

Driving under the influence of cannabis: a 10-year study of age and gender differences in the concentrations of tetrahydrocannabinol in blood

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ABSTRACT

Background Δ^9 -Tetrahydrocannabinol (THC) is the major psychoactive constituent of cannabis and its various preparations. Increasing use of cannabis for recreational purposes has created a problem for road-traffic safety. This paper compares age, gender and the concentrations of THC in blood of individuals apprehended for driving under the influence of drugs (DUID) in Sweden, where a zero-tolerance law operates. **Measurements** Specimens of blood or urine were subjected to a broad screening analysis by enzyme immunoassay methods. THC positives were verified by analysis of blood by gas chromatography-mass spectrometry (GC-MS) with a deuterium-labelled internal standard (d_3 -THC). All toxicology results were entered into a database (TOXBASE) along with the age and gender of apprehended drivers. **Findings** Over a 10-year period (1995–2004), between 18% and 30% of all DUID suspects had measurable amounts of THC in their blood (> 0.3 ng/ml) either alone or together with other drugs. The mean age [\pm standard deviation (SD)] of cannabis users was 33 ± 9.4 years (range 15–66 years), with a strong predominance of men (94%, $P < 0.001$). The frequency distribution of THC concentrations ($n = 8794$) was skewed markedly to the right with mean, median and highest values of 2.1 ng/ml, 1.0 ng/ml and 67 ng/ml, respectively. The THC concentration was less than 1.0 ng/ml in 43% of cases and below 2.0 ng/ml in 61% of cases. The age of offenders was not correlated with the concentration of THC in blood ($r = -0.027$, $P > 0.05$). THC concentrations in blood were higher when this was the only psychoactive substance present ($n = 1276$); mean 3.6 ng/ml, median 2.0 ng/ml compared with multi-drug users; mean 1.8 ng/ml, median 1.0 ng/ml ($P < 0.001$). In cases with THC as the only drug present the concentration was less than 1.0 ng/ml in 26% and below 2.0 ng/ml in 41% of cases. The high prevalence of men, the average age and the concentrations of THC in blood were similar in users of illicit drugs (non-traffic cases). **Conclusions** The concentration of THC in blood at the time of driving is probably a great deal higher than at the time of sampling (30–90 minutes later). The notion of enacting science-based concentration limits of THC in blood (e.g. 3–5 ng/ml), as discussed in some quarters, would result in many individuals evading prosecution. Zero-tolerance or limit of quantitation laws are a much more pragmatic way to enforce DUID legislation.

Keywords Blood, cannabis, drugs, DUID, road traffic accident, tetrahydrocannabinol, THC.

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INTRODUCTION

Although, in most countries, cannabis and its various preparations are classified as illicit drugs, these psychoactive substances are used widely for recreational purposes and thereby represent a problem for traffic safety [1–4]. Some countries have a fairly liberal attitude towards possession of cannabis for personal use, whereas in others

this constitutes a criminal offence [2,5,6]. Accordingly, there is much ambivalence among both politicians and scientists about the pros and cons of legalizing cannabis as a recreational drug or whether cannabinoids should be prescribed for certain medical conditions [7–9].

The pharmacologically active constituent of cannabis, hashish and marijuana is Δ^9 -tetrahydrocannabinol (THC), which displays a complex pharmaco-

kinetic profile owing to its high lipid solubility, protein binding and large distribution volume [10–12]. The forensic evidence necessary to verify that a person has used cannabis comes from analysis of THC or its main metabolites (6-hydroxy-THC and carboxy-THC) in blood, urine or other body fluid [12–14]. Knowledge of the concentrations of THC in blood or plasma is essential to allow any conclusion to be drawn about the effects of cannabis on a person's performance and behaviour and the likelihood of any drug-related impairment [15,16].

A zero-tolerance law for driving under the influence of drugs (DUID) in Sweden led to a dramatic increase (more than 12-fold) in the number of blood samples submitted by the police authorities for toxicological analysis [17]. The limit of quantitation (LOQ) for analysis of THC in blood in our laboratory is 0.3 ng/ml, and this serves as the threshold concentration for prosecution. Other countries, such as Germany, have established a consensus limit of 1.0 ng/ml THC in serum, which corresponds to 0.5 ng/ml in blood, owing to a ~ 2 : 1 serum/blood distribution ratio [18,19]. Belgium has adopted a punishable THC limit of 2.0 ng/ml in plasma (1.0 ng/ml in blood) and Switzerland enforces a limit of 1.5 ng/ml in blood [18]. In other countries where a zero-tolerance law operates, such as France, Finland and Poland, the laboratory LOQ determines the threshold limit for a DUID prosecution [18].

After alcohol, cannabis is probably the most popular psychoactive substance used for recreational purposes in western nations [3,20]. An influential group of scientists has attempted to establish science-based concentration limits for driving after use of cannabis with THC concentration in blood serving as *per se* evidence of impairment [21,22]. The scientific background for setting these limits comes from critical reviews of scientific literature and investigation of traffic crashes in which THC was identified in the driver's blood [23,24]. In addition, laboratory studies of psychomotor and cognitive skills after people smoke marijuana [25,26], as well as on-the-road driving performance, is being evaluated [27–29]. Whatever the outcome, it seems certain that the threshold concentration of THC in blood for prosecution is likely to be set fairly high, for instance 3.0 ng/ml or even higher [21,22]. What this would mean is that many individuals who had smoked marijuana or used cannabis a few hours earlier would evade prosecution. This follows because of the complex pharmacokinetics of THC, such that the concentration in blood drops below the *per se* limit for driving between the time of last use of cannabis and obtaining blood samples for toxicological analysis.

The aim of this study was to investigate the frequency of occurrence of THC in forensic blood samples from people apprehended in Sweden for DUID over a 10-year period (1995–2004). We documented the concentra-

tions of THC in blood in relation to age and gender of offenders and whether THC was the only drug present or occurred together with other psychoactive substances. For comparative purposes, a large forensic sample of individuals arrested for use of illicit drugs (non-traffic cases) was also investigated and compared with the DUID suspects.

MATERIALS AND METHODS

Collection of blood samples from impaired drivers

Motorists apprehended by the police in connection with a moving traffic offence, involvement in a crash, when stopped in connection with routine sobriety controls or reported by other road users submit first to a roadside breath-alcohol screening test. If the result of the breath-test is positive this is followed by either a more sophisticated evidential breath-alcohol test or a specimen of venous blood taken for laboratory analysis of ethanol. If the roadside breath-alcohol test is negative and the person shows signs of drug influence or impairment, then a specimen of venous blood is taken for toxicological analysis.

One central laboratory (Department of Forensic Genetics and Forensic Toxicology, National Board of Forensic Medicine, Linköping) is responsible for the toxicological analysis of blood and urine from all drivers apprehended in Sweden (population 9 million). Two specimens of venous blood are taken into 10-ml grey-stopper evacuated tubes that contain 100 mg sodium fluoride (NaF) and 25 mg potassium oxalate as preservatives (Terumo Europe NV, Leuven, Belgium). Whenever possible a specimen of urine (10 ml), preserved with 1% NaF, is also collected and if available is used to make an initial screening analysis for a wide range of abused drugs (see below). A person cannot be forced to provide a sample of urine, which means that this body fluid is not always available for analysis.

Police procedures

In connection with passing a zero-tolerance DUID law (1 July 1999) the police were allowed to examine a suspect's eyes with a flashlight to test for any reaction to light, and pupil size was measured with a pupilometer device. The existence of any gaze nystagmus was also noted, as well as other indications that might suggest use and abuse of drugs other than alcohol. The results of these simple observational tests are recorded on the arrest forms, which are sent along with the blood and urine samples for toxicological analysis. Whether or not the toxicological analysis for drugs of abuse in blood and urine proves to be negative, there are no consequences or reprimands for the arresting officers.

Determination of THC in blood samples

Specimens of blood and/or urine are screened initially by enzyme-multiplied immunoassay (EMIT) and cloned enzyme donor immunoassay (CEDIA) for the major drugs of abuse (amphetamines, opiates, cannabis, cocaine metabolite and benzodiazepines). All positive results from the screening are verified by more selective and sensitive methods [gas chromatography–mass spectrometry (GC-MS) and liquid chromatography–mass spectrometry (LC-MS)]. Prescription drugs are determined in blood by capillary gas chromatography with a nitrogen-specific detector after alkaline and neutral extraction with butyl acetate.

THC was determined in whole blood by GC-MS using selected ion monitoring (SIM) after adding a deuterium-labelled analogue (d_3 -THC) as the internal standard [30]. An exact aliquot of blood (~1 g) was extracted with *n*-pentane and the organic phase mixed with *N,O*-bis-(trimethylsilyl) trifluoroacetamide (BSTFA) and then heated to 60°C to prepare a derivative for chromatography. After cooling to room temperature the solvent was evaporated to dryness under nitrogen and the residue was dissolved in butyl acetate and transferred into auto-injector vials in readiness for GC-MS analysis. The ratio of peaks at *m/z* 386 for THC and *m/z* 389 for internal standard were used for quantitative analysis and *m/z* 303 and *m/z* 371 served as the qualifier ions. This method had an LOQ of 0.3 ng/ml, and the response of the peak area ratio (*m/z* 386 to *m/z* 389) was linear until a THC concentration in blood of 15 ng/ml was reached. If concentrations exceeded this upper limit on the standard curve then the blood sample was diluted with fresh whole blood and the analytical procedure repeated. Within-run imprecision, expressed as coefficient of variation, was 5.5% at a THC concentration of 0.5 ng/ml and 4.4% at a THC concentration of 5 ng/ml.

For the purposes of this investigation, the age, gender and concentration of THC in blood were available for all cases of drug-impaired driving over a 10-year period (1995–2004).

Evaluation of results

Frequency distributions of the concentrations of THC in blood were skewed markedly to the right, so mean, median and range of values were used as descriptive statistics. Mean and standard deviation (SD) was calculated for the age of offenders. We investigated 8794 cases of DUID in which THC was verified as present in a driver's blood either alone or together with other drugs. Subgroups were formed depending on whether THC was the only psychoactive substance present or occurred together with other drugs. Over a 5-year period (2000–2004) we examined the most common types of

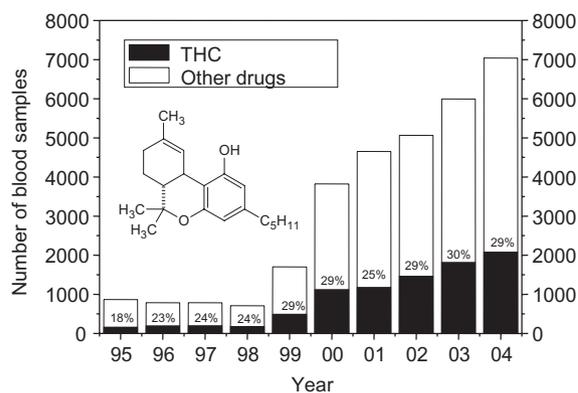


Figure 1 Development in the number of apprehended drivers over a 10-year period (1995–2004) showing the relative proportion of specimens with Δ^9 -tetrahydrocannabinol verified in blood samples

other drugs that were identified in blood together with THC.

Differences between two means were compared by Student's *t*-test and two medians by the Mann–Whitney test for non-parametric data. Two proportions were compared by χ^2 test. When more than two groups were compared, either a one-way analysis of variance (ANOVA) or a non-parametric Kruskal–Wallis test was used.

RESULTS

Development in number of DUID blood samples

Figure 1 shows the development in number of cases of DUID submitted by the police for toxicological analysis over a 10-year period (1995–2004). Note that the zero-limit law was introduced on 1 July 1999. Also shown on this graph is the proportion of blood samples that contained measurable amounts of THC, which ranged from 18% to 30% over the study period. In these cases THC was either the only drug present or occurred together with other licit or illicit drugs.

Age and gender differences in THC concentration

Table 1 compares age and gender of DUID suspects in relation to the concentrations of THC in blood either alone or together with other drugs. The proportion of men far exceeded that of women (94% versus 6%, $P < 0.001$) and the women tended to be a few years older than the men (mean age 34 ± 8.3 years compared with 32 ± 9.5 years). This small age difference was statistically significant ($P < 0.001$) owing to the large sample-sizes. A frequency distribution of the age of DUID offenders with THC in blood including descriptive statistics is shown in Fig. 2.

Table 1 Concentrations of Δ^9 -tetrahydrocannabinol (THC) in blood of apprehended drivers apprehended over a 10-year period as a function of their age and gender.

Gender	n (%)	Age, years	Blood THC conc. (ng/ml)
		Mean \pm SD	Mean (median) highest
Men	8238 (94)	32 \pm 9.5	2.1 (1.0) 67
Women	556 (6)*	34 \pm 8.3 [†]	1.4 (0.9) 30 [‡]
Both	8794 (100)	33 \pm 9.4	2.1 (1.0) 67

*Higher proportion of men (χ^2 test, $P < 0.001$). [†]Women older than men (Student's t -test, $P < 0.001$). [‡]Concentration of THC in blood of women less than men (Mann–Whitney test, $P < 0.001$). SD: standard deviation.

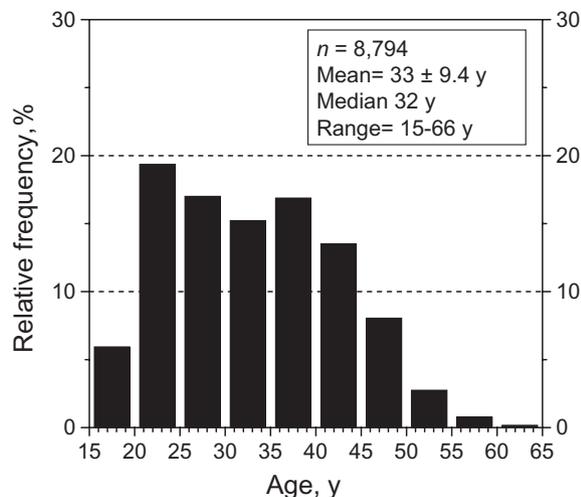


Figure 2 Relative frequency distribution of the age of apprehended drivers with Δ^9 -tetrahydrocannabinol verified as present in blood samples (1995–2004)

Figure 3 illustrates the skewed nature of the frequency distribution of THC concentrations in blood with mean (median) and highest values of 2.1 ng/ml (1.0 ng/ml) and 67 ng/ml, respectively. The average THC concentrations in blood of men (mean 2.1 ng/ml, median 1.0 ng/ml) was higher than in women (mean 1.4 ng/ml, median 0.9 ng/ml), as shown by a Mann–Whitney test, $P < 0.001$ (Table 1).

Time trends in the concentrations of THC in blood and age of offenders

Year-by-year changes in the number of blood samples with THC verified as present by GC-MS are shown in Table 2, along with the average age of offenders and the THC concentrations in blood for a 10-year period. The mean concentrations of THC in blood fluctuated over the 10-year study period, varying from 1.7 ng/ml to 2.3 ng/ml ($P < 0.001$), as did the average age of offenders, which varied from 31 \pm 6.7 years to

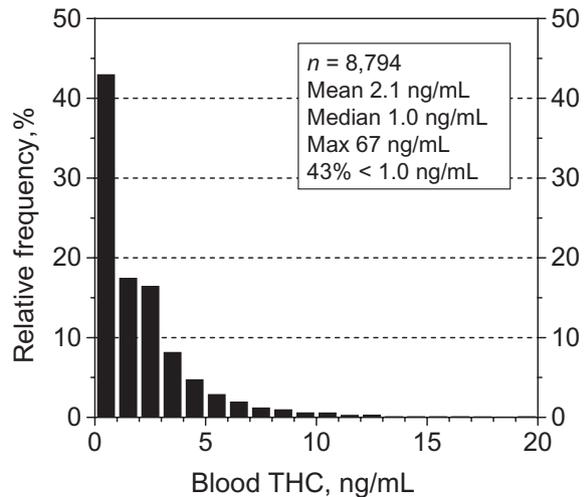


Figure 3 Relative frequency distribution of the concentrations of Δ^9 -tetrahydrocannabinol (THC) in blood samples from driving under the influence of drugs suspects apprehended over a 10-year period; $n = 38$ cases (0.43%) with a THC concentration above 20 ng/ml are not plotted for clarity

33 \pm 10.1 years ($P < 0.001$). The large sample sizes meant that these year-by-year changes were statistically significant.

Concentration of THC in blood when this was the only psychoactive substance present

Table 3 compares the age, gender and concentration of THC in blood when this was the only psychoactive drug present and when other drugs of abuse were also identified. The offenders were predominantly men in each subgroup, although those with THC as the only drug present tended to be about 3 years younger, mean 28 \pm 9.3 years compared with 33 \pm 9.3 years for THC + other drugs ($P < 0.001$).

The mean and median concentrations of THC were appreciably higher when this was the only drug present, suggesting either more recent use or more frequent use of cannabis in these individuals ($P < 0.001$). The relative frequency distribution of THC concentrations in blood when this was the only drug present is plotted in Fig. 4.

Concentrations of THC in users of illicit drug (non-traffic cases)

The ages, gender and concentrations of THC in blood of people arrested by the police for use of illicit drugs (non-traffic cases) are shown in Table 4. The results are presented according to whether THC was the only drug present or whether this occurred along with other drugs of abuse. The ages and concentrations of THC in blood for these non-traffic cases agreed well with the DUID

Table 2 Year-by-year changes in number of apprehended drivers with Δ^9 -tetrahydrocannabinol (THC) in blood in relation to mean [\pm standard deviation (SD)] age and concentration of THC in blood between 1995 and 2004.

Year	n*	Blood THC conc. (ng/ml) [†] mean (median) highest	Age, years mean \pm SD [†]	Age, years range
1995	154	1.8 (1.0) 13	31 \pm 6.7	17–50
1996	184	1.9 (1.0) 20	33 \pm 8.1	16–52
1997	187	1.7 (1.0) 30	31 \pm 7.5	17–52
1998	174	1.8 (1.0) 16	32 \pm 8.7	17–58
1999	490	1.8 (1.0) 21	32 \pm 8.5	16–58
2000	1109	1.7 (1.0) 21	32 \pm 8.9	15–58
2001	1169	1.9 (1.0) 30	32 \pm 9.0	15–60
2002	1462	2.3 (1.0) 46	32 \pm 9.4	15–66
2003	1805	2.3 (1.0) 67	33 \pm 9.9	15–63
2004	2061	2.3 (1.0) 39	33 \pm 10.1	15–63
1995–2004	8794	2.1 (1.0) 67	33 \pm 9.4	15–66

*A zero-tolerance driving under the influence of drugs law was introduced 1st July 1999. [†]Statistically significant differences in mean age (analysis of variance) and median concentrations of THC in blood (Kruskal–Wallis test) over time ($P < 0.001$).

Table 3 Age and gender differences in the concentration of Δ^9 -tetrahydrocannabinol (THC) in blood of impaired drivers with or without other drugs present.

Drugs present	Gender	n (%)	Age, years Mean \pm SD	Blood THC (ng/ml) Mean (median) highest
THC alone	Men	1236 (97)*	28 \pm 9.3	3.6 (2.0) 67
	Women	40 (3)	31 \pm 8.8 [†]	2.4 (1.0) 10 [‡]
	Both	1276 (100)	28 \pm 9.3	3.6 (2.0) 67 [§]
THC + other drugs	Men	7002 (93)*	33 \pm 9.3	1.9 (1.0) 46
	Women	516 (7)	35 \pm 8.3 [†]	1.3 (0.8) 30 [‡]
	Both	7518 (100)	33 \pm 9.3	1.8 (1.0) 46
THC all cases	Men	8238 (94)*	32 \pm 9.5	2.1 (1.0) 67
	Women	556 (6)	34 \pm 8.3 [†]	1.4 (0.9) 30 [‡]
	Both	8794 (100)	33 \pm 9.4	2.1 (1.0) 67 [†]

*Higher proportion of men than women ($P < 0.001$). [†]Women older than men ($P < 0.001$). [‡]Concentrations of THC in blood lower in women ($P < 0.001$). [§]Concentrations of THC in blood significantly higher when this was the only drug present ($P < 0.001$). SD: standard deviation.

suspects, suggesting that they represent the same population of individuals (see Table 3).

Drugs commonly identified together with THC in blood

The high prevalence of polydrug use in DUID suspects is illustrated by the data presented in Table 5. THC was the only drug identified in blood in 14% of cases; THC occurred together with alcohol (> 20 mg/100 ml) in 3.8% of cases and with amphetamines in 35% of cases. The use of cannabis, together with amphetamine as well as a benzodiazepine, was fairly common (16%). Polydrug use with a strong preference for amphetamine seems to be the norm among DUID suspects apprehended in Sweden [17].

DISCUSSION

This large-scale study of cannabis use and driving involved a comprehensive toxicological analysis of many

thousands of blood samples. The results provide a reliable picture of the concentrations of THC in blood after recreational use of cannabis preparations. The mean and median concentrations of THC were higher in apprehended drivers when this was the only psychoactive substance present. This probably reflects more recent or more intensive use of cannabis, or a more effective way to administer the active substance. The cannabis-only users tended to be a few years younger than those with multi-drugs identified in the blood (see Table 5). The higher concentration of THC might also reflect changes in the potency of cannabis preparations or residual THC in blood of heavy users from previous exposures [31].

A study of apprehended drivers in Norway ($n = 589$) with THC as the only psychoactive substance in blood reported a median THC concentration of 2.2 ng/ml and a range from 0.3 to 45 ng/ml [30]. These values agree well with our findings (median 2.0 ng/ml, range 0.3–67 ng/ml in THC-only cases [32]). Similarly, the Norwe-

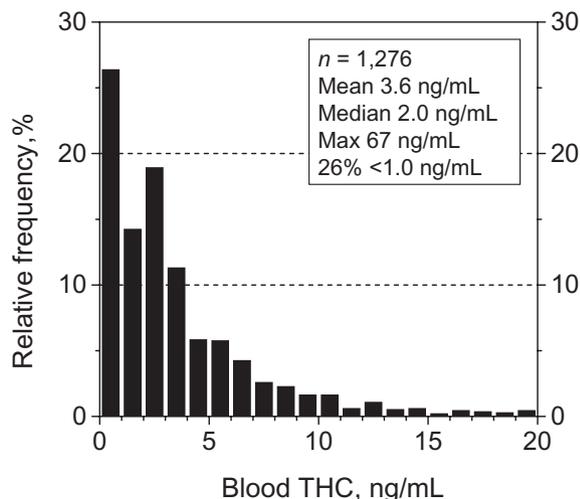


Figure 4 Relative frequency distribution of the concentrations of Δ^9 -tetrahydrocannabinol (THC) in blood samples from driving under the influence of drugs suspects when no other psychoactive substances were present; $n=20$ cases (7%) with a THC concentration above 20 ng/ml are not plotted for clarity

gian study showed a predominance of male offenders (96%) compared with 97% in Sweden. Additionally, men generally had slightly higher THC concentrations in blood than women ($P < 0.05$). In DUID suspects apprehended in Switzerland ($n = 440$), the mean and median concentrations of THC in blood were higher (5.0 ng/ml and 3.0 ng/ml) and many offenders had also used other drugs together with cannabis [16]. These differences might be related to the different potency of the cannabis preparations available in different countries, or a shorter elapsed time between last use and sampling of blood for analysis of THC.

Recreational use of cannabis or marijuana invariably involves smoking a joint. The inhalation route of administration is associated with an early occurring maximum concentration in plasma, which is often reached before smoking ceases [11]. Users of cannabis tend to become more talkative, find it easier to laugh and converse and their thought processes are altered [2,33]. More potent forms of cannabis or more frequent and intensive use causes impairment of cognitive and psychomotor functioning, which is not compatible with safe driving [34,35]. The most pronounced behavioural effects of cannabis are, however, fairly short-lived (1–3 hours) and subside when THC concentrations decrease to low levels (< 2.0 ng/ml). Establishing a threshold concentration of THC in blood above which impairment is presumed to exist is a difficult task, owing to the complex concentration–effect relationship and the phenomenon of hysteresis [13]. Concentrations of THC in the brain are probably still rising when concentrations in the plasma or blood are already declining [12,15].

Interpreting the concentration of THC in blood in relation to the time when cannabis was last used or the risk of a crash is fraught with difficulties [36,37]. The concentrations of THC in blood at the time of blood sampling will be appreciably less than at the time of arrest, which is usually 30–90 minutes earlier, and driving, which was still earlier [12]. Back-extrapolation of the measured THC concentration from time of sampling blood to the time of driving is not an option, owing to the many variable and unknown factors involved and the complex pharmacokinetic profile of THC.

Some may consider that a zero-tolerance DUID law is a somewhat draconian measure, considering the scanty experimental evidence that low concentrations of THC in blood enhance the risk of a crash [38]. However, cannabis is an illicit drug used by people for the primary purpose of ‘getting high’ and escaping from reality, and this is not compatible with performing skilled tasks such as driving [23,39]. Drugs having their sites of action in the brain have the potential to alter a person’s behaviour in a negative manner, as shown by deterioration of cognitive, sensory and/or motor functioning. There is general consensus that cannabis use leads to reckless behaviour, especially shortly after smoking a joint, and in most countries purchase, possession, selling or growing of cannabis plants are criminal offences [40,41].

Cannabis ranks second to alcohol as the psychoactive substance used most frequently in many western nations [42,43]. The 18–30% of cases shown in Fig. 1 are those motorists with THC verified in blood, although others had carboxy-THC in urine, which also verifies use of cannabis. Evidence supporting a ban on the use of cannabis before driving comes from epidemiological surveys of road-traffic fatalities with assessment of culpability for the crash [44,45]. In addition, controlled laboratory studies of cognitive and psychomotor functions after use of cannabis and, most convincingly, reports of actual driving performance [28,42,46,47]. Case–controlled studies of crash risk as a function of the concentration of THC in blood are, however, lacking, owing to the less frequent use of cannabis compared with alcohol and the difficulty in obtaining a sizable control group of drivers.

Some might argue that a zero-limit or LOQ limit for THC in blood would mean that people exposed passively to cannabis smoke run the risk of being charged with DUID. However, several controlled studies have shown that the risk of reaching measurable amounts of THC in blood after passive inhalation is virtually non-existent [48–50]. However, it is more likely that carboxy-THC, which is an inactive metabolite of THC, might be detected in urine after passive smoking [51,52]. Zero-limit DUID laws for cannabis based on analysis of carboxy-THC in blood or urine lack scientific support and cannot be defended. Another argument against analysing carboxy-

Table 4 Age, gender and concentrations of Δ^9 -tetrahydrocannabinol (THC) in blood from individuals arrested for use of illicit drugs (non-traffic cases) over a 10-year period.

<i>Use of illicit drugs (non-traffic cases)</i>	<i>Gender</i>	<i>n (%)</i>	<i>Age, years mean \pm SD</i>	<i>Blood THC (ng/ml) Mean (median) highest</i>
THC alone	Men	2292 (92)*	26 \pm 8.4	2.5 (1.0) 36
	Women	187 (8)	26 \pm 8.5	2.4 (1.0) 28
	Both	2479 (100)	26 \pm 8.4	2.5 (1.0) 36†
THC + other drugs	Men	4804 (91)*	30 \pm 8.3	1.7 (1.0) 35
	Women	467 (9)	29 \pm 8.0	1.4 (0.8) 12
	Both	5271 (100)	30 \pm 8.3	1.6 (1.0) 35
THC all cases	Men	7096 (92)*	29 \pm 8.5	1.9 (1.0) 36
	Women	654 (8)	28 \pm 8.3	1.7 (0.9) 28
	Both	7750 (100)	29 \pm 8.5	1.9 (1.0) 36

*Higher proportion of men than women ($P < 0.001$). †THC concentrations in blood significantly greater when this was the only drug present compared with multi-drug users ($P < 0.001$).

Table 5 Occurrence of Δ^9 -tetrahydrocannabinol (THC) alone or in combination with other recreational drugs in blood of apprehended drivers shown as function of mean age [\pm standard deviation (SD)] and mean (median) and maximum concentration of THC between 2000 and 2004.*

<i>Drug combinations</i>	<i>n (%)</i>	<i>Age, years Mean \pm SD†</i>	<i>Blood THC, ng/ml† mean (median) highest</i>
THC alone	1079 (14.1)	28 \pm 9.3	3.7 (2.0) 67
THC + alcohol‡	291 (3.8)	33 \pm 10.1	2.3 (1.0) 28
THC + amphetamine	2647 (34.5)	37 \pm 8.6	1.7 (1.0) 38
THC + amphetamine + alcohol‡	158 (2.1)	39 \pm 9.7	1.9 (1.0) 11
THC + amphetamine + benzodiazepines§	1193 (15.7)	33 \pm 8.7	1.4 (0.9) 19
THC + benzodiazepines§ + alcohol‡	140 (1.8)	30 \pm 9.2	2.5 (2.0) 13
THC + amphetamine + opiates	82 (1.1)	36 \pm 8.6	1.3 (0.9) 6
THC + all prescription drugs§	625 (8.2)	26 \pm 8.0	3.2 (2.0) 46
All other combinations of drugs with THC	1391 (18)	31 \pm 8.7	2.0 (1.0) 45
All cases 2000–2004	7606 (100)	33 \pm 9.6	2.1 (1.0) 67

*The blood samples were for a 5-year period 2000–04 ($n = 7606$ cases) because laboratory routines changed after 1999 regarding selection of samples for analysis if they contained alcohol. †Statistically significant differences in mean age and median concentration of THC depending on which other substances were identified in blood samples. ‡Blood alcohol concentration > 0.2 mg/g (0.02 g% or 20 mg/100 ml). §Mainly sedative-hypnotics but not opiates.

THC is that there could be residual amounts still measurable in blood and urine several days or weeks since last use [31,53].

Cannabis and its preparations are popular recreational drugs, although there are mixed feelings among policy makers about reclassification as a controlled substance and also whether cannabis-related products should be made available on prescription for certain medical conditions [1,54,55]. The argument for establishing a science-based punishable THC limit akin to the prescribed blood-alcohol concentration (BAC) limits is hard to motivate. The BAC limit varies fourfold between countries; 20 mg/100 ml (Norway, Sweden), 50 mg/100 ml (most European Union countries) and 80 mg/100 ml; (United States, Canada, Great Britain and Ireland). Establishing these blood-alcohol limits seems to

depend more on politics and alcohol policy in the countries concerned rather than scientific research.

Whether the apprehended drivers in this study with THC in blood exhibited signs and symptoms of drug influence is not available for evaluation and cannot be commented upon. However, the police must have suspected that a driver was unfit to drive or had used an illicit drug in order to proceed with obtaining blood for toxicological analysis [17]. Such indicators as the smell of cannabis inside the vehicle, discovery of drug paraphernalia or finding the drug itself will obviously warrant further investigation. A commonly recorded finding on the police arrest forms in those drivers apprehended with THC in blood was their bloodshot eyes.

The frequency distributions of THC concentrations reported here (Figs 3 and 4) are of interest to those who

Table 6 Number and cumulative percentage of driving under the influence of drugs suspects with Δ^9 -tetrahydrocannabinol (THC) in blood alone (THC only) or with other licit or illicit drugs sorted as a function of the concentration of THC.

Blood THC, ng/ml	THC + other drugs <i>n</i> * (cumulative %)	THC only <i>n</i> † (cumulative %)
0.3–0.9	3767 (43%)	333 (26%)
1.0–1.9	1533 (61%)	180 (41%)
2.0–2.9	1444 (77%)	239 (60%)
3.0–3.9	718 (85%)	143 (71%)
4.0–4.9	419 (90%)	74 (77%)
5.0–5.9	256 (93%)	73 (83%)
> 6.0	657 (100%)	234 (100%)

*All cases with THC in blood (*n* = 8794). †Cases with only THC in blood (*n* = 1276).

advocate science-based *per se* concentration limits of THC in blood for driving. A THC concentration in serum of between 7 and 10 ng/ml, which corresponds to 3.5–5.0 ng/ml in whole blood, was suggested recently as a threshold *per se* limit for prosecution [21,22]. If a threshold THC concentration of 5.0 ng/ml in blood was adopted, the results in Table 6 show that between 77% and 90% of people who had used cannabis before driving would not be liable to prosecution.

One consequence of a zero-tolerance or LOQ law is that many people will be liable to prosecution with only a trace amount of THC in blood (LOQ in our laboratory is 0.3 ng/ml). This might be hard to accept by supporters of an impairment-based DUID law, and the issue of residual THC after a period of heavy use of cannabis might need to be considered. The high solubility of THC in fat makes it likely that after prolonged daily use of cannabis there will be an accumulation of this drug in lipid compartments and a slow washout into the bloodstream after termination of use. Indeed, there is evidence that THC and its metabolites can be detected in heavy users 24 and 48 hours after last use of the drug [31].

It is worth remembering that in most countries it is illegal to buy, sell, possess or use cannabis for recreational purposes. Moreover, experience has shown that the vast majority of DUID offenders are polydrug users (Table 5) and re-arrests are very frequent, making it easier to motivate enforcement of zero-tolerance legislation [56,57]. Some countries, such as Switzerland, have set a higher THC concentration threshold for prosecution (1.5 ng/ml) in blood. This clearly accords the benefit of the doubt to people who might have smoked a joint 12 or more hours earlier or claim that they were passively exposed to cannabis smoke before or during driving.

The fact remains that so-called zero-tolerance laws or LOQ laws for DUID reflect, to a large extent, public health attitudes about use and abuse of illicit drugs. Scientists

find it virtually impossible to agree upon the concentration of a psychoactive substance in blood that leads to impairment in the vast majority of people, owing to individual differences in response, habituation, potency of the abused drug and differences related to dose, mode of administration as well as the pharmacokinetic profile. Much depends upon the experimental design and the sensitivity of the battery of cognitive and psychomotor tests used and to what extent these resemble skills relevant for driving. Using the laboratory LOQ to establish the threshold limit for prosecution is a much more pragmatic way to enforce DUID legislation. This also sends a clear and concise message to those who use illicit drugs such as cannabis that this behaviour will not be tolerated, especially in connection with driving.

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