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Prevalence of use and impairment from drugs and alcohol among trauma patients: A national prospective observational study

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ABSTRACT

Background: Being under the influence of psychoactive substances increases the risk of involvement in and dying from a traumatic event. The study is a prospective population-based observational study that aims to determine the prevalence of use and likely impairment from psychoactive substances among patients with suspected severe traumatic injury.

Method: This study was conducted at 35 of 38 Norwegian trauma hospitals from 1 March 2019 to 29 February 2020. All trauma admissions for patients aged ≥ 16 years admitted via trauma team activation during the study period were eligible for inclusion. Blood samples collected on admission were analysed for alcohol, benzodiazepines, benzodiazepine-like hypnotics (Z-drugs), opioids, stimulants, and cannabis (tetrahydrocannabinol).

Results: Of the 4878 trauma admissions included, psychoactive substances were detected in 1714 (35 %) and in 771 (45 %) of these, a combination of two or more psychoactive substances was detected. Regarding the level of impairment, 1373 (28 %) admissions revealed a concentration of one or more psychoactive substances indicating *likely impairment,* and 1052 (22 %) *highly impairment*. Alcohol was found in 1009 (21 %) admissions, benzodiazepines and Z-drugs in 613 (13 %), opioids in 467 (10 %), cannabis in 352 (7 %), and stimulants in 371 (8 %). Men aged 27–43 years and patients with violence-related trauma had the highest prevalence of psychoactive substance use with respectively 424 (50 %) and 275 (80 %) testing positive for one or more compounds.

Conclusion: The results revealed psychoactive substances in 35 % of trauma admissions, 80 % of which were likely impaired at the time of traumatic injury. A combination of several psychoactive substances was common, and younger males and patients with violence-related injuries were most often impaired. Injury prevention strategies should focus on high-risk groups and involve the prescription of controlled substances. We should consider toxicological screening in trauma admissions and incorporation of toxicological data into trauma registries.

Introduction

Traumatic injuries are among the leading causes of death and years lived with disability worldwide. Annually, 4.4 million people die because of injuries, constituting nearly 8 % of all deaths [1]. For each trauma death, an estimated 30 people are admitted to a hospital for medical treatment, and many suffer long-term reduction in physical and psychological health [2]. Deaths and disabilities caused by injuries have a major global impact on public health. Primary injury prevention, which reduces the incidence of traumatic injuries, relies on a detailed knowledge of risk factors.

Influence of psychoactive substances increases the risk of being involved in and dying from a traumatic event [3–9]. Despite this, screening for blood alcohol concentration is not routinely performed

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during trauma admissions, and additional testing for other intoxicating substances is rare in clinical settings. This is also reflected on an aggregated level where data on psychoactive substances are either absent or infrequently captured in the large national trauma registries [10–18]. Many previous studies assessing substance use among patients with traumatic injuries have focused solely on transport-related injuries [3,5,6,19–21] while others have only included alcohol intoxication in the analyses [5,21–24]. Various psychoactive substances may have significant yet diverse effects on patient physiology. Intoxication may confound patient assessment and management and is associated with higher complication rates and worse short- and long-term outcomes [25–27]. Addressing the clinical manifestations of intoxication may reduce these adverse effects.

A comprehensive description of the toxicological profile of trauma patient population is a prerequisite to understand the relationship between intoxication and injury. To our knowledge, no previous nationwide population-based study has described results from detailed toxicological analyses of blood samples obtained at trauma admission. The study aims to determine the prevalence of psychoactive substance use and estimate the level of impairment among acutely admitted trauma patients.

Methods

The study is a prospective population-based observational study that includes toxicological analysis of patients admitted for acute trauma.

Setting

Norway has a publicly funded healthcare system with 38 hospitals managing trauma patients. All trauma hospitals have multidisciplinary trauma teams to assess and manage patients with suspected severe injuries. The teams are activated by predefined criteria based on the principles described in the Centers for Disease Control and Prevention's guidelines for field triage of the injured patient [28]. All Norwegian trauma hospitals were invited to participate in a 12-month data collection period, from 1 March 2019 to 29 February 2020.

Participants

The study included all trauma patients aged 16 years or older for whom trauma teams were activated upon admission at any Norwegian trauma hospital. Foreign citizens (patients without a Norwegian national identity number) and those who could not be contacted after discharge from the hospital due to missing contact information were excluded. Furthermore, the study included only the initial hospital admissions for patients transferred between hospitals, and patients admitted multiple times for separate trauma incidences were enrolled separately.

Patient and public involvement

Representatives from the Norwegian Association of Disabled, one former patient, and a member of the National Association for the traumatically injured were actively involved in the planning and implementation of the study.

Data sources

The biological and clinical data were collected consecutively during

Table 1
Psychoactive substances included in the toxicological analysis in whole blood with three cut-off limits.

	Analytical cut-off limits ng/mL	*Cut-off limits indicating likely impaired ng/mL*	*Cut-off limits indicating highly impaired ng/mL*
Alcohol (ethanol)	0.01 %	0.05 %	0.12 %
Cannabis (tetrahydrocannabinol)	0.6	3.1	9.4
Stimulants			
Amphetamine	4.1	202.8	486.8
Methamphetamine	4.5	223.9	537.3
Cocaine	3.0	NA	NA
Benzoylecgonine[a]	2.9	NA	NA
MDMA (ecstasy)[b]	5.8	NA	NA
Opioids			
Buprenorphine	0.3	0.7	1.7
Codeine	3.0	NA	NA
Fentanyl[c]	0.7	3.4	NA
6-MAM[d]	9.8	NA	NA
Methadone	9.3	61.9	148.5
Morphine	2.9	22.8	57.1
Oxycodone	3.2	37.8	94.6
Tramadol[c]	7.9	790.1	NA
Benzodiazepines and Z-drugs			
Alprazolam	3.1	6.2	15.4
Clonazepam	1.3	3.2	7.9
Diazepam	5.7	142.4	341.7
Diclazepam	1.6	NA	NA
Flunitrazepam	1.6	3.1	7.8
Nitrazepam	2.8	42.2	98.4
Oxazepam	14.3	430.1	860.1
Zolpidem	21.5	76.8	184.4
Zopiclone	7.8	23.3	58.3

Analytical cut-off concentrations represent validated limits of quantification. Cut-off limits indicating likely or highly impaired are based on graded sanction limits in the Norwegian Road Traffic Act and correspond to a blood alcohol concentration of 0.05 % and 0.12 %, respectively [34]. NA=not applicable.

[a] Metabolite of cocaine.

[b] MDMA=3,4-Methylenedioxymethamphetamine.

[c] For fentanyl and tramadol the cut-off limits indicating likely impairment were equal to the upper reference limits in therapeutic drug monitoring [35].

[d] Heroin rapidly metabolises to 6-monoacetylmorpine (6-MAM), a unique metabolite of heroin, which rapidly metabolises to morphine. Therefore, heroin and 6-MAM may not be detectable in a blood sample taken some time after heroin exposure.

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the study period. Local trauma registrars registered the clinical data via an encrypted online web form and biological data were obtained from blood samples collected on admission as part of a routine acute primary survey by the trauma team. For the purpose of data collection for the study, samples of residual blood from the primary survey were de-identified and sent by postal mail to the Section of Drug Abuse Research, Oslo University Hospital (Oslo, Norway). Analyses for alcohol were performed with an automated enzymatic method [29], other compounds were analysed with ultra high-performance liquid chromatography coupled with tandem mass spectrometry (UHPLC-MS/MS) [30].

Variables

Table 1 presents the toxicological analyses including 24 psychoactive substances with cut-off levels.

We used three levels of analytical concentrations: the *analytical cut-off concentrations*, which represent the validated limits of quantification and indicate drug use within a few hours or days before sample collection [31]. The cut-off limits indicating *likely impaired* were equal to the graded sanction limits in the Norwegian Road Traffic Act, corresponding to a blood alcohol concentration (BAC) of 0.05 %, whereas the cut-off limits indicating *highly impaired* were equal to the graded sanction limits corresponding to a BAC of 0.12 % [32–34]. These limits were based on experimental studies of cognitive and psychomotor tests [32]. For amphetamine and methamphetamine, the blood concentrations are summarised for the cut-off limits indicating likely and highly impaired as described in the Norwegian Road Traffic Act [33]. The cut-off limits indicating likely impairment for fentanyl or tramadol were equal to the upper reference limits in therapeutic drug monitoring [35]. To determine whether morphine and codeine detected in blood samples are the result of morphine, heroin, or codeine intake, morphine/codeine ratios were used as described by Konstantinova et al. [36].

The simultaneous use of multiple drugs with similar structures and mechanisms may result in additive effects [36,37]. Benzodiazepine concentrations were converted to diazepam-equivalent concentrations and opioid concentrations to morphine-equivalent concentrations using conversion factors for blood concentrations, according to the Norwegian Road Traffic Act [34]. Equivalent doses have been established for these two drug classes and are widely acknowledged [37,38]. Morphine and diazepam equivalents were calculated according to conversion factors (*Table S1, supplementary material)*. Zolpidem and zopiclone (Z-drugs) were included in the benzodiazepine group.

Healthcare workers may administer diazepam, fentanyl, morphine, or oxycodone as part of trauma patient care. If the administration of one of these drugs was reported in the medical records prior to the blood sample collection, the blood concentration of this specific substance was set to zero. If no other substances were detected in the same blood sample, the concentration for these four substances was also set to zero. The rationale behind this was if only these substances were found in the blood sample, they were most likely administered by healthcare workers after the traumatic injury occurred, and missing in the medical record or not recorded by the local admission officer.

We categorised the substances into three groups: alcohol, medicinal drugs, and illegal drugs, to examine the use of different groups of psychoactive substances. Medicinal drugs include opioids, except heroin and 6-MAM, and benzodiazepines, except diclazepam, which is not prescribed in Norway. Illegal drugs include cannabis (tetrahydrocannabinol; THC), stimulants (cocaine and its inactive metabolite, amphetamine, methamphetamine, and 4-methylenedioxymethamphetamine [MDMA]), and heroin as well as its psychoactive metabolites 6-MAM and diclazepam.

Statistical analysis

Descriptive data were presented as whole numbers and percentages, and medians with interquartile ranges (IQR) were used as appropriate. Age was categorised into quartiles for descriptive purposes and regression analyses. The association between the prevalence of psychoactive substances and age, sex, and mechanism of injury was assessed using univariate and multivariate logistic regression. To ensure analyses on unique persons, the first admission was used for patients with more than one admission during the study period. The model outcome was a compound variable defined as the presence of any psychoactive substance at the level of likely impairment, and all assessed predictors were present in the final model. Two-tailed tests were used, and statistical significance was assumed for P-values <0.05. SPSS version 28 (IBM, Armonk, NY, USA) was used for the analysis.

Ethical considerations

The Regional Committee for Medical and Health Research Ethics (Ref. no.: 2017/1363) approved the study and waived the need for informed consent. However, all participants were informed after inclusion with the option to withdraw from the study. Patients who could not be reached by postal mail after discharge from the hospital for reasons such as no available postal address, no postal address of the next of kin in case of death, or they being foreign residents, were excluded. Oslo University Hospital (OUH) was the main study sponsor and data controller. The study complies with the 2018 General Data Protection Regulation regulations, and a Data Protection Impact Assessment was conducted in cooperation with the OUH Data Protection Officials. The study was registered in Clinical Trials prior to data collection (NCT03773614). The study conforms to the STROBE reporting guidelines, and a STROBE checklist was used to ensure appropriate reporting quality [39].

Results

During the 12-month study period, 4878 trauma admissions of 4845 patients from 35 of 38 Norwegian trauma hospitals were included (*Fig. 1*). During the study period, 31 admitted patients had records of more than one admission.

The median age was 43 years, and 68 % of the patients were male (*Table 2*). In one-quarter of the admissions, the patients were <27 years of age, and among these, 60 % were involved in transport-related traumas. Fall traumas were more common in higher age group patients, while the median age was lowest, and the proportion of males was highest in violence-related traumas.

One or more psychoactive substances were detected in 35 % of all trauma patients (*Table 3*). Alcohol was the most commonly detected substance with a median concentration of 0.17 %. Diazepam and clonazepam were the most commonly detected benzodiazepines, whereas morphine, codeine, and tramadol were the most commonly detected opioids. Cannabis and stimulants were found in 352 (7 %) and 371 (8 %) patients, respectively. Cannabis was the only psychoactive substance detected in 72 patients. Among the 31 patients admitted more than once during the study period, 22 (67 %) had detectable levels of psychoactive substances. Benzodiazepines were the most commonly detected substance (42 %), followed by alcohol (33 %), opioids (24 %), cannabis (15 %), and stimulants (15 %).

Assessing the level of impairment, 28 % of the admissions had a concentration of one or more psychoactive substances, indicating *likely impaired,* and 22 % were *highly impaired* (*Table 4)*. Among patients with detectable blood alcohol concentrations, 92 % were *likely impaired* and 72 % *highly impaired*. Among patients involved in traumas related to transport, 23 % tested positive for psychoactive substances, of which 58 % had blood concentrations corresponding to *highly impaired*. The most prevalent substances detected in traumas related to transport were alcohol and benzodiazepines. Psychoactive substances were detected in 44 % of the patients injured in falls, of which 62 % had blood concentrations indicating *highly impaired*. Patients with violence-related trauma

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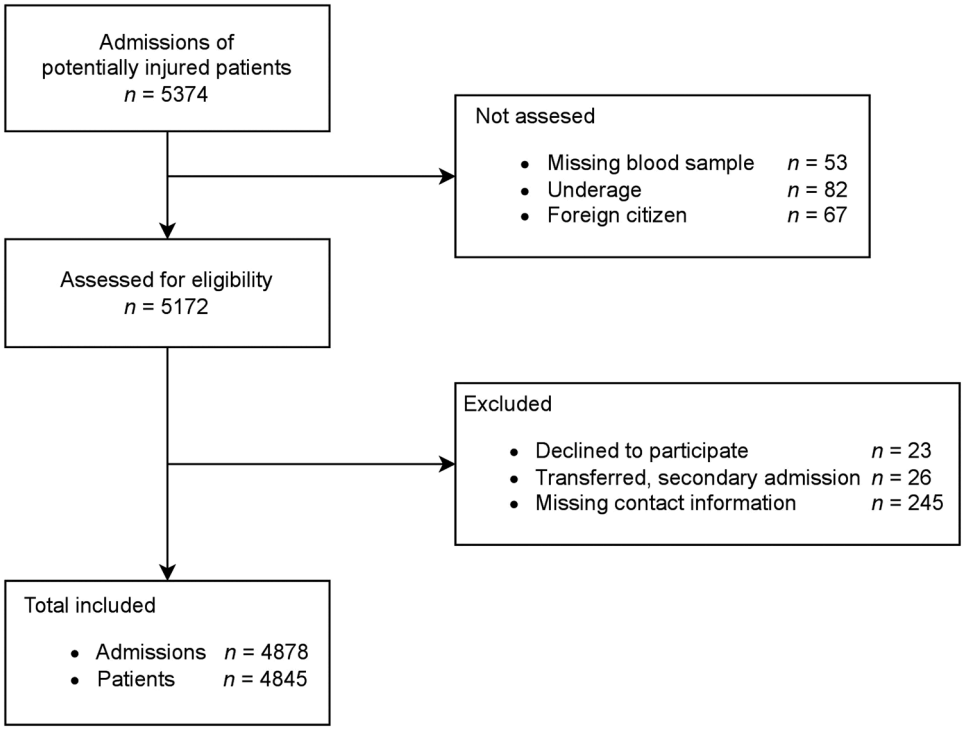

Fig. 1. Flowchart illustrating the total number of registered admissions, exclusion (and reasons for exclusion) and total number of included trauma admissions and patients.

Table 2
Descriptive characteristic of trauma admissions with median age (IQR) and sex (%) categorized by mechanism of injury.

	Transport	Fall	Violence	Other	Total
n (%)	2320 (48)	1489 (30)	344 (7)	725 (15)	4878 (100)
Median age (IQR)	38 (23–56)	57 (35–72)	33 (25–43)	41 (27–56)	43 (26–61)
Sex n (%)					
Female	775 (33)	511 (34)	60 (17)	205 (28)	1551 (32)
Median age (IQR)	38 (23–57)	58 (34–77)	35 (27–45)	32 (22–49)	43 (25–64)
Male	1545 (67)	978 (66)	284 (83)	520 (72)	3327 (68)
Median age (IQR)	37 (23–56)	57 (36–70)	33 (24–43)	44 (30–58)	43 (27–60)

IQR=interquartile range.

had the highest prevalence of psychoactive substances, with blood concentrations indicating *highly impaired* in 57 % of the cases.

A higher proportion of men tested positive for psychoactive substances (38 %) than did women (29 %). Stimulant and cannabis users had the most marked gender differences, with 86 % of stimulant users and 83 % of cannabis users being male. Among the patients with positive findings for alcohol consumption, 78 % were men. Men dominated substance use for all age groups and groups of psychoactive substances, except for benzodiazepines and opioids in the age group above 43 years (*Table 5*). In these groups, the general sex-related difference was either nulled or reversed. The highest prevalence of psychoactive substance use was noted in men aged 27–43 years, with 50 % testing positive for one or more compounds; among them, 68 % were highly impaired. Women above 61 years of age comprised the only group in which opioid and benzodiazepine use were more common than alcohol. Regardless of sex, age > 61 years was associated with the lowest prevalence of alcohol, stimulant, and cannabis use.

To assess the likelihood of alcohol or drug-related impairment at trauma admission, a regression analysis was performed using sex, age, and injury mechanism as predictors, and blood concentrations corresponding to *likely impaired* from any group of psychoactive substances as outcome variables (*Table 6*). Being male, aged between 27 and 43 years, and having injuries from falls and violence (in comparison to transport) were all factors that independently predicted impairment from psychoactive substance use. Injury from violence was the strongest predictor of the influence of intoxicating substances on a patient.

To determine the extent to which the patients used more than one group of psychoactive substances, we categorised the substances into alcohol, medicinal, and illegal compounds. Among the 1714 admissions with positive blood samples, 613 (36 %) used a combination of alcohol, medicinal drugs, or illegal drugs *Fig. 2*. The most common combinations were benzodiazepines with illegal drugs (291 admissions), and benzodiazepines with alcohol (217). admissions). In addition, psychoactive substances were combined within the groups of medicinal and illegal drugs, and when these were added, psychoactive substance use was observed in 771 (45 %) admissions.

Discussion

Psychoactive substances were found in 35 % of all trauma admissions; blood concentrations in 80 % of these indicated that the patients were likely or highly impaired at the time of injury. Two or more

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Table 3
The prevalence *n* (%) of psychoactive substances with analytical cut-off limits, median concentrations and percentage of positive cases with blood concentrations indicating likely impaired among 4878 trauma admissions.

	Prevalence *n (%)*	**Median concentration** *ng/mL (IQR)*	**Likely impaired** *%*
Any substance	1714 (35)		80
Alcohol (ethanol)	1009 (21)	0.17 % (1.1–2.1)	92
Benzodiazepines & Z-drugs	613 (13)		65
Diazepam	283 (6)	83.1 (31.1–207.5)	35
Clonazepam	214 (4)	24.5 (9.5–65.7)	91
Oxazepam	164 (3)	60.6 (24.0–162.2)	12
Zopiclone	102 (2)	19.4 (11.5–34.8)	42
Alprazolam	76 (2)	24.8 (10.1–47.7)	88
Zolpidem	42 (1)	131.5 (68.0–281.1)	71
Nitrazepam	42 (1)	28.1 (10.7–57.3)	36
Diclazepam	12 (0)	7.6 (2.8–25.4)	NA
Flunitrazepam	3 (0)	8.0 (1.7–8.0)	67
Opioids	467 (10)		46
Morphine	124 (3)	18.3 (8.7–40.7)	43
Codeine	116 (2)	29.0 (11.9–54.3)	2
Tramadol	116 (2)	122.3 (63.3–273.5)	6
Fentanyl	76 (2)	1.4 (1.0–2.9)	24
Methadone	51 (1)	168.1 (107.9–295.8)	80
Buprenorphine	49 (1)	1.0 (0.6–2.4)	71
Oxycodone	39 (1)	20.9 (9.5–46.2)	31
Heroin	21 (0)		NA
6-MAM	0 (0)		
Stimulants	371 (8)		29
Amphetamines			
Amphetamine	255 (5)	112.4 (32.7–340.4)	39
Methamphetamine	69 (1)	35.2 (8.4–112.4)	17
Cocaine			
Benzoylecgonine	137 (3)	68.9 (16.6–213.1)	NA
Cocaine	3 (0)	3.9 (3.9–3.9)	NA
MDMA (ecstasy)	27 (1)	90.3 (38.7–287.3)	NA
Cannabis (THC)	352 (7)	2.9 (1.6–6.3)	49

Heroin=morphine/codeine ratio > 1 (with both morphine and codeine concentrations above analytical cut-off limits) as an indication of heroin intake. MDMA=3,4-Methylenedioxymethamphetamine; NA=not applicable.

psychoactive substances were present in 45 % of the positive cases.

The prevalence of psychoactive substances was markedly higher in injury related to violence. This is reported in previous prevalence studies [7,24,40] and is also in line with a recent case-control study where substance abuse disorder was the strongest risk factor for a violence-related injury [41]. Prevalence was also higher in fall injuries, which corresponds well with our knowledge of the effects of alcohol and several psychoactive drugs on physiological and psychological parameters such as balance and attention. This group was also characterised by older age, a known risk factor for falls [42].

Alcohol- or drug-related impairment was relatively less common in transport related injuries. In a previous case-control study of killed car and van drivers in Norway, Gjerde and colleagues reported that the prevalence of alcohol use was approximately one in four drivers [43]. In our results the prevalence of alcohol among all transport related injury was half of this, approximately one in eight. However, the prevalence of any psychoactive substance detected in roadside surveys in the uninjured controls in the study by Gjerde was 2,24 %, i.e. one tenth of the prevalence in our results. This supports a substantial etiological role for impairment caused by psychoactive substances also among the transport related injuries in our results.

Younger males presented with the highest levels of alcohol intoxication in our study and are more susceptible to mortality and morbidity from traumatic injuries. Our findings support the claim that alcohol use is a major contributor to injury proneness [7,20–22,44,45]. However, studies based on the assessment of only transport-related injuries may underestimate the prevalence of alcohol use in the general trauma population.

Benzodiazepines and Z-drugs have well-documented concentration-related impairing effects on psychomotor performance and were the most commonly detected prescribed psychoactive drug groups in our study [46–48]. These results correspond to those of previous studies involving trauma patients [19,20,40]. Clonazepam use was surprisingly prevalent in our study, and similar to alprazolam use, it was associated with a high proportion of likely impaired patients. According to the Norwegian Prescription Database, both clonazepam and alprazolam are infrequently prescribed but easily available on the illicit drug market; our findings are therefore likely explained by mostly recreational use

Table 4
The prevalence of psychoactive substances for analytical cut-off limit, likely impaired, and highly impaired according to injury mechanism.

n	*Transport* *2320*	*Fall* *1489*	*Violence* *344*	*Other* *725*	*Total* *4878*
Substance n (%)					
Any substance					
Analytical cut-off limit	528 (23)	660 (44)	275 (80)	251 (34)	1714 (35)
Likely impaired	397 (17)	530 (36)	250 (73)	196 (27)	1373 (28)
Highly impaired	309 (13)	405 (27)	195 (57)	143 (20)	1052 (22)
Alcohol (ethanol)					
Analytical cut-off limit	287 (12)	414 (28)	179 (52)	129 (18)	1009 (21)
Likely impaired	257 (11)	386 (26)	166 (48)	118 (16)	927 (19)
Highly impaired	198 (9)	320 (22)	128 (37)	84 (12)	730 (15)
Benzodiazepines and Z-drugs					
Analytical cut-off limit	169 (7)	223 (15)	110 (32)	111 (15)	613 (13)
Likely impaired	121 (5)	119 (8)	83 (24)	75 (10)	398 (8)
Highly impaired	91 (4)	69 (5)	59 (17)	55 (8)	274 (6)
Opioids					
Analytical cut-off limit	127 (6)	195 (13)	66 (19)	79 (11)	467 (10)
Likely impaired	48 (2)	91 (6)	43 (13)	31 (4)	213 (4)
Highly impaired	21 (1)	40 (3)	23 (7)	16 (2)	100 (2)
Stimulants					
Analytical cut-off limit	126 (5)	80 (5)	103 (30)	62 (9)	371 (8)
Likely impaired	42 (2)	24 (2)	27 (8)	16 (2)	109 (2)
Highly impaired	21 (1)	12 (1)	14 (4)	9 (1)	56 (1)
Cannabis (THC)					
Analytical cut-off limit	124 (5)	68 (5)	111 (32)	49 (7)	352 (7)
Likely impaired	58 (3)	29 (2)	62 (18)	22 (3)	171 (4)
Highly impaired	21 (1)	8 (1)	17 (5)	6 (1)	52 (1)

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Table 5
The prevalence of psychoactive substances for analytical cut-off limit, likely impaired, and highly impaired according to sex and different age groups.

Sex	Female	Male	Female	Male	Female	Male	Female	*Male*
Age	*< 27*	*< 27*	*27–43*	*27–43*	*44–61*	*44–61*	*> 61*	*> 61*
n	*437*	*827*	*359*	*854*	*338*	*871*	*417*	*784*
Substance n (%)								
Any substance								
Analytical cut-off limit	97 (22)	301 (36)	117 (33)	424 (50)	108 (32)	303 (35)	123 (30)	241 (31)
Likely impaired	77 (18)	255 (31)	85 (24)	361 (43)	86 (25)	259 (30)	75 (18)	175 (22)
Highly impaired	50 (11)	188 (23)	62 (17)	288 (34)	79 (23)	216 (25)	39 (9)	130 (17)
Alcohol (ethanol)								
Analytical cut-off limit	70 (16)	207 (25)	51 (14)	240 (28)	65 (19)	193 (22)	41 (10)	142 (18)
Likely impaired	59 (14)	190 (23)	47 (13)	225 (27)	62 (18)	184 (21)	34 (8)	126 (16)
Highly impaired	36 (8)	143 (17)	37 (10)	174 (21)	56 (17)	151 (17)	25 (6)	108 (14)
Benzodiazepines and Z-drugs								
Analytical cut-off limit	20 (5)	68 (8)	48 (13)	166 (20)	48 (14)	106 (12)	71 (17)	86 (11)
Likely impaired	13 (3)	56 (7)	30 (8)	133 (16)	30 (9)	70 (8)	27 (7)	39 (5)
Highly impaired	11 (3)	41 (5)	21 (6)	111 (13)	20 (6)	50 (6)	6 (1)	14 (2)
Opioids								
Analytical cut-off limit	16 (4)	53 (6)	41 (11)	124 (15)	35 (10)	87 (10)	43 (10)	68 (9)
Likely impaired	6 (1)	19 (2)	15 (4)	65 (8)	15 (4)	47 (5)	20 (5)	26 (3)
Highly impaired	1 (0)	7 (1)	5 (1)	28 (3)	10 (3)	26 (3)	9 (2)	14 (2)
Stimulants								
Analytical cut-off limit	17 (4)	78 (9)	26 (7)	173 (21)	10 (3)	55 (6)	0 (0)	12 (2)
Likely impaired	4 (1)	11 (1)	8 (2)	55 (7)	4 (1)	23 (3)	0 (0)	4 (1)
Highly impaired	1 (0)	2 (0)	3 (1)	34 (4)	3 (1)	13 (2)	0 (0)	0 (0)
Cannabis (THC)								
Analytical cut-off limit	18 (4)	108 (13)	26 (7)	126 (15)	12 (4)	51 (6)	2 (1)	9 (1)
Likely impaired	7 (2)	55 (7)	10 (3)	54 (6)	8 (2)	31 (4)	0 (0)	6 (1)
Highly impaired	2 (1)	13 (2)	4 (1)	17 (2)	0 (0)	14 (2)	0 (0)	2 (0)

Table 6
Univariable and multivariable logistic regression models of likely impairment of any psychoactive substance adjusted for sex, age, and injury mechanism, with odds ratios (OR), 95 % confidence intervals (CI), and significance level.

	Univariable logistic regression			Multivariable logistic regression		
	OR	*95 % CI*	*P*	*OR*	*95 % CI*	*P*
Sex						
Female	Reference					
Male	1.76	(1.52–2.03)	<0.001	1.64	(1.41–1.91)	<0.001
Age (years)						
>61	Reference					
<27	1.35	(1.12–1.63)	0.002	1.73	(1.41–2.13)	<0.001
27–43	2.23	(1.86–2.68)	<0.001	2.46	(2.01–3.01)	<0.001
44–61	1.50	(1.24–1.81)	<0.001	1.81	(1.48–2.21)	<0.001
Injury mechanism						
Transport	Reference					
Fall	2.66	(2.28–3.09)	<0.001	3.20	(2.72–3.77)	<0.001
Violence	12.94	(9.97–16.80)	<0.001	11.26	(8.64–14.67)	<0.001
Other	1.75	(1.43–2.13)	<0.001	1.68	(1.38–2.06)	<0.001

[49,50]. Clonazepam and alprazolam have higher potency than other benzodiazepines [51,52], and the problem of their illegal use has been discussed in previous reports [50,53,54]. Blood samples that were positive for zolpidem, zopiclone, and diazepam also revealed high concentrations. In contrast to clonazepam and alprazolam, these medications are more frequently prescribed. Compared with the general population, the prevalence of psychoactive drug prescriptions is high among individuals involved in traumatic events [55]. In most cases, benzodiazepines were found in combination with alcohol or other psychoactive drugs. The additive, and possible synergistic, impairing effect of benzodiazepines in drug-alcohol and drug-drug combinations warrants further exploration in terms of injury prevention. We should convey their patterns of use and their association with injury proneness to all prescribers of benzodiazepines and Z-drugs.

Overconsumption of opioids [56], particularly oxycodone and fentanyl, and a rapid increase in overdose-related deaths have been described as opioid epidemics in the United States [57]. In Europe, there is wide heterogeneity among countries in opioid prescriptions and the frequency of deaths related to opioids [58]. However, opioids contribute to approximately three of four fatal overdoses in the EU [59]. Recent reports have stated that Norway has a higher frequency of opioid prescriptions than other Scandinavian countries, and users of prescription opioids now outnumber recreational heroin users among fatal overdoses related to opioids [60,61]. Although oxycodone is frequently found in fatal overdoses, its use was less prevalent in our study. We found that codeine and tramadol were more commonly detected, reflecting prescription trends, as they are also the most frequently prescribed opioids in Norway. However, in recent years, there has been a shift in opioid prescriptions with an increasing proportion of oxycodone prescription [62]. Whether this will be reflected in future toxicological profiles among patients with trauma remains to be determined. Opioid users have increased morbidity and mortality compared with non-opioid users, and traumatic injuries contribute to this. Trends in opioid prescriptions and recreational use and the toxicological trends among trauma patients need to be monitored to improve the safety of this high-risk group.

The relationship between cannabis use and injury proneness is debated. Similar to previous studies of injured patients, cannabis was the

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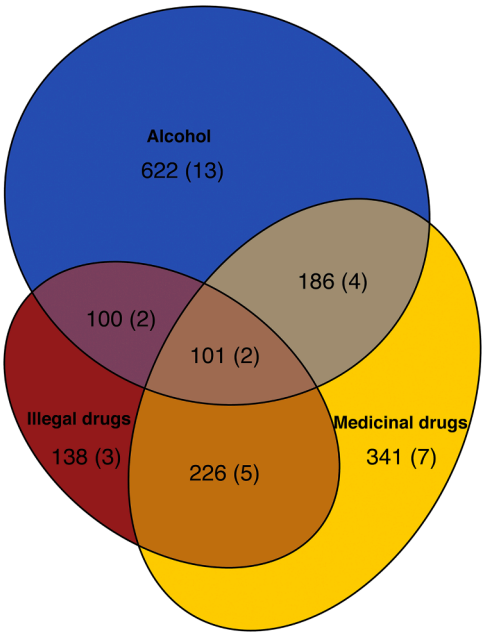

Fig. 2. Scaled Venn diagram. Prevalence *n* (%) of alcohol, medicinal and illegal drugs detected separately and in combination above analytical cut-off limits among 4878 trauma admissions.

most frequently detected drug in our study, particularly among younger males and patients with violence-related injuries [19,20,40,45,59,63]. Many recreational users of illicit drugs use a wide range of substances [59]. Our study, where only one in five samples positive for cannabis had cannabis as the only detected psychoactive substance, supports this finding. Similar to cannabis, the dose-response psychomotor impairment of stimulants may be less clear than for other psychoactive substances [47,64]. However, studies on transport safety have shown that stimulant use is associated with a higher risk of injury and death [20]. A roadside survey found amphetamines and cocaine in 0.3 % and 0.2 % of the Norwegian drivers, respectively [65]. In our study, 8 % of all admissions and 5 % of admissions from transport related injuries were influenced by a stimulant. This further supports the role of stimulants as an important risk factor for injury. Additional studies are needed to quantify increased injury proneness associated with cannabis and stimulant use, comparing the prevalence of use in injured drivers with representative controls from roadside surveys.

Polysubstance use was found in many injured patients in this study. The individual or combined contribution of various psychoactive substances to injury proneness cannot be determined because of the obvious lack of toxicological data from uninjured controls. For prescribed controlled substances, future studies linking prescription data at the individual level to toxicological results may determine the extent of illegal versus prescribed use of controlled substances. For prescribed drugs, future registry-based case-control studies can help establish the risk of injury associated with each substance.

The management of severely injured patients is a time-critical endeavor aimed at restoring normal physiology and function. Intoxication may affect all phases of trauma care, from diagnostics to rehabilitation. Given the high prevalence of alcohol and drug use in the trauma population, recognition and awareness of medical issues related to intoxication should be prioritised. For some patients addressing withdrawal symptoms during hospital admission will be of importance, while for others recognition of problematic substance use may serve as a gateway for counselling and rehabilitation services. To further increase our understanding of the physiological and clinical impacts of intoxication, we should consider routine toxicological screening of patients with suspected severe injuries. Furthermore, these data should be incorporated into the trauma registries. Future clinical studies based on combined toxicological and clinical trauma data should aim to improve the outcome of intoxicated trauma patient by identifying specific clinical manifestation of each psychoactive substance and assessing relevant therapeutic interventions.

The main strength of the study is the extensive prospective data collection, with the participation of hospitals covering 96 % of the Norwegian population. Data were collected over an entire one-year period, which eliminated seasonal variations in trauma epidemiology. Toxicological analyses of blood samples obtained from acutely admitted patients shortly after injury increase the representativeness of the toxicological results.

A limitation of the study is that it excluded patients who died before reaching a hospital and patients that were under-triaged for trauma team activation. For patients that are not received by a trauma team there is no standardised protocol to obtain blood samples immediately upon emergency department arrival. All injured patients not received by a trauma team were therefore excluded from participation.

Long-term use of psychoactive substances may lead to tolerance and individual differences in age, sex and physiology may affect the association between observed concentrations and cognitive impairment. For rapidly metabolised substances, such as 6-MAM, cocaine, and THC, concentrations are reduced from the time from the injury until blood sample collection.

The study has a cross sectional design and the lack of toxicological data in a representative uninjured control population means that of risk for traumatic injury associated with psychoactive substance cannot be quantified. Similarly, assessing causality through odds of culpability studies necessitate data on an extensive amount of injury circumstance factors that was beyond the scope of this study.

Conclusion

We detected psychoactive substances in 35 % of trauma admissions. Alcohol was the most commonly used substance, and in decreasing order, benzodiazepines, opioids, stimulants, and cannabis were detected in every eighth to fourteenth admission. Polydrug use was detected in 45 % of the positive cases. Younger males and patients with violence-related injuries were more likely to be impaired. Injury prevention strategies should focus on high-risk groups and involve the prescription of controlled substances. We should consider toxicological screening in trauma admissions and incorporation of toxicological data into trauma registries.

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Data statement

The data collected in the study were considered sensitive and protected according to the decision of The Regional Committee for Medical and Health Research Ethics and the data protection officials representing the data controller, Oslo University Hospital. Queries regarding access to anonymised aggregated data may be directed to the corresponding author.

Declaration of Competing Interest

All authors have completed the ICMJE uniform disclosure form and

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.injury.2023.111160.

References

[1] WHO. Injuries and violence - Key facts. 2021. https://www.who.int/news-room/fact-sheets/detail/injuries-and-violence (accessed April 15, 2023).
[2] WHO Europe. Fact sheet. EURO/11/05 Rev.1 2005. https://www.euro.who.int/_data/assets/pdf_file/0007/98611/fs1105e.pdf (accessed April 15, 2023).
[3] Drummer OH, Gerostamoulos D, di Rago M, Woodford NW, Morris C, Frederiksen T, et al. Odds of culpability associated with use of impairing drugs in injured drivers in Victoria, Australia. Accid Anal Prev 2020;135:105389. https://doi.org/10.1016/j.aap.2019.105389.
[4] Kuschel BM, Laflamme L, Möller J. The risk of fall injury in relation to commonly prescribed medications among older people - a Swedish case-control study. Eur J Public Health 2015;25:527–32. https://doi.org/10.1093/eurpub/cku120.
[5] Rehm J, Gmel GE, Gmel G, Hasan OSM, Imtiaz S, Popova S, et al. The relationship between different dimensions of alcohol use and the burden of disease—an update. Addiction 2017;112:968–1001. https://doi.org/10.1111/add.13757.
[6] Gjerde H, Christophersen AS, Normann PT, Mørland J. Associations between substance use among car and van drivers in Norway and fatal injury in road traffic accidents: a case-control study. Transp Res F Traffic Psychol Behav 2013;17:134–44. https://doi.org/10.1016/j.trf.2012.11.004.
[7] Bombana HS, Bogstrand ST, Gjerde H, Jamt REG, Carvalho HB de, Andreuccetti G, et al. Use of alcohol and illicit drugs by trauma patients in Sao Paulo. Brazil. Injury 2022;53:30–6. https://doi.org/10.1016/j.injury.2021.10.032.
[8] Lacey J.H., Kelley-Baker T., Berning A., Romano E., Ramirez A., Yao J., et al. Drug and alcohol crash risk: a case-control study (Report No. DOT HS 812 355). 2016.
[9] Bernhoft IM, Hels T, Lyckegaard A, Houwing S, Verstraete AG. Prevalence and risk of injury in europe by driving with alcohol, illicit drugs and medicines. Procedia Soc Behav Sci 2012;48. https://doi.org/10.1016/j.sbspro.2012.06.1259.
[10] Australia New Zealand Trauma Registry (ATR). Bi-national trauma minimum data set (BNTMDS) 2021. atr.org.au/data-set (accessed April 15, 2023).
[11] The Trauma Audit & Researh network (TARN). Procedures manual england & wales 2021. https://www.tarn.ac.uk/content/downloads/53/Procedures%20manual%20England%20&%20Wales%20Complete%20Sept%2021.pdf (accessed April 15, 2023).
[12] AUC Trauma Register DGU (DGU-TR). Guide to completion the entry sheet of TraumaRegister DGU 2020. https://www.traumaregister-dgu.de/fileadmin/user_upload/TR-DGU_-_Guide_data_entry_form.pdf (accessed April 15, 2023).
[13] Registro intraospedaliero multiregionale traumi gravi (RITG). Statistiche n.d. http://www.pprg.infoteca.it/ritg/(accessed April 15, 2023).
[14] Ringdal KG, Coats TJ, Lefering R, di Bartolomeo S, Steen PA, Røise O, et al. The Utstein template for uniform reporting of data following major trauma: a joint revision by SCANTEM, TARN, DGU-TR and RITG. Scand J Trauma Resusc Emerg Med 2008;16. https://doi.org/10.1186/1757-7241-16-7.
[15] National Trauma Registry. NTR definisjonskatalog n.d. http://www.ntr-definisjonskatalog.no (accessed April 15, 2023).
[16] American College of Surgeons National Trauma Data Bank (NTDB). Trauma quality programs (TQP) 2021. https://www.facs.org/media/mkxef10z/ntds_data_dictionary_2022.pdf (accessed April 15, 2023).
[17] Dunham CM, Chirichella TJ. Trauma activation patients: evidence for routine alcohol and illicit drug screening. PLoS ONE 2012;7:e47999. https://doi.org/10.1371/journal.pone.0047999.
[18] Alser O, Perez NP, Gebran A, Maurer LR, Ortega G, Velmahos GC, et al. Underuse and variability in substance use screening among adult trauma patients in the U.S. – a nationwide retrospective cohort study. Ann Surg 2021. https://doi.org/10.1097/SLA.0000000000005331.
[19] Kelly E, Darke S, Ross J. A review of drug use and driving: epidemiology, impairment, risk factors and risk perceptions. Drug Alcohol Rev 2004;23:319–44. https://doi.org/10.1080/09595230412331289482.
[20] Schulze H., Schumacher M., Urmeew R., Alvarez J., Bernhoft I., Gier Hg. Driving under the influence of drugs, alcohol and medicines in Europe -findings from the DRUID project 2012 Luxembourg: publications Office of the European Union. 2012. https://doi.org/10.2810/74023.
[21] Blomberg RD, Peck RC, Moskowitz H, Burns M, Fiorentino D. The Long Beach/Fort Lauderdale relative risk study. J Saf Res 2009;40:285–92. https://doi.org/10.1016/j.jsr.2009.07.002.
[22] Johnston JJE, McGovern SJ. Alcohol related falls: an interesting pattern of injuries. Emerg Med J 2004;21:185–8. https://doi.org/10.1136/emj.2003.006130.
[23] Taylor B, Irving HM, Kanteres F, Room R, Borges G, Cherpitel C, et al. The more you drink, the harder you fall: a systematic review and meta-analysis of how acute alcohol consumption and injury or collision risk increase together. Drug Alcohol Depend 2010;110:108–16. https://doi.org/10.1016/j.drugalcdep.2010.02.011.
[24] Cherpitel CJ. Alcohol and injuries: a review of international emergency room studies since 1995. Drug Alcohol Rev 2007;26:201–14. https://doi.org/10.1080/09595230601146686.
[25] DiGiorgio AM, Wittenberg BA, Crutcher CL, Kennamer B, Greene CS, Velander AJ, et al. The impact of drug and alcohol intoxication on glasgow coma scale assessment in patients with traumatic brain injury. World Neurosurg 2020;135:e664–70. https://doi.org/10.1016/j.wneu.2019.12.095.
[26] el Moheb M, Herrera-Escobar JP, Breen K, Orlas C, Haynes AN, Levy-Carrick NC, et al. Long-term outcomes of psychoactive drug use in trauma patients: a multicenter patient-reported outcomes study. J Trauma Acute Care Surg 2021;90:319–24. https://doi.org/10.1097/TA.0000000000003032.
[27] Cannon R, Bozeman M, Miller KR, Smith JW, Harbrecht B, Franklin G, et al. The prevalence and impact of prescription controlled substance use among injured patients at a Level I trauma center. J Trauma Acute Care Surg 2014;76:172–5. https://doi.org/10.1097/TA.0b013e3182ab10de.
[28] Sasser SM, Hunt RC, Faul M, Sugerman D, Pearson WS, Dulski T, et al. Guidelines for field triage of injured patients: recommendations of the National Expert Panel on Field Triage, 2011. MMWR Recomm Rep 2012;61:1–20.
[29] Kristoffersen L, Smith-Kielland A. An automated alcohol dehydrogenase method for ethanol quantification in urine and whole blood. J Anal Toxicol 2005;29:387–9. https://doi.org/10.1093/jat/29.5.387.
[30] Jørgenrud B, Skadberg E, de Carvalho Ponce J, Furuhaugen H, Berg T. Determination of the alcohol biomarker phosphatidylethanol 16:0/18:1 and 33 compounds from eight different drug classes in whole blood by LC-MS/MS. J Pharmacol Toxicol Methods 2021;107:106939. https://doi.org/10.1016/j.vascn.2020.106939.
[31] Verstraete AG. Detection times of drugs of abuse in blood, urine, and oral fluid. Ther Drug Monit 2004;26:200–5. https://doi.org/10.1097/00007691-200404000-00020.
[32] Vindenes V, Jordbru D, Knapskog AB, Kvan E, Mathisrud G, Slørdal L, et al. Impairment based legislative limits for driving under the influence of non-alcohol drugs in Norway. Forensic Sci Int 2012;219:1–11. https://doi.org/10.1016/j.forsciint.2011.11.004.
[33] Ministry of Transport. Regulations amending the regulations on fixed limits for the influence of intoxicants other than alcohol, etc. 2022. https://lovdata.no/dokument/LTI/forskrift/2022-01-24-119 (accessed April 15, 2023).
[34] Ministry of Transport. Regulations amending the regulations on fixed limits for the influence of intoxicants other than alcohol, etc. 2016. https://lovdata.no/dokument/LTI/forskrift/2016-01-12-19 (accessed April 15, 2023).
[35] Helland A, Berg JA, Gustavsen I, Nordal K, Hilberg T, Aronsen L, et al. Serum concentration measurements of addictive drugs. Tidsskr Nor Laegeforen 2016;136:400–2. https://doi.org/10.4045/tidsskr.16.0030.
[36] Konstantinova S v, Normann PT, Arnestad M, Karinen R, Christophersen AS, Mørland J. Morphine to codeine concentration ratio in blood and urine as a marker of illicit heroin use in forensic autopsy samples. Forensic Sci Int 2012;217:216–21. https://doi.org/10.1016/J.FORSCIINT.2011.11.007.
[37] Strand MC, Mørland J, Slørdal L, Riedel B, Innerdal C, Aamo T, et al. Conversion factors for assessment of driving impairment after exposure to multiple benzodiazepines/z-hypnotics or opioids. Forensic Sci Int 2017;281:29–36. https://doi.org/10.1016/j.forsciint.2017.10.022.
[38] Bech AB, Clausen T, Waal H, Vindenes V, Edvardsen HE, Frost J, et al. Postmortem toxicological analyses of blood samples from 107 patients receiving opioid agonist treatment: substances detected and pooled opioid and benzodiazepine concentrations. Addiction 2020;116:845–55. https://doi.org/10.1111/add.15211.
[39] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Int J Surg 2014;12:1495–9. https://doi.org/10.1016/j.ijsu.2014.07.013.
[40] Bakke E, Bogstrand ST, Normann PT, Ekeberg Ø, Bachs L. Influence of alcohol and other substances of abuse at the time of injury among patients in a Norwegian emergency department. BMC Emerg Med 2016;16:20. https://doi.org/10.1186/s12873-016-0085-2.
[41] Murphy S, Kruse M, Elklit A, Brink O. Risk factors for violence-related injuries in emergency departments: a Danish linkage study. Eur J Psychotraumatol 2019;10. https://doi.org/10.1080/20008198.2019.1606627.
[42] Pfortmueller CA, Lindner G, Exadaktylos AK. Reducing fall risk in the elderly: risk factors and fall prevention, a systematic review. Minerva Med 2014:105.

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[43] Gjerde H, Normann PT, Christophersen AS, Samuelsen SO, Mørland J. Alcohol, psychoactive drugs and fatal road traffic accidents in Norway: a case-control study. Accid Anal Prev 2011;43. https://doi.org/10.1016/j.aap.2010.12.034.
[44] Riuttanen A, Jäntti SJ, Mattila VM. Alcohol use in severely injured trauma patients. Sci Rep 2020;10:17891. https://doi.org/10.1038/s41598-020-74753-y.
[45] Brubacher JR, Chan H, Martz W, Schreiber W, Asbridge M, Eppler J, et al. Prevalence of alcohol and drug use in injured British Columbia drivers. BMJ Open 2016;6:e009278. https://doi.org/10.1136/bmjopen-2015-009278.
[46] Bramness JG, Skurtveit S, Mørland J. Clinical impairment of benzodiazepines - Relation between benzodiazepine concentrations and impairment in apprehended drivers. Drug Alcohol Depend 2002;68. https://doi.org/10.1016/S0376-8716(02)00188-6.
[47] Gustavsen I, Mørland J, Bramness JG. Impairment related to blood amphetamine and/or methamphetamine concentrations in suspected drugged drivers. Accid Anal Prev 2006;38:490–5. https://doi.org/10.1016/j.aap.2005.11.005.
[48] Verster JC, Volkerts ER, Schreuder AHCML, Eijken EJE, van Heuckelum JHG, Veldhuijzen DS, et al. Residual effects of middle-of-the-night administration of zaleplon and zolpidem on driving ability, memory functions, and psychomotor performance. J Clin Psychopharmacol 2002;22:576–83. https://doi.org/10.1097/00004714-200212000-00007.
[49] The Norwegian Institute of Public Health. The Norwegian Prescription Database n. d. https://www.norpd.no/(accessed April 15, 2023).
[50] Høiseth G, Middelkoop G, Mørland J, Gjerde H. Has previous abuse of flunitrazepam been replaced by clonazepam? Eur Addict Res 2015;21:217–21. https://doi.org/10.1159/000377628.
[51] Ashton H. The diagnosis and management of benzodiazepine dependence. Curr Opin Psychiatry 2005;18:249–55. https://doi.org/10.1097/01.yco.0000165594.60434.84.
[52] Mehdi T. Benzodiazepines revisited. Br J Med Pract 2012;5:a501.
[53] Dokkedal-Silva V, Berro LF, Galduróz JCF, Tufik S, Andersen ML. Clonazepam: indications, side effects, and potential for nonmedical use. Harv Rev Psychiatry 2019;27:279–89. https://doi.org/10.1097/HRP.0000000000000227.
[54] Ait-Daoud N, Hamby AS, Sharma S, Blevins D. A review of alprazolam use, misuse, and withdrawal. J Addict Med 2018;12:4–10. https://doi.org/10.1097/ADM.0000000000000350.
[55] Torp HA, Skurtveit S, Skaga NO, Gustavsen I, Gran JM, Rosseland LA. Pre-injury dispensing of psychoactive prescription drugs in a ten years trauma population: a retrospective registry analysis. Scand J Trauma Resusc Emerg Med 2021;29:125. https://doi.org/10.1186/s13049-021-00939-6.
[56] Stangeland H, Handal M, Skurtveit SO, Aakvaag HF, Dyb G, Wentzel-Larsen T, et al. Killing pain?: a population-based registry study of the use of prescription analgesics, anxiolytics, and hypnotics among all children, adolescents and young adults in Norway from 2004 to 2019. Eur Child Adolesc Psychiatry 2022. https://doi.org/10.1007/s00787-022-02066-8.
[57] Lancet. The opioid crisis in the USA: a public health emergency. The Lancet 2017;390. https://doi.org/10.1016/S0140-6736(17)32808-8. 2016.
[58] Häuser W, Buchser E, Finn DP, Dom G, Fors E, Heiskanen T, et al. Is Europe also facing an opioid crisis?—a survey of European pain federation chapters. Eur J Pain 2021;25:1760–9. https://doi.org/10.1002/ejp.1786.
[59] European Monitoring Centre for Drugs and Drug Addiction. European drug report 2022: trends and developments. Luxembourg: 2022. https://doi.org/10.2810/75644.
[60] Gjersing L, Amundsen E. Increasing trend in accidental pharmaceutical opioid overdose deaths and diverging overdose death correlates following the opioid prescription policy liberalization in Norway 2010–2018. Int J Drug Policy 2022;108:103785. https://doi.org/10.1016/J.DRUGPO.2022.103785.
[61] Skurtveit S, Odsbu I, Gjersing L, Handal M, Gilje Lid T, Clausen T, et al. Individuals dying of overdoses related to pharmaceutical opioids differ from individuals dying of overdoses related to other substances: a population-based register study. Eur Addict Res 2022;28:419–24. https://doi.org/10.1159/000526145.
[62] Muller AE, Clausen T, Sjøgren P, Odsbu I, Skurtveit S. Prescribed opioid analgesic use developments in three Nordic countries, 2006-2017. Scand J Pain 2019;19:345–53. https://doi.org/10.1515/sjpain-2018-0307.
[63] Isles S, McBride P, Gee P, Fleischer D, Kappatos D, Pandey R, et al. Prevalence of psychoactive drugs in injured patients presenting to an emergency department. Emerg Med Australas 2023;35:25–33. https://doi.org/10.1111/1742-6723.14040.
[64] Jones AW. Age- and gender-related differences in blood amphetamine concentrations in apprehended drivers: lack of association with clinical evidence of impairment. Addiction 2007;102:1085–91. https://doi.org/10.1111/j.1360-0443.2007.01802.x.
[65] Furuhaugen H, Jamt REG, Nilsson G, Vindenes V, Gjerde H. Roadside survey of alcohol and drug use among Norwegian drivers in 2016–2017: a follow-up of the 2008–2009 survey. Traffic Inj Prev 2018;19:555–62. https://doi.org/10.1080/15389588.2018.1478087.

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