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Authors	Daly, Caroline;Griffin, Eve;Ashcroft, Darren M.;Webb, Roger T.;Perry, Ivan J.;Arensman, Ella
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Frequently used drug types and alcohol involvement in intentional drug overdoses in Ireland: a national registry study

Caroline Daly[1], Eve Griffin[1], Darren M Ashcroft[2,3,] Roger T Webb[4], Ivan J Perry[1,5], Ella Arensman[1,5]

[1] National Suicide Research Foundation, University College Cork, Ireland

[2] Centre for Pharmacoepidemiology and Drug Safety, Division of Pharmacy & Optometry, School of Health Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester Academic Health Sciences Centre (MAHSC), Manchester, UK

[3] NIHR Greater Manchester Patient Safety Translational Research Centre, University of Manchester, Manchester Academic Health Sciences Centre (MAHSC), Manchester, UK

[4] Centre for Mental Health and Safety, Division of Psychology & Mental Health, School of Health Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester Academic Health Sciences Centre (MAHSC), Manchester, UK

[5] Department of Epidemiology and Public Health, University College Cork, Ireland.

Corresponding author: Ms. Caroline Daly

Address: Room 4.28, Fourth Floor, National Suicide Research Foundation, Western Gateway Building, Western Road, Cork, Ireland.

Telephone: +353 21 4205551

Email: carolinedaly@ucc.ie

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Abstract:

Background: Intentional drug overdose (IDO) is the most common form of hospital-treated self-harm, yet no study has systematically classified the range of drugs involved using a validated system. We aimed to determine the profile of patients engaging in overdose, to identify drugs frequently used and to quantify the contributions of multiple drug use and alcohol involvement.

Methods: Between 2012 and 2014, the National Registry of Deliberate Self-Harm, Ireland recorded 18,329 presentations of non-fatal intentional drug overdose (IDO) to Irish emergency departments. Information on demographic and overdose characteristics were obtained. Drugs were categorised using the Anatomical Therapeutic Chemical (ATC) classification system.

Results: Analgesics (32.4%), antidepressants (21.9%), anxiolytics (21.2%) and hypnotics and sedatives (21.0%) were the most frequently used drugs types involved in overdose. Presentations involving analgesic and antidepressant medication were more common for females whereas males more often took illegal, anxiolytic and hypnotic and sedative drugs. Overdoses with drugs other than those which affect the nervous system were identified, including musculoskeletal drugs, taken in 12.0% of presentations. Paracetamol was the most frequently used drug, particularly among females (32.0%) and persons under 25 years (21.7%). Alcohol was most often present in overdoses involving anxiolytics and illegal drugs. Multiple drug use was a factor in almost half of presentations.

Conclusions: People who engage in IDO frequently take prescription only or sales restricted drugs, often involving alcohol and/or multiple drug use. These findings highlight the importance of addressing drug and alcohol misuse, potential inappropriate prescribing and the enforcement of legislation restricting specific drug sales.

Keywords: self-harm, suicide, overdose, drug, alcohol, prescribing

1. Introduction

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The individual and societal impact of non-fatal intentional drug overdose (IDO) is significant. Its association with morbidity, repeat self-harm and suicide is well established (1-4). Intentional drug overdose is the most common form of hospital treated self-harm, involved in 65-85% of presentations in Oxford, Manchester and Derby as reported by the Multicentre self-harm study (5, 6), and in Ireland by the National Self-Harm Registry (7). Most commonly enacted by females and by persons aged under 45 years (1), IDO is associated with multiple drug use and alcohol consumption (2, 8). Alcohol is involved in between 43-59% of self-harm presentations (1, 8, 9) and is of concern due to the increased lethality of IDOs involving alcohol (10), its association with complications in medical treatment and the increased risk of long-term alcohol related death among persons who self-harm involving alcohol (11).

Psychotropic and analgesic drugs currently represent the most frequently reported drug types involved in IDO (1, 2, 12-14). Approximately one-third of IDOs in Ireland entail the use of minor tranquillisers (7), whereas paracetamol-containing medication are more common in IDO in England, as per the Multicentre study (6, 15). Additionally, benzodiazepines and antipsychotics are associated with misuse and frequent use in IDO (16, 17). Multiple drug use is an important factor in IDO, involved in 18-26% of presentations, with implications for patient treatment, outcome and controlling access to drugs (9, 17).

Earlier research indicates that the frequency and trends of drugs taken in IDO reflects their availability and prescribing in a population (13, 18-21). This association presents an opportunity for means restriction interventions, for which a current and comprehensive evidence-base regarding drugs used in IDO is essential. Studies conducted to date generally apply ad hoc classifications to drugs used in IDO, based on what are assumed to be the most common drug groups. This method of classification does not allow for the complete examination of all drugs used, resulting in many drugs being represented within a large miscellaneous ‘other drugs’ category. Moreover, these classifications often do not include drugs other than those that affect the nervous system including, for example, those used to treat the musculoskeletal, cardiovascular and respiratory disorders. Finally, the use of non-

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standardised classifications also restricts the comparability of information regarding drugs used across surveillance systems and registries.

The Anatomical Therapeutic Chemical (ATC) system is a World Health Organization (WHO) recommended classification system designed to measure drug utilisation at an internationally comparable level (22). This is the first known study of a national self-harm surveillance system to examine drugs taken in IDO according to the ATC system. The application of this system is progressive in this area as it will provide an up-to-date, standardised and complete breakdown of all drugs used in IDO, necessary to inform suicide and self-harm research, intervention and policy, whilst facilitating comparative drug utilisation research between countries and across healthcare settings. This national study examines the clinical and socio-demographic profile of patients who engage in IDO, detailing drugs used according to their ATC classification with a particular focus on quantifying the contributions of multiple drug use and alcohol involvement.

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2. Methods

2.1. National Self-Harm Registry, Ireland (NSHRI)

This is a national system that monitors the occurrence of hospital-treated self-harm. Since 2006 the Registry has collected self-harm data from all 36 acute hospitals across the Republic of Ireland. This study examines presentations of IDO for the period January 1st 2012 to

December 31st 2014. Data collection is carried out by trained Data Registration Officers (DROs). Cases of self-harm are independently identified and recorded by DROs using a combination of manual and electronic checks of emergency department presentations. For a full description of data items and procedures of the Registry, please refer to Perry et al., 2012 (7).

2.2. Recording of self-harm methods

Cases of IDO include those with ICD-10 codes of X60-X64 (overdose of drugs and medicaments). Presentations of accidental overdose with prescribed medications intended to treat specific illnesses or with illegal drugs used for recreational purposes and poisonings of undetermined intent (ICD-10 codes Y10-Y19), were not included. Cases involving other poisoning agents and alcohol-only self-poisoning cases were excluded. Drug names and quantity of tablets ingested, involving up to 13 drugs, are captured via self-reported information from the patient, ambulance service records, hospital medical records, and toxicology reports where present. Alcohol involvement prior to or during the act of IDO is captured through hospital case notes as recorded on registration or by the attending clinician, or if present in toxicology reports.

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2.3. Classification of drugs taken in IDO using the Anatomical Therapeutic Chemical (ATC) system

The ATC system categorises drugs according to the system or organ upon which they act, stratifying them according to their chemical, pharmacological and therapeutic properties, the detail of which can be found in the Guidelines for ATC Classification (22). An ATC code was applied to all drugs examined by the researcher (CD) with validation cross-checks provided by a co-author (DMA) who is a qualified pharmacist. Drugs classified within the ATC system may be used for two or more equally important indications. Such drugs were attributed one code, based on its main indication, as determined by the literature (22). Drugs were classified according to their use at the time of ATC system application, December 2016. Illegal drugs

were identified using the Misuse of Drugs Acts (23, 24). In accordance with these Acts, we identified illegal drugs as those with no or very little medicinal purposes. For IDOs involving intravenous illegal drugs, the quantities taken were recorded as missing. As a result of self-report, 2,005 (10.9%) of drugs taken were reported as 'unknown'. For a further 593 (3.2%) of drugs recorded the classification of 'unknown' was attributed to them as it was not possible to apply an ATC code based on limited information available. In the context of this paper, multiple drug use refers to the use of two or more drugs other than alcohol involved in a presentation. Single drug use refers to the use of just one drug type, other than alcohol, per presentation.

2.4. Ethical approval and data protection

The Registry has ethical approval from the National Research Ethics Committee of the Faculty of Public Health Medicine. The National Suicide Research Foundation is registered with the Data Protection Agency and complies with the Irish Data Protection Act of 1988 and the Irish Data Protection (Amendment) Act of 2003.

2.5. Statistical analysis and reporting

Statistical analyses were conducted using IBM SPSS version 22.0. We applied a threshold of $p<0.01$ to signify statistical significance. Due to the large sample size in this study many outcomes were found to be statistically significant at $p<0.05$ but overall the magnitude of identified differences was small. Where presentation numbers fell below 5 data was not published to protect the identity of individuals. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies.

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3. Results

3.1. Profile of persons engaging in IDO

During the study period 1st January 2012 to 31st December 2014 there were 18,329 self-harm presentations involving IDO, representing 67.6% of all self-harm presentations. The majority (58.7%) of presentations were made by females. As described in Table 1, presentations were proportionately highest among persons aged 15-24 years (28.3%), and decreased with increasing age. The majority of IDO presentations involved overdose only (89.5%) with self-cutting identified as the most common combined method, involved in 6.5% of IDOs. Alcohol was present in 40.6% of IDOs, more common in male presentations (44.7% vs 37.8%, x^2=86.82, df=1, p<0.01) and highest among those aged 25-34 years (25.1%, x^2=619.61, df=5, p<0.01). Almost half (47.1%) of presentations involved more than one drug type. The median

number of total tablets taken per IDO case was 23 for males (IQR: 12-40) and 20 for females (IQR: 12-35). Over one-third of presentations involved the ingestion of between 20 and 49 tablets (36.7%) and 14.0% of presentations involved 50 or more tablets.

<Table 1 here>

3.2. Classification of drug types involved in IDO

Four fifths of IDOs (80.2%) involved drugs affecting the nervous system, with musculoskeletal system drugs present in 12.0% of presentations (Table 2). Illegal drugs were involved in 6.0% of IDOs. Drugs affecting the alimentary tract and metabolism were involved in 851 presentations (4.6%) and cardiovascular system drugs were similarly common, in 3.9% of presentations.

<Table 2 here>

3.3. Nervous system drugs involved in IDO

The most commonly taken drugs in IDO are described in Table 3**.** Hypnotic and sedative drugs were involved in approximately one fifth (21.0%) of IDOs. Benzodiazepine derivatives were involved in over one in three presentations (36.4%). Analgesics were taken in almost one-third of IDOs (32.4%). Antidepressants were involved in more than one in five (21.9%) presentations. Antiepileptic drugs were involved in 8.9% of IDOs (Table 4), of which the many were either pregabalin or gabapentin (49.5%).

<Table 3 here>

3.4. Drugs most frequently involved in IDO

Table 4 illustrates the individual drugs most frequently taken in IDO. Five of these are benzodiazepine derivatives and other related drugs (diazepam, zopiclone, alprazolam, zolpidem and flurazepam), cumulatively involved in 31.1% of presentations. The most frequently used drug was paracetamol, involved in 27.8% of IDOs. Anti-inflammatory drugs ibuprofen and diclofenac, and antidepressant drugs escitalopram and venlafaxine were also frequently taken in IDO (6.6%, 2.4%, 5.1% and 3.4%).

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<Table 4 here>

3.5. Gender and age differences

Significant gender differences were found in relation to drugs involved in IDO. Musculoskeletal system drugs were significantly more common in female compared to male IDOs (14.0% vs 9.2%, x^2=94.34, df=1, p<0.01). Similarly, IDO involving analgesics and antidepressants were significantly more common in female presentations (36.4% vs. 26.7%, x^2=191.65, df=1, p<0.01 and 23.9% vs. 19.1%, x^2=59.865, df=1, p<0.01) (Table 3). In particular paracetamol was involved significantly more often in female IDOs (32.0% vs 21.7%, x^2=232.16, df=1, p<0.01). Illegal drugs were three times more common in male compared to female presentations (10.1% vs 3.1%, x2=388.66, df=1, p<0.01) (Table 2). Similarly, anxiolytic drugs were also taken significantly more frequently by males (24.2% vs 19.2%, x^2=68.388, df=1, p<0.01).

Regarding age, those under 25 years took analgesic drugs more frequently than those within the older age groups (39.9%, x^2=206.30, df=2, p<0.01). Paracetamol overdose was highest among persons under 25 years (36.2%, x^2=292.30, df=2, p<0.01) and was present in 43.8% of IDOs by females aged under 25 years. Benzodiazepine involvement increased with age and was highest for those aged 45 years and over (44.3%, x^2=502.16, df=2, p<0.01). Antidepressants were involved most commonly among those aged 45 years and over (24.7%, x^2=89.17, df=2, p<0.01). Hypnotics and sedative use in IDO was significantly higher among those aged 45 years and over (28.9%, x^2=438.00, df=2, p<0.01), involving mainly sleeping sedatives zopiclone, zolpidem and flurazepam (9.2%, 4.6% and 3.4%).

3.6. Alcohol involvement

Alcohol involvement in IDO was significantly higher in male compared to female presentations (44.7% vs 37.8%, x^2=86.82, df=1, p<0.01). Alcohol was most frequently consumed in

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presentations involving illegal drugs (47.8%) followed by anxiolytics (49.3%, x^2=154.52, df=1, p<0.01) (Table 3).

3.7. Multiple versus single drug use

As described in Table 1 presentations made by those aged 15-24 years had the highest proportion of multiple drug use when compared to other age groups (26.3%, x^2=74.55, df=5, p<0.01). The median number of tablets taken was considerably higher in multiple drug use at 27 (IQR 15-45) compared to a median of 18 (IQR 10-30) in single drug use (t=25.112, p<0.01). Of those who engaged in multiple drug use 59.5% took more than 20 tablets in their IDO presentation compared to 42.3% of those who engaged in single drug use (t=9.059, p<0.01).

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4. Discussion

4.1. Key findings

This is the first national study to descriptively profile IDO. The present study utilised a national self-harm surveillance system to describe the clinical and socio-demographic profile of persons engaging in IDO, to identify drugs used in overdose and to quantify the frequency of alcohol involvement and multiple drug use. We found that individuals engaging in IDO were most often female and young to middle aged. Alcohol use was particularly associated with being male and over 35 years, taken most often in presentations involving anxiolytics and illegal drugs. Multiple drug use was frequent; not gender-specific; most common in IDOs enacted by young-middle aged individuals, and associated with the consumption of greater quantities of tablets in overdose. The ATC classification system enabled the complete identification of the involvement of drugs used in IDO and also the identification of specific drugs used to treat physical illnesses in IDO. Analgesic, antidepressant, anxiolytic and hypnotic and sedative drugs were most commonly consumed in IDO with age, gender, alcohol involvement and multiple drug use significantly impacting the frequency of their involvement. We found paracetamol to be the most frequently used drug, with a concerning proportion of young females overdosing with the drug.

4.2. Building on existing literature

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The demographic profile of persons engaging in IDO identified by the present study is similar to that previously described (9, 16, 17). The involvement of alcohol combined with IDO was similar to some existing findings (6, 10, 17), particularly in relation to its concentration among persons aged 35-54 years (25). However, it was lower than that recently recorded by the Multicentre Self-Harm Study (41% vs 58%) (8) and the Northern Ireland Registry of Self-Harm (59%) (1). Our findings also quantify and elucidate multiple drug use in IDO, which was more frequent than that reported by Finkelstein et al., 2016 in Canada and Vancayseele et al., 2016 in Belgium (26% and 18%) (9, 17). As expected, multiple drug use was associated with higher quantities of tablets taken in overdose, which has been correlated with repeat self-harm and an increased risk of suicide (26). Our findings detailing the types of drugs used in IDO build upon those reported by Griffin et al., 2014 (1), owing to the application of ATC categorisation to our data, facilitating the comprehensive identification of drugs used in IDO. We have also described the patterns of drugs used in IDO which are intended to treat physical illnesses. The involvement of benzodiazepines in IDO was substantially higher in our study compared to their frequency as reported by the Multicentre study (36% versus 14%) (6, 16). This more frequent use of benzodiazepines in IDO signals an association between these drugs and high risk of self-harm, potentially due to differences in the accessibility of these drugs, the most notable and worthy of further research would be disparities in prescribing patterns. Analgesic use in IDO in Ireland remains proportionately lower than in England (32.4% vs 45.7%) (16), which is potentially impacted by differences in access to paracetamol. In England quantities of paracetamol which can be purchased over-the-counter in pharmacy and non-pharmacy outlets exceed those available in Ireland (27). Disparities in relation to adherence to sales restriction legislation for paracetamol have been reported (28, 29), with comparable research into adherence to sales restrictions in pharmacies required. This study too identifies the concerning use of paracetamol in IDO, with variations in its involvement determined by gender and age, as per previous research (17, 30).

4.3. Clinical and research implications

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The findings of this study provide detailed insights into the frequent use of prescription, sale-restricted and illegal drugs in IDO. We have identified populations at risk of taking prescription only drugs in IDO, a finding which can inform prescribing guidelines, in particular to those at risk of self-harm. New insights into the involvement of the range of drugs used in IDO highlights the need for physicians to also consider risk when prescribing for the management of physical illness. In line with evidence-based suicide prevention initiatives, physicians may benefit from additional training regarding the frequent use of particular drugs in IDO and measures to address issues with prescribing (31, 32). Furthermore, the commonality of multiple drug use in our sample and the association between this and repeat self-harm and suicide (26), underlines the need to monitor the availability of multiple drug types to individuals, via prescription review, particularly to those at risk of self-harm.

Means restriction has proven efficacy in relation to IDO (27, 32-37) and is increasingly recommended by national suicide prevention and drug strategies (38, 39). The frequent use of over-the-counter and restricted-sale drugs found in this study accompanied by identified issues with adherence to paracetamol sales-restrictions (28, 29) highlight the need to review the operations of existing legislation and to examine new ways of preventing individuals, particular young people, from accessing excessive quantities of drugs. Considering alcohol, the specialised care needs of patients who have engaged in IDO with alcohol will require specialist training for hospital staff in the management of these patients (10).

4.4. Strengths and limitations

In this study we used robust data from a national self-harm Registry that is internationally exclusive to this field. The use of this national dataset with full geographic coverage is unique, as endorsed by the World Health Organization (32, 40). The application of the ATC classification system (22) to our data is progressive as it has enabled the comprehensive examination of specific drugs taken in IDO, previously restricted by unstandardised methods of classification. Furthermore, this system presents considerable potential to facilitate

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comparative work with other drug utilisation statistics and datasets between countries and across healthcare settings. There are a number of limitations to this study. Information collected on drugs used in IDO was self-reported. Information on the drug dosage and source, including whether or not it was prescribed to the individual is not currently collected.

4.5. Conclusion

This study presents a comprehensive profile of individuals presenting to hospital following IDO with respect to gender, age, alcohol involvement and multiple drug use. The findings raise important concerns regarding the use of specific prescribed drugs and patient safety which should be considered in prescribing guidelines. The frequent use of over-the-counter drugs raises concerns about adherence to and enforcement of legislation regulating the sale of certain drugs. The obligation to concurrently and effectively address the specialised care needs of IDO patients with alcohol intoxication is reiterated by our findings, requiring address in terms of resources and training.

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Conflicts of interest

None declared.

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Key points

- Frequently used drugs, alcohol and multiple drug use in intentional overdose are examined using a national dataset
- Analgesics, antidepressants, anxiolytics and hypnotic and sedatives are the most frequent drug groups taken in overdose
- Paracetamol is the most common drug taken in overdose, particularly among females and those under 25 years
- Alcohol and multiple drug use are common in overdose, creating specific care needs for patients
- Issues with potential inappropriate prescribing and the enforcement of legislation regulating the sale of particular drugs require review.

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Table 1 Characteristics of Intentional Drug Overdose (IDO) involvement in self-harm acts, 2012-2014

Demographics		Male N (%)	Female N (%)	Total N (%)
		7562 (41.3)	10767 (58.7)	18329
Age	Median (IQR)	32 (23, 43)	33 (22, 45)	33 (23, 45)
	<15 years	73 (1.0)	349 (3.2)	422 (2.3)
	15-24	2105 (27.8)	3090 (28.7)	5195 (28.3)
	25-34	2041 (27.0)	2330 (21.6)	4371 (23.8)
	35-44	1613 (21.3)	2132 (19.8)	3745 (20.4)
	45-54	1088 (14.4)	1790 (16.6)	2878 (15.7)
	55+	642 (8.5)	1076 (10.0)	1718 (9.4)
IDO and self-cutting		549 (7.3)	634 (5.9)	1183 (6.5)
Alcohol involvement	All ages	3377 (44.7)	4069 (37.8)	7446 (40.6)
	<15 years	8 (0.2)	18 (0.4)	26 (0.3)
	15-24	786 (23.3)	817 (20.1)	1603 (21.5)
	25-34	908 (26.9)	963 (23.7)	1871 (25.1)
	35-44	824 (24.4)	1003 (24.6)	1827 (24.5)
	45-54	560 (16.6)	865 (21.3)	1425 (19.1)
	55+	291 (8.6)	403 (9.9)	694 (9.3)
Number of drug types	1 drug type	4077 (53.9)	5613 (52.1)	9690 (52.9)
	2 or more	3485 (46.1)	5154 (47.9)	8639 (47.1)
	3 or more	1597 (21.1)	2557 (23.7)	4154 (22.7)
	4 or more	631 (8.3)	1077 (10.0)	1708 (9.3)
	5 or more	184 (2.4)	310 (2.9)	494 (2.7)
Multiple drug use	All ages	3485 (46.1)	5154 (47.9)	8639 (47.1)
	<15 years	28 (0.8)	121 (2.3)	149 (1.7)
	15-24	889 (25.5)	1381 (26.8)	2270 (26.3)
	25-34	956 (27.4)	1192 (23.1)	2148 (24.9)

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	35-44	796 (22.8)	1092 (21.2)	1888 (21.9)
	45-54	513 (14.7)	881 (17.1)	1394 (16.1)
	55+	303 (8.7)	487 (9.4)	790 (9.1)
*Number of tablets	Median (IQR)	23 (12,40)	20 (12,35)	20 (12,37)
*Number of tablets	<10 tablets	1603 (27.3)	2104 (24.1)	3707 (25.3)
	10-19	1206 (20.5)	2304 (26.3)	3510 (24.0)
	20-49	2133 (36.3)	3238 (37.0)	5371 (36.7)
	50+	939 (16.0)	1102 (12.6)	2041 (14.0)

*Number of tablets was known for 14,628 (79.8%) of all presentations

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Table 2 Therapeutic drug groups involved in IDO according to ATC classification, 2012-2014

Drug class (ATC)	Male N (%) N=7562	Female N (%) N=10767	Total N (%) N=18329
Nervous system (N)	5910 (78.2)	8793 (81.7)	14703 (80.2)*
Musculoskeletal system (M)	698 (9.2)	1504 (14.0)	2202 (12.0)*
Illegal drugs	767 (10.1)	335 (3.1)	1102 (6.0)*
Alimentary tract and metabolism (A)	323 (4.3)	528 (4.9)	851 (4.6)
Cardiovascular system (C)	278 (3.7)	443 (4.1)	721 (3.9)
Anti-infective for systemic use (J)	170 (2.2)	367 (3.4)	537 (2.9)*
Respiratory system (R)	168 (2.2)	361 (3.4)	529 (2.9)*
Blood and blood forming organs (B)	100 (1.3)	107 (1.0)	207 (1.1)
Systemic hormonal preparations, excl. sex hormones & insulin (S)	54 (0.7)	133 (1.2)	187 (1.0)*
Genitourinary system and sex hormones (G)	23 (0.3)	56 (0.5)	79 (0.4)
Antiparasitic products, insecticides and repellents (P)	18 (0.2)	43 (0.4)	61 (0.3)
**Antineoplastic and immunomodulating agents, Various, Sensory and Dermatologicals (L,V,S,D)	25 (0.3)	33 (0.3)	58 (0.3)

*Denotes statistical significance p<0.01.

**Categories combined due to small numbers.

For 2005 (10.9%) recorded drugs taken, drug names were recorded at hospital as unknown. For 593 (3.2%) of drugs recorded the classification of unknown was attributed to them as it was not possible to attribute an ATC code based on limited information.

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Table 3: Nervous system and illegal drugs involved in IDO by gender, age, alcohol and multiple drug use, 2012-2014

Drug class (ATC)	Male N (%) N=7562	Female N (%) N=10767	<25 years N (%) N=5,618	25-44 N (%) N=8115	45+ N (%) N=4596	Total N (%) N=18329	Alcohol involvement N (%)	Multiple drug use N (%)
Nervous system (N)	5910 (78.2)	8793 (81.7)	4332 (77.1)	6592 (81.2)	3779 (82.2)*	14703 (80.2)*	6186 (42.1)	8095 (55.1)
Psycholeptics (N05)	3521 (46.6)	4336 (40.3)	1682 (29.9)	3830 (47.2)	2345 (51.0)*	7857 (42.9)*	3568 (45.4)	5185 (66.0)
Anxiolytics (N05B)	1832 (24.2)	2062 (19.2)	888 (15.8)	1963 (24.2)	1043 (22.7)*	3894 (21.2)*	1920 (49.3)	2677 (68.7)
Hypnotics & sedatives (N05C)	1610 (21.3)	2248 (20.9)	694 (12.4)	1836 (22.6)	1328 (28.9)*	3858 (21.0)	1736 (45.0)	2765 (71.7)
Antipsychotics (N05A)	769 (10.2)	1036 (9.6)	367 (6.5)	927 (11.4)	511 (11.1)*	1805 (9.8)	588 (32.6)	1441 (79.8)
Analgesics (N02)	2020 (26.7)	3923 (36.4)	2240 (39.9)	2392 (29.5)	1311 (28.5)*	5943 (32.4)*	2186 (36.8)	3515 (59.1)
Other analgesics & antipyretics (N02B)	1745 (23.1)	3576 (33.2)	2099 (37.4)	2069 (25.5)	1153 (25.1)*	5321 (29.0)*	1931 (36.3)	3082 (57.9)
Opioids (N02A)	342 (4.5)	484 (4.5)	206 (3.7)	420 (5.2)	200 (4.4)*	826 (4.5)	335 (40.6)	643 (77.8)
Antimigraine preparations (N02C)	<0.1	<0.1	<0.1	<0.1	<0.1	18 (0.1)	(<17.0)	17 (94.4)
Psychoanaleptics (N06)	1476 (19.5)	2604 (24.2)	1037 (18.5)	1900 (23.4)	1143 (24.9)*	4080 (22.3)*	1820 (44.6)	2991 (73.3)
Antidepressants (N06A)	1442 (19.1)	2570 (23.9)	991 (17.6)	1886 (23.2)	1135 (24.7)*	4012 (21.9)*	1804 (45.0)	2956 (73.7)

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Psychostimulants, agents used for ADHD and nootropics (N06B)	34 (0.4)	41 (0.4)	51 (0.9)	17 (0.2)	7 (0.2)*	75 (0.4)	20 (26.7)	44 (58.7)
Anti-dementia drugs (N06D)	5 (0.1)	5 (0.0)	0.1	<0.1	<0.1	10 (0.1)	(<20.0)	8 (80.0)
Antiepileptics (N03)	642 (8.5)	987 (9.2)	307 (5.5)	834 (10.3)	488 (10.6)*	1629 (8.9)	604 (37.1)	1286 (78.9)
Other Nervous System Drugs (N07)	203 (2.7)	124 (1.2)	79 (1.4)	194 (2.4)	54 (1.2)*	327 (1.8)*	134 (41.0)	265 (81)
Anti-Parkinson (N04)	34 (0.4)	33 (0.3)	10 (0.2)	21 (0.3)	36 (0.8)*	67 (0.4)	14 (20.9)	62 (92.5)
Anaesthetics (N01)	17 (0.2)	9 (0.1)	13 (0.2)	<0.1	<0.1	26 (0.1)	9 (34.6)	17 (65.4)
Illegal drugs	767 (10.1)	335 (3.1)	427 (7.6)	630 (7.8)	45 (1.0)	1102 (6.0)*	527 (47.8)	778 (70.6)

*Denotes statistical significance p<0.01. For 2,005 of drugs taken, drug names were recorded as unknown. For 593 of drugs recorded the classification of unknown was attributed to them as it was not possible to attribute another ATC code based on limited information.

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Table 4 Drugs frequently involved in IDO, by gender and age, 2012-2014

Drug	Male N (%) N=7562	Female N (%) N=10767	<25 years N (%) N=5618	25-44 years N (%) N=8115	45 years+ N (%) N=4596	Total N (%) N=18329
Paracetamols (N02BE01/51)	1644 (21.7)	3443(32.0)*	2034 (36.2)	1996 (24.6)	1057(23.0)	5087 (27.8)*
Diazepam (N05BA01)	1093 (14.5)	1007 (9.4)*	564 (10.0)	1064 (13.1)	472 (10.3)	2100 (11.5)*
Zopiclone (N05CF01)	739 (9.8)	953 (8.9)	291 (5.2)	860 (10.6)	541 (11.8)	1692 (9.2)*
Alprazolam (N05BA12)	583 (7.7)	843 (7.8)	314 (5.6)	713 (8.8)	399 (8.7)	1426 (7.8)*
Escitalopram (N06AB10)	337 (4.5)	592 (5.5)	275 (4.9)	432 (5.3)	222 (4.8)	929 (5.1)
Zolpidem (N05CF02)	288 (3.8)	559 (5.2)*	127 (2.3)	397 (4.9)	323 (7.0)	847 (4.6)*
Pregabalin (N03AX16)	331 (4.4)	470 (4.4)	129 (2.3)	424 (5.2)	248 (5.4)	801 (4.4)*
Venlafaxine (N06AX16)	206 (2.7)	426 (4.0)*	113 (2.0)	304 (3.7)	215 (4.7)	632 (3.4)*
Flurazepam (N05CD01)	255 (3.4)	369 (3.4)	111 (2.0)	289 (3.6)	224 (4.9)	624 (3.4)*
Ibuprofen (M01AE01)	366 (4.8)	846 (7.9)*	529 (9.4)	508 (6.3)	175 (3.8)	1212 (6.6)*
Diclofenac (M01AB05)	142 (1.9)	290 (2.7)*	159 (2.8)	200 (2.5)	73 (1.6)	432 (2.4)*
Illegal drugs	767 (10.1)	335 (3.1)*	427 (7.6)	630 (7.8)	45 (1.0)	1102 (6.0)*

*Denotes statistical significance p<0.01.

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