

## Original Article

# Recreational drug use and the emerging challenges of psychoactive substances in Malta – A case series

Jeffrey Bonnici, James Coulson, Dorothy Gauci

**Abstract**

**Introduction:** Recreational drug-related hospital admissions, excluding alcohol, appeared to be relatively constant in Mater Dei Hospital (MDH), Malta's sole public, acute general hospital. While 'classical' recreational drugs such as cocaine, heroin and Methylendioxyamphetamine (MDMA) were always seen as the main culprits, intoxications secondary to novel psychoactive substances (NPS) have recently emerged in MDH. The aim of this study was to determine the challenges of acute recreational drug intoxication, including NPS, in MDH.

**Methods:** All MDH admissions secondary to acute recreational drug intoxication between 2010 and 2015 were investigated. MDH clinical performance unit (CPU), hospital data files, hospital discharge letters and the hospital database software system were utilised for data collection. Intoxications associated with deliberate self-harm, mechanical injury and lone alcohol ingestions were excluded.

**Results:** 286 patients were admitted to MDH with recreational drug intoxication between 2010-2015, with a peak of 71 patients in 2015. 78.3% were males and the median age was 26 years. While 79% of the admissions were Maltese nationals, there was a surge in foreigner admissions, from 11.8% between 2010-2012 to 28.3% between 2013-2015 ( $p<0.001$ ). Admissions occurred mostly in spring and summer, on Saturday or Sunday, and at night. 52.4% of admissions were acutely confused. Ethanol co-ingestion (40.9%) and polydrug use (39.9%) were common in these admissions. 16% needed admission to critical care. 91.3% admissions were secondary to 'Classical' recreational drugs, mostly heroin and cocaine. In 2015, 36.6% of admissions were secondary to NPS, mostly synthetic cannabinoids (SCRA). SCRA admissions were associated with severe sympathomimetic and neuropsychiatric features. An SCRA toxidrome mnemonic (MEET\_SCRA) is proposed from the most common features of lone intoxications.

**Jeffrey Bonnici** MD, MRCEM, FEBEM, MSc. Medical Toxicology (Cardiff)\*  
Emergency Department,  
Mater Dei Hospital,  
Msida, Malta  
[jeffrey.bonnici@gov.mt](mailto:jeffrey.bonnici@gov.mt)

**James Coulson** BSc (Hons) LLM, MD, MRCP, FRCPE, MAcadMED  
Pharmacology, Therapeutics & Toxicology,  
Centre for Medical Education,  
Cardiff University,  
Heath Park, Cardiff

**Dorothy Gauci** B.Psy (Hons), MSc. (Lond) DLSHTM  
Directorate for Health Information and Research,  
Pieta', Malta

\*Corresponding Author

**Conclusion:** Recreational drugs were associated with significant hospital burden, with NPS representing a new threat to MDH and Maltese public health. The toxidrome mnemonic MEET\_SCRA could potentially aid in the identification of SCRA intoxications.

### Keywords

Novel Psychoactive substances, NPS, Recreational drugs, SCRA, Meet\_SCRA

### Introduction

Recreational drug intoxications, excluding alcohol, presenting to the Emergency department (ED) in Europe is a common problem resulting in between 0.3% to 0.45% of their ED attendances in studies by Dines et al.<sup>1</sup> and Liakoni et al.<sup>2</sup>

Similar ED data from the United States (US) shows a worse picture, with about 2.5 million patients or 2% of the total ED visits resulting from drug abuse or misuse in 2011, of which 51% were attributable to illicit drug use.<sup>3</sup> Apart from the classical psychoactive substances, NPS, often known as 'Legal Highs', started to appear worldwide in the mid-2000s, specifically designed to evade drug laws with the potential of causing grave threats to public safety.<sup>4</sup> Recent studies from European and US ED's showed an increase in reported NPS intoxications, with resulting increased challenges for these already strained departments.<sup>1,3,5</sup>

Malta is the smallest country member of the European Union, with a population of around 425,000 in 2013<sup>6</sup> and is a major tourist destination with around 1.6 million tourists every year, including many young adults.<sup>7</sup>

MDH has an inpatient bed capacity of 949 beds, including 20 intensive care beds, with the ED seeing an average of 110,000

patients per year.<sup>8</sup> A total of 27,158 patients were admitted through the ED in 2012.<sup>9</sup> Throughout the years, recreational drug-related admissions to MDH appeared to be relatively constant with cocaine, heroin and MDMA being the main culprits, especially in the summer period. This correlates well with studies showing increased prevalence of recreational drug use in places of recreation.<sup>10-11</sup>

The aim was to describe the trends and impact of recreational drugs between 2010 and 2015 on MDH, and the impact of novel psychoactive substances in the local scene. Finally, this audit will attempt to describe the toxidrome for SCRA toxicity that will hopefully aid future professionals dealing with such NPS poisonings.

### Method

All the patients admitted to MDH with acute recreational drug intoxication in the 6-year period (1<sup>st</sup> January 2010 to the 31<sup>st</sup> December 2015) were included in this retrospective study.

For the aims of this study, only patients admitted to hospital secondary to acute intoxication from a drug taken for recreational purposes 'to get a high' were included. Thus, patients with deliberate self-harm or when it was not clear whether the admissions were directly related to drug intoxication (e.g. mechanical injury or withdrawal), were excluded.

Patients admitted to hospital with lone alcohol intoxication were excluded. Patients admitted to hospital following misuse of pharmaceuticals were included only if it was deemed that these drugs were used for recreational purposes. Recreational drugs were deemed to have been involved if the patient self-reported their use, or if these were later found in drug toxicology tests, one not excluding the other. In cases where

patients abused of a recreational drug while on a prescribed medication/s, the prescribed medication/s were added to the study only if the patient self-reported its use as a recreational drug, or if drug toxicology tests tested positive for a psychotropic drug that was not their routine medication on admission. The patients admitted after intoxication from a self-reported use of a lone SCRA, were further investigated by gathering data on their baseline parameters and clinical features in an attempt to describe a SCRA toxidrome. Information was gathered through the hospital CPU data, using a clinical coding system based on discharge letters. Data was also gathered through the patient discharge notes (through an electronic case summary software database), through patient medical records, and through the use of a hospital database software system (I-Soft Clinical Manager<sup>®</sup>).

### Statistical Analysis

Continuous variables were presented as mean (standard deviation) and median (interquartile range) for non-Gaussian variables and were compared by the Mann-Whitney *U* test. Pearson's chi-square test or Fisher's exact test (where appropriate) were performed to compare multiple categorical variables, presented as number (percentage) for the time period 2010 to 2015. Since the overall numbers were small, these were also grouped in two time periods (2010-2012 and 2013-2015) so as to increase statistical significance. Data analyses was carried out via Excel<sup>®</sup> 2011 and SPSS-software, version 19.0. Armonk, NY: IBM Corp. A *p*-value <0.05 was considered statistically significant.

### Results

#### *Admissions to MDH (2010-2015)*

In total, 286 patients were admitted to

MDH with acute recreational drug intoxication in the 6-year period between 1<sup>st</sup> January 2010 and 31<sup>st</sup> December 2015. The average number of admissions in this period was 47.7, with a peak of 71 admissions in 2015.

### Patient Demographics

Male patients constituted 224 (78.3%) of the admissions between 2010 and 2015. There was no statistically significant difference across the genders during the 6-year period (Table 1). The mean (SD) age between 2010 and 2015 was 28.3 (9.68) years, while the median age (IQR, range) was 26 (20-34, 13-60) years. The median (IQR, range) age for males was 27.5 (22-35, 14-60) years while that for females was 22 (18.3-31.8, 13-50) years (*p*=0.002). 226 (79%) of all admissions to MDH between 2010 and 2015 were Maltese nationals. Foreigner admissions increased from 11.8% between 2010-2012 to 28.3% between 2013-2015 (*p*<0.001) (Table 1).

Spring and summer (Table 1) were the most common seasons for admissions, while the fewest presentations occurred in February (Fig.1).

Saturday (50, 17.5%) and Sunday (61, 21.3%) were the most common days of presentation, with Tuesday being the least common date of admission (30, 10.5%) (Fig. 2).

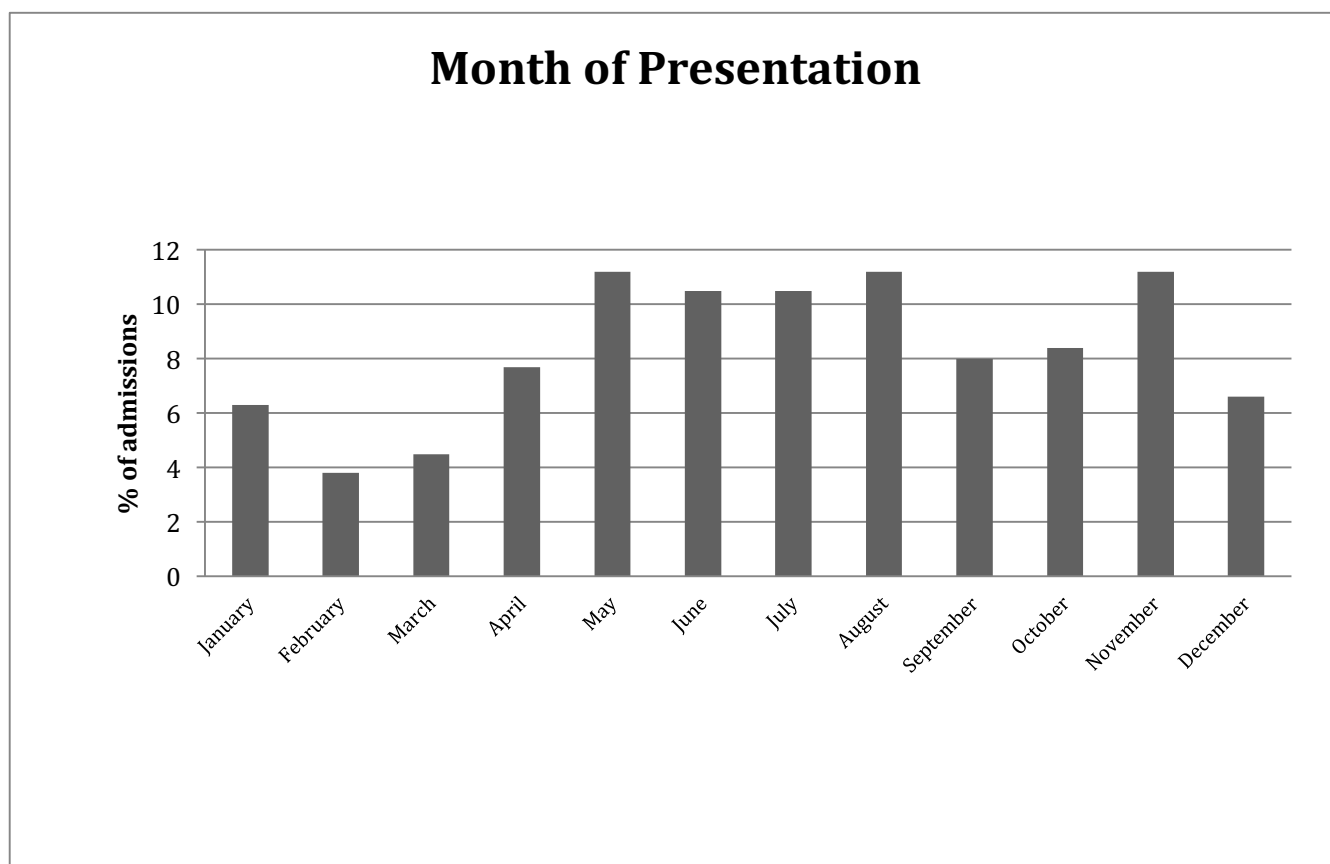
136 or 47.6% of presentations occurred during the weekend (Friday 17:00hrs-Monday 07.59hrs). There was no statistically significant difference in this trend between 2010-2015 (Table 1). 145 or 50.7% were night presentations (20:00hrs-07.59hrs). There was a statistically significant increase in night presentations in the latter years (2013-2015) as compared to the earlier years (2010-2012) (*p*=0.017) (Table 1).

**Table 2:** The number of admissions secondary to the most common recreational drugs compared across the earlier (2010-2012) and latter (2013-2015) years.

| The most common recreational drugs       | Number of admissions involving recreational drug N, percentage of admissions 2010-2015 (%) | 2010-2012      | 2013-2015        | P-value            |
|--|--|----------------|------------------|--------------------|
|  |  | N (%)          | N (%)            |                    |
| Heroin                                   | 126 (44.1)   | 62 (48.8)      | 64 (40.3)        | 0.147 <sup>#</sup> |
| Cocaine                                  | 119 (41.6)   | 48 (37.8)      | 71 (44.7)        | 0.242 <sup>#</sup> |
| MDMA/<br>methamphetamine<br>/amphetamine | 63 (22)  | 38 (29.9)      | 25 (15.7)        | 0.004 <sup>#</sup> |
| Cannabis                                 | 54 (18.5)  | 24 (18.9)      | 29 (18.2)        | 0.887 <sup>#</sup> |
| <b>SCRA</b>                              | <b>26 (9.1)</b>  | <b>0 (0)</b>   | <b>26 (16.4)</b> | <b>&lt;0.0001*</b> |
| Benzodiazepines                          | 25 (8.7)   | 11 (8.7)       | 14 (8.8)         | 0.966 <sup>#</sup> |
| <b>Synthetic<br/>Cathinones</b>          | <b>11 (3.8)</b>  | <b>9 (7.1)</b> | <b>2 (1.3)</b>   | <b>0.013*</b>      |

Statistical tests used - <sup>#</sup>: Pearson's chi square test, <sup>\*</sup>: Fisher's exact test used

**Figure 1:** Percentage admission per month (2010-2015)

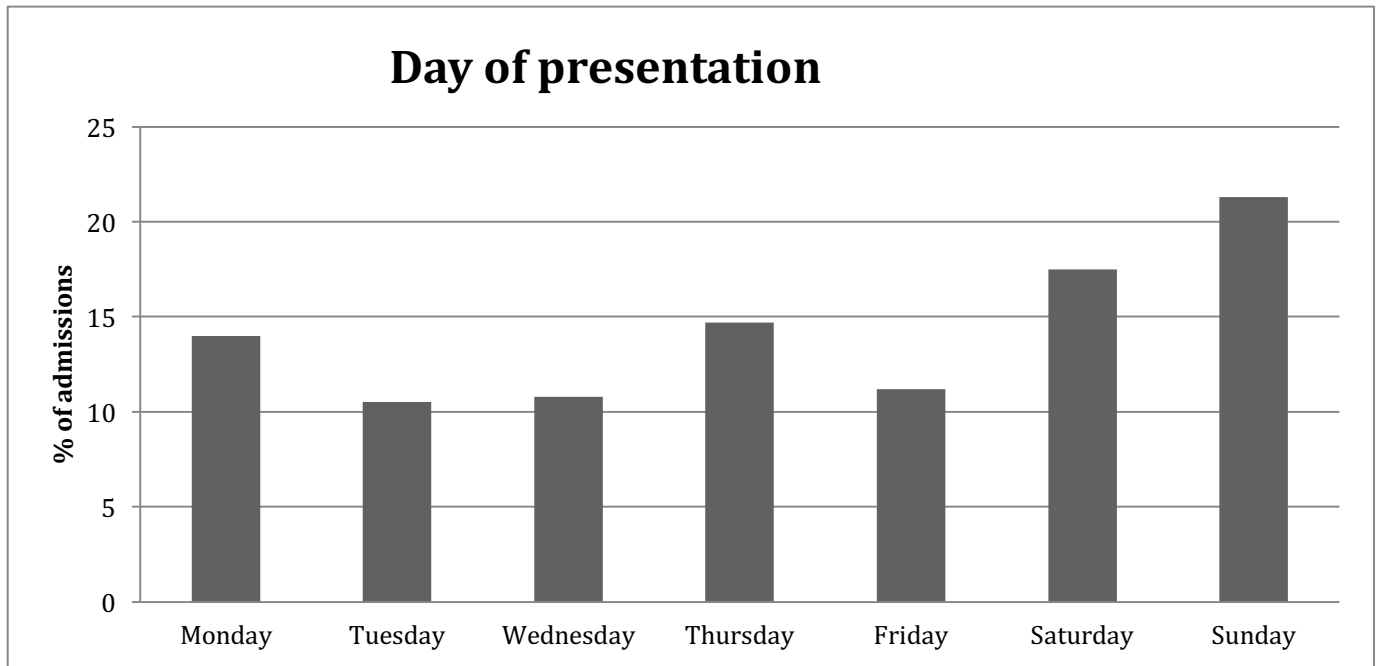


**Table 1: Multiple categorical variables with their respective p-value between 2010-2015 and for the grouped years 2010-2012 and 2013-2015.**

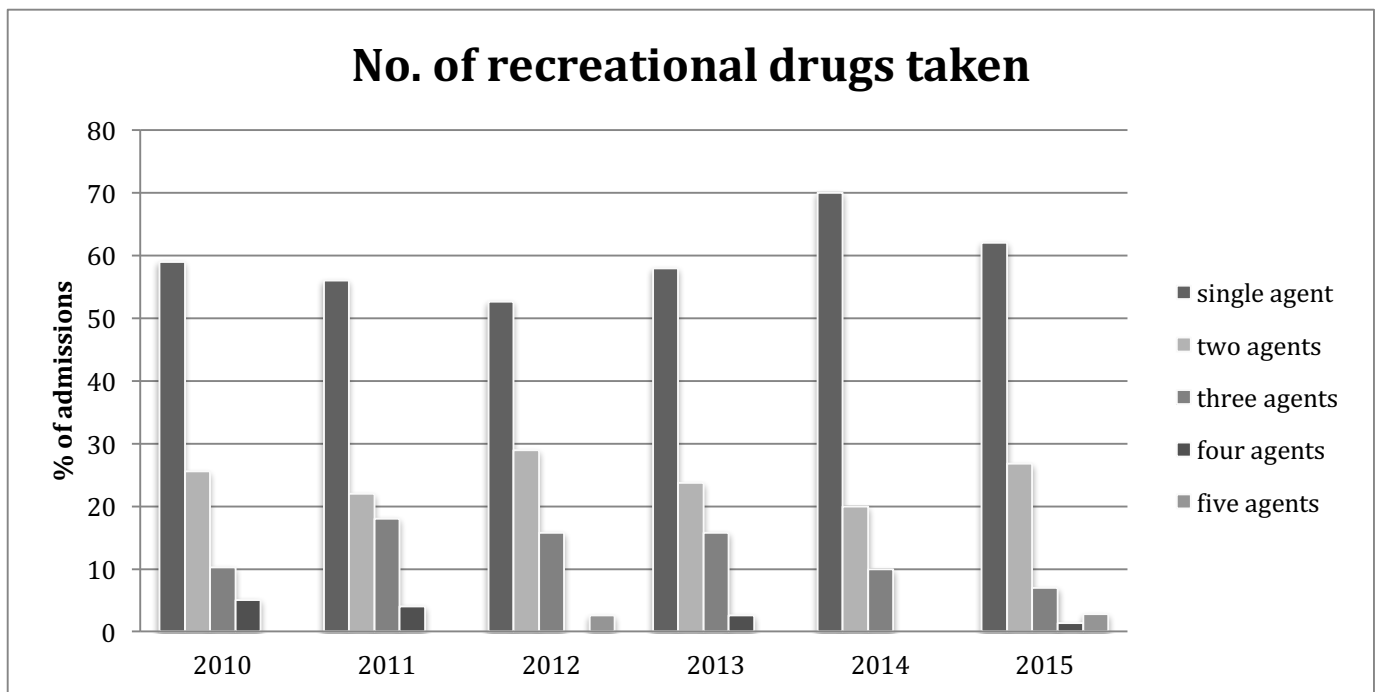
|                                   |                                    | 2010         | 2011       | 2012         | 2013         | 2014       | 2015      | P-value                  | 2010-2012  | 2013-2015     | P-value                  |
|-----------------------------------|------------------------------------|--------------|------------|--------------|--------------|------------|-----------|--------------------------|------------|---------------|--------------------------|
|                                   |                                    | N (%)        | N (%)      | N (%)        | N (%)        | N (%)      | N (%)     |                          | N (%)      | N (%)         |                          |
| <b>Gender</b>                     | Male                               | 31<br>(79.5) | 44<br>(88) | 30<br>(78.9) | 32<br>(84.2) | 39<br>(78) | 48 (67.6) | <b>0.136<sup>s</sup></b> | 105 (82.7) | 119<br>(74.8) | <b>0.11<sup>s</sup></b>  |
|                                   | Female                             | 8<br>(20.5)  | 6 (12)     | 8<br>(21.1)  | 6<br>(15.8)  | 11<br>(22) | 23 (32.4) |                          | 22 (17.3)  | 40<br>(25.2)  |                          |
| <b>Nationality</b>                | Maltese                            | 37<br>(94.9) | 46<br>(92) | 29<br>(76.3) | 31<br>(81.6) | 36<br>(72) | 47 (66.2) | <b>0.001*</b>            | 112 (88.2) | 114<br>(71.7) | <b>0.001<sup>s</sup></b> |
|                                   | Foreign                            | 2 (5.1)      | 4 (8)      | 9<br>(23.7)  | 7<br>(18.4)  | 14<br>(28) | 24 (33.8) |                          | 15 (11.8)  | 45<br>(28.3)  |                          |
| <b>Ward</b>                       | Normal                             | 35<br>(89.7) | 40<br>(80) | 35<br>(92.1) | 25<br>(65.8) | 45<br>(90) | 59 (83.1) | <b>0.028*</b>            | 110 (86.6) | 129<br>(81.1) | <b>0.261<sup>s</sup></b> |
|                                   | Critical care                      | 4<br>(10.3)  | 10<br>(20) | 3 (7.9)      | 13<br>(34.2) | 5 (10)     | 12 (16.9) |                          | 17 (13.4)  | 30<br>(18.9)  |                          |
| <b>Weekend</b>                    | No                                 | 24<br>(61.5) | 27<br>(54) | 23<br>(60.5) | 15<br>(39.5) | 21<br>(42) | 39 (54.9) | <b>0.205<sup>s</sup></b> | 74 (58.3)  | 75<br>(47.2)  | <b>0.074<sup>s</sup></b> |
|                                   | Yes                                | 15<br>(38.5) | 23<br>(46) | 15<br>(39.5) | 23<br>(60.5) | 29<br>(58) | 32 (45.1) |                          | 53 (41.7)  | 84<br>(52.8)  |                          |
| <b>Night</b>                      | No                                 | 23 (59)      | 32<br>(64) | 18<br>(47.4) | 17<br>(44.7) | 20<br>(40) | 31 (43.7) | <b>0.118<sup>s</sup></b> | 73 (57.5)  | 68<br>(42.8)  | <b>0.017<sup>s</sup></b> |
|                                   | Yes                                | 16 (41)      | 18<br>(36) | 20<br>(52.6) | 21<br>(55.3) | 30<br>(60) | 40 (56.3) |                          | 54 (42.5)  | 91<br>(57.2)  |                          |
| <b>Season</b>                     | Winter<br>(December-<br>February)  | 8<br>(20.5)  | 14<br>(28) | 7<br>(18.4)  | 4<br>(10.5)  | 8 (16)     | 7 (9.9)   | <b>0.004*</b>            | 29 (22.8)  | 19<br>(11.9)  | <b>0.006<sup>s</sup></b> |
|                                   | Spring (March-<br>May)             | 7<br>(17.9)  | 10<br>(20) | 3 (7.9)      | 11<br>(28.9) | 7 (14)     | 29 (40.8) |                          | 20 (15.7)  | 47<br>(29.6)  |                          |
|                                   | Summer (June-<br>August)           | 14<br>(35.9) | 13<br>(26) | 19<br>(50)   | 9<br>(23.7)  | 16<br>(32) | 21 (29.6) |                          | 46 (36.2)  | 46<br>(28.9)  |                          |
|                                   | Autumn<br>(September-<br>November) | 10<br>(25.6) | 13<br>(26) | 9<br>(23.7)  | 14<br>(36.8) | 19<br>(38) | 14 (19.7) |                          | 32 (25.2)  | 47<br>(29.6)  |                          |
| <b>Day of the<br/>Week</b>        | Monday                             | 7<br>(17.9)  | 6 (12)     | 8<br>(21.1)  | 3 (7.9)      | 6 (12)     | 10 (14.1) | <b>&lt;0.0001*</b>       | 21 (16.5)  | 19<br>(11.9)  | <b>0.53<sup>s</sup></b>  |
|                                   | Tuesday                            | 5<br>(12.8)  | 2 (4)      | 9<br>(23.7)  | 4<br>(10.5)  | 4 (8)      | 6 (8.5)   |                          | 16 (12.6)  | 14<br>(8.8)   |                          |
|                                   | Wednesday                          | 7<br>(17.9)  | 6 (12)     | 2 (5.3)      | 1 (2.6)      | 3 (6)      | 12 (16.9) |                          | 15 (11.8)  | 16<br>(10.1)  |                          |
|                                   | Thursday                           | 6<br>(15.4)  | 10<br>(20) | 3 (7.9)      | 4<br>(10.5)  | 7 (14)     | 12 (16.9) |                          | 19 (15)    | 23<br>(14.5)  |                          |
|                                   | Friday                             | 2 (5.1)      | 6 (12)     | 7<br>(18.4)  | 7<br>(18.4)  | 4 (8)      | 6 (8.5)   |                          | 15 (11.8)  | 17<br>(10.7)  |                          |
|                                   | Saturday                           | 3 (7.7)      | 11<br>(22) | 3 (7.9)      | 10<br>(26.3) | 10<br>(20) | 13 (18.3) |                          | 17 (13.4)  | 33<br>(20.8)  |                          |
|                                   | Sunday                             | 9<br>(23.1)  | 9 (18)     | 6<br>(15.8)  | 9<br>(23.7)  | 16<br>(32) | 12 (16.9) |                          | 24 (18.9)  | 37<br>(23.3)  |                          |
|                                   |                                    |              |            |              |              |            |           |                          |            |               |                          |
| <b>Ethanol</b>                    | No                                 | 22<br>(56.4) | 35<br>(70) | 18<br>(47.4) | 20<br>(52.6) | 26<br>(52) | 48 (67.6) | <b>0.128<sup>s</sup></b> | 75 (59.1)  | 94<br>(59.1)  | <b>1<sup>s</sup></b>     |
|                                   | Yes                                | 17<br>(43.6) | 15<br>(30) | 20<br>(52.6) | 18<br>(47.4) | 24<br>(48) | 23 (32.4) |                          | 52 (40.9)  | 65<br>(40.9)  |                          |
| <b>Number of<br/>agents taken</b> | Single                             | 23 (59)      | 28<br>(56) | 21<br>(55.3) | 22<br>(57.4) | 36<br>(72) | 44 (62)   | <b>0.574<sup>s</sup></b> | 72 (56.7)  | 102<br>(64.2) | <b>0.199<sup>s</sup></b> |
|                                   | Multiple                           | 16 (41)      | 22<br>(44) | 17<br>(44.7) | 16<br>(42.1) | 14<br>(28) | 27 (38)   |                          | 55 (43.3)  | 57<br>(35.8)  |                          |

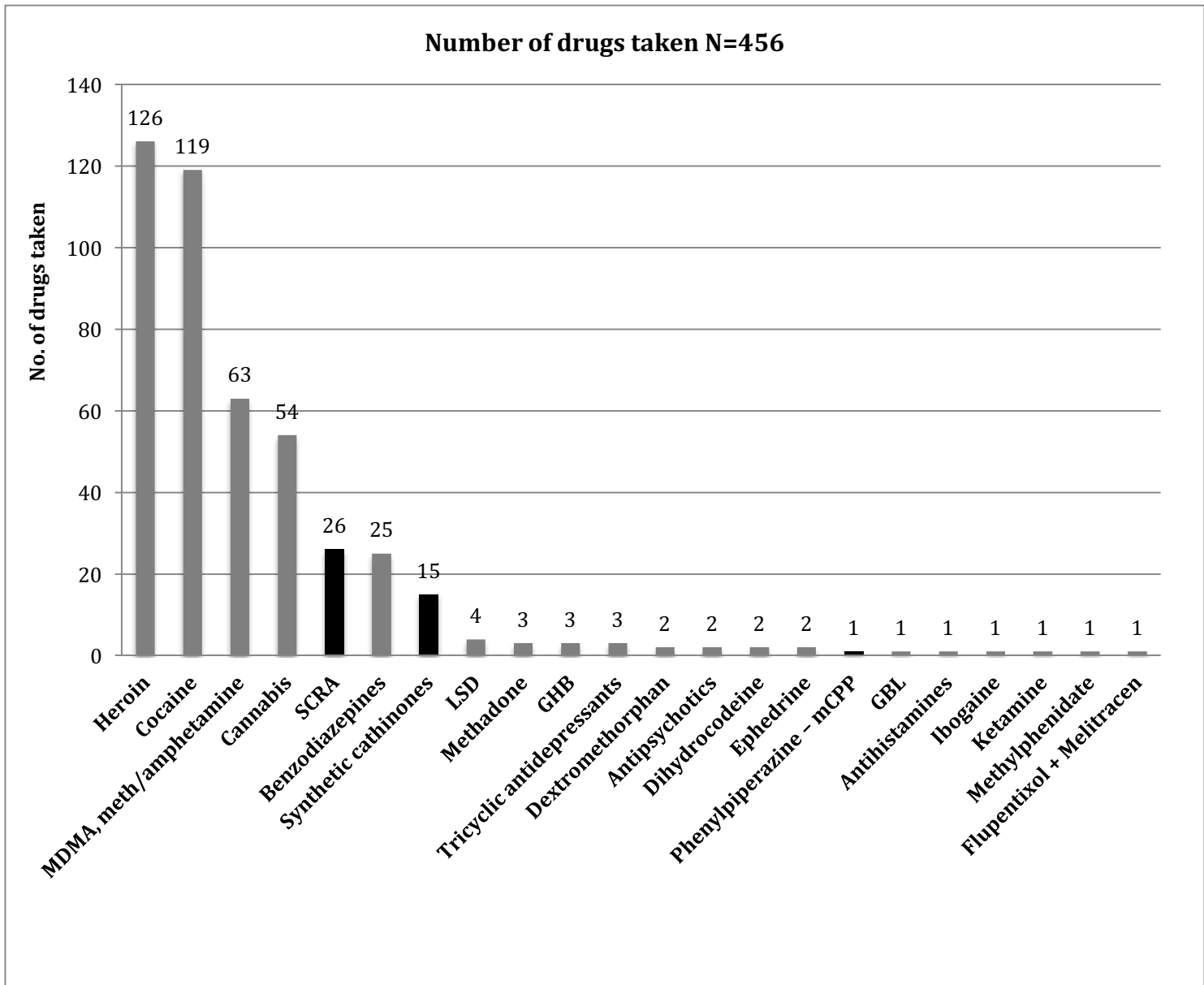
N: number; Statistical tests used - <sup>s</sup>: Pearson chi-square test; \*: Fisher's exact test

**Figure 2:** Percentage of admissions per day of the week (2010-2015).



**Figure 3:** Percentage of admissions per number of recreational drugs taken between 2010 and 2015



**Figure 4:** All the recreational drugs taken (including NPS in black), between 2010-2015.

### Recreational drugs taken

There were 456 reported recreational drugs out of a total of 284 admissions. Ethanol was co-ingested in 40.9% of all admissions, with no significant difference across the years (Table 1). As shown in Fig. 3, a single agent was involved in most admissions (172, 60.1%), with no statistically significant change in the number of drugs taken (single or multiple) across the 6-year period (Table 1).

Of the total number of drugs taken (456), ‘classical’ recreational drugs were the

most commonly involved with 362 (79.4%) of the total recreational drugs taken, while there were 42 (9.2%) reported NPS (SCRA, synthetic cathinones and phenylpiperazine) (Fig. 4).

‘Classical’ recreational drugs such as heroin, and cocaine were involved in 261 (91.3%) of the total admissions, while NPS were present in 37 (12.9%) of the admissions between 2010 and 2015. 15 of these 37 NPS admissions involved both ‘Classical’ recreational drugs and NPS. Of these NPS, SCRA were first reported in an

MDH admission in 2015, and resulted in 36.6% of all recreational drug admissions in that year.

43 (9.4%) pharmaceutical medications were taken in 34 admissions (11.9%) for recreational purposes. Of these benzodiazepines were the most common (26, 60.5%), with diazepam (16, 37.2%), being the commonest pharmaceutical drug.

### Severity of the admissions

The average length of stay (LOS) between 2010 and 2015 was 47.2 hours, while the median (IQR) LOS was 38 (23-50.9) hours. The median (IQR, range) GCS at admission to ED between 2010 and 2015 was 14 (13-15, 3-15), while the average GCS at ED was 13.2. There was no statistically significant difference in GCS between genders ( $p=0.239$ ). 27 (9.44%) patients had a GCS of less than or equal to 8 on admission (comatose), while 123 (43%) had a GCS of between 9 and 14. 47 patients (16.4%) required admission to either cardiac critical care unit (CCCU) or intensive care unit (ITU).

### Novel psychoactive substances

NPS were present in 37 (12.9%) admissions between 2010-2015, involving 42 (9.2%) reported NPS. 26 SCRA, 15 synthetic cathinones (MDPV, dimethylcathinone, mephedrone, pentadone, PVP and pyrovalerone) and 1 piperazine (mCPP) were involved. When NPS admissions were compared with Non-NPS admissions there was no statistical difference in terms of median GCS ( $p=0.297$ ), critical bed usage ( $p=0.213$ ) or median LOS ( $p=0.977$ ).

### Synthetic cannabinoid receptor agonists (SCRA)

Admissions secondary to self-reported

SCRA intoxication were analysed in order to attempt to identify a toxidrome. In total, 18 cases were included out of a total of 26 cases of self-reported SCRA use. One medical file could not be retrieved and 6 other cases had either consumed alcohol or other drugs together with SCRA. 13 (72.2%) were males and 11 (61.1%) were foreign nationals.

### MEET\_SCRA

The most common features were mydriasis (66.7%), emesis (50%), euphoria (38.9%), tachycardia (77.8%), sweating (38.9%) and seizures (22.2%), confusion [GCS<15] (77.8%), respiratory depression (44.4%), respiratory acidosis (33.3%), anxiety (61.1%)/ agitation (79.9%). From these features a mnemonic for the toxidrome of SCRA intoxication is proposed (MEET\_SCRA).

### Discussion

#### *Admissions with recreational drug intoxication*

286 patients were admitted for recreational drug intoxication between the 1<sup>st</sup> of January 2010 and the 31<sup>st</sup> of December 2015. This represents 0.18% of the total ED admissions per year in MDH.<sup>6</sup> There was however a significant increase in the number of admissions in 2015 (0.26%), which would approach European figures [1, 2].

### Demographics

The patients' age and gender ratios compared well with other European studies (median age of 26 years) with males amounting for more than three quarters of the MDH admissions.<sup>1,12</sup> 79% of the MDH recreational drug admissions were Maltese, however over the latter years there was a statistically significant increase in the number of foreigners. This was likely due to



the recent increase in immigration, with Malta recording amongst the highest population growth rates in 2013.<sup>13</sup>

Most of these admissions attended during the night and in the summer period, while Saturday and Sunday were the most common days of admission (Table 1 and Fig. 2). This correlates well with a study by Dines et al.<sup>1</sup> and with the fact that some social settings like clubbing, increase the risk of recreational drug consumption.<sup>14</sup>

### Severity of the admissions

The average LOS during this 6-year period was 47.2 hours, with a median of 38 hours. Comparison with the European study by Dines et al.<sup>8</sup> with a LOS of 4.6 hours (IQR 2.5-9.9 hours) was not possible, since this study included discharges from the ED.

The median GCS upon admission to the ED was 14 while the average GCS was 13.2. The fact that 27 (9.44%) patients were comatose and that 123 (43%) had a GCS of between 9 and 14 on admission, indicates the severity of such intoxications and compares well with other studies.<sup>1-2</sup> 47 patients (16.4%) were admitted to critical care. When comparing NPS admissions to non-NPS admissions, there was no-statistical change in terms of severity (LOS, median GCS and critical bed usage). However, note is made of the small numbers of the sample which might have affected the statistical outcome.

### Recreational drugs taken

The high rate of ethanol co-ingestion (40.9%) and poly-drug use (39.9%) in these admissions relates well with other European studies.<sup>1-2</sup>

'Classical' recreational drugs, especially heroin and cocaine were the most common recreational drugs over the 6-year period (379, 83.1%). Pharmaceutical drugs

were taken for recreational purposes in 11.9% of these admissions. In the MDH study, only 3 patients took them as a lone drug (excluding alcohol). Thus, the lone intake of a pharmaceutical drug to 'get a high' remains a very rare occurrence in MDH admissions.

### Novel psychoactive substances (NPS)

NPS were present in 37 (12.9%) of all admissions and included 42 (9.2%) reported NPS. This percentage of reported NPS was twice as common in Malta than in the European study by Dines et al.<sup>1</sup> In 2015, 27 (24.3%) NPS were reported in 26 (36.6%) admissions, hence being significantly more than the latter study. Synthetic cathinones "bath salts" were more common in the earlier years (2010-2012), and have decreased over the latter years (2013-2015) ( $p=0.013$ ) (Table 2).

The only piperazine reported, meta-Chlorophenylpiperazine (mCPP) was detected by GC/MS in 2010 and was found in a polydrug admission (together with MDMA and cocaine). The reasons for such decrease in reported synthetic cathinones and piperazines could be a change in trend use, decreased availability, or possibly the scheduling of such drugs. Mephedrone became scheduled by legal notice in Malta in 2010.<sup>15</sup> Also, the mass spectrometer of the GC-MS available at the MDH laboratory had not been functional for the last 6 months of 2015.

The fact that some users might be acquiring different contents, or actually different recreational drugs, to what they paid for, has also been mentioned in the literature.<sup>16-17</sup> This might be the reason why some patients had not self-reported the use of synthetic cathinones, even when these drugs were still not scheduled in Malta. MDPV for instance, only became scheduled in Malta in 2016.<sup>18</sup>

**Table 3: Clinically reported features of SCRA intoxications**

|   | Total Number (N) = 18 | (%)  |
|---|-----------------------|------|
| <b>Cardiovascular</b>   |                       |      |
| Tachycardia (>100bpm)   | 14                    | 77.8 |
| Bradycardia (<60bpm)  | 0                     | 0    |
| Hypotension (Systolic blood pressure<90)  | 1                     | 5.6  |
| Arrhythmias   | 0                     | 0    |
| Palpitations  | 2                     | 11.1 |
| Chest pain  | 1                     | 5.6  |
| Arrhythmias (apart from sinus tachycardia)  | 0                     | 0    |
| <b>Respiratory</b>  |                       |      |
| Hyperventilation  | 4                     | 22.2 |
| Respiratory depression: pCO <sub>2</sub> (> 45mmHg)                                 | 8                     | 44.4 |
| <b>Neurological/Psychiatric</b>   |                       |      |
| Anxiety   | 11                    | 61.1 |
| Euphoria  | 7                     | 38.9 |
| Headache  | 1                     | 5.6  |
| Agitation/Aggressiveness  | 13                    | 72.2 |
| Psychosis   | 2                     | 11.1 |
| Hallucinations  | 3                     | 16.7 |
| Amnesia   | 4                     | 22.2 |
| Seizures  | 3                     | 16.7 |
| Twitching of muscles (myoclonus)  | 2                     | 11.1 |
| Cerebellar features   | 3                     | 16.7 |
| Pupils – Mydriasis  | 12                    | 66.7 |
| Pupils – Miosis   | 0                     | 0    |
| Pre-hospital 'Alert' on AVPU scale  | 7                     | 38.9 |
| Pre-hospital 'Not Alert' on AVPU scale i.e. V, P or U /low GCS                      | 11                    | 61.1 |
| GCS on arrival to ED = 15   | 4                     | 22.2 |
| GCS on arrival to ED 9-14   | 13                    | 72.2 |
| GCS on arrival to ED < or = 8   | 1                     | 5.6  |
| <b>Others</b>   |                       |      |
| Lactate >=2.0   | 7                     | 38.9 |
| Acidosis (pH <7.35)   | 6                     | 33.3 |
| Alkalosis (pH >7.45)  | 1                     | 5.6  |
| Nausea or vomiting  | 9                     | 50   |
| Respiratory acidosis only (pH <7.45, pCO <sub>2</sub> >45mmHg, Bicarbonate > 21)    | 6                     | 33.3 |
| Metabolic acidosis only (pH <7.45, pCO <sub>2</sub> <=45mmHg, HCO <sub>3</sub> <21) | 0                     | 0    |
| Mixed metabolic and respiratory acidosis  | 2                     | 11.1 |
| Glucose level >9 <11.1  | 5                     | 27.8 |
| Glucose level >=11.1  | 2                     | 11.1 |
| Hyperthermia (>39degrees Celsius)   | 0                     | 0    |
| Hypothermia (<35 degrees Celsius)   | 3                     | 16.7 |
| Sweating  | 7                     | 38.9 |
| Acute kidney injury   | 6                     | 33.3 |
| Hypokalaemia (K <sup>+</sup> < 3.5)   | 5                     | 27.8 |

## Synthetic cannabinoid receptor agonists (SCRA)

SCRA were first reported in MDH admissions in the beginning of April 2015. From then onwards, 26 (36.6%) admissions in 2015 were from SCRA. This represented only the self-reported intoxications since there is no liquid chromatography-tandem Mass Spectroscopy (LC-MS/MS) or other analytical screen able to detect SCRA at present in Malta, and no samples were sent for testing abroad.

Sympathomimetic toxicity, respiratory complications and neuropsychiatric symptoms, were the most common reported features of lone SCRA intoxications (Table 3). This collated well with a study by Hermanns-Clausen et al.<sup>19</sup> involving a small sample of patients with confirmed SCRA intoxication.

Fourteen (77.8%) patients in the MDH study had documented tachycardia (range 102-145bpm). All of these patients were treated symptomatically for the tachycardia, and all had normalization of their heart rate within a few hours.

A significant number of patients had respiratory depression in this study, and this is supported by an early study on SCRA effects on animals.<sup>20</sup> While the study by Hermanns-Clausen et al.<sup>19</sup> does not mention respiratory depression or acidosis, it does emphasise the fact that a third of the patients displayed somnolence for several hours, “but still had sufficient respiration”. It is reasonable to assume that respiratory depression might have been present at some point during this period of decreased consciousness. 2 case reports documenting SCRA-associated respiratory depression in two young males, both of whom required intubation, were described by Jinwala and Gupta.<sup>21</sup>

In the study by Hermanns-Clausen et

al.<sup>19</sup> no patients had acute kidney injury (AKI), as defined by KDIGO<sup>22</sup> while this was present in 6 lone SCRA intoxications admitted to MDH. All of these admissions involved young males (16 to 36 years). Four of these 6 AKI's were hypotensive, or had documented fluid loss, such as sweating, vomiting or excessive physical activity. However, in 2 of these 6 cases neither rhabdomyolysis nor a pre-renal injury appear to fully explain the AKI, suggesting a SCRA-associated intrinsic AKI. AKI has been associated with SCRA in 16 US patients, with 6 out of 8 of such patients who had a renal biopsy, showing acute tubular injury, while 3 out of these patients showing features of acute interstitial nephritis.<sup>23</sup> Of these 16 patients, five required haemodialysis, most recovering within 3 days of the creatinine peak, with no reported deaths.<sup>23</sup> While MDH cases had normalisation of their levels within a maximum of 10 days, with none needing dialysis, two patients were discharged home before documented normalisation of their renal function.

Three patients (16.7%) in this study had generalised seizures, all of which were treated conservatively and none had status epilepticus. SCRA have been associated with seizure activity.<sup>24</sup>

A toxidrome mnemonic “MEET\_SCRA” is proposed from the results of this study, as an aid in diagnosing patients intoxicated with SCRA.

## Conclusion

Recreational drug use is a significant healthcare burden in MDH. Although the number of admissions is relatively small, these appear to be on the increase, with a substantial increase in 2015. More than half of such patients were confused (GCS<15), and 16.4% needed critical care.

'Classical' recreational drugs are the most common recreational drugs associated with admissions. NPS however have become an important threat from a public health perspective. More than a third of all admissions in 2015 involved a NPS (SCRA or synthetic cathinones). A large proportion of the SCRA-associated admissions were severe, with respiratory depression, acidosis and low GCS. Although SCRA symptoms appeared to improve relatively quickly, a third of patients with lone SCRA intoxication had AKI, 16.7% had seizures, and more than a quarter of such admissions needed critical care.

The use of the toxidrome mnemonic 'MEET\_SCRA' is proposed in order to facilitate patient diagnosis in cases of SCRA intoxication.

### Limitations

Since admission records was obtained from a clinical coding system based on discharge letters, admissions that had no discharge letter done were not included. Such might have occurred if the patient self-discharged or died during that admission. This study only included patients admitted to MDH. While the admissions likely reflected those patients that had the more severe symptoms, it also excludes a large cohort of patients that were discharged from the ED.

This study was based substantially on the self-reporting of recreational drugs taken, and this also depends on the patient's attitude towards possible legal repercussions.

There is currently no available LC-MS/MS in Malta, thus, SCRA and some other NPS could not be detected.

The mass spectrometer of the GC-MS in the MDH laboratory was not operational from mid-2015 onwards, due to a malfunction.

This might have resulted in less reported NPS in the latter half of 2015.

### Recommendations

Further research on the pharmacology and toxicology of recreational drugs including NPS, and their impact on hospitals locally and internationally is recommended. The use of the toxidrome mnemonic 'MEET\_SCRA' is proposed in order to facilitate patient diagnosis in cases of SCRA intoxication.

A LC-MS/MS and a better-equipped hospital laboratory would be a valuable asset in early identification of recreational drug outbreaks, such as with SCRA in 2015. In 2016, Malta joined the Euro-DEN project<sup>25</sup> which aims to identify recreational drug use presenting to European ED's. Such data can be of help to local and EU policy makers, when deciding on future healthcare implementations on this subject.

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### Ethics approval

University Research Ethics Committee (University of Malta).

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