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The role of illicit, licit, and designer drugs in the traffic in Hungary

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ABSTRACT

The aim of this study was to investigate the prevalence and pattern of psychoactive substances among suspected DUID (Driving Under the Influence of Drugs) drivers in Hungary in 2014 and 2015. Blood and/or urine samples of 1252 suspected drivers (600 in 2014 and 652 in 2015) were analyzed for classical illicit and licit drugs, stimulant designer drugs (SDDs), and for synthetic cannabinoids, with 78.3% and 79.6% positive cases for at least one substance in 2014, and 2015, respectively. Impairment was proven in 39.2% (2014) and 35.7% (2015) of all drivers tested, based on the legal criteria of Hungary. Classical illicit drugs were found to be present in blood or urine of 89–61%, drivers tested. Drivers also tested positive for legal medications in 20–22%, SDDs in 21–28%, and synthetic cannabinoids in 15–19% of all cases. This indicates a drop in prevalence for classical illicit drugs and a slight but statistically non-significant increase for the other three substance groups. The distribution of drug types in each category were: [1] classical illicit drugs: cannabis (432), amphetamine (321), and cocaine (79); [2] medicines: alprazolam (94) and clonazepam (36); [3] SDDs: pentedrone (137) and α-PVP (33); [4] synthetic cannabinoids: AB-CHMINACA (46) and MDMB-CHMICA (30). The average age of illicit drug and SDD users was 30 years, while legal medications users were 36 years old on average, and the mean age of synthetic cannabinoid users was 26.5 years. The presence of both alcohol and at least one drug in samples was found in about 10% of the cases, both years. The ratio of multi-drug use was 33.0% in 2014 and 41.3% in 2015.

Compared to former years the number of drivers who tested positive for drugs doubled in Hungary, but it is still low compared to alcohol positive cases. The relatively low detected rate of DUID can be explained by (1) combined alcohol consumption masking drug symptoms, (2) the absence of road-side tests for illicit and designer drugs and, (3) police officers not adequately trained to recognize milder symptoms of impairment. Targeted education of police officers, prompt medical examination and the use of a symptom-focused on-site survey, could improve the efficacy of DUID investigations.

Our findings are not comparable with drug consumption habits of the general driving population. The last roadside survey (DRUID EU-6 Project) was performed in Hungary in 2008–2009, prior to the mass

Abbreviations: SDDs, stimulant designer drugs; 4-BMC, 4-bromomethcathinone; 4-CMC, 4-chloromethcathinone; mCPP, m-chlorophenyl-piperazine; EDDP, 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine; 4F-α-PEP, 4-fluoro-α-pyrrolidinoheptiophenone; 2-FMC, 2-fluoromethcathinone; 4-MA, 4-methylamphetamine; 4-MeBu, 4-methylbuphedrone; 4-MEC, 4-methylethcathinone; 2-MeOD, 2-methoxy-diphenidine; 3-MMC, 3-methylmethcathinone; MeOPh, methoxyphenidine; MPA, methiopropamine; bk-MPA, 2-(methylamino)-1-(thiophen-2yl)propan-1-one; α-PEP, α-pyrrolidinoheptiophenone; α-PHP, α-pyrrolidino-hexanophenone; α-PVT, α-pyrrolidino-pentiothiophenone; α-PVP, α-pyrrolidinovalerophenone; AB-CHMINACA, *N*-[(2*S*)-1-amino-3-methyl-1-oxobutan-2-yl]-1-(cyclohexylmethyl) indazole-3-carboxamide; AB-FUBINACA, *N*-[(2*S*)-1-amino-3-methyl-1-oxobutan-2-yl]-1-[(4-fluorophenyl)methyl]indazole-3-carboxamide; AKB 48, *N*-(1-adamantyl)-1-pentylindazole-3-carboxamide; AB-PINACA, *N*-[(1*S*)-1-(aminocarbonyl)-2-methylpropyl]-1-pentyl-1*H*-indazole-3-carboxamide; ADB-FUBINACA, *N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(4-fluorobenzyl)-1*H*-indazole-3-carboxamide; AKB 48F, *N*-(adamantan-1-yl)-1-(5-fluoropentyl)-1*H*-indazole-3-carboxamide; 5F-AB-PINACA, *N*-[(2*S*)-1-amino-3-methyl-1-oxobutan-2-yl]-1-(5-fluoropentyl)indazole-3-carboxamide; JWH-018 (mb), **JWH-018 *N*-pentanoic acid**: 5-(3-(1-naphthoyl)-1*H*-indol-1-yl)pentanoic acid; MAM-2201, (1-(5-fluoropentyl)-1*H*-indol-3-yl)(4-methyl-1-naphthalenyl)-methanone; MAB-CHMINACA, *N*-[(2*S*)-1-amino-3,3-dimethyl-1-oxobutan-2-yl]-1-(cyclohexylmethyl)indazole-3-carboxamide; MDB-CHMICA, methyl (2*S*)-2-{[1-(cyclohexylmethyl)-1*H*-indol-3-yl]formamido}-3,3-dimethylbutanoate; MDMB-CHMICA, methyl (2*S*)-2-{[1-(cyclohexylmethyl)-1*H*-indol-3-yl]formamido}-3,3-dimethylbutanoate; PB-22, 1-pentyl-1*H*-indole-3-carboxylic acid 8-quinolinyl ester; UR-144 (mb), UR-144 *N*-pentanoic acid: 5-(3-(2,2,3,3-tetramethylcyclopropanecarbonyl)-1*H*-indol-1-yl)pentanoic acid; 6AM, 6-acetylmorphine; BZE, benzoyl-ecgonine; CNS, central nervous system; DUID, Driving Under the Influence of Drugs; HIFS, Hungarian Institute for Forensic Sciences; NPS, new psychoactive substances.

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spreading of designer drugs. As their appearance has drastically changed the pattern of drug consumption of the population, a new roadside survey, targeting general drivers, would be necessary.

1. Introduction

Driving under the influence of illicit and licit drugs (DUID) has been punishable in Hungary since July 1999. According to data from Country Police Headquarters approximately 10–15,000 alcohol impairment cases per year were taken to court between 2000 and 2010 (personal communication) but drug impairment was proven in less than 120 cases per year [1]. The real number of DUID cases, however, is probably much higher. A roadside survey demonstrating a higher incidence of DUID was conducted (DRUID EU-6 project) in Csongrád County (South-East Hungary, ~420,000 inhabitants), during which oral fluid samples of 2738 randomly stopped car drivers were analyzed for illicit and licit drugs in 2008–2009. The prevalence of medications that act on the central nervous system (CNS) was 3.14% and that of illicit drugs was 0.99%. Breath alcohol was also tested and was positive in 0.13% of the cases [2]. Among drivers who died in accidents in South-East Hungary (involving four counties with about 1,390,000 inhabitants) 10.7% were positive for licit drugs, 4.92% for illicit drugs, and 33.6% for alcohol during the same investigation period [3]. According to the results of these studies the ratio of DUID drivers must be much higher than it was proved between 2000 and 2010.

The widespread appearance of designer drugs has changed the pattern of drug consumption among drug users in the last five years. As there are no data available describing the frequency of designer drug consumption in general and by suspected DUID drivers in Hungary, the aim of this study was to investigate the frequency of abuse among suspected and proven DUID drivers in 2014–15 of legal psychoactive medications, classical illicit drugs, as well as new psychoactive substances.

2. Materials and methods

Blood and urine samples of 600 suspected DUID drivers were analyzed in 2014 and samples of 652 drivers in 2015. Results of subjects positive for alcohol alone were not included in the current study. Around 80–90% of the nationwide collected samples were analyzed by the National Institute of Forensic Toxicology in Budapest. The samples collected from Csongrád and Pest Counties, as well as from Districts III, VIII, and IX in Budapest were analyzed in other institutes. These regions involve about 18% of the inhabitants in Hungary. Due to the lower number of analytes identified in these institutes their results are not involved in this study.

Initial dilution, protein precipitation and centrifugation of our samples were followed by a liquid chromatography–tandem mass spectrometry assay in which classical drugs and designer drugs were identified by one MRM-transition, except for synthetic cannabinoids and their metabolites, 3,4,5-trimethoxy-amphetamine, 5-MeO-AMT, 4-MeO-α-PVP, 3,4-CTMP, 3-MeO-PCP, 4-MeO-PCP, 2C-P, fentanyl, GHB, morphine and morphine-D6-glucuronide, which were identified by two MRM-transitions. Benzodiazepines and barbiturates were identified by three MRM-transitions. After this primary screening, confirmatory analysis of the positive samples was performed according to Table 1. Details of the confirmatory UHPLC–MS/MS method for synthetic cannabinoids: all targets were identified by three MRM-transitions, default ion allowance was 30% in absolute reference ion mode, S/N values needed to be over 10, in the calibration curve the accuracy of the calibration points had to be within the range of 70%–130%. The mean of the precision for the quantified analytes was 10.2 RSD% at concentration of 0.1 ng/ml and 8.5 RSD% at concentration of

Table 1
Scheme of **v**erification of blood and urine samples tested positive during screening and direct analysis of blood samples.

Groups of substances	Sample	Extraction and derivatization	Instrumental analysis	No. of analytes
Amphetamines, cathinones, other basic drugs	Blood and urine	LLE, toluene, *on-line* deriv. by MBTFA	GC–MS, SIM	150
Ketamine derivatives, methadone, tramadol etc.	Blood and urine	LLE, toluene	GC–MS, SCAN	10
Cannabinoids	Blood Urine	SPE, deriv. by methyl iodide alkaline hydrolysis, SPE	GC–MS, SIM HPLC-DAD	4
Synthetic cannabinoids[a]	Blood Urine	SLE Enzymatic hydrolysis and SLE	UHPLC–MS/MS	100
Cocaine and metabolites	Blood Urine	SPE	HPLC–MS HPLC-DAD, HPLC–MS	3
Opiates	Blood Urine	SPE Enzymatic hydrolysis, SPE, deriv. by MSTFA	HPLC-MS GC–MS	12
GHB	Blood and urine	LLE, deriv. by MSTFA	GC–MS	1
Benzodiazepines and Z-drugs	Blood Urine	SPE	HPLC-DAD, HPLC–MS HPLC-DAD	44

No. of analytes: the total number of different analytes that can be detected by the methods.
LLE: liquid–liquid extraction, SPE: solid phase extraction, SLE: supported liquid extration, MBTFA: *N*-methyl-bis-trifluoroacetamide, MSTFA: *N*-methyl-*N*-(trimethylsilyl) trifluoroacetamide, deriv.: derivatization, GC–MS: gas chromatography–mass spectrometry, HPLC-DAD: high performance liquid chromatography with diode array detection, HPLC–MS: high performance liquid chromatography–mass spectrometry, UHPLC–MS/MS: ultra high performance liquid chromatography–tandem mass spectrometry, SIM: selective ion monitoring mode, SCAN: scanning mode.
[a] Analysis was directed to 64 mother compounds and 36 metabolites.

30.0 ng/ml, the mean of the bias was 106% and 100% at the concentrations of 2.0 and 12.0 ng/ml, respectively. The mean of the limit of detection for the quantified analytes was 0.008 ng/ml (the highest value was 0.038 ng/ml) and the mean limit of quantitation was 0.027 ng/ml (the highest value was 0.127 ng/ml). For the linearity the correlation coefficient (r^2) was above 0.97 for all quantified analytes within the range of 0.05 and 30.0 ng/ml.

The analytes identified, their cut off values, and the concentration intervals found in blood and urine samples are listed in Table 2. With the support of the Hungarian Institute for Forensic Sciences (HIFS) we used purified seized materials as standards for several designer drugs in the absence of certified chromatographic standards. In these cases only qualitative analyses were possible until certified standards became available. Qualitative results alone were collected for the following substances: 3-MMC, 4-MA, α-PVT, α-PEP, 4F-α-PEP, α-PHP, 4-CMC, bk-MPA, 2-FMC, mCPP, 4-BMC, 2-MeOD, 4-MeBu, AKB48, AB-PINACA, 5F-AMBICA, MDMB-CHMICA, ADB-PINACA, MDP-CHMICA, MAB-CHMINACA, MAM2201, 5F-MDMB-PINACA, MDMB-FUBICA, and AMB-FUBINACA, while both qualitative and quantitative results for EDDP, ethylone, pentedrone, 4-MA, α-PVP, AB-FUBINACA, ADB-FUBINACA, and AB-CHMINACA, JWH-200, 6-OH-indole-, JWH-250, *N*-5-OH-pentyl-, JWH-073, JWH-073, *N*-4-OH-butyl-, JWH-018, JWH-018 *N*-pentanoic acid, JWH-018, *N*-5-OH-pentyl-, JWH-018, *N*-5-OH-pentyl-, AM2201, *N*-4-OH-pentyl-, AM2201, 5/6-OH-indole-, JWH-081, JWH-081, *N*-5-OH-pentyl-, MAM2201, *N*-4-OH-pentyl-, JWH-019, *N*-6-OH-hexyl-, JWH-122, JWH-122, *N*-5-OH-pentyl-, UR-144 *N*-pentanoic acid, AKB48F, AKB48 *N*-pentanoic acid, AKB48, *N*-5-OH-pentyl-, JWH-018, 5-OH-indole-, JWH-210, JWH-210, 5-OH-indole-, EAM2201, PB-22, JWH-122, *N*-4-pentenyl-, THJ-018.

In Hungary, if a driver is suspected to be impaired during traffic control or in accidents without personal injury, breath alcohol is checked and, depending on the decision of the police after the

Table 2
Substances with quantitative results, their cut offs, concentration intervals, and median.

Substances	Cut off (ng/ml)		cc. interv.	Median	N	cc. interv	Median	N
	Blood	Urine	Blood (ng/ml)			Urine (ng/ml)		
Amphetamine	3	200	4–830	52.9	207	230–217,570	5195	297
MA	3	200	9.5–454	63.9	42	340–174,940	13570	55
MDA	3	200	6.6–157	20.0	9	250–5640	1400	32
MDMA	3	200	10.6–653	47.3	31	280–70,470	8775	48
THC	1	n.a.	1.2–12.5	3.66	132			
THC-OH	1	n.a.	1.2–20.1	2.5	94			
THC-COOH	2	5	3.5–135	21.0	291	8.10–5157	145	419
Cocaine	10	300				330–35000	3285	20
BZE	10	300	18.6–511	95.8	35	339–277,100	20700	67
6AM	5	5				163		1
Morphine	10	500	20.6		1	568–10,000	3000	11
Codeine	10	250	18.8		1	293–1861	472	7
GHB (μg/ml)	4	10	44.3–87.1		4	115–50,000	252	6
Tramadol	50	300	86.7–321	200	10	690–25,000	3000	8
Methadone	50	200	66.2–436		3	240–13,700	3000	10
Ketamine	10	100	61.0–436	233	8	610–15,000	3000	13
Alprazolam	5	5	6.0–346	63.0	77	7.8–370	51.9	64
Clonazepam	5	5	19.7–420	68.6	26	25.4–160	53.4	12
Diazepam	5	5	67.6–158	81.6	6			
Nordiazepam	5	5	225–266		2	13.9–266		3
Temazepam	5	5				75		1
Oxazepam	5	5				170		1
Carbamazepine	5	5	97.6–7540		4	22.4–2768		4
Lorazepam	5	5	106		1	2649		1
Cinolazepam	5	5				595		1
Midazolam	5	5	27.0–41.7		2	19.1–27.2		2
Zolpidem	5	5	100–758	192	5	304–1443		3
Zopiclone	5	5				50		1
Pentedrone	3	200	5.8–440	62.4	56	300–83,500	6600	113
4-MA	3	200	56		1	1500		1
3-MMC	3	200	26		1			
α-PVP	3	200	130–284		3	310–32,240	2935	16
4-MEC	3	200				990–4100		2
MPA	3	200	338		1			
JWH-018 (mb)	0.1	0.1	0.6		1	1.3		1
AKB 48	0.1	0.1	0.2–10.2		2			
AKB 48F	0.1	0.1	1.5–0.7		2			
AB-PINACA	0.1	0.1	2.01		1			
AB-FUBINACA	0.1	0.1	0.56–0.98		2			
MAM-2201	0.1	0.1	0.12		1			
PB-22	0.1	0.1	0.2–0.33		3			
AB-CHMINACA	0.1	0.1	0.27–22.6	1.9	17	0.5–3.79	1.0	10
MDMB-CHMICA	0.1	0.1	0.21–10	1.19	10			
MDB-CHMICA	0.1	0.1	5.49		1			
MAB-CHMINACA	0.1	0.1	2.48–25.9		3			
ADB-FUBINACA	0.1	0.1	0.27–10.0		3	0.22–10.0		3
UR-144 (mb)	0.1	0.1				10.6		1
5F-AB-PINACA	0.1	0.1	0.41		1			

Median is given if the number of quantitative results was ≥5 (about 1% of positive samples), N—number of positive samples with quantitative results, n. a.—not adequate, cc. interv.: concentration interval; UR-144 (m): UR-144 *N*-pentanoic acid metabolite; JWH-018 (mb): JWH-018 *N*-pentanoic acid metabolite.

Table 3
Gender and age distribution of positive cases.

Gender	2014		2015	
	Absolute	%	Absolute	%
Men	445	95.5	415	95.6
Women	21	4.5	19	4.4
Total	466	100	434	100

Age groups	2014		2015	
	Absolute	%	Absolute	%
<25	138	30.7	119	27.2
25–34	200	44.5	195	45.3
35–44	87	19.4	92	21.4
>45	24	5.4	26	6.1
Total	449	100	432	100
Average age	Men	Women	Men	Women
	29.3 ± 7.41 (SD)	30.1 ± 10.1 (SD)	30.3 ± 8.52 (SD)	35.1 ± 9.63 (SD)

$p > 0.05$ in all cases when comparing the 2014 and 2015 data.

investigation on the spot, the suspect is transferred to a medical ward for blood and urine sampling and for medical examination. Medical examination (pupil reaction, nystagmus, Romberg probe, finger-to-nose probe, speaking disturbance, orientation, behavior) was performed by a medical doctor to determine whether the person shows clinical signs of impairment. In accidents with personal injury medical investigation and sampling are compulsory. Immunological urine test is allowed but it is informative only for classical drugs and medicines but not for designer drugs, and the positive results always require verification. If a subject is injured in an accident, sampling and medical investigation (if possible) are performed at the medical ward, hospital or clinic where the patient is transferred to. In case of fatal outcomes samples are taken during autopsy.

According to the current practice impairment is proven if: (1) the blood/serum concentration of a classical illicit drug or alcohol exceeds the impairment limit (THC: 2 ng/ml; morphine: 20 ng/ml; amphetamine, MA, MDMA, cocaine, and benzoyl-ecgonine: 50 ng/ml, GHB: 30 μg/ml, blood alcohol: 0.5 g/l, breath alcohol: 0.25 mg/l); (2) the concentration of an illicit drug (which has no impairment limit) or of a designer drug is over the detection limit and the person produces clinical signs of impairment during the medical investigation; (3) the concentration of a medically prescribed drug acting on the central nervous system (CNS) reaches the lower limit (occasional users) or exceeds the upper limit of the therapeutic range; (4) or, in multiple-drug users the concentration of two or more substances (including alcohol) exceeds the detection limit. Blood and urine alcohol concentrations were measured in a different institute and these results were not available for us. It can cause bias in cases when a driver is seriously injured or died in an accident and breath alcohol determination is not possible. These cases are involved in the category “Breath alcohol determination was not performed or registered” in Table 4.

Finally, our results were compared to the nationwide data of illicit and designer drug seizures provided by the HIFS. Statistical analysis was performed by the chi-square test setting the probability level to $p < 0.05$.

3. Results

In 2014, samples of 600 suspected impaired drivers were analyzed resulting in 470 (78.3%) positive tests for at least one substance, and impairment was proven only in 235 cases (39.2%). In 2015, 519 (79.6%) of 652 subjects tested positive, and 233 (35.7%) were documented as impaired. There was no difference in the gender and age distribution of positive cases between the two years. The average age in 2014 for men was 29.3 ± 7.41 years and was 30.1 ± 10.1 years for women, and similarly 30.3 ± 8.52 years for men and 35.1 ± 9.63 years for women in 2015 (Table 3).

The deficiencies in driver testing are listed in Table 4. Breath alcohol was not determined or registered in 36–39%, and medical examination was not performed or registered in 13–20% of cases. Only urine samples were taken from 17 to 26% of suspects, which is sufficient to prove consumption but not impairment. The time of sampling was not registered in 11–23% of cases, and the average time period between the event and the medical investigation was too long (about 3 h). Documentation was incomplete in 41.5% of all drivers tested in 2014 and 62.1% in 2015 ($p < 0.05$) but the ratio of incomplete documentation was significantly lower for those who were deemed impaired (34.5% and 35.6%, respectively; $p < 0.05$ in both years).

Among impaired drivers clinical signs were not registered in 15 (2014), and in 30 cases (2015), and negative clinical signs were found in 84 and 67 cases, respectively. In these cases the drivers were classified as impaired because (1) the blood concentration of an active substance or breath alcohol level exceeded the impairment limit (50 out of 235 cases in 2014, and 33 out of 233 cases in 2015) or (2) two or more active substances were detected (49 cases in 2014, and 64 cases in 2015). Drivers with positive clinical signs were deemed impaired when one or more active substance was detected, including alcohol (Table 5).

In 2014, 257 subjects were tested for breath alcohol and 53 of them (20.7%) were positive. The number of positive cases was 50 out of 263 drivers (19.0%) tested in 2015. The percentage of positive cases for alcohol was 8.83% in 2014 and 7.67% in 2015 in the whole driving population while for impaired drivers it was 22.6% and 21.5%, respectively. The average breath alcohol concentrations were 0.550 and 0.532 mg/l, respectively (Table 6).

Classical illicit drugs were present in 88.5% (2014) and 60.6% (2015) of all drivers tested ($p < 0.05$). The most common classical illicit drug among suspected DUID drivers was cannabis, followed by amphetamines and cocaine. The proportion of medicines acting on the CNS was 20.2% in 2014 and 22.4% in 2015 ($p > 0.05$). The most prevalent medicines were alprazolam and clonazepam, while the frequency of other benzodiazepines, zolpidem and tramadol was lower. The frequency of stimulant designer drugs slightly increased from 21.2% to 27.9% but it was not statistically significant ($p > 0.05$). Pentedrone was the most frequent one in both years followed by α-PVP and 3-MMC in 2014, and by α-PVP, α-PHP, and 4-CMC in 2015. The ratio of synthetic cannabinoids was similar in

Table 4
Deficiencies in driver testing.

Sample	2014 N = 600	2015 N = 652
Breath alcohol determination was not performed or registered	218 (36.3%)	253 (38,8%)
Medical examination was not performed or registered	76 (12.7%)	133 (20.4%)
Only urine sample was taken	102 (17.0%)	169 (25.9%)
Time of sampling was not registered	66 (11.0%)	150 (23.0%)[+]
Average time period until sampling (mean ± SD)	182 ± 157 min	167 ± 125 min
Incomplete documentation	249 (41.5%)	405 (62.1%)[+]
Impaired cases	**2014 N = 235**	**2015 N = 233**
Breath alcohol determination was not performed or registered	70 (29.8%)[*]	75 (32.2%)[*]
Medical examination was not performed or registered	15 (6.38%)[*]	30 (12.9%)[*]
Time of sampling was not registered	27 (11.5%)	37 (15.9%)[*]
Incomplete documentation	81 (34.5%)[*]	83 (35.6%)[*]

[*] $p < 0.05$ versus the corresponding data of the sample.
[+] $p < 0.05$ between 2014 and 2015.

Table 5
Results of medical investigation of impaired drivers and deem of impairment.

	2014	2015
Number of impaired drivers	235	233
Positive clinical signs	136	136
Negative clinical signs	84	67
Medical investigation is not performed or documented	15	30
Deem of impairment		
Drivers with positive clinical signs		
According to impairment limit	34	49
Presence of an active substance without impairment limit	20	12
Multi-drug use	82	75
Drivers with negative clinical signs or with missing documentation		
According to impairment limit	50	33
Multi-drug use	49	64

the two years (15.1% and 19.0%, respectively, $p > 0.05$). AB-CHMINACA, AB-FUBINACA and AB-PINACA were the most prevalent synthetic cannabinoids in 2014, while MDMB-CHMICA, ADB-FUBINACA, and MDMB-FUBICA in 2015. The three most popular synthetic cannabinoid in 2014 were also detected in biological samples in 2015 but with lower frequency (Table 7).

The frequency ranking of substances in blood samples of impaired drivers corresponded to their frequency in the total driver population tested (Table 7). While prevalence of classical illicit and licit drugs as well as SDDs was nearly the same in 2014 and 2015, the frequency of synthetic cannabinoids doubled in 2015 ($p < 0.05$).

The ratio of multi-drug users was 33.0% (198 of 600) in 2014 and 41.3% (269 of 652) in 2015. All substances were present more frequently in combination than alone, except for cannabis and pentedrone (Table 8).

The average age of positively tested subjects was ~30 years for classical illicit drugs, 35–37 years for medicines, 30–31 years for SDDs, and 25–28 years for synthetic cannabinoids. The percentage of males varied between 96.6 and 100% for all substance groups, except for medicines (it was only 85.3% and 86.4%, respectively).

The most frequent age groups for illicit drugs and SDDs were 25–34 years both in 2014 and 2015, for medicines they were 25–34 years in 2014 and 35–44 years in 2015, for synthetic cannabinoids <25 years in 2014, and 25–34 years in 2015. The shift in age distribution of synthetic cannabinoids towards the older age-groups was statistically significant ($p < 0.05$, Table 8,Fig. 1). Sixty percent (12) of the 20 females tested positive for medicines were ≥35 years while this ratio was only 43.8% in the male population (53 of 121). This suggests that women ≥35 years are more often take medicines during driving than men. No information was available about the ratio of prescribed medicine users.

The number of drug seizures in Hungary between 2010 and 2015 is presented in Table 9. As compared to the 2010–2013 data the number of seizures increased in 2014–15 for the majority of substances and substance groups. A decrease was observed for cannabis plant and pills containing cathinones while marihuana seizure rate was nearly constant.

4. Discussion

Several epidemiological studies were performed in Europe to investigate the frequency of DUID cases but variations in study design (different substances measured, cut off values, etc.) make it difficult to compare previous findings to results from the current study [4]. In these studies, the percentage of positive cases for illicit and licit drugs among suspected DUID drivers varied between 70–90%, but the ratio where impairment was also proven was not reported [5–8]. Depending on the legislative background, different algorithms are used to determine impairment in European countries. Some countries use an approach to determine legal liability, dependent on whether a driver shows clear symptoms of impairment in his personal behavior or driving style. This approach is susceptible to error if the time interval between arrest and behavioral assessment is long (e.g. hours). It is possible that the clinical signs of impairment might wane in the interim. In most

Table 6
Breath alcohol determination.

	2014 n = 257	2015 n = 263
Positive	53 (20.6%)	50 (19.0%)
Related to all drivers investigated	8.83%	7.67%
Related to impaired drivers	22.6%	21.5%
Average breath alcohol concentration (mg/l)	0.550 [0.05–1.49]	0.532 [0.03–1.11]

Table 7
Frequency of classical illicit drugs, medicines, SDDs, and synthetic cannabinoids in samples from suspected DUID drivers.

Illicit drugs	2014				2015			
	88.5%[a]			71.5%[b]	60.6%[a,*]			61.8%[b]
	Alone	Comb.	Sum	IMP	Alone	Comb.	Sum	IMP
Cannabis	121	83	204	83	119	109	228	81
Amphetamine	43	114	157	86	41	123	164	85
MA	2	15	17	13	3	29	32	19
MDMA	2	21	23	15	1	26	27	12
Cocaine	10	33	43	14	8	28	36	9
Morphine (Heroin)	1	2	3	0	2	7	9	1
Codeine	0	3	3	0	0	4	4	1
Methadone	0	6	6	2	0	5	5	1
Ketamine	3	6	9	2	1	4	5	0
GHB	1	0	1	1	0	4	4	3
Total	183	299	482	216	175	339	514	211

Medicines	2014				2015			
	20.2%[a]			20.0%[b]	22.4%[b]			19.7%[b]
	Alone	Comb	Sum	IMP	Alone	Comb	Sum	IMP
Alprazolam	23	15	38	28	23	33	56	33
Clonazepam	7	8	15	9	9	12	21	10
Diazepam	2	3	5	3	0	1	1	1
Other benzodiazepines	4	5	9	4	1	3	4	1
Zolpidem	2	2	4	3	2	0	2	2
Tramadol	1	7	8	3	2	6	8	1
Total	39	40	79	50	37	55	92	48

SDDs	2014				2015			
	21.2%[a]			17.0%[b]	27.9%[a]			20.1%[b]
	Alone	Comb.	Sum	IMP	Alone	Comb.	Sum	IMP
Pentedrone	32	24	56	21	42	39	81	21
α-PVP	2	15	17	7	5	11	16	3
α-PEP	1	3	4	2	1	0	1	0
α-PHP					6	10	16	4
3-MMC	2	5	7	3	0	7	7	3
3-FMC	0	2	2	0				0
4-MA					0	4	4	2
4-CMC					3	16	19	2
Others	0	4	4	4	1	5	6	5
Total	35	54	89	37	58	92	150	40

Synthetic cannabinoids	2014				2015			
	15.1%[a]			11.5%[b]	19.0%[a]			22.4%[b,*]
	Alone	Comb.	Sum	IMP	Alone	Comb.	Sum	IMP
AB-CHMINACA	17	16	33	18	3	10	13	7
AB-FUBINACA	6	1	7	3	0	4	4	1
AB-PINACA	3	3	6	1	0	2	2	2
AKB-48	1	4	5	2	0	2	2	0
5-F-AMBICA	2	1	3	1	0	6	6	2
MDMB-CHMICA	1	1	2	1	7	21	28	23
ADB-FUBINACA					2	19	21	16
MDMB-FUBICA					2	11	13	10
ADB-PINACA					1	5	6	5
Others	3	5	8	4	2	14	16	10
Total	33	31	64	30	17	84	111	76

Comb: in combination, IMP: frequency of substances among impaired drivers.
[*] $p < 0.05$ versus the 2014 data.
[a] Percentage of all drivers tested.
[b] Percentage of impaired cases.

countries, strict dug limits are used for determining legal impairment: if a drug concentration above a defined cut off concentration is found in a driver's blood or oral fluid, the driver is prosecuted. A two-tiered system combines both approaches: a lighter penalty when drugs are present above a certain limit and heavier sanctions when the driver is also proven to be impaired [9].

In the current study, driver impairment in Hungary was proven in 235 cases in 2014 and in 233 cases in 2015 according to the national legislation as described in Section 2. Compared to former years, the number of cases doubled in 2014–15 but remained low [1]. Between 2000 and 2007, impairment was determined according to specific blood concentration limits. Due to this evaluation up to 116 impaired cases per year were confirmed [1]. The relatively low number of impaired cases in 2014–15 can be attributed to clinical signs of drug use likely going unrecognized, as quick tests for drugs are not available for the police to conduct on the spot screening. Many drugs produce less pronounced clinical signs than alcohol, especially at lower blood concentrations. As

Table 8
Gender distribution and average age of positive cases according to substance groups.

	2014		2015	
	Absolute	%	Absolute	%
Illicit drugs				
Men	314	96.6	302	97.1
Women	11	3.4	9	2.9
Average age	29.6 ± 7.29 y		29.7 ± 7.90 y	
Medicines				
Men	64	85.3	57	86.4
Women	11	14.7	9	13.6
Average age	34.7 ± 10.3 y		36.8 ± 11.2 y	
SDDs				
Men	78	97.5	99	97.1
Women	2	2.5	3	2.9
Average age	30.3 ± 7.51 y		30.8 ± 7.72 y	
Synthetic cannabinoids				
Men	55	98.2	66	100
Women	1	0.8	0	0
Average age	25.1 ± 5.74 y		28.2 ± 6.76 y	

SDDs: stimulant designer drugs.

police officers are not trained to recognize milder clinical symptoms, many positive cases may remain undetected. The method of drug administration and whether the positive subjects were occasional or regular drug users could also influence the severity of clinical symptoms. No data were provided about those factors to us. Clinical symptoms of one or more drugs can be masked, when in combination with alcohol; therefore, many subjects were likely investigated only for alcohol-related symptoms when they may have been under the influence of both drugs and alcohol. Deficiencies in driver testing could explain why impairment was confirmed only in 36–39% of all drivers tested. In a large percentage of the cases, only urine and no blood samples were taken (17% in 2014 and 26% in 2015). Although blood samples were missing in 9% more cases in 2015 than 2014, the difference was not statistically significant ($p > 0.05$). Medical investigation was not performed or documented in 13–20% of cases, and the average time period between the arrest and medical investigation was close to 3 h, during which the clinical signs of several drugs disappear. Importantly, clinical signs are essential criteria to establish impairment in Hungary when a single active substance with no impairment limit is detected in the blood.

Documentation was incomplete in 42–62% of all drivers tested and 35–36% of those who were considered impaired (Table 4). This might be the result of blood samples not being obtained from 17 to 26% of the tested drivers.

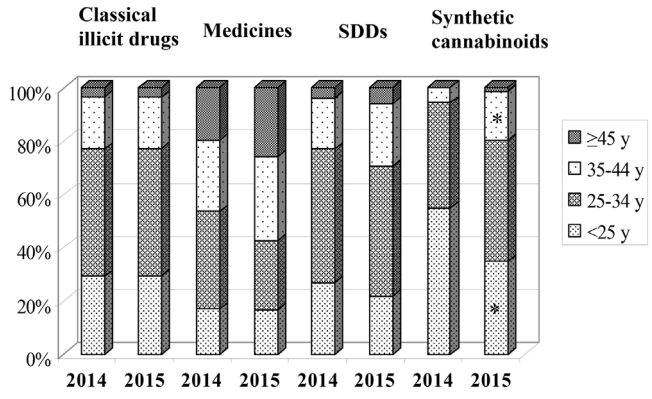

Fig. 1. Age distribution of positive cases according to substance groups (%). SDDs: stimulant designer drugs; *$p < 0.05$ versus the 2014 data.

Table 9
Number of seizures in Hungary between 2010 and 2015.

Materials	Number of seizures					
	2010	2011	2012	2013	2014	2015
Marihuana	2220	2073	2092	2040	2058	1945
Cannabis plant	213	192	193	196	146	127
Hashish	44	63	103	101	101	141
Heroin	73	22	26	32	31	48
Cocaine	132	108	118	117	143	153
Amphetamine	484	483	454	536	598	633
Metamphetamine	41	33	38	50	54	62
Ecstasy tbl. (MDMA, MDA, MDE)	9	22	91	181	213	219
Synthetic cannabinoids on plants	51	465	1298	2099	3876	2440
Synthetic cannabinoids, powder	5	51	61	60	104	90
Cathinones, powder	353	595	700	855	863	802
Cathinones, pills	60	144	174	174	40	67

Source: Hungarian Institute for Forensic Sciences, 2015.

Less than half of the suspected drivers (520 of 1252) were tested for breath alcohol. Out of the ones that were, 103 (8.2%) were determined to be positive. The breath alcohol of drivers who injured in an accident (1.5–2 g/l blood alcohol concentration) was higher than that of the overall average (0.53–0.55 mg/l) [1,10]. The simultaneous presence of alcohol and other substances in Hungary increased from 14.5 to 44.3% between 2000 and 2007 [1], and we found 8.83 and 7.67% in 2014 and 15, respectively. As these data were calculated only from cases where alcohol levels were available for us, the real percentages are probably higher. However, the penalty of drunk driving was increased in July 2013 which could have discouraged drunk driving. In comparison, the combined presence of alcohol and drugs in suspected drivers was higher in several European countries: 33% in Finland (1977–2007) [11], 18% in Denmark (1997–2006) [7], and 22% in Switzerland (2005) [8]. The ratio of multi-drug use in Hungary varied between 27–42% in the 2000–2007 time period [1] and similar results were received for 2014–15 (33–41%). In Finland for example, this ratio was 43.8% as an average between 1977 and 2007 [11].

We found a decrease in classical illicit drug prevalence, which might be due to the increasing dominance of designer drugs on the market. This tendency is also reflected by the decreasing incidence of classical illicit drug-seizures [12]. In our samples, cannabis, amphetamines, and cocaine were the most common illicit drugs, which is consistent with the frequency of those drugs in seizures (Table 8). In different European countries, the order of frequency for classical illicit drugs varies both in suspected DUID and randomly tested drivers according to the differences in black market supply and popularity [6–8,11,13,14]. The incidence of legal medications found in our samples did not considerably change compared to previous years.

In our 2-year study, the frequency of stimulant designer drugs increased by one-third in a year. Pentedrone and α-PVP were the most prevalent in both years, although they have been illegal since January 2015. In 2015, new psychoactive substances (α-PHP and 4-CMC) were detected in samples as frequently as previously established psychoactive drugs. The prevalence of synthetic cannabinoids increased in 2014 compared to previous years, but after several members of this class (AB-CHMINACA, AB-FUBINACA, AB-PINACA, and MDMB-CHMICA) were added the list of illicit drugs in January 2015, their frequency decreased, with the exception of MDMB-CHMICA (Table 6).

Overall, our data supports the general observation that the seizure of designer drugs and their presence in biological samples decreases as soon as they are included in the list of illicit drugs. From a legal prospective, until a designer drug is added on the list of New Psychoactive Substances, consumers are not punishable-only producers and distributors. Essentially, the popularity of

3 substances (pentedrone, α-PVP, and MDMB-CHMICA) outmatched the deterrent of illegal drug status and therefore the supplier system maintained them on the market. Another explanation for the discrepancy between increasing synthetic cannabinoid consumption in DUID suspects and the lower number of seizures could be the differing patterns of police activity in traffic control and illicit drug exploration during the 2 years analyzed.

It is not possible to compare the current results of this study with those of general drivers during the same time-period, as the last road-side survey targeting the general driving population in Hungary was performed in 2008–2009 (DRUID EU-6 project). That survey involved only classical illicit drugs and medications, but a number of designer drugs appeared on the black market since that time, which significantly altered the pattern of drug consumption. A new road-side survey would be necessary in order to estimate the structure and frequency of drug consumption of general drivers and to investigate their effect on traffic safety in Hungary.

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