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# Benzodiazepine use amongst young attendees of an Irish substance treatment centre

--Manuscript Draft--

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| **Abstract:** | Objective<br><br>To describe the demographic characteristics of those service-users attending Matt Talbot Services, and their current and past substance use, and to explore the use of benzodiazepines amongst this group.<br><br>Method<br><br>There were 198 service-users who attended a substance misuse treatment centre in Cork, Ireland between January 2005 and August 2011.<br><br>Results<br><br>Benzodiazepines had ever been used by 51.0%, and of these, 55.8% were regular benzodiazepine users. The mean age of first use was 14.9 ± 1.40 years. Regular users of benzodiazepines were regular users of significantly more substances (3, IQR=2-3) when compared with non-regular benzodiazepine users (1, IQR=1-2). Regular benzodiazepine users showed more behavioural signs (12, IQR=10-14) than non-regular users (9, IQR=7-12). Physical signs were significantly different between regular (8, IQR=6-11) and non-regular (5, IQR=3-10) users.<br><br>Conclusions<br><br>The effects of benzodiazepine misuse affect the individual, their family, and society as whole through hospitalisation, substance treatment and crime. Identifying regular benzodiazepine users can help reduce the burden of benzodiazepines. |

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# Abstract

**Objective**

To describe the demographic characteristics of those service-users attending Matt Talbot Services, and their current and past substance use, and to explore the use of benzodiazepines amongst this group.

**Method**

There were 198 service-users who attended a substance misuse treatment centre in Cork, Ireland between January 2005 and August 2011.

**Results**

Benzodiazepines had ever been used by 51.0%, and of these, 55.8% were regular benzodiazepine users. The mean age of first use was 14.9 ± 1.40 years. Regular users of benzodiazepines were regular users of significantly more substances (3, IQR=2-3) when compared with non-regular benzodiazepine users (1, IQR=1-2). Regular benzodiazepine users showed more behavioural signs (12, IQR=10-14) than non-regular users (9, IQR=7-12). Physical signs were significantly different between regular (8, IQR=6-11) and non-regular (5, IQR=3-10) users.

**Conclusions**

The effects of benzodiazepine misuse affect the individual, their family, and society as whole through hospitalisation, substance treatment and crime. Identifying regular benzodiazepine users can help reduce the burden of benzodiazepines.

# 1. Introduction

## 1.1. Background

Treatment for substance misuse is a global issue. In 2010, there were between 3.1 and 7.2 million people who received treatment for substance dependence (UNODC, 2012). This is similar to the estimate of treatment uptake in 2005, which was around 3.7 million people (UNODC, 2007). It can be seen that there was little change in these numbers between these two periods. In Europe however, a different trend is observed as there has been a consistent rise in the number of people accessing drug treatment. In 2005 there were approximately 326,000 people attending drug treatment centres, but by 2010 this had increased by 45% (EMCDDA, 2007b, 2012a). This increase has also been mirrored in first-time users of the treatment centres which showed that the numbers increased 38% to approximately 177,700 (EMCDDA, 2007a, 2012a). Ireland has not been left untouched by this trend, with an approximate 35% increase in the number of cases handled by treatment centres in Ireland between 2005 and 2010 (Bellerose, Carew, & Lyons, 2011). In the same period of time, there was a 59% increase in the number of new persons entering into treatment. In 2010, 9.3% of cases (equivalent to 707 people) related to those aged less than 18 years of age, which was a 75% increase in the number of adolescents in treatment in 2005.

Whilst international treatment service utilisation figures are not available nonetheless in Europe, there was a 94% increase in the number of under-25s accessing treatment between 2005 and 2010 (EMCDDA, 2012b). Lifetime drug use amongst 15-34 years olds in Ireland has increased between 2002 and 2011 by approximately 10% from 25.9% to 35.7% (National Advisory Committee on Drugs, 2011). The most commonly used drugs in the year previous in this age group in 2010/2011 were alcohol (86.3%), tobacco (37.3%), opiates other than heroin [such as codeine, oxycodone and morphine] (28.3%), cannabis (10.3%), synthetic psychoactive substances (6.7%), and

sedatives/tranquilisers (4.8%). The sedative/tranquiliser category of drugs was the only category in which a rise was observed since the previous survey done in 2006/2007. In a recent review of substance use amongst young people, benzodiazepines were the only substance reviewed whose prevalence did not decrease over its 10-year review period (Murphy, Sahm, McCarthy *et al.*, 2013). These two studies highlight that benzodiazepine misuse is not following the trend of decreasing use as other substances are.

Progress has been made in reducing of the numbers of young people using benzodiazepines in Europe. Between 1995 and 2011, the percentage of 15/16 year olds that had used benzodiazepines without a prescription decreased from 7% (Bjorn Hibell, Andersson, Bjarnason *et al.*, 1997) to 3% (Björn Hibell, Guttormsson, Ahlström *et al.*, 2012), although this is greater than 2003 levels, 2% (Bjorn Hibell, Andersson, Bjarnason *et al.*, 2004). This is in contrast to the percentage of young people who are prescribed benzodiazepines in Ireland which has decreased from 11% in 1999 (Bjorn Hibell, Andersson, Salme *et al.*, 2000) to 9% in 2011 (Björn Hibell, Guttormsson, Ahlström*, et al.*, 2012). Combining these, it can be estimated that approximately 1-in-10 Irish 15/16 year olds use benzodiazepines. Another method of measuring benzodiazepine usage amongst young people in Ireland is to look at the number of young people entering treatment services in Ireland. Between 2003 and 2008, there was a minimum of a 5-fold increase in the number of young people aged less than 18 years who received treatment for benzodiazepine use (Bellerose, Lyons, Carew *et al.*, 2010).

Benzodiazepines at therapeutic levels can have serious short-term side-effects, and chronic use can result in long-term consequences. Acute use of benzodiazepines can impair the perception of risk, which can lead to hazardous activities such as high-risk sexual behaviour and reckless driving (Dassanayake, Michie, Carter *et al.*, 2011; Griffin, Kaye, Bueno *et al.*, 2013). Benzodiazepines can also lead to paradoxical reactions such as restlessness, agitation, anxiety, aggressive behaviour, and delusions (Irish Medicines Board, 2011; Parsa, 2011). There is evidence that these paradoxical reactions are more likely to occur to those at either extremes of age i.e. a younger or older age

(Mancuso, Tanzi, & Gabay, 2004), and that combining with alcohol can increase the occurrence of violent behaviour (Forsyth, Khan, & McKinlay, 2011). Cognitive impairment is a well-documented side-effect of benzodiazepine use (M. J. Barker, K. M. Greenwood, M. Jackson *et al.*, 2004; Boeuf-Cazou, Bongue, Ansiau *et al.*, 2011; Billioti de Gage, Begaud, Bazin *et al.*, 2012), both short-term and long-term. There is evidence that these effects can remain even after treatment with benzodiazepines has ceased (Melinda J. Barker, Kenneth M. Greenwood, Martin Jackson *et al.*, 2004; Stewart, 2005), although this is not without dispute (Verdoux, Lagnaoui, & Begaud, 2005). Although not directly related to benzodiazepines, it is also interesting to note in a National Office of Suicide Prevention report that benzodiazepines were the second leading method of self-harming in Ireland, after alcohol, in 2011, resulting in 3611 hospitalisations (National Suicide Research Foundation, 2012). The significance of benzodiazepines in self-harm is such that the report views restricting access to benzodiazepines as a priority.

### 1.2. Aims

The aim of this paper is to characterise service-users who attend Matt Talbot Services (MTS) in the south of Ireland.

Objective:

To describe the demographic characteristics of those service-users attending MTS, and their current and past substance use, and to explore the use of benzodiazepines amongst this group.

## 2. Methods

### 2.1. Design

Ethical Approval for this research was gained from the Clinical Research Ethics Committee of the Cork Teaching Hospitals. The study used data collected from service-users who entered treatment with MTS between 2005 and August 2011. Applicants were initially interviewed by MTS staff to

identify those who would benefit from treatment. Those who passed the initial screening were accepted for treatment, while those not accepted were referred to alternatively-tiered services that could provide more appropriate treatment. A description of the 4-tier structure of mental health services is available elsewhere (Corrigan & O' Gorman, 2007). A total of 198 patient files were used in the study. Assessment was aided by the use of assessment forms. One of the forms included a section on the physical and behavioural impact of substance use. This was made up of 16 common behavioural symptoms and 12 physical signs of substance misuse. Service-users were asked to indicate if they had experienced any of these because of their substance misuse.

### 2.2. Analyses

Descriptive analysis of demographic data was done to provide a background of the service-user population type. Further descriptive analysis was performed on data relating to recent substance use, and examined by age and year of access to treatment. Regular benzodiazepine use was defined as benzodiazepine use in the previous month. This is a common measure of current use in the substance misuse field (National Advisory Committee on Drugs, 2011; European Monitoring Centre for Drugs and Drug Addiction, 2006). For the comparison of regular benzodiazepine users and non-regular benzodiazepine users, an independent t-test was performed on normally-distributed data, while the Mann-Whitney U test was performed on non-normally-distributed continuous/interval data. For nominal data, Pearson's chi-square analysis was performed (with Yate's continuity correction for 2x2 tables), and where expected values fell below 1 (or 5 for 2x2 tables), Fisher's Exact Test was used instead. A significance level of $\alpha$=0.05 was used for any inferential statistics calculated. All statistical analyses were performed using Predictive Analytics SoftWare Statistics (PASW; SPSS Inc. Chicago, Ill.) version 18.0.

## 3. Results

### 3.1 Demographic data

There were 198 service-users included in this study. Because of the number of incomplete forms, the sample numbers will vary between statistics; sample numbers are provided for each statistic reported.

97.9% (n=185) of service-users were male. The age of service-users that had details (n=163) ranged from 13-21 and their mean age was 16.4 years with a standard deviation (SD) of 1.25 years. Referral to the service has increased from two in 2005 up to 49 in 2010, with 29 service-users accessing treatment up to August 2011, as can be seen in Figure 1.

A breakdown of referral sources can be seen in Table 1. Juvenile Liaison officers (JLOs) were responsible for the most referrals (24.5%), while family members were the second largest group of referrals at 18.6%. Combining the referrals from JLOs and Probation officers, it can be seen that the Department of Justice is responsible for nearly half of all referrals (48.7%), whereas referrals from Department of Social Protection workers (social workers and youth centres) accounted for only 20.3% of total referrals.

Of the service-users who answered (n=184), 98.9% had ever consumed an alcoholic drink (See Table 2). The median age of first consumption was 13 years (IQR=12-14.75). Cannabis and tobacco followed closely with lifetime use at 93.9% and 92.7% respectively. Cocaine and benzodiazepines were the only remaining substances that had lifetime use levels over 50% (54.3% and 51.0% respectively).

### 3.2 Benzodiazepine use

Benzodiazepines had ever been used by 80/157 of the service-users. Of these, 43 (55.8%) service-users used benzodiazepines in the previous month, a measure of regular use (3 service-users did not answer the question). Daily use was recorded by 9 service-users, 19 service-users used benzodiazepines 2-6 times a week, and use of once a week or less was recorded for 15 service-users. The average age of first benzodiazepine use was 14.9 ± 1.40 years.

Characteristics of service-users entering treatment and their substance use history, as it relates to benzodiazepines, are examined in Table 3.

A comparative examination of regular and non-regular users showed no significant difference in the age of first benzodiazepine use, as can be seen in Table 4. Regular users of benzodiazepines were regular users of significantly more substances (3, IQR=2-3) when compared with non-regular benzodiazepine users (1, IQR=1-2).

Regular benzodiazepine users showed more behavioural signs (12, IQR=10-14) than non-regular users (9, IQR=7-12). Similarly, the physical signs were significantly different between regular (8, IQR=6-11) and non-regular (5, IQR=3-10) users. Both behavioural and physical signs were examined for differences between regular and non-regular users. Reporting of paranoia (p=0.018), loss of interest in sports and hobbies (p=0.039) and attention-seeking behaviour (p=0.022) were behaviours that differed significantly for regular and non-regular users. Pale/white skin (p=0.031) and vomiting (p=0.031) were the physical signs that were significantly different in both groups (See **Error! Reference source not found.**).

# 4. Discussion

## 4.1. Summary

This study examined the substance use history of a cohort of service-users attending an outpatient substance misuse treatment centre. An examination of these service-users' background was also conducted. The majority of those attending the service were male and the mean age was 16.4 years. The biggest source of referrals from this cohort was from Juvenile Liaison Officers, which accounted for approximately a third of all referrals. Alcohol, cannabis, and tobacco were all experimented by over 90% of attendees.

Benzodiazepines had been experimented on by over half of the attendees, while over a quarter of attendees use benzodiazepines more than once a month, and the mean age of first benzodiazepine use was 14.9 years. A comparison of regular benzodiazepine users and non-regular benzodiazepine users showed that regular users experienced more behavioural symptoms. Paranoia, attention-seeking behaviour, and loss of interest in sports were shown to occur more in regular benzodiazepine users. Regular users also reported more physical symptoms, with pallor and vomiting being significantly more common in regular users.

There is a large discrepancy between the number of males and females that attended the treatment centre. The majority of service-users in treatment centres are generally male, and this can be seen in many other studies (Che, Assanangkornchai, McNeil *et al.*, 2011). The overwhelming majority of attendees were male in this study (97.9%), and this is partially due to the aforementioned bias. However another cause must be factored in which is the mission statement of MTS was to help males that had substance dependence issues. Unofficially, they would accept females in crisis situations, so this kept the number of female clients lower than would be expected. This policy was changed in 2010 to accept both males and females. Regular admission of females should bring the gender ratio back in line with the studies shown above.

Delusions such as paranoia can be known to occur with benzodiazepine use and this effect is classed in a category known as paradoxical reactions (Irish Medicines Board, 2011). The Summary of Product Characteristics (SPC) for Valium states that delusions occur in response to using benzodiazepines predominantly in the elderly and in children (Irish Medicines Board, 2011). Attention-seeking behaviour is often a symptom of borderline personality disorder (Aviram, Brodsky, & Stanley, 2006) and histrionic disorder (Bakkevig & Karterud, 2010). Both of these disorders have been associated with benzodiazepine dependence, possibly because they are prone to depression and anxiety (Konopka, Pełka-Wysiecka, Grzywacz *et al.*, 2013).The loss of interest in sport may be related to effects of benzodiazepines. It is a common effect of regular substance use; it is listed as one of the

criteria for substance dependence in the Tenth Revision of the International Statistical Classification of Diseases and Related Health Problems (World Health Organisation, 1992). Specifically for benzodiazepines, if they are taken at clinical doses can lead to fatigue, drowsiness, decreased alertness, and depression (Irish Medicines Board, 2011). All of these side effects can lead to a decreased motivation which can result in decreased time spent on sports and hobbies.

Skin pallor in benzodiazepine use is related to benzodiazepine withdrawal and can last weeks after withdrawal (Lader, 2011). There does not appear to be a link benzodiazepine use and vomiting according to SPCs. There was a weak link in the literature that described benzodiazepines as a potential anti-emetic (Yeo, Jung, Ryu *et al.*, 2009). This suggests that vomiting may be a benzodiazepine withdrawal symptom, and there are cases reports that would support this hypothesis (Lin, Ma, & Liu, 2013), as well as evidence from primate research (Sannerud, Alien, Cook *et al.*, 1991), and reviews (Dickinson, Rush, & Radcliffe, 1990).

Looking more generally at negative behavioural and physical symptoms, regular benzodiazepine users experienced more behavioural and physical effects than non-regular users. This is to be expected as regular users will have more problems than others, however it is surprising that regular users experienced a wider spectrum of symptoms. In the case of physical symptoms, the difference is greater than 50%. It would be difficult to explain this discrepancy alone by increased benzodiazepine use; that would more likely lead to increased occurrence of similar symptoms. One possible factor that could influence this result was the difference between the numbers of regular medicines used by both groups of benzodiazepine users. Polysubstance use could account for a portion of the extra symptoms experienced by regular benzodiazepine users.

### 4.2. Limitations

This study was cross-sectional in design. The ability to generalise these data to other substance misuse centres should be done cautiously. This is a retrospective study so the researchers had no control over the design of the forms used by the staff at the MTS. This would have been advantageous as it would have been possible to customise the form so that a more thorough data could have been derived from it. Including further information on psychosocial and physical symptoms could provide a clearer picture of the experiences of these service-users. More information about the service-users' family history and their interests may help give researchers a better perspective on how their substance misuse fits in their lives.

This study surveyed adolescent service-users attending a substance misuse treatment centre. This is a specialised population that is not comparable to the general population. The level of drug use will be substantially higher among this population that among the population of adolescents in Ireland. Another factor that limits its generalisability to the general population is that the population is predominantly male. It has been mentioned previously that this is the case in other treatment centres internationally and may allow for comparison with other treatment centres.

## 5. Conclusions

This study presents data on the use of benzodiazepines among Irish adolescents attending a drug treatment centre. It is important that awareness about the level and severity of adolescent use of benzodiazepines is disseminated throughout the community, in particular among healthcare professionals. Benzodiazepines are powerful prescription medications used for a wide range of indications, including anxiety, insomnia, and epilepsy. Half of those who had taken benzodiazepines in this study became regular users. Recreational use of benzodiazepines can have acute and chronic effects, especially in a formative stage of life such as adolescence. Paranoia, attention-seeking behaviour, loss of interest in sports, pallor, and vomiting could indicate regular benzodiazepine use. Regular benzodiazepine users often are polysubstance users and the risks of mixing substances should be known. The effects of benzodiazepine misuse affect the individual, their family, and

society as whole through hospitalisation, substance treatment and crime. Identifying regular benzodiazepine users can help reduce the burden of benzodiazepines.

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Tables

Table 1.Breakdown of referrals of service users by source of referral (n=113)

| Referral source | % of total referrals (n) |
|---|---|
| Juvenile Liaison Officer | 34.5 (39) |
| Family | 18.6 (21) |
| Social Worker | 16.8 (19) |
| Probation officer | 14.2 (16) |
| Other | 5.3 (6) |
| Self | 3.5 (4) |
| Youth Centre | 3.5 (4) |
| School | 2.7 (3) |
| Other Treatment Centre | 0.9 (1) |

Table 2. Service-users that have ever used a substance

| Substance | % ever used (n) |
|---|---|
| Alcohol | 98.9 (182) |
| Cannabis | 93.9 (170) |
| Tobacco | 92.7 (153) |
| Cocaine | 54.3 (88) |
| Benzodiazepines | 51.0 (80) |
| Ecstasy | 49.4 (80) |
| Petrol | 34.2 (53) |
| Amphetamines | 28.8 (44) |
| Head shop | 51.4 (37) |
| Mushrooms | 18.5 (28) |
| Lysergic acid (LSD) | 11.8 (18) |
| Opiates | 3.4 (5) |
| Heroin | 50.0 (1) |

Table 3. Comparison of service-user characteristics of regular and non-regular benzodiazepine users

| Measure | Regular users | Non-regular users | Significance |
|---|---|---|---|
| Mean age ± S.D. (years) | 16.6 ± 1.02 | 16.7 ±1.20 | t=0.585, p=0.561 |
| Gender | | | |
| Male (%) | 97.5 | 100.0 | p=1.000 |
| Female (%) | 2.5 | 0.0 | |
| Source of referral | | | |
| Juvenile Liaison Officer (%) | 30.0 | 28.6 | |
| Probation and Welfare Officer (%) | 15.0 | 21.4 | |
| Social Worker (%) | 10.0 | 21.4 | p=0.776 |
| Other (%) | 10.0 | 0.0 | |
| Family (%) | 25.0 | 14.3 | |
| Youth Centre (%) | 10.0 | 7.1 | |
| Self (%) | 0.0 | 7.1 | |
| Median substances ever used | 7 | 7 | Z=-1.750, p=0.080 |
| Median substances used in the previous month | 3 | 1 | Z=-5.096, p<0.001* |
| Mean age of first benzodiazepine use | 14.8 | 15.2 | t=-1.105, p=0.269 |

* signifies significance ≤ 0.05

Table 4. Comparison of physical and behavioural symptoms experienced by benzodiazepine users

| Measure | Regular users | Non-regular | Significance | Total, % (n) |
|---|---|---|---|---|
| Median behavioural symptoms | 12 | 9 | Z=-2.434, p=0.015* | |
| Behavioural symptoms | | | | |
| Alcohol or prescription drugs going missing or dwindling in the house | 69.4% | 55.2% | $\chi^2$=0.859, p=0.354 | 47.7 (73) |
| Changing friends and moving away from old friends | 79.5% | 72.4% | $\chi^2$=0.153, p=0.696 | 68.9 (111) |
| Dramatic attention-seeking behaviour | 81.3% | 50.0% | $\chi^2$=5.232, p=0.022* | 65.2 (101) |
| Extreme apathy | 80.6% | 60.7% | $\chi^2$=1.960, p=0.161 | 60.0 (87) |
| Hyperactivity | 83.8% | 76.7% | $\chi^2$=0.178, p=0.673 | 67.7 (109) |
| Impulsive behaviour | 94.7% | 83.3% | p=0.227 | 79.6 (129) |
| Increased irritability | 89.7% | 74.2% | $\chi^2$=1.947, p=0.163 | 78.9 (131) |
| Increased time spent alone in room/withdrawn behaviour | 88.9% | 69.0% | $\chi^2$=2.837, p=0.092 | 63.3 (100) |
| Loss of interest in sports and hobbies | 97.3% | 80.0% | p=0.039 | 76.8 (129) |
| Low mood | 87.2% | 73.3% | $\chi^2$=1.317, p=0.251 | 70.4 (114) |
| Money/objects missing from home that could be easily converted into cash | 66.7% | 55.2% | $\chi^2$=0.477, p=0.490 | 48.4 (74) |
| Paranoia | 94.9% | 74.2% | p=0.018* | 72.0 (116) |
| Relationships with peers/siblings/parents affected | 94.4% | 80.8% | p=0.119 | 79.7 (122) |
| Suicidal ideation | 35.1% | 31.0% | $\chi^2$=0.008, p=0.930 | 28.0 (44) |
| Suicide attempts | 22.9% | 20.7% | $\chi^2$=0.000, p=1.000 | 15.7 (24) |
| Temper outbursts | 92.3% | 80.0% | p=0.163 | 79.8 (134) |
| Median physical signs | 8 | 6 | Z=-1.969, p=0.049* | |

| Measure | Regular users | Non-regular | Significance | Total, % (n) |
|---|---|---|---|---|
| Physical signs | | | | |
| Blackouts | 83.8% | 83.3% | p=1.000 | 71.4 (115) |
| Bloodshot eyes that appear glassy or vague | 85.7% | 71.4% | $\chi^2$=1.164, p=0.281 | 61.3 (93) |
| Change in appetite | 86.1% | 67.9% | $\chi^2$=2.096, p=0.148 | 61.3 (95) |
| Change in weight | 81.6% | 60.0% | $\chi^2$=2.880, p=0.090 | 62.0 (103) |
| Deterioration in appearance | 74.3% | 48.3% | $\chi^2$=3.535, p=0.060 | 54.8 (86) |
| Excessive sleeping | 59.5% | 55.6% | $\chi^2$=0.003, p=0.955 | 49.0 (77) |
| Insomnia | 79.5% | 60.7% | $\chi^2$=1.979, p=0.160 | 59.9 (97) |
| Loss of fine motor co-ordination e.g. holding a glass | 75.0% | 60.7% | $\chi^2$=0.905, p=0.341 | 46.5 (72) |
| Short-term memory loss | 91.7% | 93.1% | p=1.000 | 69.2 (108) |
| Vomiting or flushed complexion | 71.4% | 40.7% | $\chi^2$=4.702, p=0.030* | 44.1 (67) |
| White or pale face | 86.8% | 60.7% | $\chi^2$=4.654, p=0.031* | 65.9 (108) |

* signifies significance ≤ 0.05

Figure
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