaigns, should primarily be based on the results of the country reports, rather than on the general reports. Furthermore it should be taken into account, that the estimated EU prevalence means of the road side survey (D2.2.3) are based on the analyses of different body fluids. DRUID WP2 tried to compensate for this by using equivalent cut-offs to correct for differences in sample collection method. The presented prevalence values of the hospital studies are based on blood samples.

WP1 focused on experimental studies evaluating the effect of psychoactive substances on driving performance (e.g. D1.1.2a-c, D1.2.1, D1.2.2). A synthesis of the experimental and epidemiological results on risk estimates for single and combined use of psychoactive substances will be available at the end of the DRUID project (October 2011, D1.3.1). Furthermore, a detailed evaluation of legal counter measures can be found in D1.4.1. Recommendation on methods of defining cut-off values for per se legislation, are to be expected at the end of the DRUID project (D1.4.2).

In the following parts methodological information of the different DRUID studies in WP1/2 are summarized for more details see the according deliverables.

DRUID roadside survey (D2.2.3)

Within the DRUID roadside survey (D2.2.3), thirteen countries participated in a large scale prevalence study by conducting roadside surveys according to a general design. In total almost 50,000 randomly selected drivers participated between January 2007 and July 2009. In most countries the results are based on saliva samples (exceptions are: LT only blood and BE, IT, and NL saliva and blood samples). The non-response rate varied between 0% and 52%. The following table gives an overview of the number of included samples, the used body-fluid and the non-response rate per country. The prevalence of drivers tested positive for at least one psychoactive substance ranged between 2.32% (HU) and 15.01% (IT). An overview of the different illicit drug- and medication groups included in this study can be found in the annex 2. Table 13 presents an overview of the number of included samples, body-fluid, non-response rate and prevalence rate for all psychoactive substances of DRUID roadside survey. European means were estimated based on the prevalence of psychoactive substances in these thirteen different European countries. To estimate this means weight factors were used, based on the number of inhabitants of the EU countries (since data on driver kilometres were not available for all European countries) and on the European region that they represented.

Table 13: Overview of number of included samples, body-fluid, non-response rate and percentage of positive toxicological finding of DRUID roadside survey (D2.2.3)

Country	Number of included samples	Body fluid	Non-response rate	Toxicological finding positive
BE	2949	Saliva/blood	52%	10.65%
CZ	2037	Saliva	23%	2.80%
DK	3002	Saliva	5%	4.48%
ES	3174	Saliva	2%	14.85%
FI	3841	Saliva	48%	2.85%
HU	2738	Saliva	10%	2.32%
IT	1310	Saliva/blood	0%*	15.01%
LT	1264	Blood	24%	5.51%
NL	4822	Saliva/blood	5%	5.51%
NO	9236	Saliva	6%	2.97%
PL	4005	Saliva	1%	2.37%
PT	3965	Saliva	3%	9.99%
SE	6199	Saliva	38%	1.34**
Total	48542			

*mandatory test in IT; **no alcohol included in SE results

DRUID hospital study (D2.2.5)

The DRUID hospital study (D2.2.5) sampled 2,492 seriously injured drivers (cars and vans) in 6 countries (BE, DK, FI, IT, LT and NL) between October 2007 and April 2010 (in both studies with different collection periods in the participating countries) and 1,118 killed drivers (cars and vans) in 4 countries (FI, NO, PT, SE) between January 2006 and December 2009*. Almost all studies are based on blood samples (see exceptions FI, IT and SE below). The non-response rate varied between 0% and 8.5% for the seriously injured drivers (not known in DK and NL). Within the killed driver studies, post-mortem examinations are mandatory in PT, FI and SE for all people killed in road traffic accidents. "However, in practice less than 100% of the cases are analysed. For this reason these three countries have a lower percentage of missing cases compared to Norway where sampling is not mandatory" (D2.2.5 p. 27). The percentage of missing cases varied between 5.7% and 41%.. Within the hospital studies the percentage drivers tested positive for at least one psychoactive substance ranged among the seriously injured drivers between 28% (LT) and 53% (BE) and among the killed drivers between 31% (SE) and 48% (PT). An overview of the tested substance classes, groups and analytical findings within the DRUID hospital studies can be found in the 3. Tables 14 and 15 give an overview of the number of included samples, the used body-fluid and the non-response rate, percentage/number of missing cases and percentage of positive toxicological finding per country for both hospital studies

Table 14: Seriously injured drivers - number of included samples, used body-fluid, non-response rate, percentage/number of missing cases and percentage of positive toxicological finding per country (based on D2.2.5)

SERIOUSLY INJURED DRIVERS					
Country	N of included samples	Body-fluid	Non-response rate	Missing cases	Toxicological finding positive
BE	348	Blood	5.4%	105	52.6%
DK	840	Blood	Unknown*	60	30.3%
FI	54	Blood/oral fluid	8.5%	No missing cases reported	44.7%
IT	676	Blood/Urine	0%	No missing cases reported**	32%
LT	387	Blood	0%	No missing cases reported	27.8%
NL	187	Blood	Unknown	No missing cases reported	33.9%
Total	2492				

* No registration of the patients that refused is available; ** Lack of accident data such as road type, accident type,.

Table 15: Killed drivers - number of included samples, used body-fluid, non-response rate, percentage/number of missing cases and percentage of positive toxicological finding per country (based on D2.2.5)

KILLED DRIVERS					
Country	N of included samples	Body-fluid	Non-response rate	Missing cases	Toxicological finding positive
FI	483	Blood	n.a.	5.7%	42.3%
NO	193	Blood	n.a.	41%	40%
PT	285	Blood	n.a.	21%	47.7%
SE	157	Blood/Urine/Muscle tissue	n.a.	6%	30.5%
Total	1118				

While comparing the prevalence values of the hospital studies and the roadside survey it has to be clear that studies refer to different populations. The roadside survey focuses on the general driving population while the hospital studies concentrates on seriously injured and killed drivers. Moreover, the presented prevalence values within the roadside survey mainly represent single substance use (exceptions are pointed out) and within the hospital studies both, single and combined use.

DRUID case control study (D2.3.5)

The results of the roadside survey and hospital studies were melted together in the DRUID case-control study (D2.3.5) in which the substance distribution over hospital cases (D2.2.5) were compared with the substance distribution over a representative sample of control drivers in the national general road user population (D2.2.3), resulting in calculations of the relative risk of being seriously injured in an accident while tested positive for alcohol and/or other psychoactive substances (DRUID TA p. 84). These risk calculations have been carried out in 6 different European countries (BE, DK, FIN, IT, LT and NL). D2.3.5 DRAFT will be finalized by the end of the DRUID Project (October 2011), but data on seriously injured drivers from BE, DK, FI, IT, LT and NL and data on killed drivers from FI, NO, PT and SE could already be included in this deliverable.

Other included accident risk estimate studies (D2.3.1, D2.3.2, D2.3.3, D2.3.4)

Furthermore, the following DRUID studies estimating the relative risk of accident involvement for drivers impaired by alcohol and other psychoactive substances were included in this deliverable.

- D2.3.1 describes the results of a pharmacoepidemiological approach estimating the risk for traffic accident involvement of patients using psychoactive medicines in NL. Medication records were obtained under controlled conditions (regarding privacy) from community pharmacies and were linked to accident data from the same patient groups. Cases were defined as adults, who had a traffic accident between 2000 and 2007 and were driving, and received medical assistance. Controls were defined as adults, who had a driving license and had no traffic accident during the study period. In total 3963 cases and 18828 matched controls were selected for the case-control analysis (D2.3.1).
- D2.3.2 investigated the responsibility risk of positive tested car drivers for psychoactive substances, involved in fatal accidents in FR. About 7,500 car drivers were sampled from a database of approximately 10,000 drivers who were involved in a fatal road accident between October 2001 and September 2003 in FR. By means of a method adapted from a responsibility analysis developed by Robertson and Drummer (1994) car drivers were assessed as either responsible for the accident (4946 cases) or not responsible (1986 controls). After taking the toxicological analysis of each subject into account the relative risk for a car driver of being responsible for a fatal crash while driving under the influence of psychoactive substances were calculated.
- D2.3.3 investigated the responsibility risk of positive tested drivers for psychoactive substances who were killed in accidents based on in depth data of fatal motor vehicle accidents in FI. From a database of the Traffic Accident Investigation Teams in Finland accidents taking place between 2002 and 2006 were sampled and analyzed (in total 1,108 killed drivers). The focus lay on the influence of (legal) medications and alcohol. Killed drivers tested positive for alcohol (n=211) or legal (prescribed) medicines (n=46) were compared with those of sober killed drivers (n=689). In order to calculate relative risk for crash responsibility four different exposed groups were compared to their matched non-exposed groups.
- D2.3.4 compared the responsibility risk of positive tested drivers for psychoactive substances who were killed in accidents in DE, HU, LT and SK. "Data of killed drivers was sampled

prospectively by means of a database established within the DRUID-framework in the years 2008 and 2009 and increased by retrospective data. The analysis included 483 subjects, 18 years and older, killed within 10 hours after being involved in a traffic accident. Responsibility analysis was conducted with the method proposed by Robertson and Drummer (1994) which allocated the 483 subjects in 419 cases and 64 controls. Subsequently a toxicological analysis was carried out where the 23 DRUID-core substances as well as several other additional substances were screened for. An in-depth analysis of 20 killed drivers was carried out by means of a systematic accident causation catalogue" (D2.3.4 p. 4).

Experimental studies on the effect of psychoactive substances on driving performance (D1.1.2a-c, D1.2.1)

- D1.1.2a: Since many experimental studies on the effects of alcohol on human performance and driving have been published, a meta-analysis was conducted (D 1.1.2a). 450 papers published between 1950 and 2007 were included in which a total of 5,300 findings of alcohol effects on (driving) performance, social behaviours or mood are reported. The meta-analytic procedure determines for each BAC group how often significant effects were reported in these studies.
- D1.2.1 investigates the influence of stimulant drugs, their interaction with sleep deprivation and with alcohol, on actual and simulated driving. Experimental studies were designed to assess the effect of 3,4-methylmethamphetamine (MDMA; 25, 50 and 100mg) and dexamphetamine (10, 40mg) on actual and simulated driving performance.
- D1.2.2 investigates the influence of psychoactive medicines (hypnotics, analgetics, antipsychotics) on actual and simulated driving.
- D1.1.2b is a meta-analysis of empirical studies concerning the effects of medicinal and illegal drugs on safe driving. In addition detailed information about pharmacokinetics of these drugs is given.
- D1.1.2c is a meta-analysis summarizing studies on psychomotor relevant performance (1) after single dose administration of opioids, narcoanalgesics and hallucinogens to drug naïve subjects (2) in patients treated chronically with morphine or methadone / buprenorphine.

3.1 Alcohol (DUI)

3.1.1 Prevalence of alcohol in relation to road safety

Alcohol ($\geq 0.1\text{g/L}$) is the most frequently detected psychoactive substance in the driving population (estimated EU mean 3.48%) (D2.2.3) as well as in the seriously injured (range 17.7-42.5%) and in killed drivers (range 19.0-44.9%) in Europe (D2.2.5; D2.2.4; D2.3.4).

General driving population

The DRUID roadside survey showed that: Alcohol is the most frequently detected psychoactive substance in Europe. The estimated EU mean prevalence for single alcohol use ($\geq 0.1\text{g/L}$) was 3.48%, highest in IT (8.59%) followed by BE, PT, ES and LT and lowest in HU (0.15%). No alcohol information was available in SE (see figure 19 and 20).

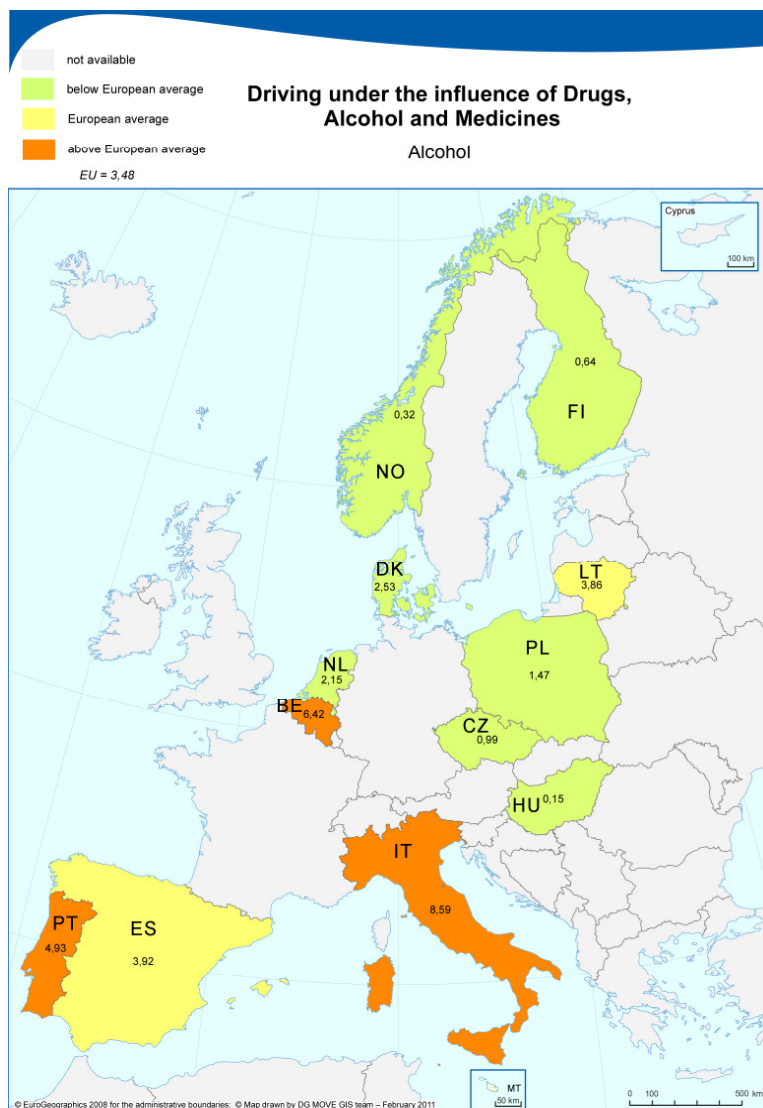


Figure 19: Geographical presentation of alcohol ($\geq 0.1\text{g/L}$) use by car drivers in the EU (D2.2.3 PART I p. 7)

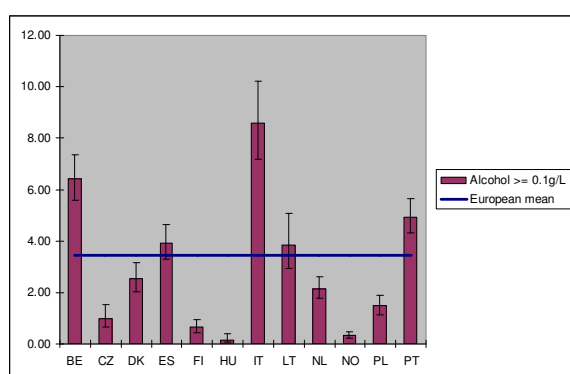


Figure 20: Prevalence of alcohol alone $\geq 0.1\text{g/L}$ by country; prevalence in percentages (D2.2.3 Part I p. 45)

The legal alcohol limit was in most countries 0.5 g/L (only CZ and HU have a zero tolerance limit for alcohol and PL, NO and SE have legal limit of 0.2g/L). Even with a cut-off level of 0.5 g/L, alcohol would still have been the most prevalent substance in European traffic with an average prevalence of 1.49%. IT (5.23%) has over twice the prevalence of the second and third ranked countries, LT (2.31%) and BE (2.16%), respectively (see figure 21). The prevalence for single alcohol use at $\geq 1.2\text{g/L}$ is highest in LT and IT (both around 1.4%). The according European average prevalence is about 0.4% (see figure 22).

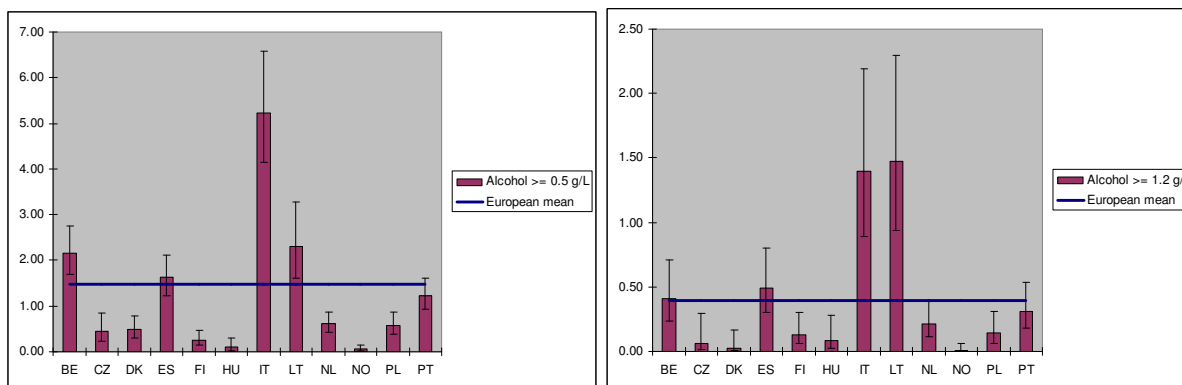


Figure 21: Prevalence of alcohol alone $\geq 0.5\text{g/L}$ by country; prevalence in percentages (D2.2.3 Part I p. 45)

Figure 22: Prevalence of alcohol alone $\geq 1.2\text{g/L}$ by country; prevalence in percentages (D2.2.3 Part I p. 46)

Single alcohol use is in general mainly prevalent in the Southern part of Europe. The highest prevalence for the TOTAL alcohol use (single + combined use) is found in IT (9.6%) followed by PT and BE (both: 6.73%) and lowest in FI (0.18%) (see table 16). The estimated EU mean for TOTAL alcohol use is 3.87%.

Table 16: Prevalence of alcohol alone and alcohol in combination with other psychoactive substances; prevalence in percentages (based on D2.2.3 PART I p. 46)

	BE	CZ	DK	ES	FI	HU	IT	LT	NL	NO	PL	PT	SE
Alcohol alone	6.42	0.99	2.53	3.92	0.64	0.15	8.59	3.86	2.15	0.32	1.47	6.42	NA
Alcohol in combination	0.31	0.05	0.10	1.14	0.08	0.03	1.01	0.03	0.24	0.07	0.00	0.31	NA
Total	6.73	1.04	2.63	5.06	0.72	0.18	9.60	3.89	2.39	0.39	1.47	6.73	NA

Seriously injured or killed drivers

In the DRUID hospital study (D2.2.5) alcohol ($\geq 0.1\text{g/L}$) was the most common toxicological finding, both in the seriously injured (range 17.7% (LT) - 42.5% (BE)) and in the killed drivers (range 19% (SE) - 44.9% (PT)). Respective findings for alcohol intoxication at $\geq 0.5\text{g/L}$ were 16.1% (LT) - 38.2% (BE) for seriously injured drivers and 16.3% (SE) – 35.1% (PT) for killed drivers. Among the positives, most had a high BAC: 90.5% of injured drivers and 87% of killed drivers had a BAC $\geq 0.5\text{g/L}$ (mean and median values of ethanol were respectively 1.59 g/L and 1.60 g/L, and 1.61g/L and 1.67g/L) (see table 17 and figure 23-24).

Table 17: Distribution of positive alcohol findings by BAC-group among seriously injured and killed drivers (based on D2.2.5)

BAC group	Seriously injured drivers		Killed drivers	
	Frequency	Percent	Frequency	Percent
0.1 \leq BAC < 0.5 g/L	58	9.5	45	12.7
0.5 \leq BAC < 0.8 g/L	48	7.9	26	7.3
0.8 \leq BAC < 1.3 g/L	103	16.9	33	9.3
BAC \geq 1.3 g/L	400	65.7	250	70.6
Total	609	100.0	354	100.0

Alcohol was the only substance among the ones tested for that appeared more often alone than in combinations. When alcohol was combined with other psychoactive substances, benzodiazepines and cannabis (THC and/or THCCOOH) were the most common associated findings (D2.2.5).

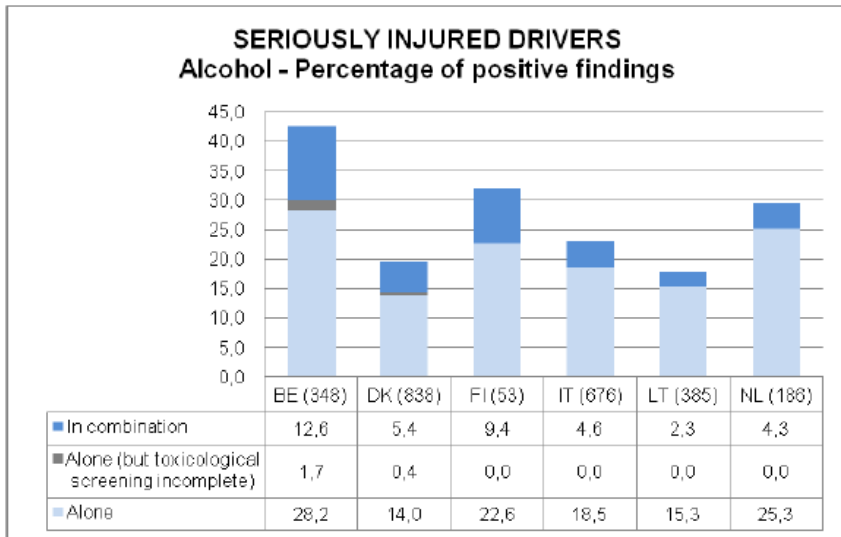


Figure 23: Seriously injured drivers – Alcohol (≥ 0.1 g/L) prevalence: detail of toxicological findings (D2.2.5 p. 60)

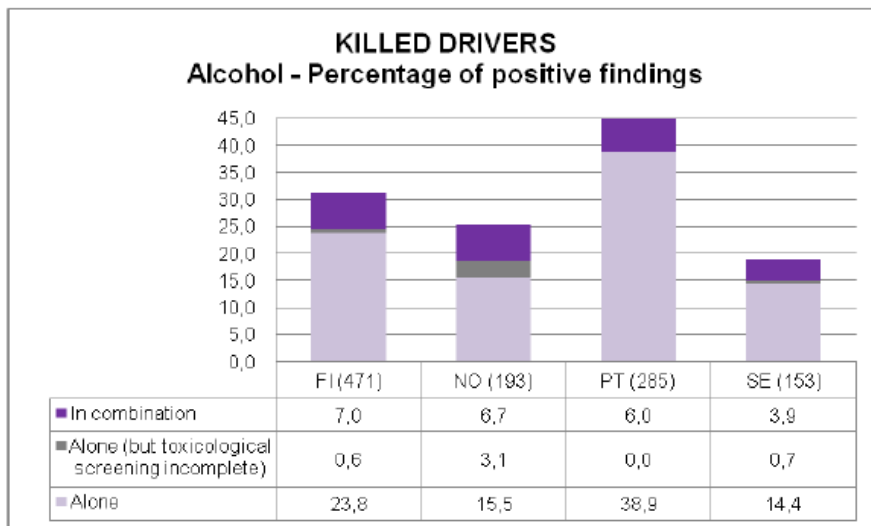


Figure 24: Killed drivers – Alcohol (≥ 0.1 g/L) prevalence: detail of toxicological findings (D2.2.5 p. 93)

Based on a fatal accidents database analysis in FR (N approx. 7,000), alcohol is the most prevalent psychoactive substance with 29% of drivers (n=1997) involved in a fatal crash tested positive for alcohol. The majority (n=1257, 63%) of positively tested drivers were severely intoxicated (blood alcohol concentration ≥ 1.2 g/L)

In the responsibility study (D2.3.4) carried out in DE, LT, HU and SK (n=483) 33% of the killed drivers were tested positive for alcohol (alcohol ≥ 0.1 g/L) as a single psychoactive substance. 67% (n=107) of positively tested drivers were severely intoxicated (BAC ≥ 1.2 g/L), a condition more frequently found in East-European samples (D2.3.4 p. 4).

3.1.2 Characteristics of drivers tested positive for alcohol

Alcohol was in the general driving population mainly detected among older male drivers, with lower BAC levels (D2.2.3). Within the accident involved drivers alcohol was mainly detected among younger male drivers with a high BAC level (D2.2.5).

General driving population

Alcohol was found to be more present in male than in female drivers in all investigated countries except in NO, where the same prevalence was found for both genders and IT where more female than male drivers were tested positive ($\geq 0.1\text{g/L}$). In most countries the proportion of alcohol-positive ($\geq 0.1\text{g/L}$) drivers (male and female) was the highest for the two oldest age groups (35-49 and 50+), except in PT where this was more present in young drivers (18-24) (D2.2.3). "In general, alcohol use is higher during night time hours than during day time hours. However, in some Eastern European countries such as HU, LT and PT this was not the case. The highest prevalence was detected in BE during weekday nights (21.05%) and weekend nights (16.60%). The 95% confidence intervals are very large for some countries; therefore it is difficult to assign exact differences between time periods for the participating countries. The proportion of alcohol use was in general the lowest at weekdays during daytime hours. However, in PT the proportion of alcohol drivers was higher during weekday hours than during weekday nights. Despite a general large proportion of high BAC drivers, no alcohol use was found during weekend nights in LT. In HU no alcohol was found at all during night time hours" (D2.2.3 PART I p. 54f).

In the general driving population the largest prevalence for alcohol is in general present at the lower BAC categories. Within the DRUID roadside survey in DK even 81% of the alcohol drivers had a BAC between 0.1 and 0.5g/L. However, in LT almost 40% of all alcohol intoxicated drivers had a BAC level of 1.2g/L or higher, while for most other countries this proportion is below 15% (D2.2.3). Among the seriously injured and killed drivers the percentage of high alcohol levels was much higher (see following chapter).

The DRUID investigation on the motives behind impaired driving (D2.2.1) carried out in SE and HU showed that drivers do not think that alcohol impairs their performance and that within this study drink drivers feel more ashamed than drug drivers. The feeling of shame appeared not to be related to a feeling that the act itself could result in an accident, but somewhat related to if their friends and relatives disapproved. Drivers whose drinking and driving was related to problems with alcohol argue that losing the licence or even to be imprisoned would not have helped them to stop re-offending; instead, they argue that the treatment programme had helped them by providing a greater insight into their own problems (D2.2.1).

Seriously injured or killed drivers

In both hospital studies significant differences were found between both gender and age groups. In general, the prevalence in males was higher than in females, with a percentage ratio approximately 70/30 in the seriously injured drivers and 83/17 in the killed drivers. The age group distribution was different in the two hospital studies, with the age group 50 and above accounting for approximately 19% of the sample in the injured drivers study and approximately 36% of the sample in the killed drivers study. In men, the two first age groups, 18-24 and 25-34, accounted for approximately 55% of the sample in the injured drivers study, and for approximately 42% of the sample in the killed drivers study. For the same two female age groups, the distribution was approximately equal to 49% in the seriously injured drivers study and to 32% in the killed drivers study.

In general, the prevalence in males was higher than in females, with a percentage ratio approximately 70/30 in the seriously injured drivers and 83/17 in the killed drivers.

The majority of seriously injured or killed drivers tested positive for alcohol within the hospital study had a high BAC level; 90.5% of injured drivers (87% of killed drivers) had a blood alcohol concentration $\geq 0.5\text{g/L}$ and 65.7% injured drivers of 70.6% killed drivers a BAC of $\geq 1.3\text{g/L}$ (D2.2.5).

Within the responsibility study (D2.3.4) carried out in DE, LT, HU and SK the majority of subjects who consumed alcohol were severely intoxicated (BAC ≥ 1.2 g/L), a condition more frequently found in East-European samples (D2.3.4).

3.1.3 Accident risk for driving with alcohol

Alcohol highly increases accident risk (e.g. D2.3.2; D2.3.3; D2.3.4; D2.3.5 DRAFT). Based on case-control studies, the relative risk of serious injury or fatality for alcohol (≥ 0.5 g/L) is found to be significantly increased compared to that of drivers below the DRUID cut-off for any substance (D2.3.5). An increased risk was associated with high BAC level, young age and speed (D2.3.3). The risk increases drastically with combined use (e.g. cannabis) (D2.3.2).

According to the French study (D2.3.2), for drivers positive for alcohol (≥ 0.1 g/L), the risk of being responsible for a fatal crash is about 8 times as high as that of sober drivers (adjusted OR 8.39 [95% CI 6.95-10.11]). For alcohol ≥ 1.2 g/L this risk increased about 19 times (adjusted OR 19.32 [95% CI 13.99-26.69]). Combined use of alcohol and cannabis multiplies the risk of causing a fatal accident ($8.39 \times 1.89 = 15.86$) (D2.3.2).

In the Finnish study (D2.3.3) killed drivers, positive for alcohol (≥ 0.5 g/L), had a risk of about 7 times as high as that of sober drivers being responsible for a fatal accident (adjusted OR 6.55 [95% CI 1.83 – 31.75]). They were more often young drivers (<36 years) and more often car than bus or lorry drivers. Significant variables associated with the responsibility were: age of the driver, driver’s BAC level and speed (D2.3.3).

In the responsibility study carried out in DE, LT, HU and SK (D2.3.4) a significant increase of the relative risk for drivers who were killed in an accident of being responsible for the accident was found for an alcohol concentration of ≥ 0.1 g/L (adjusted OR 4.57 [95% CI 2.02-10.38]) and for ≥ 1.2 g/L this was 20.84 [95% CI 3.10-140.16]. The corresponding confidence intervals are wide and therefore the precision of estimate is poor.

Table 18 gives an overview of the above mentioned results of the different responsibility studies carried out in DRUID.

Table 18: Overview of the adjusted OR estimating the risk for a driver of being responsible for a fatal accident (D2.3.2) and the risk for a killed driver of being responsible for the accident (D2.3.3; D2.3.4) when driving under the influence of alcohol.

Reference	Included country	BAC concentration in g/L			
		≥ 0.1		≥ 1.2	
		Adjusted OR	95% CI	Adjusted OR	95% CI
D2.3.2	FR	8.39	6.95-10.11	19.32	13.99-26.69
D2.3.3	FI	6.6	1.83-31.75	14.96	2.00-111.89
D2.3.4	DE, LT, HU, SK	4.57	2.02-10.38	20.85	3.10- 140.16

Although the study designs of the single DRUID risk estimation studies do not allow precise comparison of the calculated accident risks, their results show similar effects regarding the relative risk of being responsible for a fatal accident driving under the influence of alcohol.

The DRUID case-control study (D2.3.5) calculated the risk of being seriously injured or killed based on control data from the roadside survey (D2.2.3) and case data from the hospital study and study on killed drivers (D2.2.5). Odds ratios for different alcohol concentrations have been calculated by means of data from BE, DK, FI, IT, LT and NL (seriously injured drivers) and for FIN, NO and PT (killed drivers) separately for each country and for all countries as a whole. The odds ratios are adjusted for age and gender and the controls were weighted with the traffic distribution in eight time periods over the week. Table 19 shows the calculated OR (alcohol) for getting seriously injured and table 20 for getting killed based on aggregated data (D2.3.5).

Table 19: Overview of OR (alcohol alone) for getting seriously injured based on aggregated data (D2.3.5)

Reference	Included country	OR + CI	BAC concentration in g/L			
			0.1 – 0.5	0.5 – 0.8	0.8 – 1.2	≥1.2
D2.3.5 DRAFT	BE, DK, LT, NL	Crude OR	1.05	3.80	13.97	55.27
		95% CI	0.73-1.53	2.48-5.82	8.75-22.29	39.52-77.31
		Adjusted OR	1.18	3.64	13.35	62.79
		95% CI	0.81-1.73	2.31-5.72	8.15-21.88	44.51-88.58

Finland and Italy have been left out of the calculations of OR for alcohol and alcohol-drug(s) because of bias in collecting data for the control samples.

Table 20: Overview of OR (alcohol alone) for getting killed based on aggregated data (D2.3.5)

Reference	Included country	OR + 95% CI	BAC concentration in g/L			
			0.1 – 0.5	0.5 – 0.8	0.8 – 1.2	≥1.2
D2.3.5 DRAFT	NO, PT	Crude OR	9.23	42.94	34.81	450.37
		95% CI	6.07-14.05	21.99-83.86	16.02-75.65	224.06-905.25
		Adjusted OR	8.01	45.93	35.69	500.04
		95% CI	5.22-12.29	23.02-91.66	15.68-81.22	238.07-inf.

Finland has been left out of the calculations of OR for alcohol and alcohol-drug(s) because of bias in collecting data for the control sample.

The results indicate a significant increase of the relative risk of serious injury or fatality for an alcohol concentration of $\geq 0.5\text{g/L}$. Overall, the relative injury risk is estimated to be slightly increased of about 1-3 times for alcohol concentrations of 0.1-0.5g/L, medium increased of about 2-10 times for alcohol concentrations of 0.5-0.8g/L, highly increased of about 5-30 times for alcohol concentrations of 0.8-1.2g/L and extremely increased of about 20-200 times for alcohol concentrations $\geq 1.2\text{g/L}$ compared to the risk for drivers below the DRUID cut-off for any substance. The results are based on calculations of odds ratios adjusted for age and gender. The controls were weighted with the traffic distribution in eight time periods over the week. Including all alcohol concentrations at and above the DRUID cut-off ($\geq 0.1\text{g/L}$) the relative injury risk for alcohol is estimated to be about 5-10 times as high as that of drivers below the DRUID cut-off for any substance.

3.1.4 Results from experimental studies on the effect of alcohol on driving performance

Alcohol has a negative impact on driving performance and on skills related to driving (e.g. D1.1.2a). Driving tests are important to estimate impairment effects, as unspecific measures of psychomotor performance do not fully represent the driving performance decrements caused by alcohol (e.g. D1.1.2a).

The main outcomes of the DRUID meta-analysis of empirical studies concerning the effects of alcohol on safe driving (D1.1.2a) are illustrated in the following two figures. As can be seen in figure 25 there is an increase in the subjective feeling of being intoxicated already at very low BAC level: at 0.4g/L BAC 80% of the findings show a significant effect. Subjective feelings of fatigue increase with increasing BAC. There are performance decrements at BAC of 0.5g/L in 30% of the findings. At BAC of 0.8g/L about 50% of the findings are significant (see figure 26). Taking a closer look at only those findings based on driving performance assessed in driving simulators, it becomes obvious that complex tasks like driving are more affected by alcohol than simple tasks, especially at low BACs.

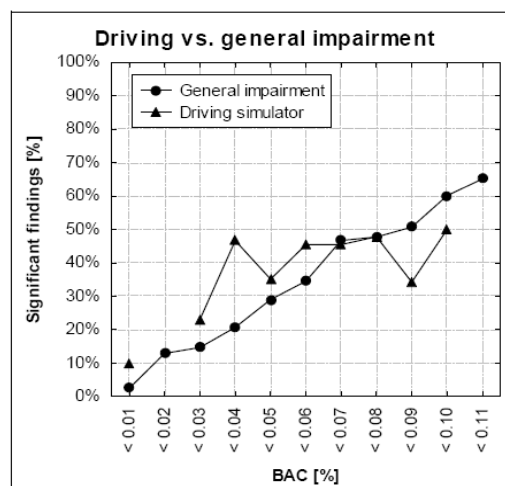
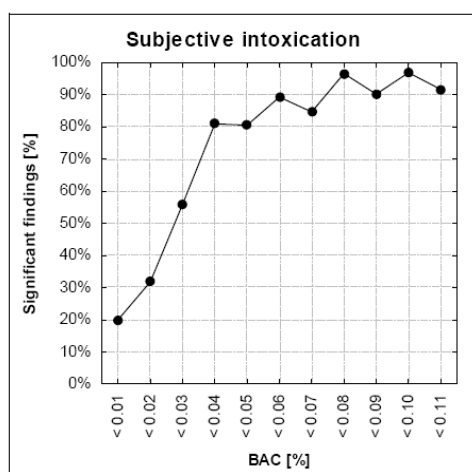


Figure 25: Subjective intoxication – percentage of significant findings per BAC group (D1.1.2a, p. 69)

Figure 26: Impairment in driving simulator tasks vs. in general – percentage of significant findings per BAC group (D1.1.2a, p.76).

Therefore it is important to conduct driving tests to estimate the impairing effects of alcohol on driving. Especially at low BACs unspecific measures of psychomotor performance do not fully represent the driving performance decrements caused by alcohol. Impairments in driving performance become obvious already at much lower BACs than in cognitive skills related to driving (D 1.1.2a).

3.1.5 Overview box – alcohol

Box 1: Summary of main DRUID results – ALCOHOL

Prevalence of alcohol in relation to road safety:

- **Alcohol ($\geq 0.1\text{g/L}$) is the most frequently detected psychoactive substance in the driving population (estimated EU mean 3.48%) (D2.2.3) as well as in the seriously injured (range 17.7-42.5%) and in killed drivers (range 19.0-44.9%) in Europe (D2.2.5; D2.2.4; D2.3.4).**
- General driving population (D2.2.3):
 - Alcohol alone ($\geq 0.1\text{g/L}$): most frequently detected substance in most countries; estimated EU mean prevalence 3.48% (range 0.15-8.59%); prevalence ranking from all investigated substances #1; main EU region: Southern Europe;
 - Alcohol alone ($\geq 0.5\text{g/L}$): estimated EU mean prevalence 1.49% (range 0.07-5.23%); prevalence ranking from all investigated substances #2;
 - Alcohol alone ($\geq 1.2\text{g/L}$): estimated EU mean prevalence about 0.40% (range 0.01-1.47%); prevalence ranking from all investigated substances #6;
 - Total alcohol (single + combined): estimated EU mean prevalence about 3.87% (range 0.18-9.6%).
- Seriously injured and killed drivers (D2.2.5; D2.2.4; D2.3.4):
 - Hospital study: alcohol ($\geq 0.1\text{g/L}$) was the most common toxicological finding, both in the seriously injured (range 17.7-42.5%) and in killed drivers (range 19.0-44.9%); Respective findings for alcohol ($\geq 0.5\text{g/L}$) were 16.1-38.2% for seriously injured drivers and 16.3– 35.1% for killed drivers (D2.2.5);
 - Fatal accident database FR (D2.2.4): prevalence rate of alcohol 25% (followed by THC, opiates, amphetamines and cocaine) (D2.2.4);
 - Responsibility study in DE, LT, HU, SK (D2.3.4): about 37% of all tested drivers were under the influence of alcohol.

Characteristics of drivers tested positive for alcohol:

- **Alcohol was in the general driving population mainly detected among older male drivers, with lower BAC levels (D2.2.3).**
- **Within the accident involved drivers alcohol was mainly detected among younger male**

drivers with a high BAC level (D2.2.5).

- General driving population (D2.2.3):
 - Most prevalent in the two oldest age groups (35-49 and 50+);
 - More prevalent in male than in female drivers;
 - Main prevalent periods: weekday nights and weekends;
 - In general the largest prevalence for alcohol is present at low BAC level (exception: LT were 40% of alcohol drivers had BAC >1.2g/L) (D2.2.3).
- Seriously injured and killed drivers (D2.2.5, D2.2.4):
 - Most prevalent in young drivers (25-35 years) (D2.2.5);
 - More prevalent in male than in female drivers (about 70/30 in seriously injured and 83/17 in the killed drivers) (D2.2.5);
 - Majority of seriously injured or killed drivers tested positive for alcohol had a high BAC level; 90.5% of injured drivers (87% of killed drivers) had BAC $\geq 0.5\text{g/L}$ (D2.2.5); majority of positive tested drivers for alcohol were severely intoxicated (BAC $\geq 1.2\text{g/L}$) (D2.2.4).
- Motives behind impaired driving (D2.2.1):
 - Drivers do not think that alcohol impairs their performance;
 - Drivers whose drinking and driving was related to problems with alcohol argue that losing the licence or even to be imprisoned would not have helped them to stop re-offending; instead, they argue that the treatment programme had helped them by providing a greater insight into their own problems.

Accident risk for driving with alcohol:

- **Alcohol highly increases accident risk (e.g. D2.3.2; D2.3.3; D2.3.4; D2.3.5 DRAFT).**
- **Based on case- control studies, the relative risk of serious injury or fatality for alcohol ($\geq 0.5\text{g/L}$) is found to be significantly increased compared to that of drivers below the DRUID cut-off for any substance (D2.3.5).**
- **An increased risk was associated with high BAC level, young age and speed (D2.3.3).**
- **The risk increases drastically with combined use (e.g. cannabis) (D2.3.2).**
- The results of the DRUID accident risk studies reveal:
 - Responsibility studies (D2.3.2, D2.3.3, D2.3.4): the risk of being responsible for a fatal crash is 5-8 times higher for a driver driving under the influence of alcohol ($\geq 0.1\text{g/L}$) than for a sober driver; severely intoxicated drivers (alcohol $\geq 1.2\text{g/L}$) have a 15-21 times higher risk of being responsible for a fatal crash compared to sober drivers.
 - Case control study (D2.3.5): relative risk of serious injury or fatality for a driver when positive for alcohol ($\geq 0.1\text{g/L}$) is estimated to be about 5-10 times (for: 0.1-0.5g/L -> 1-3 times; 0.5-0.8g/L -> 2-10; 0.8-1.2g/L -> 5-30 times; and $\geq 1.2\text{g/L}$ -> 20-200 times) as high as that of drivers below the DRUID cut-off for any substance.

Results from experimental studies on the effect of alcohol on driving performance:

- **Alcohol has a negative impact on driving performance and on skills related to driving (e.g. D1.1.2a).**
- **Driving tests are important to estimate impairment effects, as unspecific measures of psychomotor performance do not fully represent the driving performance decrements caused by alcohol (e.g. D1.1.2a).**

3.2 Illicit drugs (DUID)

3.2.1 Prevalence of illicit drugs in relation to road safety

All DRUID investigations (e.g. D2.2.3, D2.2.5, D2.3.4) show that the prevalence of illicit drugs in the driver population (estimated EU mean 1.90%) is lower than the alcohol prevalence (estimated EU mean 3.48%) (D2.2.3). Within the accident involved drivers, the majority of drugs appeared to be used in combination with other psychoactive substances (mainly alcohol) (D2.2.5). THC is generally the most frequently detected illicit drug, followed by cocaine, but the

prevalence of the different illicit substances show high national variability (e.g. D2.2.3, D2.2.5, D2.3.4).

General driving population

Within the DRUID roadside survey illicit drugs were, as a whole, most frequently detected in Southern and Western Europe. The highest prevalence was found in ES where 8.20% of all tested drivers (approximately 1 in 12) were positive for one or more illicit drugs (followed by IT: 3.92%; NL: 2.51% and PT: 1.80%). In Northern and Eastern Europe the prevalence was on average below 1% (range 0.22% SE – 0.94% BE) (see figure 27). The different estimated EU mean prevalence of the investigated substances were: THC 1.32, cocaine 0.42, amphetamine 0.08, illicit opiates 0.07% (D2.2.3).

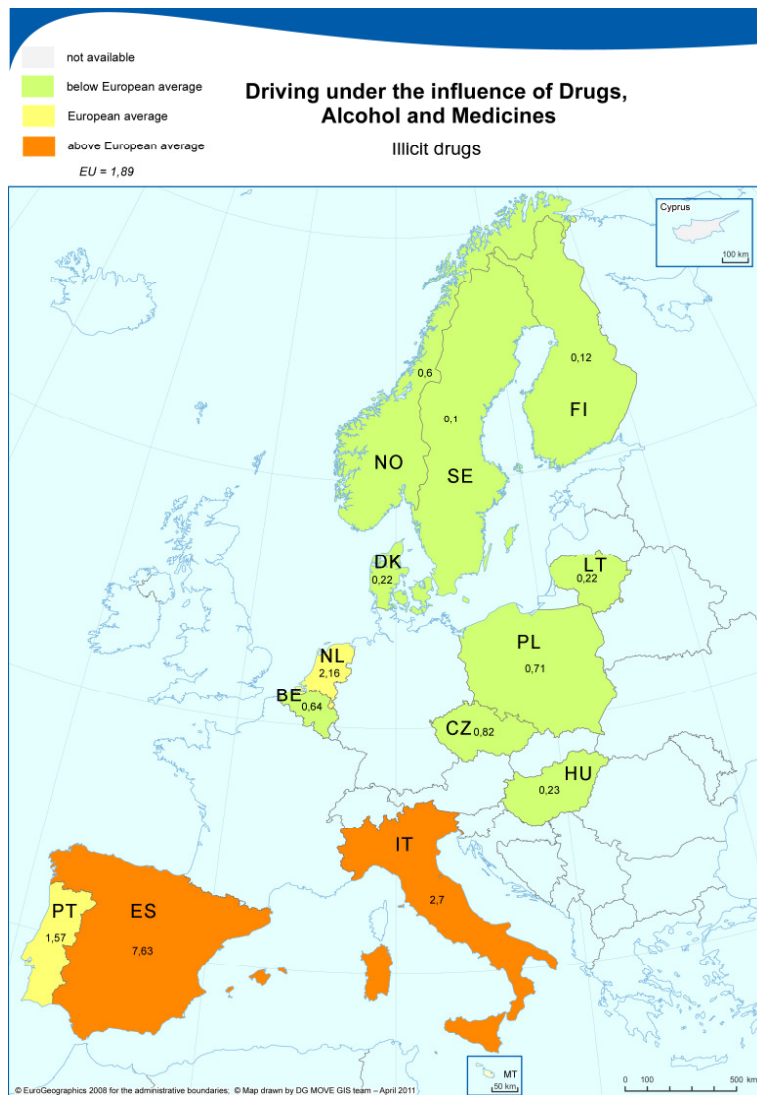


Figure 27: Geographical presentation of illicit drug use by car drivers in the EU (D2.2.3 PART I p. 6)

The results of the DRUID roadside survey in regard to different illicit drugs and combined use have been summarized as follows (D2.2.3, p. 137f):

“**THC¹** was the **most frequently detected illicit drug in traffic** (D2.2.3, 2.2.5, D2.2.4) (estimated European mean: 1.32%). It was mainly used in **ES** where the prevalence was almost four times higher than in the second ranked country, NL. On **average** between **20% and 30% of THC** use was in

¹ The THC substance group is formed by THC only. THC-COOH was detected as well in blood, but this inactive metabolite of THC will be regarded as negative.

combination with other psychoactive substances. Combinational THC use was the **highest in the Southern European countries (IT, ES, PT) and NL** (No THC was detected in LT) (see figure 28).

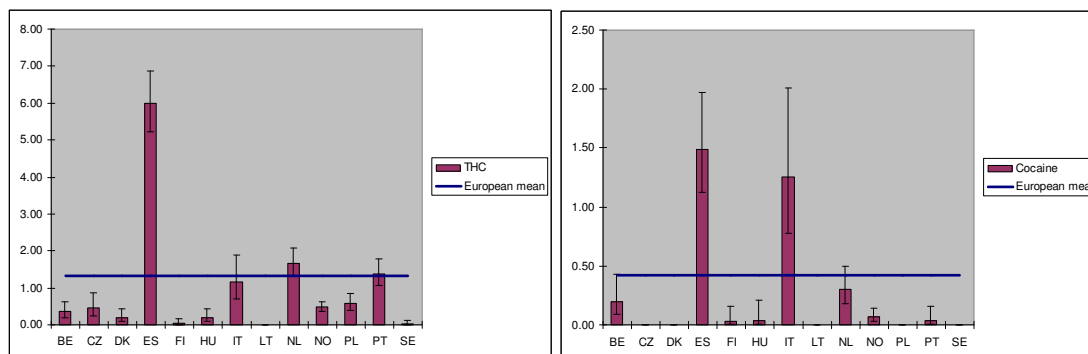


Figure 28: Prevalence of THC alone by country; prevalence in percentages (D2.2.3 Part I p. 70)

Figure 29: Prevalence of cocaine alone by country; prevalence in percentages (D2.2.3 Part I p. 63)

Cocaine² was the **second most frequently detected illicit drug** among drivers was cocaine (estimated European mean: 0.42%). The highest prevalence for cocaine was found in ES and IT. (No cocaine was detected among drivers in CZ, DK, LT, PO and SE.) On **average around half of the cocaine was detected in combination with other substances**. Only in FI and HU cocaine was solely detected in single drug use (see figure 29).

Amphetamines³ were far less frequently detected than THC and cocaine. The prevalence of amphetamines is very low in most of the 13 countries (estimated European mean: 0.08%). The CZ has the highest proportion with 0.38% which is almost the double of the proportion of the countries that are ranked second and third: LT and NL with 0.22% and 0.19% respectively. Most countries have a prevalence which is lower than 0.10%. In general amphetamines are equally often detected alone as in combinations...(No single amphetamines were detected in BE, HU, IT and PT.) (see figure 30)

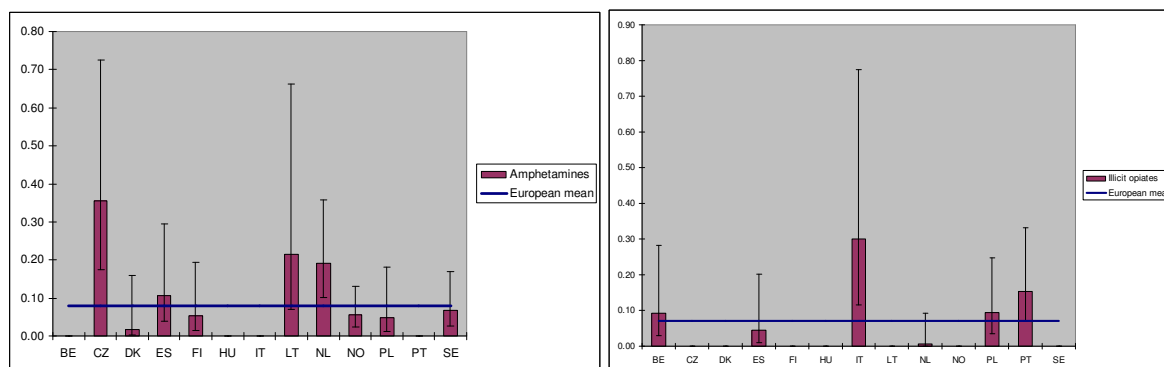


Figure 30: Prevalence of amphetamines alone by country; prevalence in percentages (D2.2.3 Part I p. 56)

Figure 31: Prevalence of illicit opiates alone by country; prevalence in percentages (D2.2.3 Part I p. 79)

Illicit opiates⁴ were barely prevalent in European traffic (estimated European mean: 0.07%). IT has the highest proportion with 0.3%. In the Northern European countries no illicit opiates were detected among drivers. In the Eastern European countries illicit opiates were only detected in PL. Illicit opiates were relatively **frequently used in combination with other psychoactive substances**. In IT the prevalence of illicit opiates in combination with other substances was 0.71% which was far higher than the single use (0.3%) (see figure 31)".

² The cocaine group includes both drivers with cocaine and with its metabolite benzoylecgonine.

³ The amphetamine drugs group consisted of amphetamine, metamphetamine, MDMA, MDA, and MDEA.

⁴ The illicit opiates group includes drivers that were positive for heroin (6-acetylmorphine) or the combination of morphine and codeine where the concentration of morphine is equal to or higher than the concentration of codeine. If the concentration of codeine is higher than that of morphine, the use was regarded as medicinal opiates and opioids use.

Alcohol-drug⁵ combinations. The Northern and Eastern European countries all had lower prevalence for the combined use of alcohol and drugs than the European average (estimated EU mean: 0.37%). In Western Europe the prevalence was around the average, while relatively the most drivers positive for alcohol and drugs were detected in **Southern Europe**. The highest prevalence was detected in ES (1.14%) and IT (1.01%) with prevalence rates just over the 1%. (In all other countries the prevalence varied between 0.00% in PL and 0.42% in PT. No information on the combined use of alcohol and drugs was available for SE.)

The relative proportion of alcohol in combination with drugs as a total of all alcohol use varies between 0% (HU) and 23% (ES). Countries with higher prevalence for single alcohol and single drug use have, as expected, higher prevalence for combined use of alcohol and drugs.

The total of single alcohol use and combined use with illicit drugs and/or psychoactive medicines is mainly prevalent in the Southern part of Europe, highest in IT (9.6%) followed by PT and BE (both: 6.73%) and lowest in FI (0.18%) (see figure 32).

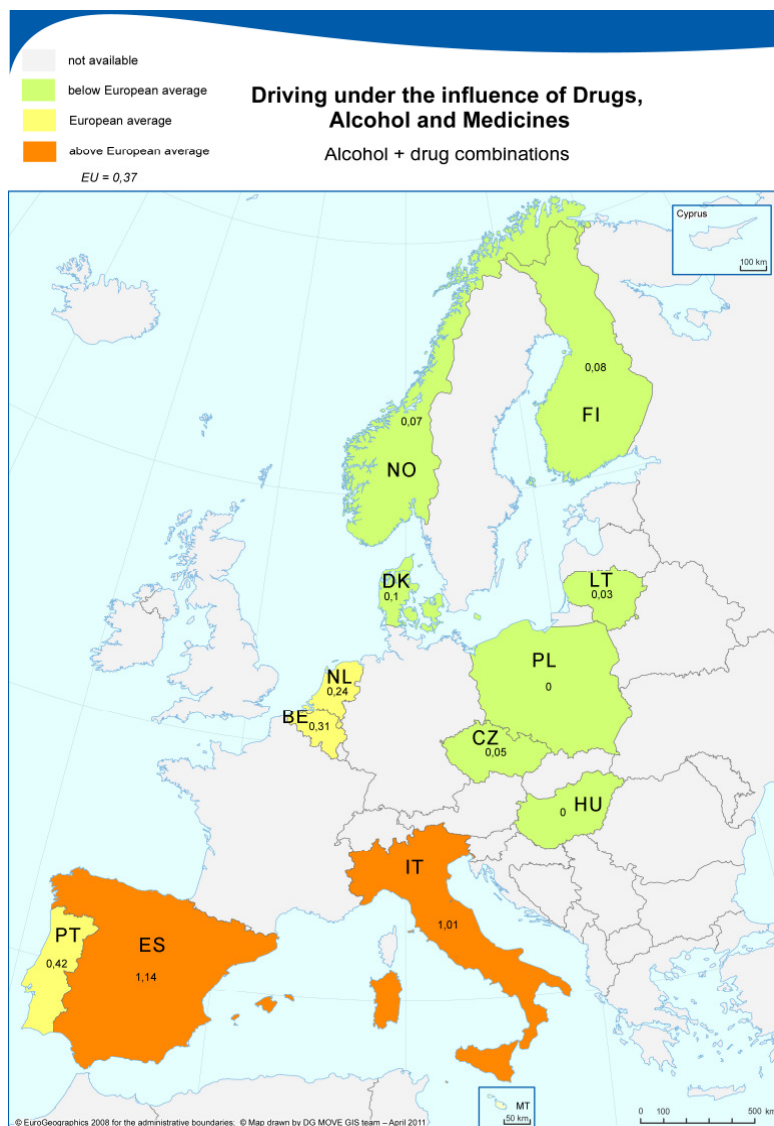


Figure 32: Geographical presentation of alcohol and drugs combinations by car drivers in the EU (D2.2.3 PART I p. 8)

Drug-drug⁶ combinations. The prevalence of drug-drug combinations among drivers was the highest in IT and ES, which were the only two countries with a prevalence higher than the European mean of

⁵ The group alcohol and drug (combination) consist of alcohol 0.1 g/L in combination with one or more other psychoactive substances, excluding THC-COOH which is regarded as negative.

⁶ The group drug-drug combinations consist of the combination of two or more other psychoactive substances other than alcohol from at least two different groups of drugs, excluding THC-COOH which is regarded as negative.

0.39%. **Most commonly used drugs in multi-drug combinations are THC, cocaine, and** (sometimes illicitly used) **benzodiazepines**, which are also the most frequently detected single psychoactive substances after alcohol.

The proportion of multi-drug use is on average around 10% of all drug use. IT had the highest proportion of multi-drug use: 22% of the drug using had been using two or more different drugs (see figure 33)”.

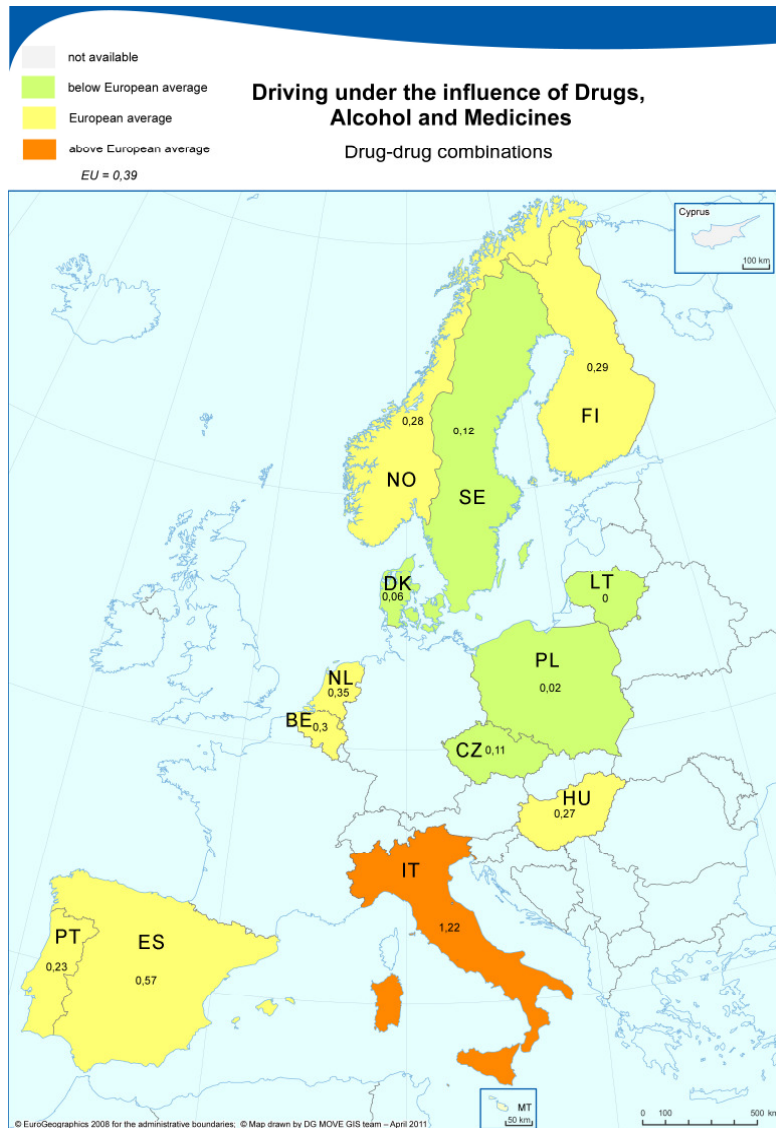


Figure 33: Geographical presentation of drug-drug combinations by car drivers in the EU (D2.2.3 PART I p. 8)

Seriously injured and killed drivers

Within the DRUID hospital study no clear picture of the distribution of illicit drugs among injured and killed drivers could be identified, as the prevalence of different substances showed great national variability (D2.2.5). In the prevalence of use among all seriously injured drivers, THC (range 0.5% (NL) - 7.6% (BE)) was the second most frequently detected substance after alcohol. Amphetamine use appears to be more common in northern Europe, while cocaine use seems to be more prevalent in southern Europe. No cases of cocaine/benzoyllecgonine were recorded in FI. In BE approximately 9.9% of the seriously injured drivers tested positive for cannabis (THC and/or THCCOOH).

In the prevalence of use among all killed drivers THC was number four (range 0% - 6.1%), after alcohol, benzodiazepines and amphetamines. NO had the highest percentage of positive findings for THC (6.1%) and PT (0.0%) the lowest. Among the killed drivers subjects positive for THC (alone or in

the presence of THCCOOH) were only found in males (D2.2.5). In PT no subjects were found positive for the amphetamine group and illicit opiates. In FI no drivers tested positive for cocaine. In both groups the majority of drugs appeared to be used in combination with other psychoactive substances (mainly alcohol) (D2.2.5).

In the FR accident databases (D2.2.4) 6.9% of all drivers involved in fatal accidents were tested positive for THC, 0.6% for amphetamines, 0.5% for cocaine and 0.9% for opiates (D2.2.4).

Within the responsibility study in DE, LT, HU and SK (D2.3.4) 10% of killed drivers with a positive toxicological screening were tested positive for illicit drugs. This corresponded to 4.3% of the whole sample⁷ (n = 483). The most common substance was cannabis (2.5% of the whole sample) (D2.3.4).

Combined use (alcohol-drug and drug-drugs) within seriously injured drivers (D2.2.5). The group of seriously injured drivers testing positive for a combination of “alcohol-drug” were within the DRUID hospital studies the second most represented group in all countries apart from Lithuania (“alcohol only” represent largest group in all six countries). The combined use of “drug-drug” represent either the third (Belgium, Denmark, Finland, Italy) or the fourth (Lithuania, The Netherlands) biggest group for percentage of positive subjects” (D2.2.5 p. 118)

In general, 75.7% of all positive tested seriously injured drivers (including all countries) used a single psychoactive substance (mainly alcohol). 17.8% tested positive for 2 substance groups (D2.2.5).

Combined use (alcohol-drug and drug-drugs) within killed drivers (D2.2.5). Within all countries the group of tested positive killed drivers for a combination of alcohol-drug was the second most represented group (“alcohol only” represent largest group in all six countries). Within the SE sample the same percentage was found for subjects testing positive for the “combination” and for the “drug-drug combination (D2.2.5).

In general, 78.7% of all positive tested killed drivers (including all countries) used a single psychoactive substance (mainly alcohol). 18.4% tested positive for 2 substance groups (D2.2.5).

3.2.2 Characteristics of drivers tested positive for illicit drugs

Illicit drugs were in general mainly detected among young male drivers, during all times of the day but mainly at the weekend (D2.2.3). Combined use of alcohol and drugs (illicit drugs and/or psychoactive medicine) is in general often prevalent among young (<35 years) male drivers during night time hours (D2.2.3). Multiple drugs (illicit drugs and/or psychoactive medicines) use is in general most common in males (D2.2.3). Age groups and time periods vary considerably by country (D2.2.3).

General driving population

Within the DRUID roadside survey the following substance specific characteristics of drivers positive for illicit drugs have been identified (D.2.2.3, p. 137f):

“THC. In general drivers who had been using THC were **males younger than 35 years**. THC was prevalent at **all days of the week during all hours** of the week in most countries. However, in BE, CZ, DK, IT and, single THC use was mainly detected during the weekend. The trend of THC use in weekends by young male drivers was confirmed by the logistic regression analysis.

Cocaine. Almost all cocaine users were younger than 50 and predominantly **male**. However, it should be taken into account that female drivers in Spain have a higher prevalence for cocaine than most male users in other countries. Cocaine was detected during **all time periods**. However, large differences in the distribution by time period exist on a country level. In FI and HU cocaine was only detected at weekdays during daytime hours. In ES it was frequently detected during all time periods. In IT it was detected frequently in all time periods except in the weekend at daytime hours. In NL single cocaine use was primarily detected during weekend nights, while in BE it was more frequently

⁷ Whole sample: all killed car drivers (N=483); Responsibility analysis was conducted with the method proposed by Robertson and Drummer (1994) which allocated the 483 subjects in 419 cases and 64 controls. Subsequently a toxicological analysis was carried out where the 23 DRUID-core substances as well as several other additional substances were screened for.

detected during weekday nights. The results of the logistic regression ...based on the data of BE, NO, HU and PT, suggest that the highest prevalence would be found among the **age group 25- 34**.

Amphetamines are mainly used by drivers **younger than 35**; (in NL and SE however, the largest proportion was formed by drivers aged 35-49 years). It is in **some countries more prevalent among male drivers and in other countries more among female drivers**. In LT the prevalence of amphetamines among female drivers was almost 20 times higher than for male drivers. This large difference could partially be caused by the small sample size of female drivers (n = 121). The distribution of amphetamines by **time period differs per country**. In NL and NO amphetamines are mainly used in night time periods. In SE it is detected during night times as well, but only on weekdays. In DK and FI amphetamine use was only detected during weekend days and in CZ and ES it was detected primarily in the weekend both during the day and during the night. In LT amphetamines were only detected in traffic during weekday hours.

Illicit opiates. Most users of illicit opiates are between **35 and 49 years old**, except for BE where most users were younger than 25. Illicit opiate use was not detected among drivers from Northern European countries (DK, FI, NO, SE) and from CZ, LT and HU. Illicit opiates are mainly used by **male** drivers. Illicit opiates were not found during weekday nights in any of the 13 countries. In IT and PT the prevalence was the highest during weekend nights, in BE, NL and ES during weekend days and in PL at weekdays during daytime”.

Alcohol and drugs combination. In general the prevalence for alcohol-drug combinations for **male** drivers is higher than for female drivers. The only exceptions are NO, where the prevalence of alcohol among male drivers was equal to that of female drivers, and Italy where the prevalence of alcohol among female drivers was even higher than that in men.

Most drivers who used alcohol and drugs in combination with each other were younger than 35 years old, except for IT, where the drugs-alcohol combination was relatively more prevalent among drivers over 35 years old.

The combined use of alcohol and drugs was mainly detected during night time hours. However, in FI, CZ and BE the prevalence during daytime hours was relatively high as well.

Drug-drug combinations were most frequently detected among drivers younger than 50 years. The distribution over the four age groups varies largely though over the different countries.

In general multi-drug use is more common among male than among female drivers. However, in CZ, SE, and especially in HU, the proportion of female users is larger.

The distribution of multi-drug use by time period varies considerable between the different countries. In Southern European countries and in NO the prevalence of drug-drug combinations was relatively high during night time hours at weekdays. The prevalence during daytime hours at weekdays was the highest in Italy and HU. The results of the logistic regression analysis also indicate no significant overall trend of time period”.

The DRUID investigation on motives behind drug impaired driving (D2.2.1) carried out in SE and HU showed that addicted drivers did not believe that they would be stopped by the police. Furthermore, they did not believe that alcohol or drugs would impair their driving and therefore they did not perceive any real risks of driving (D2.2.1).

Findings of the smartphone study in DE indicate that especially moderate substance users can realistically judge their intoxication and are responsible-minded concerning drugs in traffic (D2.2.2).

Seriously injured or killed drivers

In both DRUID hospital studies (seriously injured and killed drivers) the distribution of gender and age groups of those subjects tested positive for illicit drugs showed high national variability. Illicit drugs were in general mainly detected among male seriously injured/killed drivers and consumption tends to drop in the age group 50 and over. The majority of drugs appeared to be used in combination with other psychoactive substances (mainly alcohol) (D2.2.5 p. 63 ff):

3.2.3 Accident risk for driving with illicit drugs

Based on case-control studies, the relative risk of serious injury or fatality for different illicit substances varies between the substances. For: THC about 1-3 times; benzoyllecgonine, cocaine and illicit opiates about 2-10 times; amphetamines about 5-30 times) as high as that of

drivers below the DRUID cut-off for any substance. Some of the risk estimates for illicit drugs vary to a high degree among the single countries; others are based on few positive cases and/or controls which result in very wide confidence intervals. Therefore the estimates are uncertain. (D2.3.5; see also D1.1.2b, D1.2.1, D2.3.2). The risk multiplies with combined use (e.g. alcohol) (e.g. D2.3.2, D2.3.5).

Although the study designs of the single DRUID risk estimation studies do not allow precise comparison of the calculated accident risks (e.g. case-control studies for the risk of responsibility, case-control studies for injury risk), they point into the same direction.

The FR responsibility study indicates a significant dose effect for cannabis: risk of about twice that of drivers not positive for cannabis (≥ 1 ng/ml) (the risk for alcohol is 8 times that of drivers not positive for alcohol (< 0.01 g/L)). The increased risk effect of responsibility in fatal accidents remains significant after adjustment for age, sex and alcohol (adjusted OR 1.89 [95% CI 1.43-2.51]). There is no interaction between alcohol and cannabis on the higher risk of causing road crashes; in other words, there is merely a multiplicative effect between the two ($8.39 \times 1.89 = 15.86$). For amphetamines, cocaine and opiates no significant increase/decrease of risk of being responsible in a fatal accident could be observed (D2.3.2).

The findings of the DRUID case-control study (D2.3.5) underline the results mentioned above. Odds ratios for different illicit substances have been calculated by means of data from BE, DK, FI, IT, LT and NL (seriously injured drivers) and data from FI, NO, PT and SE (killed drivers) separately for each country and for all countries as a whole. The odds ratios are adjusted for age and gender and the controls were weighted with the traffic distribution in eight time periods over the week. Table 21 shows the calculated OR (illicit drugs) for getting seriously injured and table 22 for getting killed based on aggregated data (D2.3.5). The results indicate an increase of the relative risk of being seriously injured in an accident of about 1-30 times, with a slightly increased risk for driving with THC (of about 1-3 times), a medium increased risk for driving with benzoyllecgonine, cocaine and illicit opiates (of about 2-10 times) and a highly increased risk for driving with amphetamines (of about 5-30 times) compared to the risk for drivers below the DRUID cut-off for any substance. Note that some of the risk estimates for illicit drugs vary to a large degree among the single countries; others are based on few positive cases and/or controls which result in wide confidence intervals. Therefore these estimates are uncertain. Equivalent data for combined use are presented in table 23 and 24.

Table 21: Overview of OR (illicit drugs alone) for getting seriously injured based on aggregated data (D2.3.5)

Reference	Included country	OR + CI	Illicit drugs				
			Amphetamines	Benzoyllecgonine	Cocaine**	THC***	Illicit opiates
D2.3.5 DRAFT	BE, DK, FI, IT, LT, NL	Crude OR	9.66*	5.36*	3.41*	1.86*	4.03*
		95% CI	4.80-19.46	2.53-11.34	1.61-7.21	1.20-2.88	1.32-12.32
		Adjusted OR	8.35	3.70	3.30	1.38	2.47
		OR 95% CI	3.91-17.83	1.60-8.57	1.40-7.79	0.88-2.17	0.50-12.10

* In the case of 0 counts in one of the groups: Positive cases, negative cases, positive controls and negative controls, 0.5 was added to all four cells in the data from each such country when calculating crude OR (Greenland et al., 2000); ** Cocaine or cocaine + benzoyllecgonine; *** THC or THC + THCCOOH

Table 22: Overview of OR (illicit drugs alone) for getting killed based on aggregated data (D2.3.5)

Reference	Included country	OR 95% CI	Illicit drugs				
			Amphetamines	Benzoyllecgonine	Cocaine**	THC***	Illicit opiates
D2.3.5 DRAFT	FI, NO, PT, SE	Crude OR	25.44*	6.87*	22.34*	1.80*	10.04*
		95% CI	10.81-59.90	1.49-31.76	3.66-136.53	0.73-4.44	2.04-49.32
		Adjusted OR	24.09	n.a.	n.a.	1.33	n.a.
		OR 95% CI	9.72-59.71			0.48-3.67	

* In the case of 0 counts in one of the groups: Positive cases, negative cases, positive controls and negative controls, 0.5 was added to all four cells in the data from each such country when calculating crude OR (Greenland et al., 2000); ** Cocaine or cocaine + benzoyllecgonine; *** THC or THC + THCCOOH

Table 23: Overview of OR (combined use) for getting seriously injured based on aggregated data (D2.3.5)

Reference	Included country	OR + CI	Combined use	
			Alcohol-drug(s)	Multiple drugs
D2.3.5 DRAFT	BE, DK, LT, NL	Crude OR	31.97	
		95% CI	20.76-49.25	
D2.3.5 DRAFT	BE, DK, FI, IT, LT, NL	Adjusted OR	28.82	8.64*
		95% CI	18.41-45.11	5.85-12.75
D2.3.5 DRAFT	BE, DK, FI, IT, LT, NL	Crude OR		8.64*
		95% CI		5.85-12.75
D2.3.5 DRAFT	BE, DK, FI, IT, LT, NL	Adjusted OR		8.01
		95% CI		5.34-12.01

Finland and Italy have been left out of the calculations of OR for alcohol and alcohol-drug(s) because of bias in collecting data for the control samples

* In the case of 0 counts in one of the groups: Positive cases, negative cases, positive controls and negative controls, 0.5 was added to all four cells in the data from each such country when calculating crude OR (Greenland et al., 2000)

Table 24: Overview of OR (combined use) for getting killed based on aggregated data (D2.3.5)

Reference	Included country	OR 95% CI	Combined use	
			Alcohol-drug(s)	Multiple drugs
D2.3.5 DRAFT	NO, PT	Crude OR	41.22	
		95% CI	22.59-75.24	
D2.3.5 DRAFT	FI, NL, PT, SE	Adjusted OR	31.52	16.77
		95% CI	16.83-59.05	9.95-28.27
D2.3.5 DRAFT	FI, NL, PT, SE	Crude OR		16.77
		95% CI		9.95-28.27
D2.3.5 DRAFT	FI, NL, PT, SE	Adjusted OR		18.51
		95% CI		10.84-31.63

Finland has been left out of the calculations of OR for alcohol and alcohol-drug(s) because of bias in collecting data for the control sample. Sweden did not include alcohol positive drivers in the control sample.

3.2.4 Results from experimental studies on the effect of illicit drugs on driving performance

Experimental studies have shown that the dose equivalent for BAC 0.5g/L-3.7ng/mL THC (range 3.1-4.5ng/mL) for oral administration and 3.8 ng/mL (range 3.3-4.5ng/mL) for smoked administration (D1.1.2b, see also D1.4.2 for more information on cut-offs equivalent to BAC 0.5g/L). Experimental studies evaluating the effect of stimulants on driving (MDMA and dexamphetamine) did not reveal impairing effects on driving performance. However, the stimulant effects of MDMA and dexamphetamine are not sufficient to overcome or compensate driving impairments produced by concomitant of alcohol use or sleep deprivation (D1.1.2b, D1.2.1).

Stimulants. The experimental studies on stimulants (D1.2.1) in WP1 showed that 3,4-methylmethamphetamine (MDMA; 25, 50 and 100mg) and dexamphetamine (10, 40mg) did not reveal impairing effects or increased risk caused by the drug consumption itself (low doses of stimulant drugs produce neutral or even stimulating effects on a range of psychomotor functions). It should be noted that doses of stimulants administered in the studies conducted within DRUID have been relatively low for (some) recreational drug users. But it was not possible to assess high doses due to medical and ethical constraints.

As stimulant drug consumption is often combined with sleep deprivation and/or concomitant alcohol use experimental studies investigated these effects. Sleep deprivation itself generates the same degree of impairment as BAC 0.8g/L. An increased risk taking behaviour could be observed only in combination with additional alcohol consumption. Stimulant effects of MDMA and amphetamine are not sufficient to overcome or compensate driving impairments produced by concomitant alcohol use or by sleep deprivation. The pharmacological effects of stimulants and the effects of drug use setting (e.g. poly-drug use, concomitant alcohol use and sleep deprivation) are closely intertwined and significantly contribute to degree of driver impairment. Very often users of stimulating drugs are not aware of post acute fatigue effects. They need to be educated about this effect and its possible implications on driving safety (D1.2.1).

Based on meta-analyses of experimental studies (D1.1.2b) no negative influence of stimulants on the fitness to drive can be stated. In summary there are more findings of performance improvements than of performance impairments. Dexamphetamine is the agent on which most studies are available

(dosage 1mg to 36 mg). Recent studies focused on the impact of designer amphetamine MDMA (ecstasy) on performance. In those studies more improvements than impairments were found, as well. Accordingly there is no performance decrement during the time of action after consumption of “normal” doses (40mg to 125mg) (D1.1.2b).

Cocaine has similar acute effects as amphetamines. From a meta-analysis of experimental studies no negative influence on the fitness to drive could be stated. Only some case-reports and non-experimental publications revealed negative effects. But overall there is a lack of studies focusing on impairments during the post acute phase (D1.1.2b).

On **Cannabis (THC)** 21 studies with 482 effects in total (doses 7.5 to 39mg) were included into a meta-analysis of the effects of oral administration of THC on performance (D 1.1.2b). This analysis reveals that the impairment caused by 3.7ng/mL THC (range 3.1 to 4.5ng/mL) is equal to that caused by 0.5g/L BAC. An additional meta-analysis on the effects of smoking of THC on performance leads to a comparable result. 78 studies with a total of 888 effects (doses 1 to 52 mg) were included in that meta-analysis. The dose equivalent to 0.5g/L BAC is 3.8ng/mL (range 3.3 to 4.55ng/mL). Therefore the results of both meta-analyses are in agreement (D1.1.2b).

3.2.5 Overview box – illicit drugs

Box 2: Summary of main DRUID results – ILLICIT DRUGS

Prevalence of illicit drugs in relation to road safety:

- **All DRUID investigations (e.g. D2.2.3, D2.2.5, D2.3.4) show that the prevalence of illicit drugs in the driver population (estimated EU mean 1.90%) is lower than the alcohol prevalence (estimated EU mean 3.48%) (D2.2.3).**
- **Within the accident involved drivers, the majority of drugs appeared to be used in combination with other psychoactive substances (mainly alcohol) (D2.2.5).**
- **THC is generally the most frequently detected illicit drug, followed by cocaine, but the prevalence of the different illicit substances show high national variability (e.g. D2.2.3, D2.2.5, D2.3.4).**
- General driving population (D2.2.3):
 - Illicit drugs: estimated EU mean for one or more illicit substances 1.90% (range 0.22-8.20%); main EU region: Southern Europe;
 - THC alone: estimated EU mean prevalence 1.32% (range 0-5.99%); prevalence ranking from all investigated substances #3; main EU region: Southern Europe; on average 20-30% of THC use was in combination with other psychoactive substances;
 - Cocaine alone: estimated EU mean prevalence 0.42%, (range 0-1.49%); prevalence ranking from all investigated substances #5; main EU region: Southern Europe; on average around 50% of cocaine use was in combination with other psychoactive substances;
 - Amphetamine alone: estimated EU mean prevalence 0.08%; (range 0-0.38%); prevalence ranking from all investigated substances #11; main EU region: no specific region; on average around 50% of amphetamine use was in combination with other psychoactive substances;
 - Illicit opiates alone: estimated EU mean prevalence 0.07%; (range 0-0.30%); prevalence ranking from all investigated substances #12; main EU region: Southern Europe; illicit opiates were relatively frequently used in combination with other psychoactive substances;
 - Alcohol ($\geq 0.1g/L$) - drug combinations: estimated EU mean prevalence 0.37% (range 0.0-1.14%); prevalence ranking from all investigated substances #8; main EU region: Southern Europe; relative proportion varies between 0-23%; Countries with higher prevalence for single alcohol and single drug use have, as expected, higher prevalence for combined use of alcohol and drugs;
 - Drug-drug combinations: estimated EU mean prevalence 0.39% (range 0-1.22%); prevalence ranking from all investigated substances #7; main EU region: Northern Europe; most commonly used drugs in multi-drug combinations are THC, cocaine, and benzodiazepines; proportion of multi-drug use is on average around 10% of all drug use (highest in IT where 22% of the drug using had been using two or more different drugs).

- Seriously injured and killed drivers (D2.2.5; D2.2.4; D2.3.4):
 - Hospital study: no clear picture of the distribution of illicit drugs among injured and killed drivers could be identified, as the prevalence of different substances showed great national variability. Seriously injured drivers: THC (range 0.5-7.6%) second most common toxicological finding after alcohol. Amphetamine use more common in northern Europe; cocaine use more prevalent in southern Europe. Killed drivers: THC was number four (range 0- 6.1%), after alcohol, benzodiazepines and amphetamines. Combined user (alcohol-drug and drug-drugs): The majority of drugs appeared to be used in combination with other psychoactive substances (mainly alcohol). The group of alcohol-drug combined users were within the seriously injured drivers and killed drivers second most represented group in almost all countries. The combined use of “drug-drug” represent either third or fourth biggest group for percentage of positive subjects among seriously injured drivers (D2.2.5).
 - Responsibility study in DE, LT, HU, SK (D2.3.4): about 4.3% of all tested drivers were under the influence of illicit drugs (mainly cannabis).

Characteristics of drivers tested positive for illicit drugs:

- ***Illicit drugs were in general mainly detected among young male drivers, during all times of the day but mainly at the weekend (D2.2.3).***
- ***Combined use of alcohol and drugs (illicit drugs and/or psychoactive medicine) is in general often prevalent among young (<35 years) male drivers during night time hours (D2.2.3).***
- ***Multiple drugs (illicit drugs and/or psychoactive medicines) use is in general most common in males (D2.2.3).***
- ***Age groups and time periods vary considerably by country (D2.2.3).***
- General driving population (D2.2.3):
 - Cannabis in drivers in traffic (D2.2.3):
 - Most prevalent among young drivers (18-34 years);
 - 2-3 times more prevalent in male than in female drivers;
 - Main time period differs per country.
 - Cocaine in drivers in traffic (D2.2.3):
 - Almost all cocaine users younger than 50 years; within logistic regression (BE, NO, HU PT) highest prevalence would be found among the age group 25- 34;
 - 2 times more prevalent in male than female drivers;
 - Main time period differs per country.
 - Amphetamines in drivers in traffic (D2.2.3):
 - Most prevalent among young drivers (18-35 years);
 - The gender effect differs by country;
 - Main time period differs per country.
 - Illicit opiates (D2.2.3):
 - Most prevalent among middle aged drivers (35-49 years);
 - More prevalent in male than in female drivers;
 - Main time period differs per country.
 - Alcohol and drugs combination (D2.2.3):
 - Most prevalent among young drivers (18-34);
 - More prevalent in male than in female drivers;
 - Most commonly detected in night-time hours.
 - Drug-drug combination (D2.2.3):
 - Mainly detected in middle aged drivers (<50);
 - More prevalent in male than in female drivers;
 - Main time period differs per country.
- Seriously injured and killed drivers (D2.2.5):
 - Most prevalent in young and middle aged drivers (<50 years),
 - More prevalent in male than in female drivers;
 - The majority of drugs appeared to be used in combination with other psychoactive substances (mainly alcohol).

- Motives behind impaired driving (D2.2.1; D2.2.2):
 - Addicted drivers did not believe that they would be stopped by the police (D2.2.1)
 - They did not believe that alcohol or drugs would impair their driving and therefore they did not perceive any real risks of driving (D2.2.1).
 - Findings indicate that especially moderate substance users can realistically judge their intoxication and are responsible-minded concerning drugs in traffic (D2.2.2).

Accident risk for driving with illicit drugs:

- **Based on case-control studies, the relative risk of serious injury or fatality for different illicit substances varies between the substances. For: THC about 1-3 times; benzoylecgonine, cocaine and illicit opiates about 2-10 times; amphetamines about 5-30 times) as high as that of drivers below the DRUID cut-off for any substance. Some of the risk estimates for illicit drugs vary to a high degree among the single countries; others are based on few positive cases and/or controls which result in very wide confidence intervals. Therefore the estimates are uncertain. (D2.3.5; see also D1.1.2b, D1.2.1, D2.3.2).**
- **The risk multiplies with combined use (e.g. alcohol) (e.g. D2.3.2, D2.3.5).**
- DRUID accident risk studies:
 - Responsibility study FR (D2.3.2): drivers involved in fatal accidents and positive for cannabis (≥ 1 ng/ml), had a risk of about twice as high as that of drivers not positive for cannabis (adjusted OR 1.89 [95% CI 1.43-2.51]) (in comparison alcohol: 8 times as high (adjusted OR 8.39 [95% CI 6.95-10.11])). Combined use of alcohol and cannabis multiplies the risk of causing a fatal accident ($8.39 \times 1.89 = 15.86$).
 - Case control study (D2.3.5): relative risk of serious injury or fatality for a driver when positive for different illicit substances is estimated to be about 1-30 times (for: THC -> 1-3 times; benzoylecgonine and cocaine -> 2-10; amphetamines 5-30 times) as high as that of drivers below the DRUID cut-off for any substance.

Results from experimental studies on the effect of illicit drugs on driving performance

- **Experimental studies have shown that the dose equivalent for BAC 0.5g/L-3.7ng/mL THC (range 3.1-4.5ng/mL) for oral administration and 3.8 ng/mL (range 3.3-4.5ng/mL) for smoked administration (D1.1.2b, see also D1.4.2 for more information on cut-offs equivalent to BAC 0.5g/L).**
- **Experimental studies evaluating the effect of stimulants on driving (MDMA and dexamphetamine) did not reveal impairing effects on driving performance. However, the stimulant effects of MDMA and dexamphetamine are not sufficient to overcome or compensate driving impairments produced by concomitant of alcohol use or sleep deprivation (D1.1.2b, D1.2.1).**

3.3 Medicines

3.3.1 Prevalence of psychoactive medicines in relation to road safety

DRUID studies indicate that some selected psychoactive medicines (benzodiazepines, medicinal opiates and opioids and Z-drugs) are less prevalent in the driving population (estimated EU mean 1.4%) (D2.2.3) as well as is in seriously injured drivers (D2.2.5) compared to alcohol (estimated EU mean 3.48%) and illicit drugs (estimated EU mean 1.90%). Among the killed drivers the presence of benzodiazepines was the second most frequent toxicological finding after alcohol (D2.2.5). Psychoactive medicines, such as (frequently used) antidepressants, anti-epileptics and antipsychotics, were not included in the DRUID studies. Therefore an underestimation of prevalence should be considered. In most countries benzodiazepines were the most common psychoactive medicines in traffic but as for illicit drugs the prevalence of the different psychoactive medicines show high national variability (D2.2.3, D2.2.5). Epidemiological studies indicate a major increase in the consumption of antidepressants and drugs used in addictive disorders in the general population in Europe within the last years (D2.1.1).

General driving population

Within the DRUID roadside survey the prevalence rates for psychoactive medicines were in most countries (7 out of 13) between 1.4 - 1.8% (estimated EU mean 1.36%). The highest prevalence was found in BE and PT just below 3% and the lowest in PL (0.17%) (see figure 34). In general benzodiazepines were the most prevalent psychoactive medicine in traffic (estimated European mean: 0.90%). Medicinal opiates and opioids were less prevalent (estimated European mean: 0.35%) and Z-drugs were very seldom detected in EU countries (estimated European mean: 0.09%), except in NO where they were detected among 0.69% of all drivers.

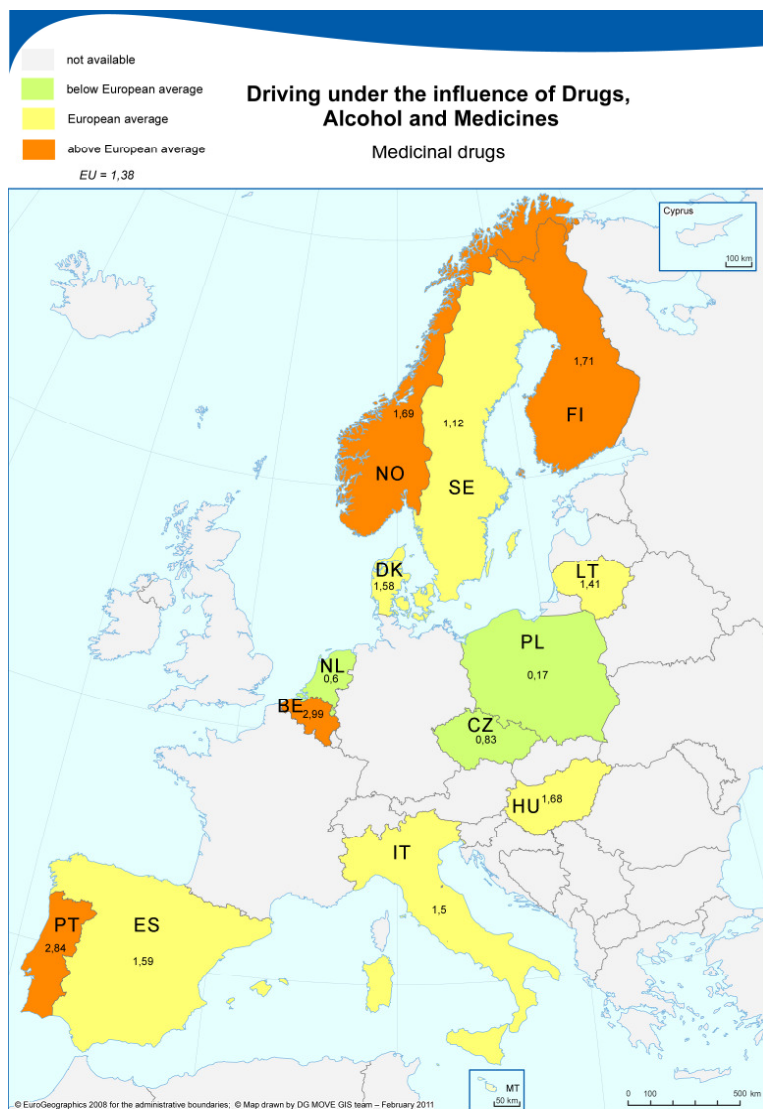


Figure 34: Geographical presentation of psychoactive medicine use by car drivers in the EU (D2.2.3 PART I p. 7)

The prevalence of different psychoactive medicines shows high national variability. The according results have been summarized within the DRUID roadside survey as follows (D2.2.3 PART I p. 141f)):

“**Benzodiazepines**⁸ were detected in all 13 countries. The highest prevalence was detected in PT, followed by BE, HU, ES and LT. The average European mean was 0.90%. Benzodiazepines were not often used in **combination** with other psychoactive substances. In **most** countries the proportion was around **15%**. However in IT almost half of all benzodiazepines were used in combination (see figure 35).

⁸ The benzodiazepines group consists of diazepam, nordiazepam, oxazepam, lorazepam, alprazolam, flunitrazepam, and clonazepam.

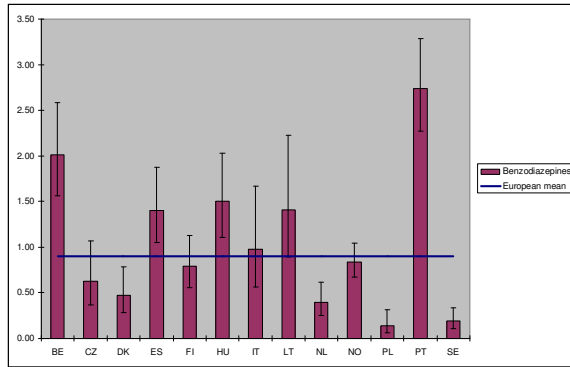


Figure 35: Prevalence of benzodiazepines alone by gender; prevalence in percentages (D2.2.3 Part I p. 86)

Medicinal opiates and opioids⁹ (estimated European mean: 0.35%). The highest prevalence was found in DK followed by BE, SE, FI and IT. No medicinal opiates and opioids were detected among drivers in LT. In HU, IT and PT medicinal opiates and opioids are relatively often used in combination with other psychoactive substances. In CZ, ES and PL only single use was detected (see figure 36).

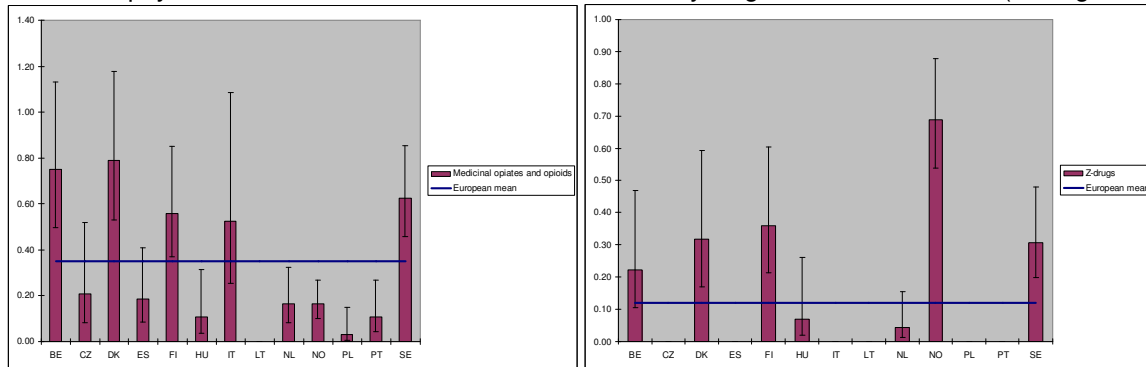


Figure 36: Prevalence of medicinal opiates and opioids alone by country; prevalence in percentages (D2.2.3 Part I p. 102)

Figure 37: Prevalence Z-drugs alone by country; prevalence in percentages (D2.2.3 Part I p. 95)

Z-drugs¹⁰ were **not commonly** detected among European drivers (estimated European mean: 0.09%). The prevalence is the highest in the Northern European countries (NO, FI, DK, SE), followed by BE, HU and the NL. In all other countries no Z-drugs were detected among drivers. Z-drugs were relatively often combined with other psychoactive substances in FI and HU. In DK only single use of Z-drugs was detected. In BE, NO, SE and NL the relative proportion of combinational use of Z-drugs varied between 9% and 26% (see figure 37)."

Seriously injured and killed drivers

Within the hospital study the prevalence use among all seriously injured drivers, of benzodiazepines (range 0-10.2%) was third most frequent finding after alcohol (range 17.7-42.5%) and THC (range 0.5-7.6%). The highest prevalence was found in FI (10.2%) and lowest in NL (0.0%). The prevalence of amphetamines ranged between 0.1 % (IT) and 4.2% (DK) and those for cocaine and/or benzoylecgonine between 0.0% (FI) and 5.4% (IT). No positive findings for Z-drugs were recorded in IT and LT. LT had almost a double amount of positive subjects for medicinal opioids compared with the other countries in the study.

Within all killed drivers benzodiazepines (range 1.8% (PT) - 13.3% (FI)), were the second most found substance group after alcohol ($\geq 0.1\text{g/L}$; range 19.0 - 44.9%), followed by amphetamine (range 0.0% (PT) – 7.4% (NO)). However, it should be noted that three of the participating countries (FI, NO and SE) are part of the Scandinavian area where the use of amphetamines is generally higher than in the southern European countries. SE had a double amount of subjects positive for medicinal opioids compared with the other three countries (D2.2.5).

⁹ The medicinal opiates and opioids group consists of morphine, codeine, methadone and tramadol.

¹⁰ The Z-drugs group consists of zolpidem and zopiclone.

Within the responsibility study in DE, LT, HU and SK (D2.3.4) 13% of the killed drivers positive for psychoactive substances were tested positive for psychoactive medicines which represented 5.6% of the whole sample (n=483). The most common substances were benzodiazepines (3.7% of the whole sample¹¹) (D2.3.4).

3.3.2 Characteristics of drivers tested positive for psychoactive medicines

Psychoactive medicines were in general mainly detected among older female drivers during daytime hours (D2.2.3).

General driving population

Within the DRUID roadside survey the following specific characteristics of drivers impaired by psychoactive medicines have been identified (D.2.2.3, p. 139f). The information in regard to drivers impaired by Z-drugs is based on a very small sample and was not included within this Deliverable.

“Benzodiazepines. The highest prevalence for **single benzodiazepine use** was detected among drivers aged **35 years and older**. However, in IT most benzodiazepines were used by young drivers aged 18-24. Unlike for illicit drugs, benzodiazepine use is relatively more frequently detected among **female** drivers. Especially in LT the proportion of female drivers was much higher than that of male drivers. In DK, FI and PL the proportion of benzodiazepine use was higher among male drivers though. Benzodiazepines were most commonly detected during **daytime** in many of the countries. Only in PL and PT relatively more drivers were positive for the use of benzodiazepines during night time hours. This trend was generally confirmed by the logistic regression analysis.

Medicinal opiates and opioids were mainly detected among drivers of **35 years and older**.

In most countries the proportion of **female** drivers is larger, except for ES, FI, NO, and PT where the proportion of male drivers positive for medicinal opiates and opioids was larger. The logistic regression results indicate a general higher prevalence among female drivers as well. The distribution over the four different DRUID time periods varies largely, but in general highest prevalence was detected during **daytime hours**. In DK though, most medicinal opiates and opioids were detected in weekend nights and in FI during weeknights”.

Seriously injured or killed drivers

In both DRUID hospital studies (seriously injured and killed drivers) the distribution of gender and age groups of those subject positive for psychoactive medicines showed high national variability. Psychoactive medicines were in general mainly detected among male seriously injured/killed drive. The percentage of positives appeared to be generally higher in older age groups (>35 years). The majority of psychoactive medicines within seriously injured/killed drivers appeared to be used in combination with other psychoactive substances (mainly alcohol and benzodiazepines) (D2.2.5 p. 86 ff):

3.3.3 Accident risk for driving with psychoactive medicines

Alcohol impaired driving is the main problem in traffic safety, but also psychoactive medicines can constitute a problem in traffic safety. Therefore, both health care providers and patients should be properly informed and aware of the potential risks associated with the use of psychoactive medicines (link WP4/7). Based on case-control studies, the relative risk of serious injury or fatality for benzodiazepines + Z-drugs and medicinal opioids) is estimated to be about 2-10 times (medicinal opioids in the upper part of the interval; benzodiazepines + Z-drugs in the lower part of the interval) as high as that of drivers below the DRUID cut-off for any substance (D2.3.5).

Although the study designs of the single DRUID risk estimation studies do not allow precise comparison of the calculated accident risks, they point into the same main direction.

¹¹ Whole sample: all killed car drivers (N=483)

Within NL relative accident risk study of patients using psychoactive medicines (D2.3.1) an increased traffic accident risk was also seen in: new (inexperienced) users, intermediate and long half-life benzodiazepine users, female users, and young/middle-aged users (these associations were not always statistically significant). The risk of being involved in an accident is highest for users of modern antidepressants (1.76, CI: 1.38-2.24), followed by patients who use combinations of psychoactive medicines (1.55, CI: 1.20-2.02), and patients using at least one psychoactive medication (1.28, CI: 1.12-1.46) (D2.3.1).

In the DRUID case-control study (D2.3.5) odds ratios for different medicines have been calculated by means of data from BE, DK, FI, IT, LT and NL (seriously injured drivers) and data from FI, NO, PT and SE (killed drivers) separately for each country and for all countries as a whole. The odds ratios are adjusted for age and gender and the controls were weighted with the traffic distribution in eight time periods over the week. Table 25 shows the calculated OR (medicine) for getting seriously injured and table 26 for getting killed based on aggregated data (D2.3.5).

Table 25: Overview of OR (medicine) for getting seriously injured based on aggregated data (D2.3.5)

Reference	Included country	OR 95% CI	Medicine	
			Benzodiazepines + Z-drugs	Medicinal opioids
D2.3.5 DRAFT	BE, DK, FI, IT, LT, NL	Crude OR	1.73	7.99*
		95% CI	1.19-2.51	5.73-11.15
D2.3.5 DRAFT	BE, DK, FI, IT, LT, NL	Adjusted OR	1.99	9.06
		95% CI	1.36-2.91	6.40-12.83

* In the case of 0 counts in one of the groups: Positive cases, negative cases, positive controls and negative controls, 0.5 was added to all four cells in the data from each such country when calculating crude OR (Greenland et al., 2000)

Table 26: Overview of OR (medicine) for getting killed based on aggregated data (D2.3.5)

Reference	Included country	OR 95% CI	Medicine	
			Benzodiazepines + Z-drugs	Medicinal opioids
D2.3.5 DRAFT	FI, NO, PT, SE,	Crude OR	5.11	4.82
		95% CI	3.72-7.02	2.61-8.88
D2.3.5 DRAFT	FI, NO, PT, SE,	Adjusted OR	5.40	4.82
		95% CI	3.90-7.46	2.60-8.93

The results of the DRUID case-control study (D2.3.5) indicate a medium increased relative risk of being seriously injured in an accident for benzodiazepines + Z-drugs and for medicinal opioids of about 2-10 times higher than that of drivers below the DRUID cut-off for any substance. There is, however, a tendency that the risk for benzodiazepines + Z-drugs lies in the lower part of the interval whereas the risk for medicinal opioids lies in the upper part of the interval.

3.3.4 Results from experimental studies on the effect of psychoactive medicines on driving performance

Psychoactive medicines can impair driving performance (e.g. D1.2.2, D1.1.2b, D1.1.2c). Besides the agent itself there are many factors influencing the degree of impairment (e.g. galenics, route of administration, dose, time period between administration and driving, concomitant use of other (medicinal) drugs, habituation). Zopiclone (7.5mg) and alprazolam (0.5mg) produced significant driving impairment in patients as well as in healthy controls during morning driving 10-11 hrs after drug intake (D1.2.2). The impairing potential of Codilprane® varies with age (D1.2.2). Single doses (10 and 20mg) of Dronabinol (Marinol®) impaired road tracking performance of occasional cannabis users (representing acute effects of Dronabinol) during on-the-road driving tests in a dose related manner. Those impairments were bigger than the impairment caused by BAC of 0.5g/L (D1.2.2). After habituation transdermal application of opioid analgesics as well as oral administration of slow release formulations of opioid analgesics caused no impairment in patients suffering from chronic pain (D1.2.2). Even at low dosages methadone and buprenorphine caused impairment when given as a single dose to healthy subjects. No clear evidence exists if patients under maintenance treatment are able to drive safely. Many maintenance patients use other substances in addition, so it is recommended that a screening for other substances is done if a maintenance patient should be allowed to drive (D1.1.2c).

The main results of D1.2.2 can be summarized as follows:

Standardized driving tests demonstrated that nocturnal intake of **zopiclone** (7.5mg) and **alprazolam** (0.5mg) produced significant driving impairment in patients as well as in healthy controls during morning driving 10-11 hrs after drug intake. Whereas chronic users did not experience any sedative effects of zopiclone and alprazolam, infrequent users and healthy users reported feelings of reduced alertness and sleep. This lack of awareness of the (residual) sedative effects of zopiclone and alprazolam may lead insomnia and anxious patients to the false belief that car driving is safe during treatment with these drugs.

Codiliprane® is a combination of codeine and paracetamol available on the European market. Results of the driving test data indicate that the impairing potential of Codiliprane® varies with age. Codiliprane did not impair driving performance when administered to young, healthy volunteers, even at high doses. But Codiliprane® produced driving impairment when administered to elderly healthy volunteers even at low doses.

Single doses (10 and 20mg) of **Dronabinol** (Marinol®) impaired road tracking performance of occasional cannabis users (representing acute effects of Dronabinol) during on-the-road driving tests in a dose related manner. Those impairments were bigger than the impairment caused by BAC of 0.5g/L. The effects of Dronabinol on driving performance of heavy cannabis users (representing chronic use of Dronabinol) were less pronounced or even absent. This suggests that tolerance to the impairing effects develops.

Driving performance of a sample of patients suffering from chronic non-cancer pain under long-term treatments with opioid analgesics (**transdermal Fentanyl, transdermal Buprenorphine, slow-release Oxycodone (sometimes in combination with naloxone), slow-release Hydromorphone or slow-release Morphine**) was not impaired compared to a sample of healthy controls.

Some performance measures in driving tests of schizophrenic patients with a history of psychotic episodes treated with **Risperidone** or **Paliperidone** were impaired (D1.2.2).

Within D1.1.2c studies dealing with application of a single dose of **opioids, narcoanalgesics** and **hallucinogens** have been summarized. For all substances at least impairment in certain groups of tasks has been found, although this does not necessarily mean that this would increase the accident risk in real traffic. In an overview the impairing doses and concentrations are related to the half-life of the drugs, which gives an idea how long the impairment can be assumed for the respective substance. Patients treated chronically with morphine showed no impairment compared to untreated patients (although in comparison to healthy volunteers impairment in psychomotor (and probably in cognitive) abilities was found. Pain by itself reduces psychomotor functions.

Substances used in maintenance treatment (methadone, buprenorphine) cause impairment even at low dosages when given as a single dose to healthy subjects. There is no clear evidence if patients treated chronically are able to drive, as there are huge interindividual differences. Many of maintenance patients use other substances additionally, so it is recommended that a screening for other substances should always be done if a maintenance patient should be allowed to drive (D1.1.2c).

Meta-analysis on experimental studies showed that there are many factors influencing the degree of impairment caused by the intake of a medicinal drug, e.g. active agent, galenics, route of administration, dose, time of administration (in the day, in the night), time period between administration and performance requirement, compliance and disposition of the patient as well as concomitant use of additional drugs. Generally speaking the start of a therapy is the most crucial phase with respect to performance impairment. Derived from published studies D 1.1.2b provides in a meta-analytic approach detailed information for major medicinal drugs (psycholeptics, anxiolytics, hypnotics and sedatives, psychoanaleptics, antidepressants and antihistamines) on the kind of performance impairments (see figure 38 as an example), the duration of the impairment and the degree of impairment caused by a certain dosage of a given active agent.

It is, at most, more the dose than the agent itself that determines the degree of performance impairment. In addition the available information of a specific active agent is summarized and information on the dosage causing an impairment equivalent to 0.5g/L BAC is given (see table 27 as example).

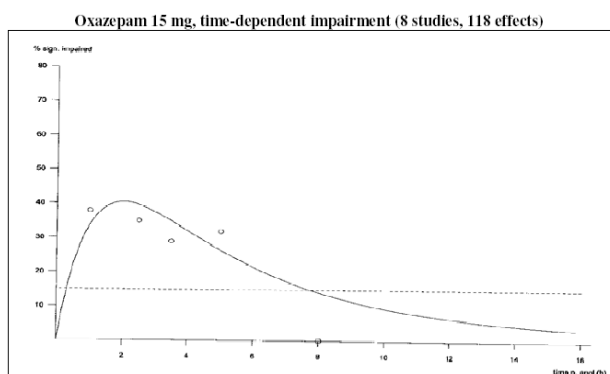


Figure 38: Oxazepam 15 mg, time-dependent impairment (D 1.1.2 B, p. 57).

Table 27: Oxazepam, summary of results.

Summary	N05BA04 Oxazepam	
Single administration		
Number of studies	26	
Number of effects	377	
Checked doses (mg)	10 - 90	
Recommended dose (mg)	10 - 30 / day	
Tabularly evaluable doses (mg)	15	30
No. studies / no. effects	8 / 118	11 / 115
Max. sign. impaired test results (%)	41 (34 - 46)	52 (46 - 61)
Hour p.a. of maximum impairment	2.0 (1.25 - 2.0)	2.25 (2.25 - 2.5)
Alcohol equivalence of max. imp. (%)	0,05 - 0,08	>0,08
Duration p.a. until <15% impairment (h)	7.75 (7.75 - 11.5)	9.0 (9.0 - 10.0)
Degree of impairment	104 (89 - 121)	170 (142 - 235)
0,05% alcohol equ. (ng/mL)	(330) ((300 - 390))	
% of max. rec. dose (mg)	(218) of 10 ((199 - 258))	

Blood specimens are often drawn several hours after the actions. Pharmacokinetic data makes it possible to calculate the concentration of a given active agent at action time and to explain the effects at the time of the incident. Based on a comprehensive meta-analysis of pharmacokinetic studies time courses of plasma-concentration and other pharmacokinetic parameters (see figure 39 as example) are given for a huge number of major psychoactive medicines in this deliverable.

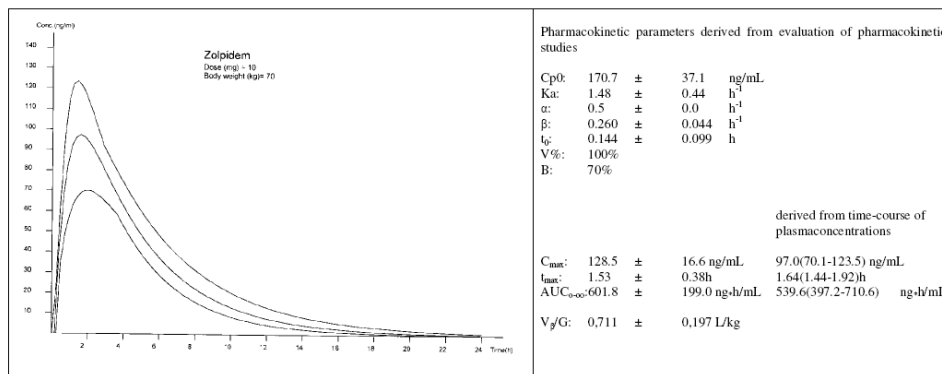


Figure 39: Plasma concentration-time curve of zolpidem after oral administration. (D 1.1.2 B, p. 469).

Further information on the effect of medicines on driving performance based on the literature have been evaluated and categorized in WP4 (classification, see according chapter and deliverables).

3.3.5 Overview box – psychoactive medicines

Box 3: Summary of main DRUID results – PSYCHOACTIVE MEDICINES

Prevalence of psychoactive medicines in relation to road safety:

- ***DRUID studies indicate that some selected psychoactive medicines (benzodiazepines, medicinal opiates and opioids and Z-drugs) are less prevalent in the driving population (estimated EU mean 1.4%) (D2.2.3) as well as is in seriously injured drivers (D2.2.5) compared to alcohol (estimated EU mean 3.48%) and illicit drugs (estimated EU mean 1.90%). Among the killed drivers the presence of benzodiazepines was the second most frequent toxicological finding after alcohol (D2.2.5). Psychoactive medicines, such as (frequently used) antidepressants, anti-epileptics and antipsychotics, were not included in the DRUID studies. Therefore an underestimation of prevalence should be considered.***
- ***In most countries benzodiazepines were the most common psychoactive medicines in traffic but as for illicit drugs the prevalence of the different psychoactive medicines show high national variability (D2.2.3, D2.2.5).***
- ***Epidemiological studies indicate a major increase in the consumption of antidepressants and drugs used in addictive disorders in the general population in Europe within the last years (D2.1.1).***
- General driving population (D2.2.3):
 - Psychoactive medicines: estimated EU mean for one or more psychoactive medicine 1.36% (range 0.17-2.99%); main EU region: no specific region;
 - Benzodiazepines alone: estimated EU mean 0.90% (range 0.14-2.73%); prevalence ranking from all investigated substances #4; main EU region: Southern Europe; not often used in combination with other psychoactive substances (proportion around 15% in most countries);
 - Medicinal opiates and opioids alone: estimated EU mean 0.35% (range 0.00-0.79%); prevalence ranking from all investigated substances #9; relatively often used in combination with other psychoactive substances; in CZ, ES and PL only single use was detected;
 - Z-drugs alone: estimated EU mean 0.09% (range 0-0.69%); prevalence ranking from all investigated substances #10; relatively often combined with other psychoactive substances.
- Seriously injured and killed drivers (D2.2.5; D2.2.4; D2.3.4):
 - Hospital study: no clear picture of the distribution of psychoactive medicines among injured and killed drivers could be identified, as the prevalence of different substances showed great national variability. Seriously injured drivers: benzodiazepines (range 0.0-10.2%) were third most frequent finding after alcohol and THC. Killed drivers:

benzodiazepines (range 1.8-13.3%), were the second most found substance group after alcohol, followed by amphetamine (D2.2.5).

- Responsibility study in DE, LT, HU, SK (D2.3.4): about 6% of all tested drivers were under the influence of psychoactive medicines (mainly benzodiazepines).

Characteristics of drivers tested positive for psychoactive medicines:

- ***Psychoactive medicines were in general mainly detected among older female drivers during daytime hours (D2.2.3).***
- General driving population (D2.2.3):
 - Benzodiazepines in drivers in traffic (D2.2.3):
 - Most prevalent among middle aged and older drivers (35+);
 - More prevalent in female than in male drivers;
 - Most commonly detected in daytime hours.
 - Medicinal opiates in drivers in traffic (D2.2.3):
 - Most prevalent among middle aged and older drivers (35+);
 - More prevalent in female than in male drivers;
 - Most commonly detected in daytime hours.
- Seriously injured and killed drivers (D2.2.5):
 - Most prevalent in middle aged and older drivers (35+);
 - More prevalent in male than in female drivers;
 - The majority of psychoactive substances appeared to be used in combination with other psychoactive substances (mainly alcohol and benzodiazepines).

Accident risk for driving with psychoactive medicines:

- ***Alcohol impaired driving is the main problem in traffic safety, but also psychoactive medicines can constitute a problem in traffic safety. Therefore, both health care providers and patients should be properly informed and aware of the potential risks associated with the use of psychoactive medicines (link WP4/7). Based on case-control studies, the relative risk of serious injury or fatality for benzodiazepines + Z-drugs and medicinal opioids) is estimated to be about 2-10 times (medicinal opioids in the upper part of the interval; benzodiazepines + Z-drugs in the lower part of the interval) as high as that of drivers below the DRUID cut-off for any substance (D2.3.5).***
- DRUID accident risk studies:
 - NL study (D2.3.1): The risk of being involved in an accident is highest for users of modern antidepressants (1.76, CI: 1.38-2.24), followed by patients who use combinations of psychoactive medicines (1.55, CI: 1.20-2.02), and patients using at least one psychoactive medication (1.28, CI: 1.12-1.46).
 - Case control study (D2.3.5): The medium increase of the relative risk of serious injury or fatality for a driver when positive for benzodiazepines + Z-drugs and medicinal opioids) is estimated to be about 2-10 times (higher risk for medicinal opioids; lower risk for benzodiazepines + Z-drugs) (D2.3.5).

Results from experimental studies on the effect of psychoactive medicines on driving performance

- ***Psychoactive medicines can impair driving performance (e.g. D1.2.2, D1.1.2b, D1.1.2c). Besides the agent itself there are many factors influencing the degree of impairment (e.g. galenics, route of administration, dose, time period between administration and driving, concomitant use of other (medicinal) drugs, habituation).***
- ***Zopiclone (7.5mg) and alprazolam (0.5mg) produced significant driving impairment in patients as well as in healthy controls during morning driving 10-11 hrs after drug intake (D1.2.2).***
- ***The impairing potential of Codiliprane® varies with age (D1.2.2).***
- ***Single doses (10 and 20mg) of Dronabinol (Marinol®) impaired road tracking performance of occasional cannabis users (representing acute effects of Dronabinol) during on-the-road driving tests in a dose related manner. Those impairments were bigger than the impairment caused by BAC of 0.5g/L (D1.2.2).***
- ***After habituation transdermal application of opioid analgesics as well as oral administration of slow release formulations of opioid analgesics caused no impairment***

in patients suffering from chronic pain (D1.2.2).

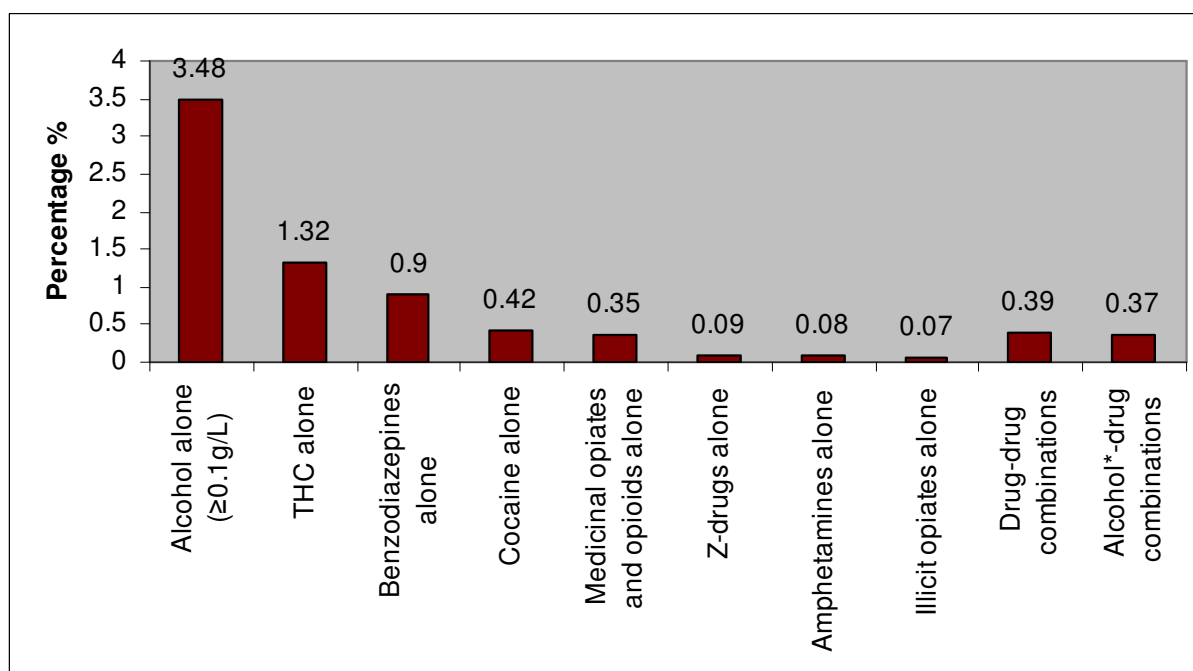
- *Even at low dosages methadone and buprenorphine caused impairment when given as a single dose to healthy subjects. No clear evidence exists if patients under maintenance treatment are able to drive safely. Many maintenance patients use other substances in addition, so it is recommended that a screening for other substances is done if a maintenance patient should be allowed to drive (D1.1.2c).*

3.4 Summary of the problem situation

The DRUID investigations show that alcohol impaired driving is the biggest problem (prevalence and risk estimation) in all EU MS. Therefore, **main focus of countermeasures on European-** as well as on **national** levels should always lie on preventing **alcohol** impaired driving. The prevalence distribution of other psychoactive substances than alcohol (illicit drugs, psychoactive medicines) shows more national variability. “In terms of preventive measures and legislative considerations alcohol should be emphasized as a key substance which presents a permanent threat to road safety in Europe” (D2.3.4 p. 4).

Estimated EU prevalence means and risk estimate data can form the basis for defining common thresholds within the community. The gathered national prevalence data on alcohol and other psychoactive substances provides the basis for specifying national countermeasures in more details (e.g. D2.2.3, D2.2.5). “National roadside surveys on the prevalence of substance use in traffic on a regular, say, annual or bi-annual base would be a helpful tool to monitor the trend of drink and drug driving” (D2.2.3 PART I p. 10).

The following estimations of EU mean prevalence of psychoactive substances based on the DRUID road side survey (D2.2.3) have been presented within this review (figure 40). A more detailed overview of the estimated European prevalence of psychoactive substances and killed can be found in D2.2.3 PART I p. 9 (annex 4).



*Alcohol (≥0.1g/L)

Figure 40: Estimated EU mean prevalence of use of psychoactive substances in traffic based on D2.2.3

Table 28 shows the percentage of driver positive for one or more substances (mutually exclusive groups) within the DRUID hospital studies (D2.2.5).

Table 28: Percentage of drivers positive for one or more substances (mutually exclusive groups) (D2.2.5 p. 4)

MUTUALLY EXCLUSIVE GROUPS - Percentage of drivers positive for the substance groups										
Toxicological finding	Seriously injured drivers						Killed drivers			
	BE (325)	DK (831)	FI (47)	IT (676)	LT (385)	NL (186)	FI (459)	NO (165)	PT (285)	SE (141)
Negative	47.4	69.7	55.3	68.0	72.2	66.1	57.7	60.0	52.3	69.5
Alcohol only	30.2	14.1	25.5	18.5	15.3	25.3	24.4	18.2	38.9	15.6
Amphetamine only	0.9	1.0	0.0	0.0	0.3	1.1	0.7	1.2	0.0	2.1
Benzoyllecgonine only	0.0	0.0	0.0	0.7	0.3	1.1	0.0	0.0	0.0	0.0
Cocaine	0.0	0.0	0.0	0.6	0.3	0.0	0.0	0.0	0.0	0.0
THCCOOH only	0.6	1.6	0.0	0.4	0.3	0.0	N.A.	N.A.	1.1	0.0
THC	1.5	0.6	2.1	1.6	0.3	0.5	0.0	1.8	0.0	0.7
Illicit opiates only	0.0	0.0	0.0	0.7	0.0	0.0	0.0	0.0	0.0	0.0
Benzodiazepines only	1.5	1.2	0.0	0.4	2.3	0.0	5.2	1.8	0.7	0.0
Z-drugs only	0.9	0.5	2.1	0.0	0.0	0.5	1.7	1.2	0.0	2.8
Medicinal opioids only	1.2	2.5	0.0	1.8	5.7	0.5	1.5	0.6	0.7	0.7
Alcohol + drug combination	13.2	5.4	10.6	4.6	2.3	4.3	7.2	7.9	6.0	4.3
Drug + drug combination	2.5	3.5	4.3	2.5	0.8	0.5	1.5	7.3	0.4	4.3
Total	100	100	100	100	100	100	100	100	100	100

Table 29 gives an overview of the presented adjusted OR for getting seriously injured and killed based on aggregated data (D2.3.5). Note that some of the risk estimates for illicit drugs vary to a large degree among the single countries; others are based on few positive cases and/or controls which result in wide confidence intervals. Therefore these estimates are uncertain.

Table 29: Overview of OR for getting seriously injured and killed drivers based on aggregated data (D2.3.5)

	Substance	Included country	OR for getting seriously injured		Included country	OR for getting killed		Risk of injury
			Adjusted OR	95% CI		Adjusted OR	95% CI	
Alcohol (BAC) alone	0.1-0.5g/L	BE, DK, LT, NL	1.18*	0.81-1.73	NO, PT	8.01	5.22-12.29	slightly increased
	0.5 - 0.8g/L	BE, DK, LT, NL	3.64	2.31-5.72	NO, PT	45.93	23.02-91.66	medium increased
	0.8 - 1.2g/L	BE, DK, LT, NL	13.35	8.15-21.88	NO, PT	35.69	15.68-81.22	highly increased
	≥1.2g/L	BE, DK, LT, NL	62.79	44.51-88.58	NO, PT	500.04	238.07-inf.	extremely increased
Illicit drugs alone	Amphetamines	BE, DK, FI, IT, LT, NL	8.35	3.91-17.83	FI, NO, PT, SE	24.09	9.72-59.71	highly increased
	Benzoyllecgonine	BE, DK, FI, IT, LT, NL	3.70	1.60-8.57		n.a.	n.a.	medium increased
	Cocaine**	BE, DK, FI, IT, LT, NL	3.30	1.40-7.79		n.a.	n.a.	medium increased
	THC***	BE, DK, FI, IT, LT, NL	1.38*	0.88-2.17	FI, NO, PT, SE	1.33*	0.48-3.67	slightly increased
	Illicit opiates	BE, DK, FI, IT, LT, NL	2.47*	0.50-12.10		n.a.	n.a.	medium increased
Medicines Alone	Benzodiazepines + Z-drugs	BE, DK, FI, IT, LT, NL	1.99	1.36-2.91	FI, NO, PT, SE	5.40	3.90-7.46	medium increased
	Medicinal opioids	BE, DK, FI, IT, LT, NL	9.06	6.40-12.83	FI, NO, PT, SE	4.82	2.60-8.93	medium increased
Combined use	Alcohol-drug****	BE, DK, LT, NL	28.82	18.41-45.11	NO, PT	31.52	16.83-59.05	extremely increased
	Drug-drug	BE, DK, FI, IT, LT, NL	8.01	5.34-12.01	FI, NO, SE, PT	18.51	10.84-31.63	highly increased

* not significant **Cocaine or cocaine + benzoyllecgonine; ***THC or THC + THCCOOH; ****Alcohol ≥0.1g/L; more precise substance definitions can be found in Annex 3: Substance classes, groups and the analytical findings within DRUID hospital studies

Table 30 shows the estimated increase of relative risk of serious injury or fatality based on case control studies. Note that some of the risk estimates for illicit drugs vary to a large degree among the single countries; others are based on few positive cases and/or controls which result in wide

confidence intervals. Therefore these estimates are uncertain. Furthermore, an overview of the main results of all investigated substances in the DRUID road side survey (D2.2.3) and case-control study (D2.3.5) can be found in the annex 5.

Table 30: Overview of estimated increase of relative risk of serious injury or fatality based on case control studies (D2.3.5).

	Substance	Estimated relative risk of serious injury or fatality based on case control studies	Risk of injury
Alcohol (BAC) Alone	0.1-0.5g/L	1-3x	slightly increased
	0.5 - 0.8g/L	2-10x	medium increased
	0.8 - 1.2g/L	5-30x	highly increased
	≥1.2g/L	20-200x	extremely increased
Illicit drugs Alone	Amphetamines	5-30x	highly increased
	Benzoyllecgonine	2-10x	medium increased
	Cocaine*	2-10x	medium increased
	THC**	1-3x	slightly increased
	Illicit opiates	2-10x	medium increased
Medicines Alone	Benzodiazepines + Z-drugs	2-10x	medium increased
	Medicinal opioids	2-10x	medium increased
Combined use	Alcohol-drug***	20-200x	extremely increased
	Drug-drug	5-30x	highly increased

*Cocaine or cocaine + benzoyllecgonine; **THC or THC + THCCOOH; ***Alcohol ≥0.1g/L; more precise substance definitions can be found in Annex 3: Substance classes, groups and the analytical findings within DRUID hospital studies

4 Countermeasures

4.1 Enforcement (WP3)

DRUID WP3 conducted a large scale scientific and practical evaluation of on-site screening for impairing psychoactive substances other than alcohol in drivers. The main focus was on illegal drugs. A number of on-site drug screening devices were first practically evaluated, followed by an analytical evaluation of devices that were deemed promising, followed by a cost-benefit analysis of the use of such devices (D3.3.1). Furthermore, current selection criteria, based on signs of impairment, before using on-site screening devices were also part of the evaluation. Selection criteria should allow the police to check for suspicious signs leading to a conclusion of possible drug usage. WP3 aim was to describe a good police practice and to formulate an advice on effective legislation for an effective drug driving enforcement. The results should improve the possibilities of detecting drug-driving in Europe, providing a good grounding for harmonising the European police requirements for on-site drug screening.

Both, the practical experiences of police officers as well as scientific evidence should be bared in mind while evaluating and implementing standards for drug-driving enforcement. Out of police perspective the following recommendations for drugs and driving legislation have been formulated within the DRUID project:

- Illicit substances: zero tolerance for known illicit substances, impairment limits for psychoactive substances not yet mentioned in Traffic Acts (zero tolerance does NOT mean analytical zero values; see D1.4.2);
- Medicines: driving with medicines on prescription is allowed. Police should be able to require prescription as evidence. The advice of labels of medicines should be respected (conform classification DRUID WP4). Illegal use is considered as illicit drug use;
- Police enforcement: random selection should be possible, but applied in a prudent way due to high cost and required time of screening;
- Screening: operational acceptable oral fluid screening device is desirable. If its screening result is negative, but clinical signs of impairment are present, the subject can still be under suspicion (e.g. GHB). An extensive Drug Recognition Evaluation (DRE) is not believed to have an added value besides drug testing, as it is very time-consuming and therefore not practical
- Evidence: confirmation analysis of an oral fluid sample by an appointed forensic laboratory is preferred. Blood is the alternative;
- Driving license: in case of suspicion of addiction, drivers can be tested for their suitability or capability to drive a motor vehicle. Based on a medical, psychological or other examination the driving license could be withdrawn (see also D5.1.1, D6.2).

Very often control strategies and detection methods are not standardised and very time consuming. Essential elements to optimise this enforcement practice are seen in (1) the training of police officers in drug recognition, (2) the development of sensitive and specific detection devices and (3) the deliberate use of control strategies.

4.1.1 Training for police officers in drug recognition

DRUID WP3 developed and evaluated a **checklist for clinical signs of impairment (CSI)** in order to see if visible signs of impairment can be used as preceding selection criteria for performing an on-site test. The checklist was based on several existing checklists, e.g. one developed for the German police and previously used in the European IMMORTAL (Impaired Motorists, Methods Of Roadside Testing and Assessment for Licensing) project.

The results of the evaluations of the current CSI checklist were so far not very promising. The checklist scored a **low sensitivity value** (Dutch study, sensitivity: 32% if self-reported drug use was included, and a meagre 13% if only signs and symptoms were considered), low correlation of symptoms and actual presence of drugs (Belgian study) or there were difficulties in correlating the symptoms to actual drug use due to the insufficient data collection (Finnish study). **Training of police officers will probably improve the results** of the CSI checklists.

4.1.2 Development of on-site drug screening devices

The quality of an oral on-site screening device depends on both scientific as well as practical needs; both should be taken into account while developing and implementing screening devices into police practice. The following police user requirements and specifications (PURS) for oral fluid screening devices have been formulated:

Requirements for training of police officers on the use of oral fluid screening devices:

- Police officers trained by police instructors (0,5 – 1 hour);
- Police instructors trained by manufacturer (1 – 2 hours);
- Learning by demonstrating;
- Learning by doing;
- Information about do's and don'ts;
- Clear hygienic and safety measures;
- Instruction card for each officer during training;
- Material available through police intranet;
- All materials in native language.

Requirements for operational use of these devices:

- 75% of tests qualified as simple to operate;
- Hygienic use of device;
- Sufficient amount of collected oral fluid;
- Detectable substances at least Cannabis, Cocaine, Opiates, Amphetamines(analogues);
- At least 75% of the tests should be correct for at least one of the substances;
- Indication lines should remain visible for at least 3 minutes.

Requirements for documentation:

- Device user manual in native language;
- Device instruction card for each trained officer;
- CD ROM or DVD available for each force/unit;
- (User manual for electronic reader).

The classic scientific test performance indicators are sensitivity, specificity and accuracy, but also positive predictive values and negative predictive values, calculated with drug prevalence for the population for which the screening is intended, should be considered as factors when selecting which on-site device to use. Within the DRUID evaluation studies test performance was assessed based on both DRUID and manufacturer cut-offs. Sensitivity, specificity and accuracy performance values of 80% or more were set as a desirable target value.

The tested substance classes within the DRUID evaluation were amphetamine, metamphetamines (including ecstasy (MDMA)), cannabis, cocaine, opiates, benzodiazepines and phencyclidine (PCP).

DRUID 6th Framework Programme - D 7.3.2 Main DRUID results to be communicated to different target groups

Eight out of 13 devices were selected as promising based on practical police on-site test requirements (i.e. Mavand RapidSTAT, Securetec Drugwipe 5+, Branam Oratect XP, Varian Oralab 6, Innovacon OrALert, Cozart DDS, Dräger Drug Test 5000 and Biosensor BIOSENS¹²) and 3 out of 8 devices were evaluated positive within the scientific evaluation (Dräger Drug Test 5000, Mavand RapidSTAT and Securetec Drugwipe 5+). None of the tests reached the target value of >80% for sensitivity, specificity and accuracy for all the separate tests they comprised (see table 31).

Table 31: Overall test performance of the different drug screening devices within the DRUID investigation (WP3)

Substance	Sensitivity	Specificity	Accuracy
Cannabis	11-59%	90-100%	84-98%
Amphetamines	0-87%	90-100%	84-98%
Cocaine	13-50%	99-100%	86-100%
Opiates	69-90%	81-100%	75-99%
Benzodiazepines	48-67%	94-100%	77-100%

However, there were tests that performed already on a promising level for one or more substance classes. Within the DRUID investigation the DrugTest 5000 had the best overall results followed by the Rapid STAT, which performed at a similar level, except for the cocaine test which was somewhat less sensitive. Best performing device in terms of sensitivity for amphetamines was within the DRUID study the DrugWipe 5+. None of the 8 tested on-site screening devices in the scientific evaluation attained 80% sensitivity for cannabis which is the most commonly used illegal drug and for cocaine. Further testing of the cocaine tests is desirable due to the low prevalence and the low concentrations encountered in this study. There are several countries in Central and Southern Europe for which these two substance classes are of special interest (e.g. ES).

The results of the DRUID evaluation of each drug screening device “need to be viewed in the context of the study population on which they were tested (e.g. test in clinics, coffee shops, at the roadside). For some of the devices, a full performance evaluation was not possible for all of the test strips on the panel due to low prevalence of the substance(s) in question. Sensitivity is usually enhanced to some extent if the study population has a high prevalence for the screened drug and if the concentrations of the drugs contained in the samples from the study population are high because of recent consumption. Conversely, when interpreting specificity values it should be noted that when a population with a low prevalence of the desired substance is tested, specificity can be expected to be high. Such a population can also be expected to result in higher accuracy results in a similar manner. Also, it should be borne in mind that sensitivity, specificity and accuracy are specific for this study and the study populations investigated in this study. Positive predictive values and negative predictive values, calculated with drug prevalence for the population for which the screening is intended, should be considered as factors too when selecting which on-site device to use” (D3.2.2 p. 95).

Since the finalisation of the EU projects ROSITA II, which also evaluated screening devices (2005), no significant improvements concerning the quality of oral fluid screening devices were achieved. Consequently, there seems to be a strong **need for improving the quality of oral on-site screening devices, particular for detecting cannabis**. Further research is needed on the test performance of on-site oral screening devices for cocaine.

4.1.3 Deliberate use of control strategies

The choice of control strategy depends on the specific characteristics of the problem situation (prevalence and risk estimates WP1-2). Main outlines of a **common standard enforcement procedure should be formulated on EU level**. The implementation of specific enforcement activities should be based on the specific characteristics of the problem situation on national level. One of the advantages of a common standard would be that it would also stimulate the competition within the respective industries to develop valid and reliable detection devices.

The DRUID cost-benefit-analysis (CBA¹³; an assessment to what degree (increased) enforcement of driving under the influence of drugs is profitable in economic terms for society, together with an

¹² During specific enforcement activities where a great number of persons should be tested in a limited period of time.

¹³ The CBA will be updated in 2011, based on final DRUID results regarding the prevalence and risk of drug driving (WP1-2).

assessment of which devices for such enforcement are more profitable) which was based on good practice and scientific research has shown that an increased drug-driving enforcement is potentially **cost-beneficial**, especially for countries that currently have a low enforcement level. It will **NOT** be **beneficial** if this increase is **financed** (time and money) **at the cost of drink-driving enforcement**. Thus, also within an economic perspective alcohol impaired driving is the biggest problem.

The **quality** of an on-site **screening device** seems to have a strong **influence on the cost-benefit outcome**. Screening devices that performed better than average showed a cost-benefit ratio which was almost twice as high as the ratio of devices that performed less than average (although higher sensitivity in detecting drug-driving will increase the safety benefits, the enforcement costs, particularly following a positive test, dominate to such an extent that high specificity is relatively more important than high sensitivity).

An increasing number of countries are planning to introduce on-site saliva screening as a legal method to detect drugged drivers (e.g. BE and NL). Two major benefits of saliva screening for drugs are that saliva collection is much less invasive than urine collection and that it better detects recent drug use (than in urine, sweat or hair), especially in the case of cannabis.

“Theoretically, the largest general deterrence effects on drug-driving may be expected from large-scale random drug testing, as is the case with random breath testing for alcohol (Homel, 1998¹⁴). However, the time-consuming process of on-site oral fluid screening, in combination with the quite high cost of the devices and the relatively low sensitivity for cannabis, which in many countries is the most frequently used illegal drug, will probably prevent large-scale random drug testing in practice.

For cost-benefit purposes, a working method to preselect suspected drivers for on-site drug screening would be desirable. Unfortunately, the evaluation of the CSI (clinical signs of impairment) checklist in this project did not give very encouraging results. Apparently, at least for persons with little observational training for clinical signs of impairment, or only relatively short-term experience of this, symptoms of drug use remain easily undetected. Also, correlation between signs of impairment and findings in oral fluid was not very good. However, proper training and long-term experience of observing clinical signs of impairment could reasonably be expected to yield better results.

The **effectiveness** of drug-driving enforcement can be further **enhanced by preselecting times and places** with a likelihood of elevated numbers of drug positive drivers and by **targeting alcohol positive drivers**. This is not only because alcohol positive drivers are likely to have a higher exposure to drugs than alcohol negative drivers, but also due to the fact that the risk of combined alcohol and drug use is extremely high (D3.3.1 p. 28f)”.

4.1.4 Overview box – Enforcement

Box 4: Summary of main DRUID results – ENFORCEMENT

<ul style="list-style-type: none"> • DRUID provides guidelines for everyday drug-driving police enforcement and installs scientific demands for on-site screening for impairing psychoactive substances other than alcohol in drivers (e.g. legal frame, basic standards of procedure and devices) (D3.1.1, D3.2.1, D3.2.2).
<ul style="list-style-type: none"> • First enforcement priority should always lie on alcohol, other drugs are second priority (D3.3.1).
<ul style="list-style-type: none"> • Characteristics of the problem situation on national level determine the focus (and devices) of drug enforcement (D3.3.1).
<ul style="list-style-type: none"> • Increase of drug enforcement is potentially cost-beneficial, especially for countries that currently have a low enforcement level. It will NOT be beneficial if this increase is financed (time and money) at the cost of drink-driving enforcement (D3.3.1).
<ul style="list-style-type: none"> • The effectiveness of drug-driving enforcement can be enhanced by e.g. (D3.3.1): <ul style="list-style-type: none"> ○ Using on-site screening devices which fulfil practical as well as scientific requirements (two major benefits of saliva screening for drugs are that saliva collection is much less invasive than urine and blood collection and that it better detects recent drug use than in urine, sweat or hair; Cost-Benefit Analysis (CBA): emphasis on high specificity). ○ Ideally large-scale random drug testing (largest general deterrence effects) is done,

¹⁴ Homel R. Policing and Punishing the Drinking Driver: A Study of General and Specific Deterrence. Research in Criminology. Springer Verlag; 1998.

but this is not feasible in practice since the devices are too expensive and take too much time for sample collection and analysis. The effectiveness can also be enhanced by: pre-selection of time, place and target group (e.g. alcohol impaired drivers), based on specific characteristics of the problems (national and regional level).

- Clinical Signs Inventory (CSI) checklist as working method to preselect suspected drivers for on-site drug screening, did not give very encouraging results; more experience and better training of police may improve the results.

4.2 Classification (of driving impairing medicines) (WP4)

The establishment of criteria for a European categorization will have to serve most of the needs of all parties involved: health professionals, drug regulatory agencies, drug manufacturers and patients. For patients to make the best (and safest) use of their medicines, clear warnings and symbols are needed.

(1) For health professionals

DRUID has produced a categorization/labelling for existing medicines, as well as producing specific information for health professionals (physicians and pharmacists) to be delivered to the driver patient. For each category information for developing directions for health care professionals and warning levels and warning symbols has been presented. The categorization system could be seen as a tool to improve prescribing and dispensing procedures both at a national and European level, and, therefore, as a instrument to better inform and involve HCPs (Health Care Professionals) [Talbot & Stephens, 2004]. With this respect, it is important that HCPs know the fundamentals of the categorization system, and, consequently, use it properly in order to fully inform their patients about the risks of driving under the influence of impairing medicines. Furthermore, HCPs should be able to distinguish between the four levels of impairment, and, therefore, if possible, choose the least impairing medication within the same therapeutic group. Moreover, this system should encourage HCPs to update their knowledge on medicines and driving in order to be prepared to answer questions that patients might have on this topic (de Gier et al., 2009; AFSSAPS, 2009).

The DRUID categorization system should also be used as a tool to motivate health care professionals to provide patients with clear information, communicate to patients the risk associated with driving under the influence of medicines, and start HCP-patient discussion leading to both safer prescriptions and the patient's conscious decision whether to drive or not (Talbot & Stephens, 2004; de Gier et al., 2009).

Finally it is recommended, that the development of supplementary information for health care professionals. A guideline (e.g. prescribing and dispensing guidelines) should be developed to explain the use of the categorization system to HCPs and to serve as a support in the decision making process.

(2) For drug regulatory agencies

Recently has been approved SmPC guidelines, in September 2009 (which applies as from 1st of May 2010), by EMA, based on the DRUID WP4 proposal categories a) no or negligible influence, b) minor, c) moderate influence, and d) major influence on driving fitness are specified with some important guidance in special circumstances.

This consensus on the wording in the Patient Information Leaflet is another and important step to harmonize information to patients on a medicine's impairing effects on fitness to drive. However, it is acknowledged by the Pharmaco-vigilance Working Party and WP4 partners that at the Member States' level more activities are needed in order to reinforce the awareness of patients on the effects of medicines on fitness to drive, e.g. by the use of an alerting pictogram on the product packaging or further stratification of the number of categories of risk with a maximum of four.

Several meetings have taken place in collaboration with national agencies. For instance, in AFSSAPS (Agence Française de Sécurité Sanitaire des Produits de Santé) on February 28th 2008, where DRUID partners attended a "regular" meeting of the French Medicinal Agency regarding medicines and driving. The criteria used and the experience on labelling medicines regarding to driving in France was shown.

The attendance at the Pharmacovigilance Working Party (PhVWP) at EMA (European Medicinal Agency) has also been of great value for the development of WP4 tasks.

However, the DRUID categorization system is, although it may have benefitted from many other early experiences, a new categorization.

However, the DRUID classification system is, although it may have benefited from many other early experiences, is a new categorization that can help at drugs regulatory agencies to harmonize their contents about the categorization / labeling of medicines.

(3) Drug manufacturers and patients

DRUID WP4 partners have produced patient-oriented information for each one of the medicines categorized.

The aim of producing this patient-oriented information is to help physicians and pharmacists (and other health professionals) in providing appropriate information to their patients. It is true that Patient Information Leaflets contain some sort of information regarding driving. However, DRUID WP4 partners considered that it is also quite important that health professionals provide further information for medicines and driving to their patients

Clear warnings and symbols are needed so patients use their medicines in the most optimal (and safest) way possible. Since the patient package leaflet is the most accessible source of information for patients, it would also be advisable to develop an effective strategy to communicate the risk related to the use of medicines and driving. For instances, a straightforward grading system could be included in the patient package leaflet and the use of pictograms (warning labels) could be printed on the medication box to provide clear directions for patients.

4.2.1 DRUID methodology on categorization/labelling on medicines and driving

The development of the DRUID categorization/labelling system was based on the criteria that were established by the DRUID WP4 partners, and based on their consensus.

The DRUID WP4 expert group established and agreed that, according to its influence on the ability to drive, a medicine could be categorized as follows regarding driving (see table 32):

- category 0 (no or negligible influence on fitness to drive);
- category I (minor influence on fitness to drive);
- category II (moderate influence on fitness to drive);
- category III (severe influence on fitness to drive).

This was in line with the recent approved SmPC guidelines adopted in September 2009 (which applies as from 1st of May 2010) by EMA, based on the DRUID WP4 proposal submitted for consideration by the CMD(h), as a response during the consultation phase of the revision of the SmPC guidelines in February/March 2008, proposing that in section 4.7 "Effects on ability to drive and use machines"....., specify whether the medicinal product has a) no or negligible influence b) minor; c) moderate influence or d) major influence on these abilities....(see also:

http://ec.europa.eu/health/documents/eudralex/vol-2/index_en.htm

http://ec.europa.eu/health/files/eudralex/vol-2/c/smpc_guideline_rev2_en.pdf)

Table 32: DRUID categorization/labelling system for medicines and driving (version February 2010).

Information for physicians and pharmacists		Warning for patients (with warning symbols and standard descriptions per country)
Description of categories with levels of impairment (compared with alcohol)	Information on how to advise their patients	
Category 0 Presumed to be safe or unlikely to produce an effect on fitness to drive.	Confirm that the medicine will be safe for driving, provided that combinations with alcohol and other psychotropic medicines are excluded.	[no warning needed]
Category 1 Likely to produce minor adverse effects on fitness to drive.	Inform the patient that impairing side effects may occur especially during the first days and that they have a negative influence on his/her driving ability. Give the patient the advice not to drive if these side effects occur.	Warning level 1 Do not drive without having read the relevant section on driving impairment in the package insert.
Category 2 Likely to produce moderate adverse effect on fitness to drive.	Inform the patient about the possible impairing side effects and the negative influence on his/her driving ability. Advise the patient not to drive during the first few days of the treatment. If possible prescribe a safer medicine, if effective and acceptable by the patient.	Warning level 2 Do not drive without advice of a health care professional. Read the relevant sections on driving impairment in the package insert before consulting the physician or pharmacist.

Category 3 Likely to produce severe effects on fitness to drive or presumed to be potentially dangerous.	Inform the patient about the possible impairing side effects and the negative influence on his/her driving ability. Urgently advise the patient not to drive. Consider prescribing a safer medicine, if acceptable by the patient.	Warning level 3 Do not drive. Seek medical advice after a period of treatment about the conditions to restart driving again.
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In summary, categorization of a medicine on driving includes several steps of evaluation (table 33):

1. Pharmacodynamic and pharmacokinetic data;
2. Pharmacovigilance data (including prevalence of unwanted effects reported in the SmPC);
3. Experimental and epidemiological data;
4. Additional data derived from the Patient Information Leaflet (PIL) and existing categorization systems;
5. Synthesis.

Table 33: Methodology of DRUID categorization/labelling system for medicines and driving

Categorization based on SmPC section 4.7	Data to be used for assigning the category				
	Pharmacodynamic & -kinetic data	Pharmacovigilance Data	Experimental & epidemiology data	Additional data	Synthesis
a) No or negligible influence	No influence expected	No demonstration of CNS side effects or other unwanted effects on driving	No demonstration of impairment	No further data on impairment	No or negligible influence
b) Minor influence	No influence expected	Some demonstration of CNS side effects or unwanted effects that impair driving	Some impairment in some experimental studies. Slight increased risk demonstrated in epidemiological studies	Some data on possible impairment	Minor influence
c) Moderate influence	Moderate influence expected	Demonstration of CNS side effects (not severe) or unwanted effects that impair driving	Impairment of driving performance is seen in various experimental studies. In epidemiological studies a significant increased risk is demonstrated	Various data on impairment (not severe)	Moderate influence
d) Major influence	Severe influence expected	Demonstration of CNS side effects (severe) or unwanted effects that impair driving	Gross impairment of driving performance or performance related to driving is repeatedly seen. In epidemiological studies a significant and meaningful increased risk is demonstrated	Data on severe impairment	Major influence

Specific sections of the SmPC and PIL were used to retrieve details on the active substance presentation, indications, posology, administration, pharmacodynamic and pharmacokinetic profile, section 4.7 on effects on the ability to drive and use machines, and section 4.8 undesirable effects related to driving and operating machines.

During the activities in Task 4.3 on categorization of the existing medicines, the occurrence of undesirable effects was considered as key information for categorising some medicines, in circumstances that information on experimental studies for assessing a medicine's effect on driving or skills related to driving or epidemiological data were lacking or limited. For that reason, section 4.8 of the SmPC was used (as well as specific literature search), if necessary. Recently, EMA has started to use the following categorization on frequency of undesirable effects, side effects or adverse reactions:

- very common (>1/10);
- common (>1/100, <1/10);
- uncommon (>1/1,000, <1/100);
- rare (>1/10,000, <1/1,000);
- very rare (<1/10,000);

- not known (cannot be estimated from the available data, since no valid estimate can be derived from clinical trials or epidemiological studies).

DRUID Partners have taken into account this categorization of undesirable effects, side effects or adverse reactions in their categorization framework for medicines and driving. Firstly by considering those effects categorized as very common (>1/10) and common (>1/100, <1/10), and secondly, those undesirable effects that can potentially impair the fitness to drive safely. In case rare or very rare unwanted effects or certain severely impairing effects occur, for example sudden sleep attacks, DRUID Partners recommend that this should be mentioned in the patient information leaflet.

The following criteria were used for assigning a medicine to a specific category, in case experimental or epidemiological data are lacking (table 34).

Table 34: Relationship of “undesirable effects category” in SmPC to DRUID category

Declaration of undesirable effects that can potentially impair the fitness to drive safely	DRUID category
Very common (> 1/10) (Medications with very common side effects affecting the ability to drive)	Category 2 or higher
Common (>1/100, <1/10) (Medications that have only common side effects that affect the ability to drive)	Category 1
Rare (>1/10,000, <1/1,000) or very rare (<1/10,000) (Medications that have not very common or common side effects that affect the ability to drive, only rare or very rare side effects)	Category 0

In the following table all relevant potentially undesirable effects to be considered when categorising the effects of medicines on driving are listed (table 35).

Table 35: Undesirable effects that can impair fitness to drive grouped by system organ class

System organ class	Selection of undesirable effects that can impair the fitness to drive safely
Nervous system disorders	<ul style="list-style-type: none"> ▪ Somnolence, dizziness, drowsiness ▪ Confusion - cognitive disorder- disorientation – co-ordination disturbances ▪ Involuntary movement disorders: ataxia, tremor, Parkinsonism, acute dystonic (dyskinesia) and dyskinetic reactions (dystonia) ▪ Convulsions – seizures ▪ Muscle weakness
Psychiatric disorders	<ul style="list-style-type: none"> ▪ Perception disturbances (hallucination, visual hallucination, auditory hallucination, illusion) ▪ Psychotic reactions and psychotic disorder (including paranoia psychosis) ▪ [Other: Emotional lability, mood swings, aggression, nervousness, irritability, personality disorders, thinking abnormal, abnormal behaviour, euphoric mood, restlessness (emotional state of excitement), depersonalisation]
Eye disorders	<ul style="list-style-type: none"> ▪ Diplopia or double vision ▪ Blurred vision ▪ Accommodation disorders ▪ Visual acuity reduced ▪ Photophobia ▪ [Other: visual field defect, peripheral vision loss, altered visual depth perception, oculozygic crisis].
Ear and Labyrinth disorders	<ul style="list-style-type: none"> ▪ Vertigo ▪ Hearing loss ▪ [Other: buzzing, tinnitus]
Metabolism and nutrition disorders	<ul style="list-style-type: none"> ▪ Hypoglycaemia
Vascular disorders	<ul style="list-style-type: none"> ▪ Hypotension

4.2.2 Categorization, labelling and patient oriented information for relevant therapeutic groups of medicines available on EU market

The aim of WP4 was to provide a categorization for the relevant therapeutic groups of medicines available on the European Union Market.

In this way, DRUID task 4.3 was able to provide categorization, labelling and patient-oriented information for the following ATC groups (The Anatomical Therapeutic Chemical –ATC- classification system; <http://www.whocc.no/>).

Individual medicines were categorized according to the DRUID classification system:

- A - ALIMENTARY TRACT AND METABOLISM
- B - BLOOD AND BLOOD FORMING ORGANS
- C - CARDIOVASCULAR SYSTEM
- D - DERMATOLOGICALS
- M - MUSCULO-SKELETAL SYSTEM
- N - NERVOUS SYSTEM
 - N01 ANESTHETICS
 - N02 ANALGESICS
 - N03 ANTIEPILEPTICS
 - N04 ANTIPAKINSON
 - N05 PSYCHOLEPTICS
 - N05A Antipsychotics
 - N05B Anxiolytics
 - N05C Hypnotics and sedatives
 - N06 PSYCHOANALEPTICS
 - N06A Antidepressant
 - N06B Psychostimulants, agents used for ADHD and Nootropics
 - N06C Psycholeptics and psychonaleptics in combination
 - N06D Anti-dementia drugs
 - N07 OTHER NERVOUS SYSTEM DRUGS
- R - RESPIRATORY SYSTEM
- S - SENSORY ORGANS

Furthermore, Fact Sheets were produced for the N01-N07 (nervous system) and R06 (respiratory system) ATC groups of medicines. Each fact sheet contains information on: source of information, presentations, indications, posology and method of administration, pharmacodynamic and pharmacokinetic properties, possible side-effects related to driving, Summary of Product Characteristics (SmPC) section 4.7 effects on effects on ability to drive and use machines, leaflet section on driving and using machines, studies on psychomotor performance and risk studies, current categorization in some EU countries, proposed DRUID based categorization, information for the patient, and place and date of agreement by the DRUID WP4 members.

Table 36 shows the DRUID categorization of the medicines in the ATC groups (the Anatomical Therapeutic Chemical –ATC- classification system; <http://www.whocc.no/>), A, B, C, D, M, N, R and S evaluated in DRUID WP4, while table 37 shown the DRUID categorization of the medicines from N01 to N07.

The DRUID project has proposed for analysis and categorization a total of 3,037 medicines from these ATC groups. Of these 3,037 medicines, 1,495 have not been categorized, because they are not available on the European Union market (not available on DRUID WP4 countries Belgium, France, Greece, Germany, Netherlands, and Spain, as well as in the UK and Ireland), as there is no sense in categorizing/labelling medicines which are not available (see table 36-37).

Table 36: DRUID categorization on medicines and driving: number of medicines categorized by ATC group

ATC GROUP	Not evaluated. Not available at EU market	DRUID Categorization						TOTAL
		0	I	II	III	MC	DC	
A - ALIMENTARY TRACT AND METABOLISM	243	234	69	8	1	4	4	563
B - BLOOD AND BLOOD FORMING ORGANS	86	135	1	1			2	225
C - CARDIOVASCULAR SYSTEM	246	90	200	11		1		548
D - DERMATOLOGICALS	156	192	1			4		353
M - MUSCULO-SKELETAL SYSTEM	88	22	44	28	15			197
N - NERVOUS SYSTEM	346	9	30	86	53	36		560
R - RESPIRATORY SYSTEM	195	62	24	32	10	5	14	342
S - SENSORY ORGANS	153	31	31	6	11	18	16	266
TOTAL	1513	775	400	172	90	68	36	3054

MC = Multiple categories; D= Depending on the medicine in combination

Table 37: Number of medicines from the ATC group, N-nervous system medicines, categorized in each DRUID category

ATC GROUP	Not evaluated. Not available at EU market	DRUID Categorization						TOTAL
		0	I	II	III	MC	DC	
N-NERVOUS SYSTEM								
N01 ANESTHETICS	31	3	3	1	12	10		60
N01A Anesthetics, general	20				11	1		32
N01B Anesthetics, local	11	3	3	1	1	9		28
N02 ANALGESICS	93	2	7	10	3	7		122
N02A Opioids	31				2	7		40
N02B Other analgesics and antipyretics	52	2	6	1	1			62
N02C Antimigraine preparations	10		1	9				20
N03 ANTIEPILEPTICS	23			14	4	2		43
N03A Antiepileptics	23			14	4	2		43
N04 ANTIPAKINSON	16		3	16		1		36
N04A Anticholinergic agents	10			4		1		15
N04B Dopaminergic agents	6		3	12				21
N05 PSYCHOLEPTICS	107		4	16	26	12		165
N05A Antipsychotics	31			13	8	9		65
N05B Anxiolytics	23		1	3	7	1		35
N05C Hypnotics and sedatives	53		3		11	2		69
N06 PSYCHOANALEPTICS	62	2	10	20	7	1		102
N06A Antidepressant	37	1	7	12	7	1		65
N06B Psychostimulants, agents used for ADHD and Nootropics	22		3	4				29
N06C Psycholeptics and psychonaleptics in combination	2							2
N06D Anti-dementia drugs	1	1		4				6
N07 OTHER NERVOUS SYSTEM DRUGS	14	2	3	9	1	3		32
N07A Parasympathomimetics	6			2		1		9
N07B Drugs used in addictive disorders	2	2	1	4	1	2		12
N07C Antivertigo preparations	2		1	2				5
N07X Other nervous system drugs	4		1	1				6
TOTAL	346	9	30	86	53	36		560

MC = Multiple categories; D= Depending on the medicine in combination

As can be seen in the following figure 41, the distribution of the 1,541 categorized medicines was as follows: Category 0 – 50,3%, Category I – 26%, Category II – 11,2%, Category III – 5,8%, Multiple category – 4,4% and the Depending on the medicine in combination 2,3%.

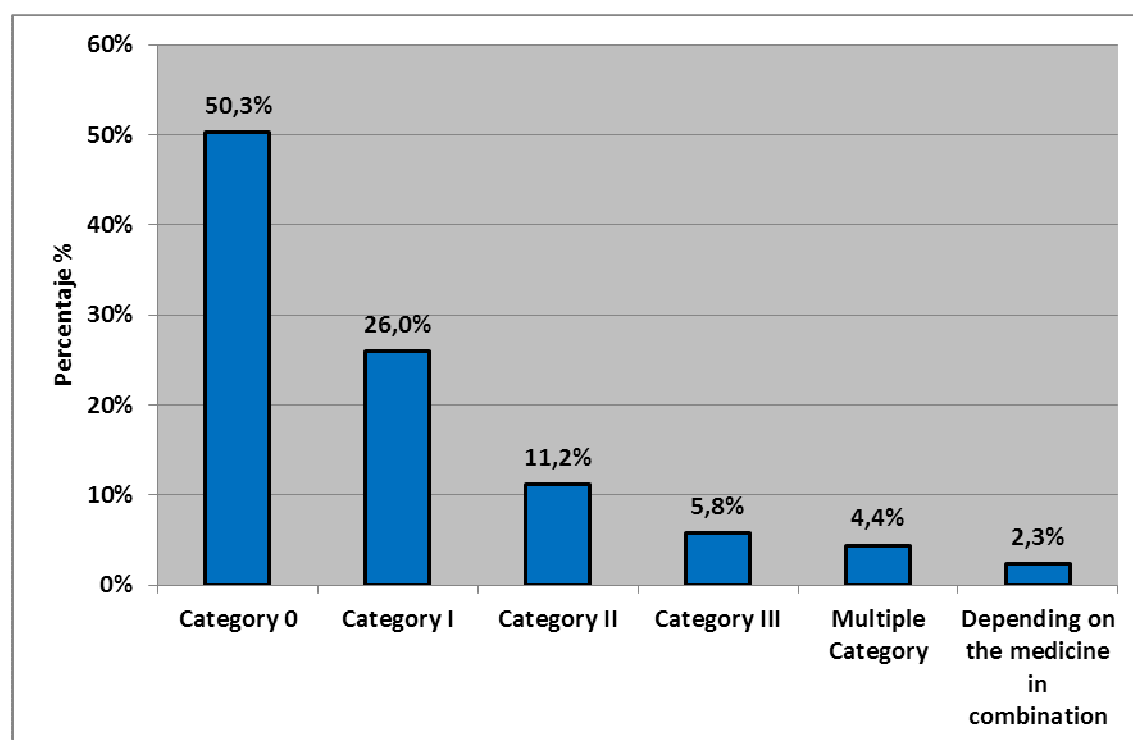


Figure 41: Percentage of medicines categorized within each DRUID category

4.2.3 Establishment of criteria for a European Categorization System for Medicines and Driving: proposals for harmonising criteria towards an European system

After the development of the input for establishing criteria for a European categorization system, progress and steps forward have been achieved in discussing these proposals with the Pharmacovigilance Working Party (PhVWP) of the Committee for Medicinal Products for Human Use (CHPM), whose meetings are held monthly at the European Medicines Agency (EMA).

The PhVWP came to a consensus based on a compromise, that a common approach should be developed which:

- Takes into account scientific evidence.
- Recognises different national approaches and experiences.
- Acknowledges the difficulty of having a consistent classification for all medicines based on current scientific evidence.
- Ensures that any information on the influence of medicines on fitness to drive should be simple and patient-centred, and therefore should be reflected in the Patient Leaflet, although information directly provided to the patient by prescribers and/or pharmacists is very relevant.
- Recognises that in addition to the legal, social, medical, and pharmacological aspects of the issue, individual responsibility of the patients plays an important role that should be considered and reflected in the appropriate way in the product information of any medicine.

Currently national approaches differ substantially: from France at one end of the extreme, where labelling with pictograms on the medicine box at three levels according to impairing properties of the medicine was enforced in 2005, to Sweden at the other end where labelling with the red triangle was removed from medicines in 2007. Sweden amended their labelling in response to patient surveys which revealed that the red triangle pictogram was misunderstood, and therefore replaced the pictogram with a generic warning in the patient leaflet.

A consensus within the PhVWP was reached that a basic 2 tier framework would be developed as a basis for warnings to be presented to the patient through the Patient Leaflet. This differentiates between medicines with a relevant potential influence on driving and those which do not.

4.2.4 Policy implications

During the development of task 4.2, the following agreements were reached with the PhVWP:

“Conclusions and recommendations

Input for the further development of criteria for a European categorization system is based on the following conclusions derived from the activities in Work Package 4.

General conclusions

1. The overview of perspectives in classification systems shows the evolution in the development of the classification systems, from an effort to achieve consensus about the various categories and descriptions from a scientific perspective to efforts for informing health care professionals (e.g. Belgium, the Netherlands, Spain) to efforts for introducing warning symbols and directions for patients, as end users, in a legal framework (e.g. in France, Spain and Slovenia).
2. It has been made clear by the developments and experiences in various countries that categorization of medicines is possible, needed and well accepted by all parties that have an interest in the safe use of medicines.

Conclusions at the level of developing criteria

1. At the level of categorising medicines it was agreed that several factors (e.g. pharmacodynamics, pharmacokinetics, pharmacovigilance data, experimental and epidemiological data, individual sensitivity, conditions of use) need to be considered for evaluating the medicines' overall potential to impair fitness to drive.
2. In circumstances where information on experimental studies or epidemiological data are lacking, the occurrence of pharmacodynamic effects resulting in undesirable effects that have the potential to impair the fitness to drive based on information in section 4.8 of the SmPC, was considered as key information for categorising some medicines.

3. The revised SmPC Guidelines (adopted in September 2009 and to be applied as from 1st of May 2010) show four descriptions of potential levels of influence on fitness to drive (a-d in section 4.7.). DRUID and the PhVWP concluded, however, that an evidence based approach supported a two tier system of warnings which may be supported by symbols or pictograms.
4. Warning levels, symbols and pictograms (in combination with a short explanation in writing) to inform patients can be developed.

Recommendations

It is clear that the establishment of criteria for a European categorization system for medicines and driving should be based on the involvement of all relevant stakeholders. Their input is needed for developing legislation, guidelines and procedures for assigning driving impairing medicines to the appropriate category and for developing information to support health care professionals in prescribing and dispensing driving impairing medicines and patients for safely using these medicines. The following recommendations will guide further activities after the completion of the DRUID project:

1. There is a need to improve information related to effects on driving in the PIL. Information to patients who are advised to use medicines that may impair driving fitness needs to be improved by simple and patient-centered directions based on a clear categorization system and reflected in the PIL.
2. A basic 2-tier risk categorization system with standard wordings for the PIL is recommended for medicines without a potential influence on driving fitness (Level 1, reflective of SmPC descriptions; a) no or negligible influence or b) minor influence) and for medicines with a potential relevant influence on driving fitness (Level 2, reflective of SmPC descriptions; c) moderate influence and d) major influence).
3. Clarification of criteria for the evidence in forming the categorizations, as described as a)-d) in the SmPC (section 4.7) into the 2 levels, should be derived in a collaborative effort of DRUID experts and the members of the PhVWP of CHMP, among other partners, preferably with support of EU bodies, such as DG Sanco and DG Move.
4. The development of supplementary information for patients (e.g. warning levels, pictograms) and health care professionals (prescribing and dispensing guidelines), in support of the categorization system, could be guided with input provided by the DRUID project (D 4.2.1., D 4.3.1., D 7.3.2. and D 7.4.2.) as well as by experiences in EU Member States" (D4.2 p. 55ff).

More information can be found in D4.2 p. 47-54 and D4.3 p. 13-35.

4.2.5 Overview box – Classification

Box 5: Summary of main DRUID results – CLASSIFICATION

DRUID WP4 proposed four level classification and a labelling system regarding the influence of medicines on driving performance (D4.2.1, D4.3.1):

- category 0: no or negligible influence on fitness to drive (no warning needed);
- category 1: minor influence on fitness to drive (warning level 1);
- category 2: moderate influence on fitness to drive (warning level 2);
- category 3: major influence on fitness to drive (warning level 3).

DRUID WP4 developed a methodology to categorize the influence of medicines on driving performance. The categorization is based on an evaluation of the following issues/steps (D4.3.1):

- conditions of use of the medicine at the European Union market;
- pharmacodynamic and pharmacokinetic data;
- pharmacovigilance data (including prevalence of unwanted effects reported in the SmPC);
- experimental and epidemiological data ;
- additional data derived from the Patient Information Leaflet (PIL) and existing categorization systems, and information from other sources;
- synthesis of the available information;
- DRUID categorization and labelling of the psychoactive medicine.

Over 3000 medicines were reviewed and over 1500 of them were categorized in regard to their influence on driving performance (D4.3.1, D4.4.1):

- Medicines in the relevant therapeutic groups that are currently on the market have been categorized according to the DRUID classification system (ATC groups: A, B, C, D, N01-N07, M01-M03, R01-R06, S).
- The DRUID project has proposed for analysis and categorization a total of 3,054 medicines from these ATC groups. Of these 3,054 medicines, 1,513 have not been categorized (49,5%), because they are not available on the European Union market.
- The distribution of the 1,541 categorized medicines was as follows: Category 0 – 50,3%,

<p>Category I – 26%, Category II – 11,2%, Category III – 5,8%, Multiple category – 4,4% and the Depending on the medicine in combination 2,3%.</p> <ul style="list-style-type: none"> Detailed Fact Sheets were elaborated for the N01-N07 (nervous system) and R06 (respiratory system) therapeutic groups of medicines, including information on possible side-effects related to driving, reference studies on psychomotor performance and risk studies, the proposed DRUID categorization level, and relevant information for the patient.
<p>Within DRUID WP4 partners have produced patient-oriented information for each one of the medicines categorized (D4.3.1, D4.4.1).</p> <ul style="list-style-type: none"> The aim of producing this patient-oriented information is to help physicians and pharmacists (and other health professionals) in providing appropriate information to their patients. Although Patient Information Leaflets contain some sort of information regarding driving, DRUID WP4 partners considered that it is also quite important that health professionals provide further information for medicines and driving to their patients.
<p>DRUID WP4 categorization and labelling should be integrated in existing computerized prescribing and dispensing systems for physicians/pharmacists (D7.4.2, D4.3.1).</p>
<p>Policy implications (D4.2.1, D4.3.1):</p> <ul style="list-style-type: none"> The DRUID WP4 categorization was in line with the recent approved SmPC guidelines adopted in September 2009 (which applies as from 1st of May 2010) by EMA, based on the DRUID WP4 proposal submitted for consideration by the CMD(h), as a response during the consultation phase of the revision of the SmPC guidelines in February/March 2008, proposing that in section 4.7 "Effects on ability to drive and use machines"....., specify whether the medicinal product has a) no or negligible influence b) minor; c) moderate influence or d) major influence on these abilities.... DRUID results are compatible with any existing national classification system (e.g. FR, ES) and could be integrated in them. The following agreements were reached with the PhVWP (recommendations): <ul style="list-style-type: none"> There is a need to improve information related to effects on driving in the PIL. Information to patients who are advised to use medicines that may impair driving fitness needs to be improved by simple and patient-centred directions based on a clear categorisation system and reflected in the PIL. A basic 2-tier risk categorisation system with standard wordings for the PIL is recommended for medicines without a potential influence on driving fitness (Level 1, reflective of SmPC descriptions; a) no or negligible influence or b) minor influence) and for medicines with a potential relevant influence on driving fitness (Level 2, reflective of SmPC descriptions; c) moderate influence and d) major influence). Clarification of criteria for the evidence in forming the categorisations, as described as a)-d) in the SmPC (section 4.7) into the 2 levels, should be derived in a collaborative effort of DRUID experts and the members of the PhVWP of CHMP, among other partners, preferably with support of EU bodies, such as DG Sanco and DG Move. The development of supplementary information for patients (e.g. warning levels, pictograms) and health care professionals (prescribing and dispensing guidelines), in support of the categorisation system, could be guided with input provided by the DRUID project (D 4.2.1, D 4.3.1, D 7.3.2 and D 7.4.2) as well as by experiences in EU Member States.

4.3 Rehabilitation (WP5)

Sanctions are necessary, but are only the ultima ratio. The driving population must be informed about the problem (risk / danger) and must be convinced in a way that opens self-responsible behaviour. In case of contraveners, individually tailored rehabilitation measures should be offered aiming at regaining the driving ability.

Driver rehabilitation (DR) was defined in DRUID WP5 as "a collective term for specific secondary interpersonal prevention measures that focus on attitudinal and behavioural changes of drink- (DUI) and drug-driving (DUID) offenders"; structural interventions like alcohol ignition interlock systems were no primary focus of the investigation. The primary aim of DR is to avoid new traffic offences and/or to re-integrate the individual into the traffic system without imposing a risk on other traffic participants. Alcohol ignition interlock programmes can be an additional option for DUI offenders but they can not substitute treatment, as they are only effective as long as they are installed.

DRUID WP5 aimed at providing updated comprehensive knowledge (incl. scientific evidence, previous projects (e.g. ANDREA), experiences in- and outside Europe) on DR for intoxicated drivers, in order to file recommendations on good/best DR practices for DUI/DUID offenders, and to propose adequate DR schemes for different groups of DUI/DUID offenders. With focus on the European situation, actual in-depth information from DR providers was specially considered via an EU-wide survey.

The DRUID WP5 investigation has shown that DUI/DUID **rehabilitation helps to prevent people from impaired driving** and restores their mobility in a safe way. **European standard group intervention programmes for DUI offenders show an average recidivism reduction rate of 45.5% but with a variation of 15 - 71%.**

At the time of the DRUID WP5 investigation, at least 47 providers in 12 European countries were carrying out DR services on a regular base. The provider survey gathered information on 87 programmes (53 for DUI offenders, 21 for DUID offenders, 13 for mixed groups). It is clear that the majority of current DR measures focus on DUI offenders, which corresponds to the higher prevalence of alcohol-impaired, as compared to drug-impaired, driving. Although the DR implementation in the national contexts varies to a great extent, the approaches for **non-dependent** DUI/DUID offenders are rather similar. Furthermore, DR courses are generally very positively evaluated by participants across Member States and also similar change effects are obtained.

4.3.1 Recommendations on good DUI/DUID rehabilitation practices

The within DRUID WP5 developed Driver Rehabilitation Evaluation Tool (DRET) consolidates the different WP5 investigations and includes the main Europe-wide standards and recommendations of good/best practices on national system level (legal implementation, assignment, quality management) as well as on single programme level (prior assessment; programme operation, content and evaluation) for DUI/DUID rehabilitation measures. This user-friendly tool is aimed as support for implementation, assessment or evaluation of existing or new DR systems or programmes, and could be the starting point of a European networking and documentation process of DR measures.

Main elements of effective DR are seen in (1) the assignment procedure (2) the matching of different rehabilitation options according to the needs of different offenders and (3) a quality management system (D5.2.4):

(1) Recommendation on assignment to DR

- **Legal regulation** of DR participation should be established in order to systematically bring offenders to intervention.
- A **linkage** of participation in **DR and licensing procedure** is considered as important, e.g. participation in DR as a precondition for the reduction of the suspension period or for license re-instatement.
- In general regulations on DR participation should care for an **early access** of the offender to specific measures in order to minimize the risk of problem escalation and secondary delinquency.
- In case of **suspicion of addiction** a (fitness to drive) **driver assessment** prior to DR should be carried out in order to match offenders to appropriate treatment. In all other cases **formal criteria** (such as high BAC-level, re-offending within five years, refusal of test) might be sufficient to directly assign DUI/DUID offenders to DR or at least to counselling in order to initiate problem awareness and screen for a severe alcohol or drug problem. DR participation should be **mandatory for high-risk offenders, repeat offenders and young (novice) drivers**.

(2) Rehabilitation options according to needs of different offenders

- Different types of DUI/DUID offenders have **different needs** and require different types of rehabilitation.
- The **intensity** of intervention should **increase with the severity of the problem** behaviour. **Addicted DUI/DUID offenders** should be at least **separated** from non-addicted offenders. If possible DUI and DUID offenders (excluding combined use of alcohol and drugs) should not be mixed within these groups as both groups do not only differ regarding the drug and its legality/illegality but also in relevant socio-demographic and offence related aspects. Scientific evidence regarding the latter group still has to be improved.

- **European standard group DR interventions** (6-12 participants; psychological-therapeutic approach with educative elements; lead by specially qualified course leader or psychologist respectively) can be recommended as a good practice example for non-addicted DUI/DUID offenders.
- Information exchange between experts from DR interventions and addiction treatment should be encouraged.

(3) Quality management system for DR

- **QM systems** in DR schemes are **necessary** to create transparency of procedures by fixing rules and instructions (standards) for carrying out DR services. The compliance with the standards is a medium to create confidence and a necessary condition for the trust of all sides: legislators, authorities, individuals and the public. WP5 developed a decision-tree which may serve as an evaluation tool for already established resp. newly introducing QM systems, focussing on the essential criteria (on European, country, provider and programme level) to be met in order to implement a comprehensive QM system. Optimally (to enhance EU harmonisation), these **standards** are defined **on European level**. A **(national) quality management body** should be installed which has an independent, authoritative position to execute the operative quality management tasks in driver rehabilitation.
- Applied programmes should be evaluated on a regular basis regarding their effectiveness for traffic safety.

(4) European initiative

DRUID WP5 strongly supports a **preventive DR concept** which is compatible with the overall objective of mobility of European citizens without endangering traffic safety. Therefore, the following initiatives are recommended on **European level**:

1. A basic statement on DR should be included in the EU Road Safety Act, stating that **driver rehabilitation for non-dependent DUI/DUID offenders should be an integrated part of a comprehensive countermeasure system in Europe**. Participation should be legally regulated in order to systematically bring offenders to intervention.
2. In a next working step, **European guidelines for legally regulated DR systems and procedures** should be established taking the WP5 results (DRET) into account.

This European initiative would support the application of adequate, effective, uniform and high quality DR measures for DUI/DUID offenders in the Member States, above all in countries, which newly implement this measure on national level.

4.3.2 Overview box – Rehabilitation

Box 6: Summary of main DRUID results – REHABILITATION

<ul style="list-style-type: none"> • DUI/DUID rehabilitation helps to prevent people from impaired driving and restores their mobility in a safe way (D5.1.1, D5.2.4).
<ul style="list-style-type: none"> • DR should be an integrated part of a comprehensive countermeasure system. This should be stated on EU level (D5.1.1, D5.2.4).
<ul style="list-style-type: none"> • Main outlines of rehabilitation procedures should be formulated on EU level (guidelines for legal regulations and standardised procedure). DRUID WP5 developed Europe-wide standards and recommendations of good practice for DUI/DUID rehabilitation measures, which were couched into the form of a user friendly tool (Development of Driver Rehabilitation Evaluation Tool, DRET) for implementation, assessment or evaluation of existing or new DR systems or programmes. It can be the starting point of a European networking and documentation process of DR measures (D5.2.4).
<ul style="list-style-type: none"> • Recommendation on assignment to DR (D5.1.1, D5.2.4): <ul style="list-style-type: none"> ○ Legal regulation of DR participation should be established in order to systematically bring offenders to intervention. ○ A linkage of participation in DR and licensing procedure is considered as important, e.g. participation in DR as a precondition for the reduction of the suspension period or for license re-instatement. ○ Formal criteria for directly assigning DUI/DUID offenders to DR (or at least to counselling) should be established in order to initiate problem awareness and screen for a severe alcohol or drug problem. WP5 proposes to use high BAC-level (above 1.6g/L), re-offending within five years, and refusal of test as assignment criteria.

<ul style="list-style-type: none"> ○ Driver assessment prior to DR should be obligatory in case of suspicion of addiction in order to match offenders to appropriate treatment. ○ DR participation should be mandatory for high-risk offenders, repeat offenders and young (novice) drivers.
<ul style="list-style-type: none"> ● Rehabilitation options according to needs of different offenders (D5.1.1, D5.2.1, D5.2.4): <ul style="list-style-type: none"> ○ Different types of DUI/DUID offenders have different needs and require different types of rehabilitation. The intensity of intervention should increase with the severity of the problem behaviour. Addicted DUI/DUID offenders should be at least separated from non-addicted offenders. If possible DUI and DUID offenders should not be mixed within these groups. ○ European standard group DR interventions (6-12 participants; psychological-therapeutic approach with educative elements; led by specially qualified course leader or psychologist respectively) can be recommended as a good practice example for non-addicted DUI/DUID offenders. ○ Information exchange between experts from DR interventions and addiction treatment should be encouraged.
<ul style="list-style-type: none"> ● Quality related requirements of DR (D5.2.3, D5.2.4): <ul style="list-style-type: none"> ○ The importance of implementation of quality management systems on European, national and driver rehabilitation provider level is stressed. ○ Quality management requirements should be established on a legal base in order to achieve uniform quality management standards. Optimally, these standards are defined on European level. ○ A (national) quality management body should be installed which has an independent, authoritative position to execute the operative quality management tasks in driver rehabilitation.
<ul style="list-style-type: none"> ● Alcohol ignition interlock programmes can be effective for DUI offenders in combination with rehabilitation (D5.1.1, D5.2.4).

4.4 *Withdrawal (of driving license) (WP6)*

The European Road Safety Action Programme as well as many of the national safety programmes within the European states is stressing the importance and effectiveness of the different enforcement measures to improve road safety. Enforcement is one of the most cost effective measures and needs no investment like changes in road infrastructure and vehicles do. In order to support this European Transport Policy and to be able to implement European Traffic Enforcement Recommendations DRUID WP6 investigated different attempts made in Europe (27 EU countries, Switzerland, Norway and Croatia) to combat DUI/DUID and discussed their experience with countermeasures and prevention. Aim was to bring together those different solutions and to come closer to a "best practice" procedure to be recommended to the Member States.

The DRUID WP6 recommendations are based on the national practices in Europe, the empirical evidence of withdrawal effectiveness and expert opinions.

4.4.1 Overview of national strategies

DRUID WP6 set up a comprehensive overview of legal systems as well as practices in European countries (27 EU countries, Switzerland, Norway and Croatia) with respect to withdrawal of a driving licence due to impaired driving, i.e., driving under the influence of alcohol, illicit drugs or medicine. The results reveal that the strategies are very heterogeneous, hence, a clustering of strategies or countries is difficult. Considering the fact that the national legal regulations in case of withdrawal differ considerably, the overall valid recommendation can be made **that regulations in European countries regarding withdrawal and accompanying measures should be harmonized**. The following recommendations, which are mainly based on empirical primary results and expert opinions, can be elements of such a uniform withdrawal system.

These recommendations have been summarized in D6.2 as follows (D6.2 p. 49ff):

4.4.2 General recommendations on withdrawal and conditional withdrawal

DRUID WP6 derived “the following recommendations which are valid for substance impaired driving in general, including all problem groups (DUI, DUID, substitution treatment and chronic medical treatment).

The analysis has shown that **withdrawal is** a considerable **effective** general and special deterrent factor, if sanction certainty and celerity are provided (above all immediate withdrawal/suspension of driving licence and a high level of perceived detection risk). Sanction severity is less important. In all investigated countries the combination of licence withdrawal and treatment/rehabilitation shows more deterrent effects (higher level of general and special deterrence) than licence withdrawal as stand-alone measure. Especially in case of addiction or misuse, punitive sanctions alone are not able to serve as a considerable deterrent factor, because these sanctions are not able to combat the underlying drinking problem. The distinction between withdrawal and driving ban is in general not able to serve as a considerably additional deterrent element, as the **re-granting procedure** (e.g. a check of fitness to drive/medical-psychological examination) **is a more important deterrent factor than the revocation procedure**. The imposition of driving licence measures shows a higher correlation with the level of deterrence than other sanctions (e.g. imprisonment or fines).

The **withdrawal duration** should be between **3 and 12 months**. Shorter withdrawal periods, especially short-term driving bans (12 – 24 hours), are commonly not effective. Longer withdrawal periods lead to an increase of driving without a driving licence.

The DRUID WP5 analysis has shown that DUI/DUID rehabilitation helps to prevent people from impaired driving and restores their mobility in a safe way. The measure of driver rehabilitation is in itself an effective special deterrent factor but cannot substitute driving licence measures. **Driver rehabilitation should be an integrated part of a comprehensive countermeasure system in Europe. Participation** in driver rehabilitation should also be **legally regulated** and obligatory in order to bring high-risk offenders systematically to an intervention or treatment.

A **conditional withdrawal** (including a conditional re-instatement of the licence) supports a re-integration process and respectively minimizes the social segregation effects, but has to be **combined with rehabilitative measures** and close monitoring in order to achieve measurable effects. Possible conditions are for example: driving is allowed for important activities (e.g. for work and treatment/rehabilitation), installation of an alcohol ignition interlock or regular medical checks.

DRUID WP6 was not able to conclude on a final recommendation on either administrative or criminal procedure: advantages of an administrative procedure are seen in the sanction celerity and sanction certainty (especially in case of per se legislation); disadvantages of a criminal procedure are related to huge differences in the severity of the imposed sanctions” (D6.2 p. 49f; see also D1.4.1).

4.4.3 Further recommendations for specific problem groups

(1) DUI

In regard to DUI DRUID WP6 recommends “**per se laws with a graduated system of withdrawal and additional measures depending on the BAC level**.

In cases of high levels of alcohol intoxication, re-offending within five years, and refusals of alcohol tests, a medical-psychological **assessment** is necessary for the decision on fitness to drive and further intervention. Medical follow-up controls should be imposed in individual cases in the frame of fitness to drive; whereby frequency and intensity should depend on the individual case.

In regard to DUI **rehabilitation** DRUID recommends to provide at least **two levels** of intervention: (1) less intense rehabilitative measures for non-dependent offenders (European standard group intervention as good practice) and (2) an intense treatment for dependent offenders (established addiction therapy in the health sector). The assignment procedure should be defined and formal criteria should be fixed which lead directly to participation.

Participation in an **alcohol ignition interlock** programme should not substitute a minimum period of full licence withdrawal, but should be offered as an option in **exchange for a reduced length of licence suspension**. The **duration** of the programme should be **criterion-based**, i.e. the offender

should not be released from the programme before he/she proved to drive sober in a stable way (= at least 6 months without starting failure for first offenders, 12 months without starting failure for repeat offenders). An interlock programme should always **include at least strict medical counselling or even psychological support**.

Interlock legislation must include supplementary provisions that prohibit a driver from asking someone else to provide a breath sample in an attempt to start the vehicle and driving a vehicle not equipped with an interlock device. The interlock **restriction must be clearly marked on the driver's licence** in order to assure enforcement in case of programme violations" (D6.2 p. 50; see also D1.4.1).

(2) DUID

In general, "the system of **withdrawal** and additional measures for DUID should be **in line with the system regarding alcohol**.

In case of DUID, including refusal of drug test, a driver **assessment should always be carried out** for the decision on fitness to drive and further intervention, **unless threshold values for DUID are defined**. As in the case of DUI, medical follow-up controls have to be imposed in individual cases in the frame of fitness to drive. The frequency and intensity should depend on the individual case.

Rehabilitative interventions for non-dependent and dependent offenders have to be provided (European standard group intervention as good practice and established addiction therapy in the health sector)" (D6.2. p. 51, see also D1.4.1).

(3) Patients in substitution treatment

"There should be **no basic difference made between patients in substitution treatment and patients in other medicinal treatments**.

Each patient in substitution therapy **has to be assessed individually** regarding fitness to drive. Thereby, the assessment and evaluation model should be adaptable to the specific case: addictions to others substances (e.g. alcohol, benzodiazepines) are exclusion criteria, patients treated with diamorphine (pharmacological heroine) are not fit to drive, substitution substance (Methadone vs. Buprenorphine vs. Morphine) and the height of the daily dosage in milligrams are no criteria for the (decision about the) fitness to drive. The adequacy of the substance and dosage for each client is a crucial issue; in cases of intake of other disease-related prescribed medicines, tests of cognitive performance are recommended, especially for older long-term using patients.

Based on the fitness to drive examination, a conditional licence with regular follow-up controls is recommendable. Thereby, **follow-up controls** are related to **alcohol-driving** abstinence (separation of drinking and driving) as well as abstinence of relevant parallel **consumption of other drugs**, a follow-up period after tapering the dose (treatment end) should be defined individually" (D6.2 p. 51; see also D1.4.1).

(4) Patients in long-term treatment with psychoactive medicines

"Patients should be adequately informed on possible impairing effects and how to recognize them (link to WP4).

The usage compliance with prescription and misuse has to be distinguished. In the latter case, the legal procedure and consequences should be in line with DUID. Legal measures should only be taken after an incident in traffic, whereby impairment is the key for sanctioning.

Based on a medical expertise / assessment, an individual solution can be developed. Thus, no approach solely on substance classes is needed. A model of conditional licensing (after a full withdrawal) is recommendable" (D6.2 p. 50f, see also D1.4.1).

4.4.4 Overview box – Withdrawal

Box 7: Summary of main DRUID results – WITHDRAWAL

<ul style="list-style-type: none">Regulations in European countries regarding withdrawal and accompanying measures should be unified as far as possible and as far as they do not intervene with other national strategies against DUI/DUID. So far, national strategies are very heterogeneous, hence a clustering of strategies or countries is difficult (D6.2).
<p>General recommendations on withdrawal and conditional withdrawal (D6.2.):</p> <ul style="list-style-type: none">Sanction certainty and celerity are crucial for the general and special deterrent impact of sanctions, above all immediate withdrawal/suspension of driving licence and a high level of perceived detection risk.The imposition of driving licence measures shows a higher correlation with the level of deterrence than other sanctions (e.g. imprisonment or fines).Withdrawal duration should be set between 3 and 12 months. The deterrent impact of shorter and longer durations has not been proven by empirical primary research; a longer withdrawal period leads in general to an increase in driving without a licence.Generally, the combination of withdrawal and rehabilitation/treatment is connected with higher levels of deterrence than the sole imposition of each measure.A conditional withdrawal (including a conditional re-instatement of the licence) supports a re-integration process and can be applied if certain requirements are met. Possible conditions are, above all rehabilitative/treatment measures, but also installation of an alcohol ignition interlock and/or regular medical checks.DRUID WP6 was not able to conclude on a final recommendation on either administrative or criminal procedure: advantages of an administrative procedure are seen in the sanction celerity and sanction certainty (especially in case of per se legislation); disadvantages of a criminal procedure are related to huge differences in the severity of the imposed sanctions.
<p>Further recommendations for specific problem groups (D6.2):</p> <ul style="list-style-type: none">DUI drivers:<ul style="list-style-type: none">A graduated system of withdrawal and additional measures - depending on the BAC level - should be introduced.Driver assessment and rehabilitation should be legally regulated and based on defined criteria (see WP5)An alcohol ignition interlock could be offered as an option in exchange for a reduced length of licence suspension and should include at least strict medical counselling or even psychological support.DUID drivers:<ul style="list-style-type: none">General DUI deterrent principles are also valid for DUID.As long as no threshold values for DUID are defined, driver assessment should always be carried out to assess the fitness to drive and to decide on further rehabilitation/treatment.Patients in substitution treatment:<ul style="list-style-type: none">Each patient in substitution therapy has to be assessed individually regarding fitness to drive.A conditional licence, based on the fitness to drive examination, is recommendable combined with follow-up controls, above all focussing on abstinence of parallel consumption of other drugs.Patients in long-term treatment with psychoactive medicines:<ul style="list-style-type: none">Legal measures should be taken only after an incident in traffic; impairment is the key indicator for sanctioning.A model of conditional licensing, based on the fitness to drive examination, is recommendable.

4.5 Guidelines and risk communication (WP7)

Health care professionals need to be informed about the potential road safety risk associated with the use of medicines. The availability of clear information with respect to the medicinal categorisation system (WP4) will contribute to more driver-patient safety and better use of medicines. Physicians and pharmacists are key actors to forward this information to patients. Practice guidelines and protocols to make physicians and pharmacists aware of their role and to provide them with relevant information needed to be developed. The emphasis should lay on using relatively safer medicines if available, and

on improving warnings and advices to patients how to act responsibly if using medicines that have the potential to impair driving. These measures should be supported by adequate training activities and supporting tools (e.g. integrated in software package of daily practice).

DRUID WP7 generally aims at providing guidelines and tools that will increase the general awareness of accident risks involved with the use of psychoactive substances (alcohol, illicit drugs and medicines). The main focus lays on improving the risk communication between health care professional and patients, but also other target groups (general public, young drivers, policy makers on EU and national level) were addressed within this work package.

The specific objectives of DRUID WP7 were: (1) to review the **state-of-the-art** of existing campaigns regarding psychoactive substances by using different media, focussed on the general public and health care professionals, as well as the documented effectiveness of those campaigns and knowledge translation; (2) to development of **prescribing and dispensing guidelines for physicians and pharmacists** to select the least impairing medicine within a therapeutic class and to provide patient information that will meet the patient's needs; (3) to develop recommendations for improving the procedures for assessing fitness to drive within the framework of **Council Directive 91/439/EEC** (on driving licences), allowing doctors to exert a responsibility in this process without incurring possible penal proceedings in the event of an accident occurring after a positive decision from their side; (4) to develop information materials aimed at the general public, young drivers, drivers as patients, physicians and pharmacists and policy makers on EU and national level and health care professionals; and (5) to evaluate practice guidelines and protocols in every day medical and pharmaceutical practice by focussing on different practice models, with and without the application of Information and Communication Technologies (ICT), as well as the evaluation of risk communication to patients and to young drugs consuming drivers (DRUID Technical Annex p. 105).

4.5.1 Recommendations and guidelines for communication

In order to develop guidelines on informing different target groups regarding driving under the influence of alcohol, drugs and medicines, different investigations were conducted in WP7:

- state-of-the-art review of existing DUI/DUID information campaigns (75 campaigns from 13 different countries) (D7.1.1 p. 81f);
- state-of-the-art review of theoretical background for information campaigns (EU CAST project) (D7.3.1);
- experts' on-line survey on the criteria for the design of prototype documents for information regarding psychoactive substances and driving (D7.3.1).

This input together with the more general literature review on risk communication theories (D7.3.2 Part I) are presented as framework for extracting target group specific information (D7.3.2 Part III) from the gathered main DRUID results (D7.3.2 Part II).

The main results of the campaigns' review can be summarized as follows (D7.1.1 p. 81f):

- The focus of campaigns (content, target group, media etc.) should be selected according to the specific characteristic of problem situation and risk group.
- Most of the retrieved DUI/DUID information campaigns were conducted through mass media. The type of medium used the most is brochures, followed by posters, written press, websites, booklets, TV commercials, radio spots, leaflets, tutorials or another type of medium.
- Most campaigns are organized by governmental agencies and road safety organisations.
- Evaluation studies of the campaigns are often lacking. Information on the impact of the campaign was only found in 7 cases. As the evaluations were performed in many different ways, it was not possible to draw conclusions concerning the association between the design of the campaigns and their effectiveness (D7.1.1).

The EU project Campaigns and Awareness-raising Strategies in Traffic Safety (CAST: www.cast-eu.org) emphasized the following key points for developing and evaluating campaigns:

- "Target audience: A key factor of success of road safety communication strategies is the identification of the target audience since this enables defining the best way to reach the targeted individuals. Furthermore, segmenting the target audience enhances the likelihood of success of the message and strategy in reaching and involving the intended audience. Once the target audience is defined, it is very important to find out and to know what the audience

wants and what their needs are, as well as what will have the greatest effect on changing their behaviour.

- Analysing the situation: The background of a campaign refers to results from the: in-depth analysis of the problematic behaviour and possible solutions; identification of the target group at risk and how to reach and influence them; translation of the overall campaign goal into specific objectives.
- Message: An effective message strategy, based on the communication objectives, is essential for the success of a campaign. It can be subdivided into content strategy (what will be said) and execution strategy (how and by whom it will be said).
- Means and features (media): Target segments' factors as well as media-related factors should be taken into account when choosing the type(s) of communication and media. Target audience factors include aperture (or opening), which is the audience's general habits, general interests and media habits. Media-related factors include the ability of media vehicles and combined actions to reach the target audience, and the communication capacity of media vehicles and combined actions.
- Communication objectives: This refers to the translation of the general goal of the campaign (based on the problem analysis) into the expected effects (objectives). It should be defined which behaviour (= primary objectives) is to be adapted by the target group to realise the general goal of the campaign. Furthermore, the factors that can contribute (i.e. knowledge, beliefs, attitudes ... = secondary objectives) to reaching the primary objectives can be defined. The specific campaign objectives are used during the evaluation of a campaign. Therefore, objectives should be clearly defined with their levels of accomplishment (e.g. % increase of knowledge) in order to evaluate the success (effectiveness)" (D7.3.2 p. 10f).

Experts' opinions (D 7.3.1.) on information documents on DUI/DUID were:

- Medicines and illicit drugs should be addressed separately.
- Much more attention should be paid to the elderly, either in campaigns addressed to the public in general as well as to the aged patients who drive.
- Illicit drugs and medicines should be dealt with by substance group.
- With regard to illicit drugs, most emphasis should be given to risks caused by use of cannabis followed by illicit use of benzodiazepines and stimulants such as ecstasy, amphetamines and cocaine.
- With regard to medicines, priority should be given to medicines used in anaesthesia (general anaesthetics) followed by analgesics, hypnotics and sedatives, ophthalmologic medicines and anti-epileptics and anti-psychotics, anxiolytics, drugs used in addictive disorders and psycho-stimulants.
- With regard to the content, the main focus should lie on the risks and effects of the substances on driving. For "general public", "driver as patients" and the "younger public", also information on sanctions should be included. For the "general public", also information on the size of the phenomenon (data on epidemiology) is considered important. For "physicians/pharmacists" and "policy makers", information should be included on the size of the phenomenon and current legislation.

4.5.2 Guidelines and professional standards

Based on existing guidelines and a survey among driving licensing authorities and experts (feedback from 18 EU countries; response rate 62%), DRUID WP7 concluded that guidelines and standards for health care professionals pertaining to medicines and driving are generally lacking in most European MS although decision support for example at the start of a treatment is needed for selecting the least impairing medicines. "Strict and binding regulations concerning prescribing and dispensing of psychoactive medicines, which might have an impact on the driving performance, are the exception rather than the rule. The compiled guidelines are typically recommendations not regulations. The role, responsibilities and tasks of physicians and pharmacists are "not defined uniformly" and, "in most cases, physicians and pharmacists will not be made legally responsible" when one of their patients [taking a driving impairing medicine(s)] is made responsible for a traffic accident" (D7.2.1 p. 4).

Recommendations on improving the Council Directive 91/439/EEC

DRUID WP7 derived eight recommendations on improving the procedures for assessing fitness to drive within the framework of Council Directive 91/439/EEC (on driving licences). The

recommendations aim at allowing medical doctors to exert a responsibility in this process without incurring possible penal proceedings in the event of an accident occurring after a positive decision from their side.

- “Some of the recommendations point at the vague terms that are used in Article 15 (such as substance abuse, regular use, both for medicines and illicit drugs, etc.), whereas more internationally accepted terms exist”.
- It is also recommended “to include the underlying cause or reason for taking medicines, as well as all co-morbidity factors, while assessing fitness to drive.
- Another recommendation points at the term combinations of medicines with central nervous system activity. (...) This is especially of interest for drivers with co-morbidities and in case of polypharmacy.
- It is also recommended to apply the DRUID (WP4) categorisation system for medicines affecting driving performance in developing national requirements for fitness to drive.
- Finally it is recommended that in situations where physicians will advise a patient to start driving again after a period in which the advice was given not to drive while using the medicine, specific procedures are needed to structure the consultation and to manage the risk of litigation in case an accident could occur.

(for more details see D7.2.1 p. 55-59)” (D7.2.1 p. 5; D7.2.2 p. 64)”. The WP7 team stress that these suggestions should be discussed in working groups/expert rounds with physicians, pharmacists, driving licensing authorities and policy makers in order to reach a consensus at European level.

Prescribing and dispensing guidelines for physicians and pharmacist

Reference is made to the developed guidelines in ICADTS and a stepwise approach for prescribing and dispensing safe medicinal treatment to drivers (see table 38).

The emphasis should be given to shared decision making between health care professionals and patients and on documentation of patient consultations (to avoid liability issues).

Table 38: Prescribing and Dispensing guidelines form ICADTS, 2001¹⁵

Prescribing Guidelines	Dispensing Guidelines
1. Realize that the use of some psychoactive medicines has been associated with an increased risk of causing an injurious accident and that patients should receive this information.	1. Discuss with prescribing physicians what patient information (written and oral) should be provided at the first delivery of a particular impairing medicine
2. Consider an alternative in the light of experimental research showing large differences between the effects on driving performance of various medicines within the same therapeutic class.	2. Inform the prescribing physician that alternative drugs exist in case a medicine in class II or III has been prescribed, and inform the patient.
3. Start with the lowest doses of psychoactive medical medicines and whenever possible avoid multiple dosing over the day.	3. Advise the physician to prescribe the lowest effective dose of a particular psychoactive medicine and to avoid multiple dosing over the day. Inform the patient.
4. Do not reflexively "double the dose" if patients fail to respond to psychoactive medication.	4. Advise the physician to try another medicine if the patient reports a lack of efficacy after beginning of treatment and inform the patient. If higher doses are needed advise the patient to use the largest part before sleep (if compatible with the therapeutic regimen).
5. Avoid prescribing different psychoactive medicines in combination.	5. Explain to the patient that poly-therapy with psychoactive medicines is always an experiment with the patient's safety and avoid to driving if treatment can not be adjusted.
6. Do not rely solely upon the manufacturers' advice for counselling patients about the effects of medicine upon driving.	6. Explain to the patient why warnings provided by the manufacturer about their medicine's effects on driving are vague, illogical and sometimes misleading.
7. Advise patients concerning the ways they can minimize the risk of causing a traffic accident if it is impossible to avoid prescribing an obviously impairing medicine or one with unknown impairing potential (see next table).	7. Advise the patient the ways they can minimize the risk of causing a traffic accident if they have to use a drug with an impairing potential (see next table).
8. Monitor the patient's driving experience with the drug.	8. Monitor the patient's driving experience with the drug (e.g. at the first refill) and report back to the physician or ask the patient to inform the physician.

¹⁵ International Council on Alcohol Drugs and Traffic Safety (ICADTS) Working Group Report on Prescribing and Dispensing Guidelines for Medicinal Drugs that Affect Driving Performance, 2001. <http://www.icadts.org/>

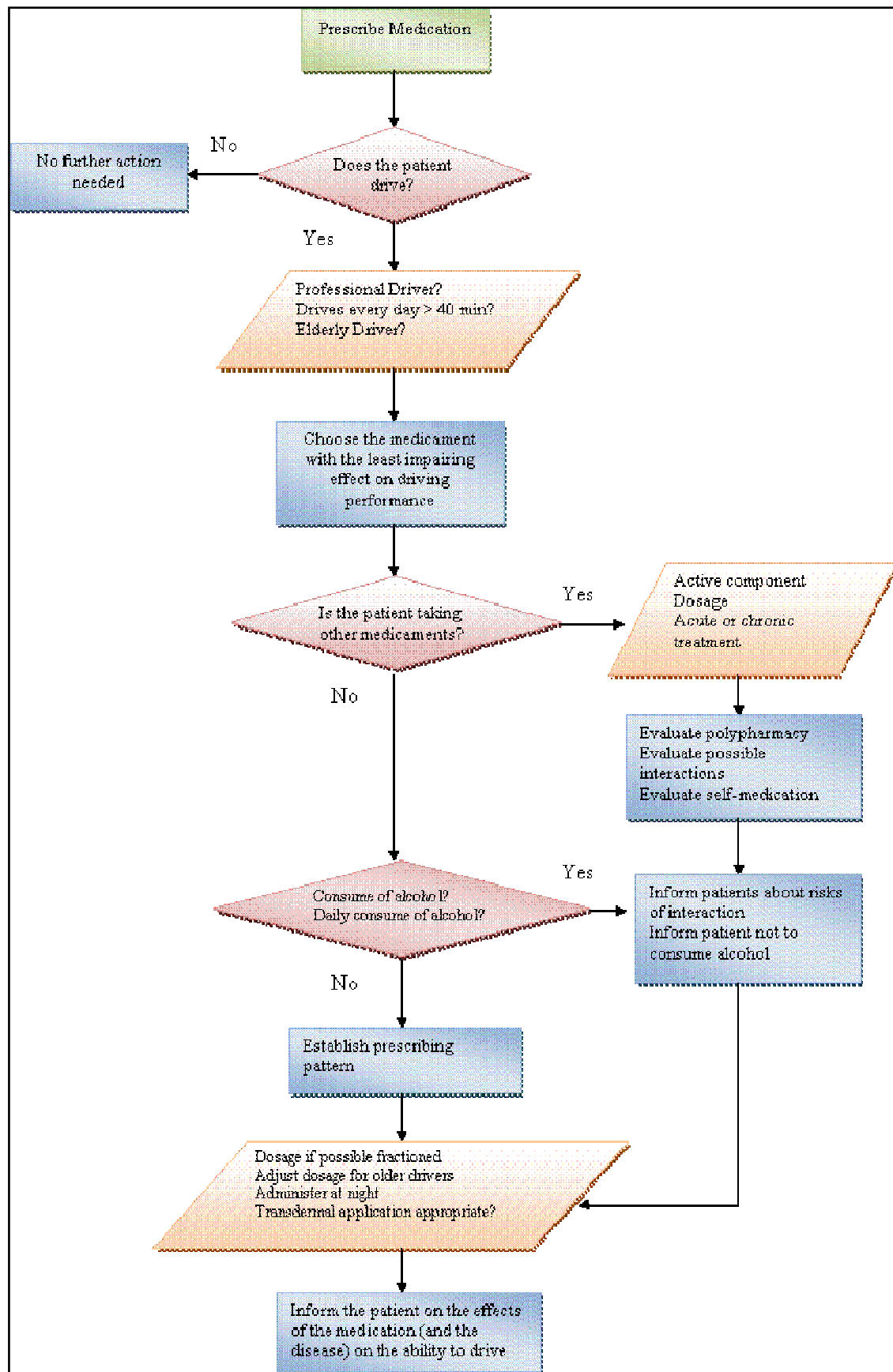


Figure 42: Prescription of medicines to patients who drive a vehicle (Álvarez, 2006).

Checklist with issues for documenting the decision-making process to avoid liability issues (D7.4.1 p. 28):

Actions to be checked during the consultation:

- Advise not to combine psychoactive medication.
- Check whether the patient is willing and able to follow the treatment plan.
- Advise the patient to be aware of possible side-effects.
- Advise the patient to report on these side-effects during a follow up visit.

Documentation of the following items:

- tests done and / or information gathered in assessing fitness to drive;
- assessment of patient's decision-making competence based on advices given;
- patient's understanding of impairing properties of the medication;
- specific actions to achieve fitness to drive (changes in medication or instructions for use);
- follow up visit for evaluation of interventions (advices given, self-assessment of patient).

In order to easy access protocols and guidelines should be integrated in existing computer software used by health care professionals in daily practice. DRUID WP7 developed or adjusted information to be used in existing software packages (see D7.2.2) which have been evaluated in BE, ES and NL (see D. 7.4.2.).

4.5.3 ICT and paper tools for physicians and pharmacists

DRUID WP7 developed several tools which can be used to aid the prescribing and dispensing process in considering possible driving impairing effects: a training paper tool aiming to inform and sensitise health care professionals on this issue, as well as supportive software including the relevant medicinal risk information and categorisation (WP4) which can either be installed in existing daily used software packages (integrated) or be used as a stand-alone tool (USB). Furthermore, a paper tool (compendium) including the individual medicinal risk categorisation and (WP4) Fact Sheets was developed. (see also DRUID CD-rom demonstration D7.2.2). These tools have been evaluated in BE, ES and NL and preliminary results are presented in the following part.

4.5.4 Evaluation of risk communication

Pictograms for showing risk

Two studies on the risk communication to patients have been carried out in ES and NL and one on the risk communication to young drugs consuming drivers in DE. The results of these studies can be found in Part I of this deliverable (D7.3.2 Part I).

The primary aims of the studies were

- to evaluate the effectiveness of the *rating model pictogram* (showing four possible categories or risk of impairment levels in different colours, presented in a bar, and a black triangle in the assigned category; with or without side-text explaining how to act) in communicating risk associated with driving impairing medicines to patients, and
- to assess patients' level of understanding and intention to change driving behaviour by looking at various pictograms.

A comparison with a similar and already existing (in France) pictogram with or without side-text how to act was conducted (*triangle model pictogram*; a single black triangle on the box with a specific colour for a assigned risk of impairment level)

Patients visiting a community pharmacy and actively participating in traffic (in NL) and patients visiting health services, such as pharmacies, primary care physicians and hospitals, with or without a driving license (in ES) were interviewed. The results show that:

- All pictograms (different categories presented in the two models) were found to be clear, informative, easy, understandable, not complex, and not ambiguous.
- Respondents' opinions of categories II and III of the rating model were those associated with more dangerous situations compared to respective categories as shown with the triangle model.
- Respondents' likelihood to change driving behaviour is significantly higher with the rating model pictogram than with the triangle model.

- Respondents stated that they would be likely to change their driving behaviour by driving less frequently. No statistically significant differences were found between both types of models.
- About 40% of the respondents would change their driving behaviour by not driving anymore, if refrain from driving is advised whenever a category III medicine is prescribed. 60% of the respondents who first saw category III pictograms from the rating model would not drive anymore, against 43.3% of those who saw the homologue triangle model.
- Respondents' preference in understanding the pictogram for explaining a side-text warning and for showing the level of impairment was significantly higher for the rating model. A negative correlation between age and pictogram model of preference was found: older participants were more in favour of the triangle model than younger participants.

Prescribing/dispensing guidelines and supporting tools

The above mentioned practice guidelines and protocols as well as supporting tools have been evaluated in everyday medical and pharmaceutical practice in BE, ES and NL (D7.4.2).

The results of these studies will be available at the end of the DRUID Project (October 2011), but preliminary findings could already be included in this deliverable.

Preliminary evaluation results based on the consolidated database (including common NL, ES and BE results) indicate a positive effect of training on and implementation of the DRUID guidelines (as intervention):

- After training on and implementation of the DRUID dispensing guidelines, pharmacists had significant positive changes in reported behaviour (increased consideration in informing patients about medicines' impairing effects regarding driving), attitudes and awareness about medicines' dispensing and driving and actual knowledge about categories of medicines and their effect on driving behaviour.
- With regard to physicians, significant differences (in the expected direction) were observed between the control and intervention groups for attitudes and reported behaviour after the training and implementation phase of the DRUID prescribing guidelines.
- Overall, health care professionals are very satisfied with and strongly prefer ICT supporting tools which are integrated in their prescribing/dispensing software systems over other supporting tools. The participating ICT software providers expressed high interest to continue offering these additional tools (which had to be stopped after the study period since update of the information was no longer guaranteed).

Risk communication towards young consumers of alcohol and drugs

During a DRUID-workshop on risk communication media- and communication-experts recommended putting a strong emphasis on the risks of drink driving. They favoured the idea to include into the target group even younger people just reaching the phase of getting a driving license, thus extending the target group to adolescents and young adults of 15-24 years. The effectiveness of adequate, general preventive approaches should be investigated, as well as special focussed preventive measures for certain smaller subgroups (lifestyle types). It was suggested, to check for efficient approaches via social networks (internet) or personal contacts (peers).

To gain a closer look on the target group a formative evaluation was started in form of a representative sampling with 800 young people. The sampling focused on:

- status of information and need for information on alcohol/drugs and driving;
- personal involvement;
- relevant attitudes and behavioural aspects;
- subjective norms;
- subjective risk perception;
- acceptance and credibility of certain media and mediators.

The results of the workshop and the formative evaluation are part of DRUID Deliverable 7.4.3.

4.5.5 Overview box – Guidelines and risk communication

Box 8: Summary of main DRUID results – GUIDELINES/RISK COMMUNICATION

Reviewing DUI/DUID information and education campaigns (D7.1.1; D7.3.1; D7.3.2 at hand):

- The focus of campaigns (content, target group, media etc.) should be selected according to the specific characteristic of problem situation and risk group. The majority of the retrieved campaigns concerned driving under the influence of drugs, aimed at young people (this is not reflecting the actual problem situation) (D7.1.1, D7.3.1).
- Campaigns are more successful if they are targeted (specific issues, groups, etc.). Therefore, large campaigns should be designed as sets of a larger number of activities on a smaller scale (D7.1.1, D7.3.1).
- Campaigns should be evaluated (D7.1.1, D7.3.1).
- Key points for developing and evaluating campaigns have been formulated in the EU project CAST (www.cast-eu.org) (target audience, analysing the situation, message, means and features (media) and communication objectives) (D7.3.1).
- The report at hand is aiming at extracting main DRUID information per target group (general public, young drivers, drivers as patients, physicians and pharmacists and policy makers on EU and national level) based on the theoretic frame of CAST (campaigns) and a more general literature review on risk communication (D7.3.2 at hand).

Guidelines and professional standards (D7.2.1, D7.4.1):

- Guidelines and standards for health care professionals pertaining to medicines and driving are generally lacking in most European MS (D7.2.1).
- Decision support at the start of a treatment is needed for selecting the least impairing medicines (D7.2.1).
- Eight recommendations on improving the procedures for assessing fitness to drive within the framework of Council Directive 91/439/EEC (on driving licences) have been formulated within DRUID WP7. They aim at allowing doctors to exert a responsibility in this process without incurring possible penal proceedings in the event of an accident occurring after a positive decision from their side. These suggestions should be discussed in working groups/expert rounds with physicians, pharmacists, driving licensing authorities and policy makers in order to reach a consensus at European level (D7.2.1).
- Emphasis in prescribing and dispensing guidelines for physicians and pharmacist should be given to shared decision making (health care professional together with the patient) and documentation of patient consultation (to avoid liability issues). Recommendations on the content of prescribing and dispensing guidelines for physicians and pharmacists have been formulated within DRUID WP7. Protocols and guidelines should be integrated in existing computer software used by health care professionals in daily practice (7.4.1).

ICT and paper tools for prescribing and dispensing medicines (D7.2.2):

- DRUID WP7 developed materials to be used in existing software packages for supporting integrated application in prescribing and dispensing practices as well as in stand-alone software packages and paper tools in which risk categorisation and Fact Sheets provided in WP4 are made accessible for physicians and pharmacists (see also DRUID CD-rom demonstration) (D7.2.2).

Evaluation on risk communication (D7.4.2Draft; D7.4.3Draft):

- The use of pictograms on medicine boxes for risk communication to patients is effective in explaining a risk of impairment level after using a driving impairing medicine. Patients' likelihood to drive less frequently under the influence of a medicine is higher if the pictogram shows reference to all possible risk levels, and identifies the selected risk level from a rating bar model as compared to a single triangle model without explanation of possible risk levels. Younger patients (more in favour) and older patients (less in favour) differ in their preference for more complex presentations of risk of impairment levels in a pictogram.
- Preliminary evaluation results based on the consolidated database (including common NL, ES and BE results) indicate a positive effect of the DRUID guidelines. Overall, health care professionals are very satisfied with and strongly prefer ICT supporting tools which are integrated in their dispensing/prescribing tools over other supporting tools (D7.4.2Draft).
- Preliminary results of D7.4.3 show that the emphasis should be given to drink driving prevention, targeting the age group 15-24 year. Preventive measures should be differentiated into general preventive approaches (e.g. campaigns) and special focussed preventive measures for certain smaller subgroups (lifestyle types e.g. personal communication). The effectiveness of approaches should be analyzed in-depth based on representative samples (according results for e.g. DE will be available at the end of the DRUID project) (D7.4.3Draft).

Part III. Extraction per target group

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Within this chapter key elements of risk communication (Part I) and main DRUID results (Part II) for and about specific target groups are extracted. The organisation of this Chapter is structured in a way that information addressed to a specific target group is presented in a complete manner. As a result content repetition in the text for each target group is possible. For their own convenience readers interested in the content for and about one specific target group are not guided to different sections of the Chapter.

1 General public

1.1 Key elements of risk communication

The aim of risk communication addressed to the general public is to (i) make them aware that the use of psychoactive substances (including some medicines) is not always compatible with car driving, (ii) support them to make their own problem definition, according to personal beliefs and expectations of risk, with or without the help of a (healthcare) professional, (iii) allow them to decide how to manage the risk in their daily life activities.

For addressing risk communication messages to the *general public*, the following issues need to be considered:

1. Factors that play a role in perceiving and accepting risk (see Part I. 3.2. Risk acceptability) For driving under the influence of psychoactive substances it seems obvious to address these factors carefully in defining messages of risk communication to the general public. A trusted organization, credible and with an eye on values and interests that people feel important can do a proper job in convincing them that, although DUI is a voluntary risk, it will not be completely controlled by the person due to the effects of psychoactive substances.
2. Groups with higher socioeconomic status are more likely to benefit from an increasing flow of information on many issues, including drugs and driving issues. However, there are many contributory factors that could reduce the knowledge gap. First of all a content domain related factor, people might feel that health issues are more relevant to them than other issues, also certain groups could experience a greater impact of information due to the channel that was chosen, and used more frequently by them (e.g. internet applications, newsgroups), and individual motivational factors. It is expected that users of ICT technologies will use the information “on demand”, allowing them to control the media technologies and attempts to change their behaviour. This, however, is also a risk for widening the knowledge gap, because access could be determined by socioeconomic status and necessary skills.
3. The “power” of any single channel of communication (being mass media or interpersonal) may depend on the complexity of the behaviour change being sought. If the change is less complex, a single channel of communication may lead to development of the promoted behaviour. If, however, the behaviour change is more complex an individual will need the use of multiple sources of information and the application of multiple channels of communication.

1.2 Extraction of main DRUID results

Problem situations

Alcohol

- **Prevalence:** Alcohol ($\geq 0.1\text{g/L}$) is the most frequently detected psychoactive substance in the driving population (estimated EU mean 3.48%) (D2.2.3) as well as in the seriously injured (range 17.7-42.5%) and in killed drivers (range 19.0-44.9%) in Europe (D2.2.5; D2.2.4; D2.3.4).

- Alcohol was in the general driving population mainly detected among older male drivers, with lower BAC levels (D2.2.3).
- Within the accident involved drivers alcohol was mainly detected among younger male drivers with a high BAC level (D2.2.5). Alcohol appeared most often alone compared to other substances. When alcohol was combined with other psychoactive substances, benzodiazepines and cannabis (THC and/or THCOOH) were the most common associated findings (D2.2.5; D2.3.4).
- **Risk:** Alcohol has a negative impact on driving performance and highly increases accident risk (e.g. D1.1.2a, D2.3.2; D2.3.3; D2.3.4; D2.3.5 DRAFT).
- Based on case- control studies, the relative risk of serious injury or fatality for alcohol (≥ 0.5 g/L) is estimated to be significantly increased compared to that of drivers below the DRUID cut-off for any substance (D2.3.5) The risk increases dramatically with the alcohol concentration.
- An increased risk was associated with high BAC level, young age and speed (D2.3.3).
- The risk multiplies with combined use (e.g. cannabis) (D2.3.2).
- The general finding is that alcohol use in traffic is already risky at low BAC levels, especially for younger drivers who have less driving experience than older drivers. Alcohol affects the driving behaviour by increasing the reaction time and decreasing concentration, coordination and tracking. Furthermore, alcohol leads to more risk-taking behaviour and affects decision making and planning, since drivers overestimate their skills and underestimate the risk due to the effects of alcohol (Kelly et al., 2004; Steyvers & Brookhuis, 1996) (D2.2.3).
- **Motives behind DUI:** Drivers do not think that alcohol impairs their performance; Drivers whose drinking and driving was related to problems with alcohol argue that losing the licence or even to be imprisoned would not have helped them to stop re-offending; instead, it they argue that the treatment programme had helped them by providing a greater insight into their own problems; factors influencing the decision to DUI/DUID: risk perceptions (e.g. beliefs in the objective danger/effect of the substance on driving ability, perceived chance to be involved in an accident / fear of injuring others, perceived chances to get caught / to lose DL), knowledge (effects of alcohol, safe alcohol consumption levels for driving), subjective norm/social norms and expectations/peer pressure (D2.2.1).
- Clear information about sanctions (certainty/celerity) of DUI is required (D6.2, D1.4.1).
- For more details see overview box 1.

Illicit drugs

- **Prevalence:** All DRUID investigations (e.g. D2.2.3, D2.2.5, D2.3.4) show that the prevalence of illicit drugs in the driver population (estimated EU mean 1.90%) is lower than the alcohol prevalence (estimated EU mean 3.48%) (D2.2.3).
- Within the accident involved drivers, the majority of drugs appeared to be used in combination with other psychoactive substances (mainly alcohol) (D2.2.5).
- THC is generally the most frequently detected illicit drug, followed by cocaine, but the prevalence of the different illicit substances show high national variability (e.g. D2.2.3, D2.2.5, D2.3.4).
- Illicit drugs were in general mainly detected among young male drivers, during all times of the day but mainly at the weekend (D2.2.3).
- Combined use of alcohol and drugs (illicit drugs and/or psychoactive medicine) is in general often prevalent among young (<35 years) male drivers during night time hours (D2.2.3).
- Multiple drugs (illicit drugs and/or psychoactive medicines) use is in general most common in males (D2.2.3).
- Age groups and time periods vary considerably by country (D2.2.3).
- **Risk:** Based on case-control studies, the relative risk of serious injury or fatality for different illicit substances varies between the substances. For: THC about 1-3 times; benzoylecgonine, cocaine and illicit opiates about 2-10 times; amphetamines about 5-30 times as high as that of drivers below the DRUID cut-off for any substance (D2.3.5 DRAFT; see also D1.1.2b, D1.2.1, D2.3.2). Some of the risk estimates for illicit drugs vary to a high degree among the single

countries; others are based on few positive cases and/or controls which result in very wide confidence intervals. Therefore the estimates are uncertain.

- Experimental studies have shown that the dose equivalent for BAC 0.5g/L-3.7ng/mL THC (range 3.1-4.5ng/mL) for oral administration and 3.8 ng/mL (range 3.3-4.5ng/mL) for smoked administration (D1.1.2b, see also D1.4.2 for more information on cut-offs equivalent to BAC 0.5g/L).
- The risk multiplies with combined use (e.g. alcohol) (e.g. D2.3.2, D2.3.5).
- Experimental studies evaluating the effect of stimulants on driving (MDMA and dexamphetamine) did not reveal impairing effects on driving performance. However, the stimulant effects of MDMA and dexamphetamine are not sufficient to overcome or compensate driving impairments produced by concomitant of alcohol use or sleep deprivation (D1.1.2b, D1.2.1).
- **Motives behind DUID:** Addicted drivers did not believe that they would be stopped by the police. They did not believe that alcohol or drugs would impair their driving and therefore they did not perceive any real risks of driving (D2.2.1). Findings indicate that especially moderate substance users can realistically judge their intoxication and are responsible-minded concerning drugs in traffic (D2.2.2).
- Clear information about sanctions (certainty/celerity) of DUID is required (D6.2, D1.4.1).
- For more details see overview box 2.

Medicines

- **Prevalence:** DRUID studies indicate that some selected psychoactive medicines (benzodiazepines, medicinal opiates and opioids and Z-drugs) are less prevalent in the driving population (estimated EU mean 1.4%) (D2.2.3) as well as is in seriously injured drivers (D2.2.5) compared to alcohol (estimated EU mean 3.48%) and illicit drugs (estimated EU mean 1.90%). Among the killed drivers the presence of benzodiazepines was the second most frequent toxicological finding after alcohol (D2.2.5). Psychoactive medicines, such as (frequently used) antidepressants, anti-epileptics and antipsychotics, were not included in the DRUID studies. Therefore an underestimation of prevalence should be considered.
- In most countries benzodiazepines were the most common psychoactive medicines in traffic but as for illicit drugs the prevalence of the different psychoactive medicines show high national variability (D2.2.3, D2.2.5).
- Epidemiological studies indicate a major increase in the consumption of antidepressants and drugs used in addictive disorders in the general population in Europe within the last years (D2.1.1).
- Psychoactive medicines were in general mainly detected among older female drivers during daytime hours (D2.2.3).
- **Risk:** Alcohol impaired driving is the main problem in traffic safety, but also psychoactive medicines can constitute a problem in traffic safety. Therefore, both health care providers and patients should be properly informed and aware of the potential risks associated with the use of psychoactive medicines (link WP4/7).
- Based on case-control studies, the relative risk of serious injury or fatality for benzodiazepines + Z-drugs and medicinal opioids is estimated to be about 2-10 times (medicinal opioids in the upper part of the interval; benzodiazepines + Z-drugs in the lower part of the interval) as high as that of drivers below the DRUID cut-off for any substance (D2.3.5).
- The risk of being involved in an accident for medicine users compared to non-users is highest for users of modern antidepressants (1.76, CI: 1.38-2.24), followed by patients who use combinations of psychoactive medicines (1.55, CI: 1.20-2.02), and patients using at least one psychoactive medication (1.28, CI: 1.12-1.46) (D2.3.1).
- **Awareness:** Medicines (in contrast to illicit drugs) must be used to cure or alleviate indispositions or diseases, with regulated dose and under (effects') control of a physician, it is important that (both health care workers and) patients are aware of the possible driving impairing effects.
- General information that medicines, including over-the-counter medication, can have an influence on driving performance.
- Always read the package leaflet (3 warning levels), pictogram.

- Ask your physician/pharmacists for additional information on impairing effects of a medicine
 - Awareness for clinical signs of impairment; signs to look out (e.g. blurred or double vision, difficulty concentrating or remaining alert, surprise at normal occurrences while driving, difficulty in remembering how the destination was reached, difficulty in driving straight, frequently driving in the wrong line or in the middle of the road...).
 - Medication and alcohol together can greatly increase adverse effects.
 - Take especially care during the first few days of the treatment, especially several hours after taking the medication.
 - Always follow the instructions of the physician/pharmacist on how to use the medicine: at the time and with the dosage indicated.
 - Never use medicines prescribed for others.
 - If you have to drive frequently, tell your physician. He/she will try to find the medication which interferes least with your fitness to drive.
 - Clear information about fitness to drive assessment and sanctions (certainty/celerity) of driving under the influence of medicines are required (D6.2, D1.4.1).
- For more details see overview box 3.

2 Drivers as patients

2.1 Key elements of risk communication

The aim of risk communication addressed to the patients is to (i) make the patient aware that the use of psychoactive medication is not always compatible with car driving, (ii) support them to make their own problem definition, according to personal beliefs, opportunities to use alternative transportation and expectations of risk, due to individual circumstances of disease and treatment, with or without the help of a healthcare professional, (iii) allow them to decide how to manage the risk in their daily life activities.

For addressing risk communication messages to the *drivers as patients*, the following issues need to be considered:

1. Factors that play a role in perceiving and accepting risk (see Part I. 3.2. Risk acceptability) For driving under the influence of psychoactive substances it seems obvious to address these factors carefully in defining messages of risk communication to the drivers as patients. A trusted organization, credible and with an eye on values and interests that people feel important can do a proper job in convincing them that, although DUI is a voluntary risk, it will not be completely controlled by the person due to the effects of psychoactive substances.
2. Focus on messages that respect patient involvement in shared decision-making and information allowing the patient to decide on certainty about the best option.
3. Groups with higher socioeconomic status are more likely to benefit from an increasing flow of information on many issues, including drugs and driving issues. However, there are many contributory factors that could reduce the knowledge gap. First of all a content domain related factor, people might feel that health issues are more relevant to them than other issues, also certain groups could experience a greater impact of information due to the channel that was chosen, and used more frequently by them (e.g. internet applications, newsgroups), and individual motivational factors. It is expected that users of ICT technologies will use the information “on demand”, allowing them to control the media technologies and attempts to change their behaviour. This, however, is also a risk for widening the knowledge gap, because access could be determined by socioeconomic status and necessary skills.
4. The “power” of any single channel of communication (being mass media or interpersonal) may depend on the complexity of the behaviour change being sought. If the change is less complex, a single channel of communication may lead to development of the promoted behaviour. If, however, the behaviour change is more complex an individual will need the use of multiple sources of information and the application of multiple channels of communication.
5. Informing the drivers as patients about issues that they can discuss with a trusted person, e.g. health care professional in the case of impairing medicines, implies that those trusted person’s need to be informed about the risk problems and possible solutions for solving these. It is crucial that information campaigns to the patients as drivers should be preceded by information activities towards the trusted parties.

2.2 Extraction of main DRUID results

Problem situation

Medicines

- **Prevalence:** DRUID studies indicate that some selected psychoactive medicines (benzodiazepines, medicinal opiates and opioids and Z-drugs) are less prevalent in the driving population (estimated EU mean 1.4%) (D2.2.3) as well as is in seriously injured drivers (D2.2.5) compared to alcohol (estimated EU mean 3.48%) and illicit drugs (estimated EU mean 1.90%). Among the killed drivers the presence of benzodiazepines was the second most frequent toxicological finding after alcohol (D2.2.5). Psychoactive medicines, such as (frequently used) antidepressants, anti-epileptics and antipsychotics, were not included in the DRUID studies. Therefore an underestimation of prevalence should be considered.
- In most countries benzodiazepines were the most common psychoactive medicines in traffic but as for illicit drugs the prevalence of the different psychoactive medicines show high national variability (D2.2.3, D2.2.5).
- Epidemiological studies indicate a major increase in the consumption of antidepressants and drugs used in addictive disorders in the general population in Europe within the last years (D2.1.1).
- Psychoactive medicines were in general mainly detected among older female drivers during daytime hours (D2.2.3).
- **Risk:** Alcohol impaired driving is the main problem in traffic safety, but also psychoactive medicines can constitute a problem in traffic safety. Therefore, both health care providers and patients should be properly informed and aware of the potential risks associated with the use of psychoactive medicines (link WP4/7).
- Based on case-control studies, the relative risk of serious injury or fatality for benzodiazepines + Z-drugs and medicinal opioids is estimated to be about 2-10 times (medicinal opioids in the upper part of the interval; benzodiazepines + Z-drugs in the lower part of the interval) as high as that of drivers below the DRUID cut-off for any substance (D2.3.5).
- The risk of being involved in an accident for medicine users compared to non-users is highest for users of modern antidepressants (1.76, CI: 1.38-2.24), followed by patients who use combinations of psychoactive medicines (1.55, CI: 1.20-2.02), and patients using at least one psychoactive medication (1.28, CI: 1.12-1.46) (D2.3.1).
- For more details see overview box 3.

Countermeasures

General information

- Patients need to be informed about the potential effect of their disease (fitness to drive) and their medication on driving performance.
- Relevant therapeutic classes (DRUID classification system): alimentary tract and metabolism, blood and blood forming organs, cardiovascular system, dermatologicals, nervous system (anesthetics, analgesics, anti-epileptics, anti-parkinson drugs, psycholeptics, psychoanaleptics, other nervous system drugs), musculo-skeletal system, respiratory system (antihistamines for systemic use), sensory organs.
- For patients receiving psychoactive medicines for chronic or long term treatment it is important to check their fitness to drive regarding the pathology (e.g. diabetes, epilepsy, or substitution treatments in addiction); for some pathologies a medical examination is required.
- Patients need be informed about the possibility of criminal sanction in case of accident after being advised by physician not to drive: legal aspects.
- Key actors to provide this information to the patient are prescribing physicians and dispensing pharmacists.
- Patients should always check the risk information in the package insert (multi-level classification + risk communication pictogram is recommended).
- Patients should be advised about the ways they can recognize signs of impaired driving performance (such as drowsiness, dizziness or sleepiness in particular during the first period of treatment (1-2 weeks), if these side effects occur the patient should not drive).

- Patients should be advised to report to their prescribing doctor or dispensing pharmacist on side effects during a follow up visit after the first 2 weeks of treatment. Based on the outcomes of the assessment, after this visit or any follow-up visit, driving might be possible taking into account some personalised advice (e.g. on adjusting lifestyle, not changing dosages, or take most of the daily dose at night).
- Patients should be advised not to combine psychoactive medication with the use of alcohol or other medicines that might affect the central nervous system, because this may increase the impairing effect on the patient's fitness to drive.
- Clear information about fitness to drive assessment and sanctions (certainty/celerity) of driving under the influence of medicines is required. DRUID recommends that legal measures (withdrawal) should be taken only after an incident in traffic; impairment is the key indicator for sanctioning. A model of conditional licensing, based on the fitness to drive examination, is recommendable (D6.2, D1.4.1).

Further information in case of addictive disorder

- Alcohol and drug dependent drivers are, by EU legislation, not considered fit to drive (Directive 91/439/EEC) (D5.1.1, D5.2.4).
- Driver assessment prior to DR should be obligatory in case of suspicion of addiction in order to match offenders to appropriate treatment. The intensity of intervention should increase with the severity of the problem behaviour (D5.1.1, D5.2.4).
- Within DR addicted DUI/DUID offenders should be at least separated from non-addicted offenders. If possible DUI and DUID offenders should not be mixed within these groups (D5.1.1, D5.2.4).
- Information exchange between experts from DR interventions and addiction treatment should be encouraged (D5.1.1, D5.2.4).
- Clear information about fitness to drive assessment and sanctions (certainty/celerity) of driving under the influence of medicines are required. DRUID recommends that: each patient in substitution therapy has to be assessed individually regarding fitness to drive; for patients in substitution treatment, a conditional licence, based on the fitness to drive examination, is recommendable combined with follow-up controls, above all abstinence of parallel consumption of other drugs (D6.2, D1.4.1).
- Alcohol ignition interlock programmes can be an additional option for DUI offenders but they can not substitute treatment, as they are only effective as long as they are installed (D5.1.1, D5.2.4, D6.2).
- For more details see overview box 5-8.

3 Young drivers

The DRUID consortium decided to put an extra emphasis on the risk communication with young drivers. Therefore, an extra task was dedicated to analyse in-depth the risk communication about impaired driving with young people (T7.4.3). Preliminary results of D7.4.3 show that the emphasis should be given to drink driving prevention, targeting the age group 15-24 year. Preventive measures should be differentiated into general preventive approaches (e.g. campaigns) and special focussed preventive measures for certain smaller subgroups (lifestyle types e.g. personal communication). The effectiveness of approaches should be analyzed in-depth based on representative samples (according results for e.g. DE will be available at the end of the DRUID project) (D7.4.3Draft).

3.1 Key elements risk communication

The aim of risk communication addressed to young drivers is to (i) make them aware that the use of psychoactive substances (including some medicines) is not always compatible with car driving, (ii) support them to make their own problem definition, according to personal beliefs, opportunities to use alternative transportation and expectations of risk, due to individual circumstances of substance use, with or without the help of a (healthcare) professional, (iii) allow them to decide how to manage the risk in their daily life activities.

For addressing risk communication messages to the *young drivers*, the following issues need to be considered:

1. Factors that play a role in perceiving and accepting risk (see Part I. 3.2. Risk acceptability). For driving under the influence of psychoactive substances it seems obvious to address these factors carefully in defining messages of risk communication to young drivers. A trusted organization, credible and with an eye on values and interests that young people feel important can do a proper job in convincing them that, although DUI is a voluntary risk, it will not be completely controlled by the person due to the effects of psychoactive substances.
2. Groups with higher socioeconomic status are more likely to benefit from an increasing flow of information on many issues, including drugs and driving issues. However, there are many contributory factors that could reduce the knowledge gap. First of all a content domain related factor, people might feel that health issues are more relevant to them than other issues, also certain groups could experience a greater impact of information due to the channel that was chosen, and used more frequently by them (e.g. internet applications, newsgroups), and individual motivational factors. It is expected that users of ICT technologies will use the information “on demand”, allowing them to control the media technologies and attempts to change their behaviour. This, however, is also a risk for widening the knowledge gap, because access could be determined by socioeconomic status and necessary skills.
3. The “power” of any single channel of communication (being mass media or interpersonal) may depend on the complexity of the behaviour change being sought. If the change is less complex, a single channel of communication may lead to development of the promoted behaviour. If, however, the behaviour change is more complex an individual will need the use of multiple sources of information and the application of multiple channels of communication.

3.2 Extraction of main DRUID results

This chapter summarizes extracted DRUID information for and about the target group (young drivers) on general level, more in-depth information will be available within D7.4.3 at the end of the DRUID project).

Alcohol

- **Prevalence:** Alcohol ($\geq 0.1\text{g/L}$) is the most frequently detected psychoactive substance in the driving population (estimated EU mean 3.48%) (D2.2.3) as well as in the seriously injured (range 17.7-42.5%) and in killed drivers (range 19.0-44.9%) in Europe (D2.2.5; D2.2.4; D2.3.4).
- Alcohol was in the general driving population mainly detected among older male drivers, with lower BAC levels (D2.2.3).
- Within the accident involved drivers alcohol was mainly detected among younger male drivers with a high BAC level (D2.2.5). Alcohol appeared most often alone compared to other substances. When alcohol was combined with other psychoactive substances, benzodiazepines and cannabis (THC and/or THCCOOH) were the most common associated findings (D2.2.5; D2.3.4).
- **Risk:** Alcohol has a negative impact on driving performance and highly increases accident risk (e.g. D1.1.2a, D2.3.2; D2.3.3; D2.3.4; D2.3.5 DRAFT).
- Based on case- control studies, the relative risk of serious injury or fatality for alcohol ($\geq 0.5\text{g/L}$) is estimated to be significantly increased compared to that of drivers below the DRUID cut-off for any substance (D2.3.5). The risk increases dramatically with the alcohol concentration.
- An increased risk was associated with high BAC level, young age and speed (D2.3.3).
- The risk multiplies with combined use (e.g. cannabis) (D2.3.2).
- The general finding is that alcohol use in traffic is already risky at low BAC levels, especially for younger drivers who have less driving experience than older drivers. Alcohol affects the driving behaviour by increasing the reaction time and decreasing concentration, coordination and tracking. Furthermore, alcohol leads to more risk-taking behaviour and affects decision making and planning, since drivers overestimate their skills and underestimate the risk due to the effects of alcohol (Kelly et al., 2004; Steyvers & Brookhuis, 1996) (D2.2.3).
- **Motives behind DUI:** Drivers do not think that alcohol impairs their performance; Drivers whose drinking and driving was related to problems with alcohol argue that losing the licence or even to be imprisoned would not have helped them to stop re-offending; instead, it they argue that the treatment programme had helped them by providing a greater insight into their

own problems; factors influencing the decision to DUI/DUID: risk perceptions (e.g. beliefs in the objective danger/effect of the substance on driving ability, perceived chance to be involved in an accident / fear of injuring others, perceived chances to get caught / to lose DL), knowledge (effects of alcohol, safe alcohol consumption levels for driving), subjective norm/social norms and expectations/peer pressure (D2.2.1).

- Clear information about sanctions (certainty/celerity) of DUI is required (D6.2, D1.4.1).
- The important role of alcohol in social activities and the high susceptibility to peer pressure is specifically stressed among young persons. The combination of some specific young (novice) drivers' constellations of lifestyle and drinking/drug taking habits with the lack of driving experience is considered to bring this group at higher risk for and when DUI/DUID. Schulze (1999) investigated the lifestyle of young drivers. He classified the data of his German sample (18 to 24 years) into five categories. Two types were of special interest: "Action type" – drivers who were found to consume alcohol several times a week, drinking high amounts and also consumed marijuana several times or regularly; and "Looking for a kick" type – drivers who drive less often, but have more frequent driving accidents as they often tend to violate norms and rules. This group had the highest percentage of marijuana consumers and highest amount of alcohol consumption of 18 to 24 years olds. Drug and alcohol re-offenders (recidivists) tend to be significantly younger at the first offence than those who do not re-offend. Driver rehabilitation participation should be mandatory for high-risk offenders, repeat offenders and young (novice) – to grab the problem in an early stage – drivers (D5.1.1).
- Lower BAC thresholds are current practice for young drivers in three countries (Germany, Luxemburg and Croatia) and for novice drivers in nine countries (Austria, Germany, Greece, Latvia, Lithuania, Luxembourg, the Netherlands, Slovenia and Spain). Furthermore, some countries have more severe sanctions for young drivers driving under the influence of alcohol (Germany, Bulgaria and Cyprus), illicit drugs (Bulgaria and Cyprus) and medicines (Cyprus). Novice drivers are often also young drivers, which mean that in countries with more severe sanctions for novice drivers, young drivers will also receive more severe sanctions (D6.1 p. 23ff).
- For more details see overview box 1.

Illicit drugs

- **Prevalence:** All DRUID investigations (e.g. D2.2.3, D2.2.5, D2.3.4) show that the prevalence of illicit drugs in the driver population (estimated EU mean 1.90%) is lower than the alcohol prevalence (estimated EU mean 3.48%) (D2.2.3).
- Within the accident involved drivers, the majority of drugs appeared to be used in combination with other psychoactive substances (mainly alcohol) (D2.2.5).
- THC is generally the most frequently detected illicit drug, followed by cocaine, but the prevalence of the different illicit substances show high national variability (e.g. D2.2.3, D2.2.5, D2.3.4).
- Illicit drugs were in general mainly detected among young male drivers, during all times of the day but mainly at the weekend (D2.2.3).
- Combined use of alcohol and drugs (illicit drugs and/or psychoactive medicine) is in general often prevalent among young (<35 years) male drivers during night time hours (D2.2.3).
- Multiple drugs (illicit drugs and/or psychoactive medicines) use is in general most common in males (D2.2.3).
- Age groups and time periods vary considerably by country (D2.2.3).
- **Risk:** Based on case-control studies, the relative risk of serious injury or fatality for different illicit substances varies between the substances. For: THC about 1-3 times; benzoylcgonine, cocaine and illicit opiates about 2-10 times; amphetamines about 5-30 times as high as that of drivers below the DRUID cut-off for any substance (D2.3.5 DRAFT; see also D1.1.2b, D1.2.1, D2.3.2). Some of the risk estimates for illicit drugs vary to a high degree among the single countries; others are based on few positive cases and/or controls which result in very wide confidence intervals. Therefore the estimates are uncertain.
- The risk multiplies with combined use (e.g. alcohol) (e.g. D2.3.2, D2.3.5).
- **Illicit drug effects:** Experimental studies have shown that the dose equivalent for BAC 0.5g/L-3.7ng/mL THC (range 3.1-4.5ng/mL) for oral administration and 3.8 ng/mL (range 3.3-

4.5ng/mL) for smoked administration (D1.1.2b, see also D1.4.2 for more information on cut-offs equivalent to BAC 0.5g/L).

- Experimental studies evaluating the effect of stimulants on driving (MDMA and dexamphetamine) did not reveal impairing effects on driving performance. However, the stimulant effects of MDMA and dexamphetamine are not sufficient to overcome or compensate driving impairments produced by concomitant alcohol use (increased risk taking behaviour) or sleep deprivation (sleep deprivation generates same degree of impairing effects as under the influence of BAC 0.8g/L); Users of stimulating drugs need to be educated about this effect and its possible dangers. The pharmacological effects of stimulants and the effects of drug use setting (e.g. poly-drug use, concomitant alcohol use and sleep deprivation) are intertwined and significantly contribute to driver impairment (D1.1.2b, D1.2.1).
- **Motives behind DUID:** Addicted drivers did not believe that they would be stopped by the police. They did not believe that alcohol or drugs would impair their driving and therefore they did not perceive any real risks of driving (D2.2.1). Findings indicate that especially moderate substance users can realistically judge their intoxication and are responsible-minded concerning drugs in traffic (D2.2.2).
- Clear information about sanctions (certainty/celerity) of DUID is required (D6.2, D1.4.1).
- For more details see overview box 2.

4 Physicians and pharmacists

4.1 Key elements risk communication

The aim of risk communication addressed to physicians and pharmacists is to (i) make them aware that the use of psychoactive medication is sometimes not compatible with car driving, depending upon the patient's treatment, lifestyle and disease conditions, provided that good information has been provided to the patient, (ii) support them to develop their own strategy of selecting the least impairing medicine (iii) allow them to decide how to guide the patient in the best way to manage the risk in their daily life activities.

For addressing risk communication messages to *physicians and pharmacists*, the following issues need to be considered:

1. A trusted organization, credible and with an eye on values and interests that physicians and pharmacists feel important, need to be involved in preparing risk communication messages to physicians and pharmacists.
2. Physicians and pharmacists should be made aware that in patient information activities the focus needs to be on messages that respect patient involvement in shared decision-making and information allowing the patient to decide on certainty about the best option (not to drive x days after the start of treatment, or refrain from driving till medical conditions have been tested to be improved).
3. Physicians and pharmacists should be informed that in giving risk communication messages to patients, certain groups could experience a greater impact of information due to the channel that was chosen, and used more frequently by them (e.g. internet applications, newsgroups), and individual motivational factors. It is expected that patients who use ICT frequently will use the information "on demand", allowing them to control the media technologies and attempts to change their behaviour. Knowledge about the content of these sources is required in order to be prepared for discussions with their patients.
4. Physicians and pharmacists should be aware that campaigns aiming at informing the general public about issues that they can discuss with a trusted person, e.g. health care professional in the case of impairing medicines, implies that those trusted persons need to be informed about the risk problems and possible solutions for solving these. It is crucial that physicians and pharmacists should be informed about these issues before public campaigns will be launched.
5. Physicians and pharmacists should be supported by practical information on how to prescribe or dispense impairing medicines to their patients, presented in clear instructions during their daily work routines using ICT supported tools.

4.2 Extraction of main DRUID results

Problem Situation

Medicines

- **Prevalence:** DRUID studies indicate that some selected psychoactive medicines (benzodiazepines, medicinal opiates and opioids and Z-drugs) are less prevalent in the driving population (estimated EU mean 1.4%) (D2.2.3) as well as is in seriously injured drivers (D2.2.5) compared to alcohol (estimated EU mean 3.48%) and illicit drugs (estimated EU mean 1.90%). Among the killed drivers the presence of benzodiazepines was the second most frequent toxicological finding after alcohol (D2.2.5). Psychoactive medicines, such as (frequently used) antidepressants, anti-epileptics and antipsychotics, were not included in the DRUID studies. Therefore an underestimation of prevalence should be considered.
- In most countries benzodiazepines were the most common psychoactive medicines in traffic but as for illicit drugs the prevalence of the different psychoactive medicines show high national variability (D2.2.3, D2.2.5).
- Epidemiological studies indicate a major increase in the consumption of antidepressants and drugs used in addictive disorders in the general population in Europe within the last years (D2.1.1).
- Psychoactive medicines were in general mainly detected among older female drivers during daytime hours (D2.2.3).
- **Risk:** Alcohol impaired driving is the main problem in traffic safety, but also psychoactive medicines can constitute a problem in traffic safety. Therefore, both health care providers and patients should be properly informed and aware of the potential risks associated with the use of psychoactive medicines (link WP4/7).
- Based on case-control studies, the relative risk of serious injury or fatality for benzodiazepines + Z-drugs and medicinal opioids is estimated to be about 2-10 times (medicinal opioids in the upper part of the interval; benzodiazepines + Z-drugs in the lower part of the interval) as high as that of drivers below the DRUID cut-off for any substance (D2.3.5).
- The risk of being involved in an accident for medicine users compared to non-users is highest for users of modern antidepressants (1.76, CI: 1.38-2.24), followed by patients who use combinations of psychoactive medicines (1.55, CI: 1.20-2.02), and patients using at least one psychoactive medication (1.28, CI: 1.12-1.46) (D2.3.1).
- For more details see overview box 3.

Countermeasures

General information

- Patients need to be informed about the potential effect of their disease and their medication on driving performance (for more information see also information provided for patients in D7.3.2 Part II chapter 2.2).
- Key actors to provide this information to the patient are prescribing physicians and dispensing pharmacists.
- Physicians/pharmacists need to be informed about their responsibilities and possible penal proceedings in the event of accidents occurring after a positive decision from their side that driving is possible in a responsible manner.

Information about counselling the patient-driver regarding medication and driving

- Guidelines for prescribing and dispensing medicines: decision supporting tools to select the least impairing medicines at the start of a treatment; emphasis on shared decision making (health care professional together with the patient) and documentation of patient consultation (to avoid liability issues); checklist with issues for documenting the decision-making process to avoid liability issues (D7.4.1 p. 28): (1) Actions to be checked during the consultation: advise not to combine psychoactive medication; check whether the patient is willing and able to follow the treatment plan; advise the patient to be aware of possible side-effects; advise the patient to report on these side-effects during a follow up visit (2) Documentation of the following items: tests done and / or information gathered in assessing fitness to drive; assessment of patient's decision-making competence based on advices given; patient's understanding of impairing

properties of the medication; specific actions to achieve fitness to drive (changes in medication or instructions for use); follow up visit for evaluation of interventions (advice given, self-assessment of patient); protocols and guidelines should be integrated in existing computer software used by health care professionals in daily practice). DRUID developed such supporting tools which have been evaluated in BE, ES and NL. Preliminary evaluation results based on the consolidated database of the three countries indicate a positive effect of the DRUID guidelines: After training on and implementation of the DRUID dispensing guidelines, pharmacists had significant positive changes in reported behaviour (increased consideration in informing patients about medicines' impairing effects regarding driving), attitudes and awareness about medicines' dispensing and driving and actual knowledge about categories of medicines and their effect on driving behaviour. With regard to physicians, significant differences (in the expected direction) were observed between the control and intervention groups for attitudes and reported behaviour after the training and implementation phase of the DRUID prescribing guidelines. Overall, health care professionals are very satisfied with and strongly prefer ICT supporting tools which are integrated in their dispensing/prescribing tools over other supporting tools (D7.4.2Draft).

- DRUID WP4 proposed four level classification and a labelling system regarding the influence of medicines on driving performance, from category 0 (no or negligible influence on fitness to drive) to category 3 (major influence on fitness to drive). The DRUID WP4 categorization was in line with the recent approved SmPC guidelines adopted in September 2009 (which applies as from 1st of May 2010) by EMA (D4.3.1, D4.4.1).
- Medicines in the relevant therapeutic groups that are currently on the market have been categorized according to the DRUID classification system (ATC groups: A, B, C, D, N01-N07, M01-M03, R01-R06, S) (D4.3.1, D4.4.1).
- Most of them were Category 0: 50.3%, while 5.8% were Category III (Major influence in fitness to drive). DRUID results are compatible with any existing national classification system (e.g. FR, ES) and could be integrated in them (D4.3.1, D4.4.1).
- Detailed Fact Sheets were elaborated for the N01-N07 (nervous system) and R06 (respiratory system) therapeutic groups of medicines, including information on possible side-effects related to driving, reference studies on psychomotor performance and risk studies, the proposed DRUID categorization level, and relevant information for the patient (D4.3.1, D4.4.1).
- Risk communication pictogram (rating model, bar form): Evaluation studies in ES and NL have indicated that the use of pictograms on medicine boxes for risk communication to patients is effective in explaining a risk of impairment level after using a driving impairing medicine. Patients' likelihood to drive less frequently under the influence of a medicine is higher if the pictogram shows reference to all possible risk levels, and identifies the selected risk level from a rating bar model as compared to a single triangle model without explanation of possible risk levels. Younger patients (more in favour) and older patients (less in favour) differ in their preference for more complex presentations of risk of impairment levels in a pictogram.

Fitness to drive assessment and licensing withdrawal

- Clear information about fitness to drive assessment and sanctions (certainty/celerity) of driving under the influence of medicines are required (D6.2, D1.4.1).
- DRUID recommends that legal measures (withdrawal) should be taken only after an incident in traffic; impairment is the key indicator for sanctioning. A model of conditional licensing, based on the fitness to drive examination, is recommendable (D6.2).
- Each patient in substitution therapy has to be assessed individually regarding fitness to drive. A conditional licence, based on the fitness to drive examination, is recommendable combined with follow-up controls, above all focussing on abstinence of parallel consumption of other drugs.
- DRUID recommendations for patients in long-term treatment with psychoactive medicines: Legal measures should be taken only after an incident in traffic; impairment is the key indicator for sanctioning. A model of conditional licensing, based on the fitness to drive examination, is recommendable.

Further information in case of addictive disorder

- Alcohol and drug dependent drivers are, by EU legislation, not considered fit to drive (Directive 91/439/EEC) (D5.1.1, D5.2.4).
- Driver assessment prior to DR should be obligatory in case of suspicion of addiction in order to match offenders to appropriate treatment. The intensity of intervention should increase with the severity of the problem behaviour (D5.1.1, D5.2.4).

- Within DR addicted DUI/DUID offenders should be at least separated from non-addicted offenders. If possible DUI and DUID offenders should not be mixed within these groups (D5.1.1, D5.2.4).
- Information exchange between experts from DR interventions and addiction treatment should be encouraged (D5.1.1, D5.2.4).
- Alcohol ignition interlock programmes can be an additional option for DUI offenders but they can not substitute treatment, as they are only effective as long as they are installed (D5.1.1, D5.2.4, D6.2).
- For more details see overview box 5-8.

5 Policy makers at EU level

5.1 Key elements risk communication

The aim of risk communication addressed to European policy makers is to (i) make them aware that the use of psychoactive substances (including some medicines) is not always compatible with car driving, (ii) support them to make their own problem definition, according to personal beliefs and professional responsibilities within the European context, (iii) provide them opportunities to use risk management tools (such as the risk management framework) in discussing risk control with relevant European stakeholders, (iii) allow them to decide how to contribute to the management of the risk in European society.

For addressing risk communication messages to *policy makers* on an EU level, the following issues need to be considered:

3. Policy makers need to be addressed with information on risk communication using the risk management framework (see table 1, p. 17). This will allow them to understand that DRUID outcomes describing the risk of driving under the influence of alcohol, illicit drugs or psychoactive medicines, can serve the purpose of discussing EU policy measures, e.g. EU risk control measures.
4. European stakeholders need to be involved in the development of a risk management framework for risk communication aiming at European bodies, such as:
 - Directorate General for Health and Consumer Affairs of the EC (DG SANCO);
 - Directorate-General for Mobility and Transport of the EC (DG MOVE);
 - Trans-European Transport Network Executive Agency of the EC (TEN-T EA);
 - European Transport Safety Council (ETSC);
 - European Parliament;
 - European Commission;
 - European Medicines Agency (EMA);
 - European professional organisation of pharmacists, physicians, psychologists and other health professionals;
 - International Alliance of Patients' Organisations (IAPO);
 - European Association of Pharmaceutical Manufacturers;
 - other bodies...

5.2 Extraction of main DRUID results

Alcohol is the most serious problem compared to illicit drugs and psychoactive medicines in traffic in all investigated EU Member States (e.g. prevalence, risk estimates and cost-benefit-analysis of enforcement measures). Consequently, the first priority of countermeasures should always lie on alcohol; other psychoactive substances are second priority.

The results of the DRUID studies in regard to the problem situation can generally be used in selecting overall activities and target groups in the policy field of psychoactive substance use in traffic across Europe. However, the results indicate, that the prevalence of psychoactive substances by gender, age and time period varies largely per country. "Therefore, recommendations for national activities regarding, e.g., policy issues, enforcement, education or campaigns, should primarily be based on the results of the country reports, rather than on the general report" (D2.2.3 PART I p. 10).

Problem Situation (WP1/2)

Alcohol

- Alcohol ($\geq 0.1\text{g/L}$) is the most frequently detected psychoactive substance in the driving population (estimated EU mean 3.48%) (D2.2.3) as well as in the seriously injured (range 17.7-42.5%) and in killed drivers (range 19.0-44.9%) in Europe (D2.2.5; D2.2.4; D2.3.4).
- Alcohol was in the general driving population mainly detected among older male drivers, with lower BAC levels (D2.2.3).
- Within the accident involved drivers alcohol was mainly detected among younger male drivers with a high BAC level (D2.2.5).
- Alcohol has a negative impact on driving performance and highly increases accident risk (e.g. D1.1.2a, D2.3.2; D2.3.3; D2.3.4; D2.3.5 DRAFT).
- Based on case- control studies, the relative risk of serious injury or fatality for alcohol ($\geq 0.5\text{g/L}$) is estimated to be significantly increased compared to that of drivers below the DRUID cut-off for any substance (D2.3.5) The risk increases dramatically with the alcohol concentration.
- An increased risk was associated with high BAC level, young age and speed (D2.3.3).
- The risk multiplies with combined use (e.g. cannabis) (D2.3.2).
- For more details see overview box 1.

Illicit drugs

- All DRUID investigations (e.g. D2.2.3, D2.2.5, D2.3.4) show that the prevalence of illicit drugs in the driver population (estimated EU mean 1.90%) is lower than the alcohol prevalence (estimated EU mean 3.48%) (D2.2.3).
- Within the accident involved drivers, the majority of drugs appeared to be used in combination with other psychoactive substances (mainly alcohol) (D2.2.5).
- THC is generally the most frequently detected illicit drug, followed by cocaine, but the prevalence of the different illicit substances show high national variability (e.g. D2.2.3, D2.2.5, D2.3.4).
- Illicit drugs were in general mainly detected among young male drivers, during all times of the day but mainly at the weekend (D2.2.3).
- Combined use of alcohol and drugs (illicit drugs and/or psychoactive medicine) is in general often prevalent among young (<35 years) male drivers during night time hours (D2.2.3).
- Multiple drugs (illicit drugs and/or psychoactive medicines) use is in general most common in males (D2.2.3).
- Age groups and time periods vary considerably by country (D2.2.3).
- Based on case-control studies, the relative risk of serious injury or fatality for different illicit substances varies between the substances. For: THC about 1-3 times; benzoylecgonine, cocaine and illicit opiates about 2-10 times; amphetamines about 5-30 times as high as that of drivers below the DRUID cut-off for any substance (D2.3.5 DRAFT; see also D1.1.2b, D1.2.1, D2.3.2). Some of the risk estimates for illicit drugs vary to a high degree among the single countries; others are based on few positive cases and/or controls which result in very wide confidence intervals. Therefore the estimates are uncertain.
- Experimental studies have shown that the dose equivalent for BAC 0.5g/L-3.7ng/mL THC (range 3.1-4.5ng/mL) for oral administration and 3.8 ng/mL (range 3.3-4.5ng/mL) for smoked administration (D1.1.2b, see also D1.4.2 for more information on cut-offs equivalent to BAC 0.5g/L).
- The risk multiplies with combined use (e.g. alcohol) (e.g. D2.3.2, D2.3.5).
- Experimental studies evaluating the effect of stimulants on driving (MDMA and dexamphetamine) did not reveal impairing effects on driving performance. However, the stimulant effects of MDMA and dexamphetamine are not sufficient to overcome or compensate driving impairments produced by concomitant of alcohol use or sleep deprivation (D1.1.2b, D1.2.1).
- For more details see overview box 2.

Medicines

- DRUID studies indicate that some selected psychoactive medicines (benzodiazepines, medicinal opiates and opioids and Z-drugs) are less prevalent in the driving population (estimated EU mean 1.4%) (D2.2.3) as well as is in seriously injured drivers (D2.2.5) compared to alcohol (estimated EU mean 3.48%) and illicit drugs (estimated EU mean

1.90%). Among the killed drivers the presence of benzodiazepines was the second most frequent toxicological finding after alcohol (D2.2.5). Psychoactive medicines, such as (frequently used) antidepressants, anti-epileptics and antipsychotics, were not included in the DRUID studies. Therefore an underestimation of prevalence should be considered.

- In most countries benzodiazepines were the most common psychoactive medicines in traffic but as for illicit drugs the prevalence of the different psychoactive medicines show high national variability (D2.2.3, D2.2.5).
- Epidemiological studies indicate a major increase in the consumption of antidepressants and drugs used in addictive disorders in the general population in Europe within the last years (D2.1.1).
- Psychoactive medicines were in general mainly detected among older female drivers during daytime hours (D2.2.3).
- Alcohol impaired driving is the main problem in traffic safety, but also psychoactive medicines can constitute a problem in traffic safety. Therefore, both health care providers and patients should be properly informed and aware of the potential risks associated with the use of psychoactive medicines (link WP4/7).
- Based on case-control studies, the relative risk of serious injury or fatality for benzodiazepines + Z-drugs and medicinal opioids is estimated to be about 2-10 times (medicinal opioids in the upper part of the interval; benzodiazepines + Z-drugs in the lower part of the interval) as high as that of drivers below the DRUID cut-off for any substance (D2.3.5).
- The risk of being involved in an accident for medicine users compared to non-users is highest for users of modern antidepressants (1.76, CI: 1.38-2.24), followed by patients who use combinations of psychoactive medicines (1.55, CI: 1.20-2.02), and patients using at least one psychoactive medication (1.28, CI: 1.12-1.46) (D2.3.1).
- For more details see overview box 3.

Countermeasures (WP3-7)

Countermeasures always have to be seen as a comprehensive countermeasure system.

Enforcement (WP3)

- DRUID provides guidelines for everyday policy enforcement and installs scientific demands for on-site drug screening (e.g. legal frame; basic standards of on-site screening procedure; basic standards for on-site screening detection devices).
- Cost benefit analyses have shown that first enforcement priority should lie on alcohol; other psychoactive substances are second priority.
- For more details see overview box 4. Furthermore, a detailed evaluation of legal countermeasures from the perspective of criminology can be found in D1.4.1

Classification (of driving impairing medicines) (WP4)

- DRUID WP4 proposed four level classification and a labelling system regarding the influence of medicines on driving performance, from category 0 (no or negligible influence on fitness to drive) to category 3 (major influence on fitness to drive). The DRUID WP4 categorization was in line with the recent approved SmPC guidelines adopted in September 2009 (which applies as from 1st of May 2010) by EMA.
- DRUID WP4 reviewed over 3000 medicines and over 1500 of them were categorized in regard to their influence on fitness to drive: Most of them were Category 0: 50.7%, while 6% were Category III (Major influence in fitness to drive). DRUID results are compatible with any existing national classification system (e.g. FR, ES) and could be integrated in them.
- Politicians should promote that the DRUID WP4 categorization and labelling be integrated in existing computerized prescribing and dispensing systems for physicians/pharmacists at the various EU member states.
- There is a need to improve information related to effects on driving, particularly in the Patient Information Leaflet (PIL). Information to patients who are advised to use medicines that may impair driving fitness needs to be improved by simple and patient-centred directions based on a clear categorisation system and reflected in the PIL.
- For more details see overview box 5.

Rehabilitation (WP5)

- It should be stated on EU level that Driver Rehabilitation should be an integrated part of a comprehensive countermeasure system.

- Main outlines of rehabilitation procedures should be formulated on EU level (guidelines for legal regulations and standardised procedure). DRUID WP5 developed Europe-wide standards and recommendations of good practice for DUI/DUID rehabilitation measures, which were couched into the form of a user friendly tool (Development of Driver Rehabilitation Evaluation Tool, DRET) for implementation, assessment or evaluation of existing or new DR systems or programmes. It can be the starting point of a European networking and documentation process of DR measures.
- For more details see overview box 6.

Withdrawal (of driving license) (WP6)

- Regulations in European countries regarding withdrawal and accompanying measures should be unified. So far, national strategies are very heterogeneous. Hence a clustering of strategies or countries is difficult.
- DRUID WP6 developed Europe-wide recommendations on withdrawal and conditional withdrawal for the general driving population and specific problem groups such as DUI/DUID drivers, patients in substitution or other long-term treatment with psychoactive medicines (see also D1.4.1).
- For more details see overview box 7.

Guidelines for health care professionals (WP7)

- Decision support at the start of a treatment is needed for selecting the least impairing medicines. Therefore, guidelines and standards for health care professionals pertaining to medicines and driving could be initiated on EU level (D7.2.1).
- Eight recommendations on improving the procedures for assessing fitness to drive within the framework of Council Directive 91/439/EEC (on driving licences) have been formulated within DRUID WP7. These suggestions should be discussed in working groups/expert rounds with physicians, pharmacists, driving licensing authorities and policy makers in order to reach a consensus at European level (D7.2.1).
- The implementation of existing protocols and guidelines into existing computer software used by health care professionals could be stimulated by e.g. incentives for organisations for maintaining databases and software companies.
- For more details see overview box 8.

Risk communication (WP7)

- The focus of campaigns (content, target group, media etc.) should be selected according to the specific characteristic of problem situation and risk group (D7.1.1, D7.3.1).
- Campaigns are more successful if they are targeted (specific issues, groups, etc.). Therefore, large campaigns should be designed as sets of a larger number of activities on a smaller scale (D7.1.1, D7.3.1).
- Campaigns should be evaluated (D7.1.1, D7.3.1). The EU project CAST provides guidelines in designing and evaluating campaigns (D7.1.1; D7.3.1).
- Risk communication pictograms on medicine boxes are effective in communicating risk to the patient (rating models are preferred over no rating indications) (study: ES NL) (D7.3.2).
- Prescribing and dispensing guidelines show a positive effect (e.g. reported behaviour, attitude) after training and implementation phase (study: BE, ES, NL). Health care professionals strongly prefer ICT supporting tools which are integrated in their daily dispensing/prescribing software packages (D7.4.2).
- The emphasis of risk communication towards young people should be given to drink driving prevention, targeting the age group 15-24 year. Preventive measures should be differentiated into general preventive approaches (e.g. campaigns) and special focussed preventive measures for certain smaller subgroups (lifestyle types e.g. personal communication). The effectiveness of approaches should be analyzed in-depth based on representative samples (according results for e.g. DE will be available at the end of the DRUID project) (D7.4.3Draft).
- For more details see overview box 8.

6 Policy makers at national level

6.1 Key elements risk communication

The aim of risk communication addressed to national policy makers to (i) make them aware that the use of psychoactive substances (including some medicines) is not always compatible with car driving, (ii) support them to make their own problem definition, according to personal beliefs and professional responsibilities within the national context, (iii) provide them opportunities to use risk management tools (such as the risk management framework) in discussing risk control with relevant national stakeholders, (iii) allow them to decide how to contribute to the management of the risk in their own society.

For addressing risk communication messages to *policy makers* on a national level, the following issues need to be considered:

1. National policy makers need to be addressed with information on risk communication using the risk management framework (see also table 1, p.17). This will allow them to understand that DRUID outcomes describing the risk of driving under the influence of alcohol, illicit drugs or psychoactive medicines, can serve the purpose of discussing national policy measures, e.g. national risk control measures.
2. National stakeholders need to be involved in the development of a risk management framework for risk communication aiming at national bodies, such as:
 - Ministry of (Public) Health;
 - Ministry of Transport;
 - National Medicines Agency;
 - National professional organisation of pharmacists, physicians, psychologists and other health professionals;
 - National Alliance of Patients' Organisations;
 - National Association of Pharmaceutical Manufacturers;
 - National Association Traffic Safety Institutes;
 - other bodies...

6.2 Extraction of main DRUID results

Problem Situation (national level)

- Alcohol is also on national level the most frequent problem compared to illicit drugs and medicines in traffic in all EU Member States (prevalence, risk estimates, CBA enforcement) (e.g. D2.2.3; D2.2.4; D2.2.5). Consequently, the main focus of countermeasures should lie on alcohol followed by illicit drugs and medicines.
- Recommendations for national activities regarding, e.g. enforcement, education or campaigns, should primarily be based on country specific characteristics of the problem situation (not on EU means) (see country specific reports e.g. D2.2.3, D2.2.5).
- For more details see overview box 1-3.

Countermeasures (national level)

In general countermeasures always have to be seen as comprehensive countermeasure system.

Enforcement (WP3)

- Characteristics of the problem situation on national level determine the focus (and devices) of drug enforcement.
- Increase of drug enforcement is potentially cost-beneficial, especially for countries that currently have a low enforcement level. It will NOT be beneficial if this increase is financed at the cost of drink-driving enforcement.
- DRUID provides guidelines for everyday policy enforcement and installs scientific demands (e.g. legal frame; basic standards of on-site screening procedure; basic standards for on-site screening detection devices).

- “National roadside surveys on the prevalence of substance use in traffic on a regular, say, annual or bi-annual base would be a helpful tool to monitor the trend of drink and drug driving” (D2.2.3 PART I p. 10).
- For more details see overview box 4, D1.4.1 and D1.4.2.

Classification (of driving impairing medicines) (WP4)

- National specific risk communication strategies would help to implement a Europe-wide classification and labelling system regarding the influence of medicines on driving performance (including the suggested common pictogram (rating model, bar form)).
- For more details see overview box 5.

Rehabilitation (WP5)

- The quality standards of DR rehabilitation which should be defined on EU level should be controlled by a (national) quality management body which has an independent, authoritative position to execute the operative quality management tasks in driver rehabilitation.
- Applied programmes should to be evaluated on a regular basis regarding their effectiveness for traffic safety
- DRUID WP5 developed Europe-wide standards and recommendations of good practice for DUI/DUID rehabilitation measures, which were couched into the form of a user friendly tool (Development of Driver Rehabilitation Evaluation Tool, DRET) for implementation, assessment or evaluation of existing or new DR systems or programmes. It can be the starting point of a European networking and documentation process of DR measures.
- For more details see overview box 6.

Withdrawal (of driving licence) (WP6)

- Regulations in European countries regarding withdrawal and accompanying measures should be unified. So far, national strategies are very heterogeneous. Hence a clustering of strategies or countries is difficult.
- DRUID WP6 developed Europe-wide recommendations on withdrawal and conditional withdrawal for the general driving population and specific problem groups such as DUI/DUID drivers, patients in substitution or other long-term treatment with psychoactive medicines (see also D1.4.1).
- For more details see overview box 7, D1.4.1 and D1.4.2. .

Guidelines for health care professionals (WP7)

- The implementation of existing protocols and guidelines into existing computer software used by health care professionals could be stimulated by e.g. incentives for software companies.
- For more details see overview box 8.

Risk communication (WP7)

- The focus of campaigns (content, target group, media etc.) should be selected according to the specific characteristic of problem situation and risk group (D7.1.1, D7.3.1).
- Campaigns are more successful if they are targeted (specific issues, groups, etc.). Therefore, large campaigns should be designed as sets of a larger number of activities on a smaller scale (D7.1.1, D7.3.1).
- Campaigns should be evaluated (D7.1.1, D7.3.1). The EU project CAST provides guidelines in designing and evaluation campaigns (D7.1.1; D7.3.1).
- For more details see overview box 8.

More detailed information on legal countermeasures for the policy makers on national level can be found in D1.4.1 which recommends different sanctions for different target groups, D1.4.2 which discusses how to implement sanctions in regard to per se legislation (e.g. definitions of cut-offs) and D1.3.1 which derives risk estimates based on the results of WP1/2.

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DRUID deliverables reviewed within this report

All of these deliverables will be available on the DRUID homepage (http://www.druid-project.eu/cln_031/nn_107534/Druid/EN/deliverables-list/deliverables-list-node.html?__nnn=true) at the latest at the end of the project (15.10.2011).

- D1.1.2a: Schnabel E., Hargutt V., Krüger H.-P. (2010): Meta-analysis of empirical studies concerning the effects of alcohol on safe driving. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 1.1.2a
- D1.1.2b: G. Berghaus G., Sticht G., Grellner W., Lenz D., Naumann Th., Wiesenmüller S. (2010): Meta-analysis of empirical studies concerning the effects of medicines and illegal drugs


- including pharmacokinetics on safe driving. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 1.1.2b
- D1.1.2c: Strand M.C., Fjeld B., Arnestad M., Mørland J. (2011): Psychomotor relevant performance: 1. After single dose administration of opioids, narcoanalgesics and hallucinogens to drug naïve subjects 2. In patients treated chronically with morphine or methadone / buprenorphine. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 1.1.2c
- D1.2.1: Ramaekers J. (2011): The influence of stimulant drugs on actual and simulated driving. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 1.2.1
- D1.3.1: (will be available at the end of the DRUID project. Okt. 2011): Concentration- impairment functions for the most relevant psychoactive substances based on experimental and epidemiological research. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 1.3.1
- D1.4.1: Krismann M., Schöch H., Knoche A., Volker Hargutt V., Klipp S.(2011): Evaluation of legal measures to combat DUI / DUID. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 1.4.1
- D1.4.2: (will be available at the end of the DRUID project. Okt. 2011): Per se limits - Methods of defining cut-off values for zero tolerance. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 1.4.2
- D2.1.1: Ravera S., De Gier J.J. (2008): Prevalence of Psychoactive Substances in the General Population. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 2.1.1
- D2.2.1: Forward S. (2010): Motives behind risky driving – driving under the influence of alcohol and drugs. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 2.2.1
- D2.2.2: Walter M., Hargutt V., Krüger H-P. (2011): Prevalence of psychoactive substances and consumption patterns in traffic, based on a smartphone survey in Germany. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 2.2.2
- D2.2.3, Part I: Houwing S., Hagenzieker M., Mathijssen R., Bernhoft I. M., Hels T., Janstrup K. Van der Linden T., Legrand S.-A., Verstraete A. (2011): Prevalence of alcohol and other psychoactive substances in drivers in general traffic Part I: General results. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 2.2.3 Part I
- D2.2.3, Part II: Houwing S., Hagenzieker M., Mathijssen R., Bernhoft I. M., Hels T., Janstrup K. Van der Linden T., Legrand S.-A., Verstraete A. (2011) : Prevalence of alcohol and other psychoactive substances in drivers in general traffic Part II: Country reports. Review version. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 2.2.3 Part II
- D2.2.4: Amoros E., Gadegbeku B. and the SAM Group (2010): Prevalence study: Main illicit psychoactive substances among all drivers involved in fatal road crashes in France. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 2.2.4
- D2.2.5: Isalberti C., Van der Linden T., Legrand S.-A., Verstraete A., Bernhoft I., Hels T., Olesen M., Houwing S., Houtenbos M., Mathijssen R.,(2011): Prevalence of alcohol and other psychoactive substances in injured and killed drivers. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 2.2.5
- D2.3.1: Ravera S., de Gier J.J. (2010): Relative accident risk of patients using psychotropic medicines in the Netherlands: A pharmacoepidemiological study. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 2.3.1
- D2.3.2: Gadegbeku B., Emmanuelle Amoros E. and the SAM group (2010): Relative risk estimates for alcohol and other psychoactive substances impaired drivers in fatal accidents, based on the

- responsibility approach in France. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 2.3.2
- D2.3.3: Laapotti S., Keskinen E. (2009): Relative risk of impaired drivers who were killed in motor vehicle accidents in Finland. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 2.3.3
- D2.3.4: Thorsteinsdóttir K., Mühlhäußer J., Paul L., Lottner S., Schick S., Hell W. (2006): Responsibility study: Psychoactive substances among killed drivers in Germany, Lithuania, Hungary and Slovakia. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 2.3.4
- D2.3.5 (DRAFT): Hels, T., Bernhoft I. M., Lyckegaard, A., Houwing S., Hagenzieker M., Legrand S.-A., Isalberty, C., Van der Linden T., Verstraete A. (2011): Risk of injury by driving with alcohol and other drugs. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 2.3.5
- D3.1.1: Cor K. (2009): Evaluation of oral fluid Screening devices by TISPOL to Harmonise European police Requirements (ESTHER). DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 3.1.1
- D3.2.1: Blencowe T., Lillsunde P. (2009): Protocol of “workshop on drug driving detection by means of oral fluid screening. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 3.2.1
- D3.2.2: Blencowe T., Anna Pehrsson A., Lillsunde P. (2010): Analytical evaluation of oral fluid screening devices and preceding selection procedures. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 3.2.2
- D3.3.1: Veisten K., Houwing S., Mathijssen R.(2010): Cost-benefit analysis of drug driving enforcement by the police. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 3.3.1
- D4.1.1: Pil K., Raes E., Van den Neste T., Goessaert A., Veramme J., Verstraete A. (2008): Review of existing classification efforts. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 4.1.1
- D4.2.1: De Gier J.J., S. Ravera S., Monteiro S.P., Álvarez F.J. (2011): Establishment of criteria for a European categorisation system for medicinal drugs and driving. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 4.2.1
- D4.3.1: Gómez-Talegón T., Fierro I., M. Del Río C., Álvarez F.J. (2011): Establishment of framework for classification/categorisation and labelling of medicinal drugs and driving. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 4.3.1
- D4.4.1: Álvarez F.J. (2011): Classification of medicinal drugs and driving: a synthesis report. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 4.4.1
- D5.1.1: Boets, S., Meesmann, U., Klipp, S., Bukasa, B., Braun, E., Panosch, E., Wenninger, U., Roesner, S., Kraus, L. & Assailly, J-P. (2008). State of the Art on Driver Rehabilitation: Literature Analysis & Provider Survey. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 5.1.1
- D5.2.1: Bukasa B., Klipp S., Braun E., Panosch E., Wenninger U., Boets S., Meesmann U., Ponocny-Seliger E., Assailly J-P. (2008): Good practice : in-depth analysis of recidivism reasons & analysis of change process and components in driver rehabilitation courses. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 5.2.1
- D5.2.2: Bukasa B., Braun E., Wenninger U., Panosch E., Klipp S., Escrihuela-Branz M., Boets S., Meesmann U., Roesner S., Kraus L., Gaitanidou L., Assailly J-P. (2008): Development of an integrated evaluation instrument for driver rehabilitation measures. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 5.2.2
- D5.2.3: Klipp S., Escrihuela-Branz M., Boets S., Meesmann U., Roesner S., Kraus L., Panosch E., Bukasa B., Braun E., Wenninger U., Siegrist S. (2008): Quality management systems

- established along with driver rehabilitation schemes. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 5.2.3
- D5.2.4: Bukasa B., Braun E., Wenninger U., Panosch E., Klipp S., Boets S., Meesmann U., Roesner S., Kraus L., Gaitanidou L., Assailly J-P., Billard A. (2008): Validation of existing driver rehabilitation measures. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 5.2.4
- D6.1.1: Kærup S., Larson L., Godler K., Žlender B. (2009): State-of-the-Art Regarding Withdrawal of Driving Licence in Connection with Sanctions for Impaired Driving – Results of Questionnaires. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 6.1.1
- D6.2.1: Bukasa B., Salamon B., Klipp S., Krisman M., Larsen L., Krašovec B., Merc K., Žlender B., Schnabel E. (2011): Recommendations on Withdrawal. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 6.2.1
- D7.1.1: Raes E., Pil K., Van den Neste T., Verstraete A. (2007): Task 7.1 Review of guidelines, booklets and other resources: state of the art. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 7.1.1
- D7.2.1: De Gier J.J., Heissing M., Álvarez F.J., Tant M. (2009): Recommendations for improving medical guidelines for assessing fitness to drive in patients who use psychotropic medicines. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 7.2.1
- D7.2.2: Monteiro S., De Gier J.J. (2011): Guidelines and Professional Standards. Report + CD or DVD with examples of ICT supported protocols for prescribing and dispensing of medicines affecting driving performance, and for informing patients who use other psychoactive substances than medicines. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 7.2.2
- D7.3.1: Álvarez F.J., Fierro I., Boets S., Meesmann U., Pil K. (2009): Prototypes of booklets, posters, messages for risk communication including a script for a TV-clip. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 7.3.1
- D7.4.1: Margaritis, D., Toulidou K., Ravera S., Monteiro S., De Gier J. J., Boets S., Meesmann U., Álvarez F.J. (2009): Training Manual for Physicians and Pharmacists on Medicinal drug and Driving. Evaluation and implementation of new technologies. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 7.4.1
- D7.3.2 DRAFT: Meesmann U., Boets S., De Gier J.J., Monteiro S., Álvarez F.J., Fierro I. (2011): Main DRUID results to be communicated to different target groups (the one which we are writing). DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 7.3.2
- D7.4.2 DRAFT: Toulidou K., Margaritis D., Spanidis P., Monteiro S., Ravera S., De Gier J.J., Boets S., Meesmann U., Tant M., Legrand S.-A., Van der Linden T., Verstraete A., Fierro I., Gómez-Talegón T., Martin L., Álvarez F.J. (2011): Report on the implementation, evaluation and new technologies of practice guidelines and information materials. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 7.4.2
- D7.4.3 DRAFT: Heißing M., Holte H., Schulze H., Baumann E., Klimmt C. (2011) DRUID outcomes and risk communication to young drivers. DRUID (Driving under the Influence of Drugs, Alcohol and Medicines). 6th Framework programme. Deliverable 7.4.3

Annex

Annex 1: Questionnaire used in the Spanish study

													
MEDICAMENTOS Y CONDUCCIÓN													
<p>Este estudio forma parte del proyecto europeo DRUID, y se hace conjuntamente con la Agencia Española de Medicamentos y Productos Sanitarios del Ministerio de Sanidad y Política Social, así como con la Junta de Castilla y León, Consejería de Sanidad – Sacyl.</p> <p>Nos sería de gran utilidad conocer su opinión a cerca de los medicamentos y la conducción. Por favor, lea con atención cada una de las preguntas y marque la casilla <input checked="" type="checkbox"/> para indicar su respuesta.</p> <p>En esta encuesta no tiene que poner su nombre, ni ningún dato que le identifique personalmente. El presente estudio ha sido aprobado por el Comité Ético de Investigación Clínica de la Facultad de Medicina, Universidad de Valladolid.</p> <p>Muchas gracias por su participación.</p>													
Con la financiación de:													
													
<table border="1" style="width: 100%; border-collapse: collapse;"><tr><td style="width: 50%; padding: 5px;">Sexo: <input type="checkbox"/> Varón <input type="checkbox"/> Mujer</td><td style="width: 50%; padding: 5px;">¿Cuál es su edad? años</td></tr></table>		Sexo: <input type="checkbox"/> Varón <input type="checkbox"/> Mujer	¿Cuál es su edad? años										
Sexo: <input type="checkbox"/> Varón <input type="checkbox"/> Mujer	¿Cuál es su edad? años												
<table border="1" style="width: 100%; border-collapse: collapse;"><tr><td style="width: 50%; padding: 5px;">¿Tiene permiso de conducir? <input type="checkbox"/> Si → cuál.....</td><td style="width: 50%; padding: 5px;">¿Cuántos kms conduce al año?</td></tr></table>		¿Tiene permiso de conducir? <input type="checkbox"/> Si → cuál.....	¿Cuántos kms conduce al año?										
¿Tiene permiso de conducir? <input type="checkbox"/> Si → cuál.....	¿Cuántos kms conduce al año?												
<table border="1" style="width: 100%; border-collapse: collapse;"><tr><td colspan="2" style="padding: 5px;">¿Cuál es su nivel de estudios?</td></tr><tr><td colspan="2" style="padding: 5px;"><input type="checkbox"/> No completó la educación primaria (EGB)</td></tr><tr><td colspan="2" style="padding: 5px;"><input type="checkbox"/> Completó la educación primaria (EGB)</td></tr><tr><td colspan="2" style="padding: 5px;"><input type="checkbox"/> Bachillerato elemental o ESO</td></tr><tr><td colspan="2" style="padding: 5px;"><input type="checkbox"/> Bachillerato superior o COU</td></tr><tr><td colspan="2" style="padding: 5px;"><input type="checkbox"/> Diploma ó licenciatura Universitaria</td></tr></table>		¿Cuál es su nivel de estudios?		<input type="checkbox"/> No completó la educación primaria (EGB)		<input type="checkbox"/> Completó la educación primaria (EGB)		<input type="checkbox"/> Bachillerato elemental o ESO		<input type="checkbox"/> Bachillerato superior o COU		<input type="checkbox"/> Diploma ó licenciatura Universitaria	
¿Cuál es su nivel de estudios?													
<input type="checkbox"/> No completó la educación primaria (EGB)													
<input type="checkbox"/> Completó la educación primaria (EGB)													
<input type="checkbox"/> Bachillerato elemental o ESO													
<input type="checkbox"/> Bachillerato superior o COU													
<input type="checkbox"/> Diploma ó licenciatura Universitaria													
<table border="1" style="width: 100%; border-collapse: collapse;"><tr><td style="width: 70%; padding: 5px;">¿Sabía que algunas medicinas pueden influir en la capacidad para conducir?</td><td style="width: 10%; padding: 5px; text-align: center;"><input type="checkbox"/></td><td style="width: 20%; padding: 5px; text-align: center;"><input type="checkbox"/></td></tr><tr><td style="padding: 5px;"></td><td style="padding: 5px; text-align: center;">Si</td><td style="padding: 5px; text-align: center;">No</td></tr><tr><td style="padding: 5px;">¿Conocía la existencia de un pictograma sobre conducción (triángulo de borde rojo con fondo blanco y un coche en el centro) en los envases de algunos medicamentos?</td><td style="padding: 5px; text-align: center;"><input type="checkbox"/></td><td style="padding: 5px; text-align: center;"><input type="checkbox"/></td></tr><tr><td style="padding: 5px;"></td><td style="padding: 5px; text-align: center;">Si</td><td style="padding: 5px; text-align: center;">No</td></tr></table>		¿Sabía que algunas medicinas pueden influir en la capacidad para conducir?	<input type="checkbox"/>	<input type="checkbox"/>		Si	No	¿Conocía la existencia de un pictograma sobre conducción (triángulo de borde rojo con fondo blanco y un coche en el centro) en los envases de algunos medicamentos?	<input type="checkbox"/>	<input type="checkbox"/>		Si	No
¿Sabía que algunas medicinas pueden influir en la capacidad para conducir?	<input type="checkbox"/>	<input type="checkbox"/>											
	Si	No											
¿Conocía la existencia de un pictograma sobre conducción (triángulo de borde rojo con fondo blanco y un coche en el centro) en los envases de algunos medicamentos?	<input type="checkbox"/>	<input type="checkbox"/>											
	Si	No											

Presentación de un envase de un medicamento con el **pictograma europeo**

En su opinión, ¿qué significado tiene para Vd. el pictograma sobre conducción?:

¿Cómo evaluaría usted el grado de influencia de este medicamento en la conducción?, es decir, el riesgo que tiene usar ese medicamento y conducir vehículos:

<input type="checkbox"/> Alto riesgo	<input type="checkbox"/> Riesgo moderado	<input type="checkbox"/> Bajo riesgo	<input type="checkbox"/> Sin riesgo	<input type="checkbox"/> No lo sé
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Supongamos que a usted le prescriben este medicamento en el que aparece el pictograma sobre conducción en el envase. ¿Con qué frecuencia conduciría en el periodo en el que estuviese tomando este medicamento?

<input type="checkbox"/> Con la misma frecuencia	<input type="checkbox"/> Menos frecuentemente	<input type="checkbox"/> Bastante menos frecuentemente	<input type="checkbox"/> Casi no conduciría	<input type="checkbox"/> No conduciría
--	---	--	---	--

¿Qué haría usted si le prescribiesen este medicamento con un pictograma sobre la conducción en su envase?

<input type="checkbox"/> Conduciría sin tomar otras medidas	<input type="checkbox"/> No conduciría sin haber leído antes el prospecto	<input type="checkbox"/> No conduciría sin el consejo de un médico o farmacéutico	<input type="checkbox"/> No conduciría hasta que me lo indicara el médico
---	---	---	---

Según su opinión, valore del 1 al 10 (1-negativo, 10-positivo), el pictograma es:

	1	2	3	4	5	6	7	8	9	10	
Innecesario	o	o	o	o	o	o	o	o	o	o	Útil
No informativo	o	o	o	o	o	o	o	o	o	o	Informativo
Incomprensible	o	o	o	o	o	o	o	o	o	o	Comprensible
Complejo	o	o	o	o	o	o	o	o	o	o	Sencillo

¿Qué probabilidad existe de que usted cambie su comportamiento sobre conducir, cuando le prescriban o dispensen un medicamento con este pictograma sobre medicamentos y conducción?

<input type="checkbox"/> Muy improbable	<input type="checkbox"/> Improbable	<input type="checkbox"/> Ni probable/ni improbable	<input type="checkbox"/> Probable	<input type="checkbox"/> Muy probable
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Presentación de otro envase de un medicamento con **un segundo pictograma europeo**

Hasta ahora ha respondido a las preguntas sobre el pictograma acerca del efecto de la medicación en la conducción.

Ahora le mostraremos un nuevo tipo de pictograma sobre la conducción.

En su opinión, ¿Cuál de los dos pictogramas sobre medicamentos y conducción es más comprensible?	
<input type="checkbox"/> El primer pictograma	<input type="checkbox"/> El segundo pictograma

¿Por qué?: _____

En su opinión, ¿Cuál de los dos pictogramas le da mejor información sobre el grado de deterioro en la conducción ocasionado por el medicamento?	
<input type="checkbox"/> El primer pictograma	<input type="checkbox"/> El segundo pictograma

¿Por qué?: _____

¿Qué cambiaría usted, si pudiera, del pictograma para hacerlo más claro?: _____
--

Consumo de medicamentos en la actualidad

¿Está tomando medicinas en la actualidad?	<input type="checkbox"/> Si: cuántas.....	<input type="checkbox"/> No
---	---	-----------------------------

¿Alguna de las medicinas que Vd. toma tiene pictograma sobre medicamentos y conducción?		
<input type="checkbox"/> Si, cuántas.....	<input type="checkbox"/> No	<input type="checkbox"/> No lo sé

¿Ha recibido en algún momento información acerca del posible efecto de alguno de los medicamentos que toma sobre su capacidad de conducir?		
<input type="checkbox"/> Si, sobre el medicamento:	<input type="checkbox"/> No	<input type="checkbox"/> No lo sé

Annex 2: Definition of different illicit drug- and medication groups within the DRUID roadside survey (D2.2.3)

- “The **THC** substance group is formed by THC only. THC-COOH was detected as well in blood, but this inactive metabolite of THC will be regarded as negative.
- The **cocaine** group includes both drivers with cocaine and with its metabolite benzoylecgonine.
- The **amphetamine** drugs group consisted of amphetamine, methamphetamine, MDMA, MDA, and MDEA.
- The **illicit opiates** group includes drivers that were positive for heroin (6-acetylmorphine) or the combination of morphine and codeine where the concentration of morphine is equal to or higher than the concentration of codeine. If the concentration of codeine is higher than that of morphine, the use was regarded as medicinal opiates and opioids use.
- The **benzodiazepines** group consists of diazepam, nordiazepam, oxazepam, lorazepam, alprazolam, flunitrazepam, and clonazepam.
- The **medicinal opiates and opioids** group consists of morphine, codeine, methadone and tramadol.
- The **Z-drugs** group consists of zolpidem and zopiclone
- The group **alcohol and drugs (combinations)** consist of alcohol 0.1 g/L in combination with one or more other psychoactive substances, excluding THC-COOH which is regarded as negative.
- The group **drug-drug combinations** consist of the combination of two or more other psychoactive substances other than alcohol from at least two different groups of drugs, excluding THC-COOH which is regarded as negative” (D2.2.3).

Annex 3: Substance classes, groups and the analytical findings within DRUID hospital studies (D2.2.5 p. 37)

Type	No.	Group	Analytical findings
Alcohol	512	alcohol	ethanol
Illicit drugs	1	amphetamines	amphetamine methamphetamine or methamphetamine + amphetamine MDMA or MDMA + MDA MDEA or MDEA + MDA MDA
	2	cocaine/1	benzoylecgonine
	4	cocaine/2	cocaine + benzoylecgonine or cocaine
	8	cannabis/1	THCCOOH
	16	cannabis/2	THC or THC+THCCOOH
	32	illicit opiates	6-acetylmorphine or 6-AM + codeine or 6-AM + morphine or 6-AM + codeine + morphine or (morphine + codeine and morphine>= codeine)
Medicinal drugs	64	benzodiazepines	diazepam diazepam + nordiazepam or diaz + oxaz or diaz + nordiaz + oxaz nordiaz or nordiaz + oxaz oxazepam lorazepam alprazolam flunitrazepam or flunitrazepam + 7-aminoflunitrazepam clonazepam or clonazepam + 7-aminoclonazepam
	128	Z-drugs	zolpidem zopiclone
	256	medicinal opioids	morphine codeine or (codeine + morphine and codeine> morphine) methadone tramadol
Various combinations		drug-alcohol	
		drug-drug	

“For calculating prevalence, substances of the same type were combined into following substance groups: alcohol, amphetamines, cocaine/1, cocaine/2, cannabis/1, cannabis/2, illicit opiates, benzodiazepines, Z-drugs, and medicinal opioids. Substance groups are aggregated into the following substance classes: alcohol, illicit drugs, medicines and following combinations: drug-alcohol and drug-drug. This last class is specified as a combination of different substance groups. For example: zolpidem + cocaine will be considered a drug-drug combination but zolpidem + zopiclone will be considered a single use of z-drugs” (D2.2.5 p. 37).

Annex 4: Overview of the estimated European prevalence of psychoactive substances; prevalence in percentage; 95% confidence intervals in italics (D2.2.3 PART I p. 9)

		Inhabitants (million)	negative	amphetamines	cocaine	THC	illicit opiates	benzodiazepines	Z-drugs	medicinal opiates and opioids	alcohol	alcohol-drugs	drugs-drugs
Northern Europe	DK	5.4	95.52 <i>94.72 - 96.2</i>	0.02 <i>0 - 0.16</i>	-	0.2 <i>0.09 - 0.43</i>	-	0.47 <i>0.28 - 0.79</i>	0.32 <i>0.17 - 0.59</i>	0.79 <i>0.53 - 1.18</i>	2.53 <i>2.02 - 3.15</i>	0.1 <i>0.03 - 0.3</i>	0.06 <i>0.02 - 0.24</i>
	FI	5.3	97.15 <i>96.58 - 97.63</i>	0.05 <i>0.02 - 0.19</i>	0.03 <i>0.01 - 0.16</i>	0.04 <i>0.01 - 0.17</i>	-	0.79 <i>0.56 - 1.13</i>	0.36 <i>0.21 - 0.6</i>	0.56 <i>0.37 - 0.85</i>	0.64 <i>0.43 - 0.94</i>	0.08 <i>0.03 - 0.23</i>	0.29 <i>0.16 - 0.52</i>
	NO	4.7	97.03 <i>96.67 - 97.38</i>	0.06 <i>0.02 - 0.13</i>	0.06 <i>0.03 - 0.14</i>	0.48 <i>0.36 - 0.64</i>	-	0.84 <i>0.67 - 1.05</i>	0.69 <i>0.54 - 0.88</i>	0.16 <i>0.1 - 0.27</i>	0.32 <i>0.23 - 0.46</i>	0.07 <i>0.03 - 0.15</i>	0.28 <i>0.19 - 0.42</i>
	SE	9.1	98.66 <i>98.34 - 98.92</i>	0.07 <i>0.03 - 0.17</i>	-	0.03 <i>0.01 - 0.12</i>	-	0.19 <i>0.11 - 0.33</i>	0.31 <i>0.2 - 0.48</i>	0.63 <i>0.46 - 0.86</i>	NA	NA	0.12 <i>0.06 - 0.25</i>
	Total	93.3	97.32	0.05	0.02	0.16	0.00	0.51	0.56	0.40	1.20	0.17	0.05
Eastern Europe	CZ	10.3	97.2 <i>96.39 - 97.83</i>	0.36 <i>0.17 - 0.72</i>	-	0.46 <i>0.25 - 0.86</i>	-	0.62 <i>0.36 - 1.07</i>	-	0.21 <i>0.08 - 0.52</i>	0.99 <i>0.65 - 1.53</i>	0.05 <i>0.01 - 0.28</i>	0.11 <i>0.03 - 0.38</i>
	HU	10.1	97.68 <i>97.04 - 98.18</i>	-	0.04 <i>0.01 - 0.21</i>	0.19 <i>0.08 - 0.44</i>	-	1.5 <i>1.11 - 2.03</i>	0.07 <i>0.02 - 0.26</i>	0.11 <i>0.04 - 0.32</i>	0.15 <i>0.06 - 0.38</i>	-	0.27 <i>0.13 - 0.54</i>
	LT	3.4	94.49 <i>93.09 - 95.61</i>	0.22 <i>0.07 - 0.66</i>	-	-	-	1.41 <i>0.9 - 2.23</i>	-	-	3.86 <i>2.93 - 5.06</i>	0.03 <i>0 - 0.36</i>	-
	PL	38.2	97.63 <i>97.11 - 98.05</i>	0.05 <i>0.01 - 0.18</i>	-	0.57 <i>0.38 - 0.85</i>	0.09 <i>0.04 - 0.25</i>	0.14 <i>0.06 - 0.31</i>	-	0.03 <i>0.01 - 0.15</i>	1.47 <i>1.14 - 1.9</i>	-	0.02 <i>0 - 0.14</i>
	Total	96.7	97.57	0.09	0.01	0.47	0.06	0.52	0.08	0.02	1.10	0.09	0.01
Southern Europe	ES	44.5	85.15 <i>83.87 - 86.34</i>	0.11 <i>0.04 - 0.3</i>	1.49 <i>1.12 - 1.97</i>	5.99 <i>5.22 - 6.87</i>	0.05 <i>0.01 - 0.2</i>	1.4 <i>1.05 - 1.87</i>	-	0.19 <i>0.09 - 0.41</i>	3.92 <i>3.3 - 4.66</i>	1.14 <i>0.83 - 1.58</i>	0.57 <i>0.36 - 0.89</i>
	IT	59.1	84.99 <i>82.95 - 86.82</i>	-	1.25 <i>0.78 - 2.01</i>	1.15 <i>0.7 - 1.89</i>	0.3 <i>0.12 - 0.78</i>	0.97 <i>0.57 - 1.67</i>	-	0.53 <i>0.25 - 1.09</i>	8.59 <i>7.19 - 10.23</i>	1.01 <i>0.59 - 1.71</i>	1.22 <i>0.75 - 1.97</i>
	PT	10.6	90.01 <i>89.04 - 90.91</i>	-	0.03 <i>0.01 - 0.16</i>	1.38 <i>1.07 - 1.8</i>	0.15 <i>0.07 - 0.33</i>	2.73 <i>2.27 - 3.29</i>	-	0.11 <i>0.04 - 0.27</i>	4.93 <i>4.29 - 5.64</i>	0.42 <i>0.26 - 0.67</i>	0.23 <i>0.12 - 0.44</i>
	Total	128.6	85.52	0.04	1.23	3.06	0.19	1.30	0.36	0.00	6.43	0.87	1.01
Western Europe	BE	10.6	89.35 <i>88.18 - 90.41</i>	-	0.2 <i>0.09 - 0.43</i>	0.35 <i>0.19 - 0.64</i>	0.09 <i>0.03 - 0.28</i>	2.01 <i>1.57 - 2.59</i>	0.22 <i>0.1 - 0.47</i>	0.75 <i>0.5 - 1.13</i>	6.42 <i>5.59 - 7.36</i>	0.31 <i>0.16 - 0.58</i>	0.3 <i>0.16 - 0.58</i>
	NL	16.4	94.49 <i>93.81 - 95.1</i>	0.19 <i>0.1 - 0.36</i>	0.3 <i>0.18 - 0.5</i>	1.67 <i>1.34 - 2.07</i>	0.01 <i>0 - 0.09</i>	0.4 <i>0.25 - 0.62</i>	0.04 <i>0.01 - 0.15</i>	0.16 <i>0.08 - 0.32</i>	2.15 <i>1.78 - 2.6</i>	0.24 <i>0.13 - 0.42</i>	0.35 <i>0.22 - 0.56</i>
	Total	181.4	92.46	0.12	0.26	1.15	0.04	1.03	0.39	0.11	3.83	0.33	0.27
Weighted European mean		500.0	92.57	0.08	0.42	1.32	0.07	0.90	0.35	0.12	3.48	0.39	0.37

Source: D2.2.3 PART I p.9

“This table shows the prevalence per substance group and per country as well as the estimated European means. The European mean can be used to distinguish per substance whether country prevalence is around, below or above this European mean. The table presents the spread of the prevalence around the estimated European mean. A yellow colour of a particular prevalence value indicates that the European mean lies within the 95% confidence interval of the prevalence. A green coloured value indicates that the confidence interval suggests that it is below the European mean, and a red coloured value indicates that the confidence interval suggests that it is above the European mean” (D2.2.3 PART I p. 5).

Annex 5: Overview of the main results of all investigated substances in the DRUID road side survey (D2.2.3) and case-control study (D2.3.5)

	ALCOHOL (alone)			PSYCHOACTIVE MEDICINES (alone)			ILLCIT DRUGS (alone)				COMBINED USE	
	Alcohol (≥0.1g/L)	Alcohol (≥0.5g/L)	Alcohol (≥1.2g/L)	Benzodia-zepines	Z-drugs	Medicinal opiates and opioids	Ampheta-mines	Cocaine	THC	Illicit opiates	Alcohol (0.1g/L) and drugs	Drug-drug
Mean prevalence (D2.2.3)	3.48%	1.49%	ca. 0.4%	0.90%	0.09%	0.35%	0.08%	0.42%	1.32%	0.07%	0.37%	0.39%
Prevalence ranking	#1	#2	#6	#4	#10	#9	#11	#5	#3	#12	#8	#7
Highest prevalence (D2.2.3)	Italy (8.59%)	Italy (5.23%)	Lithuania and Italy (about 1.4%)	Portugal (2.73%)	Norway (0.69%)	Denmark (0.79%)	Czech Republic (0.38%)	Spain (1.49%)	Spain (5.99%)	Italy (0.3%)	Spain (1.14%)	Italy (1.22%)
Main European region (D2.2.3)	Southern Europe	No specific region	No specific region	Southern Europe	Northern Europe	Northern Europe	No specific region	Southern Europe	Southern Europe	Southern Europe	Southern Europe	Southern Europe
Main gender effect (D2.2.3)	Male drivers			Female drivers	Female drivers	Female drivers	Differs per country	Male drivers	Male drivers	Male drivers	Male drivers	Male drivers
Main age effect (D2.2.3)	Differs per country			35 years and older	Drivers 50 years and older	35 years and older	Young drivers (18-34)	Drivers (18-49)	Young drivers (18-34)	Drivers 35-49	Young drivers (18-34)	Drivers younger than 50
Main time period effect (D2.2.3)	Weekday nights and weekends			Daytime hours	Daytime hours at weekdays	Daytime hours	Differs per country	Differs per country	Differs per country		Night time hours	Differs per country
Relative risk of serious injury or fatality compared to sober drivers (D2.3.5)	5-10x ¹		20-200x	2-10x (for benzodiazepines + Z-drugs and for medicinal opioids)			5-30x	2-10x (for benzoyllecgonine and for cocaine)	1-3x	2-10x	20-200x	5-30x

NA = not available; ¹ For different concentrations: 0.1 – 0.5g/L: 1-3x; 0.5 - 0.8g/L: 2-10x; 0.8 - 1.2g/L: 5-30x

