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Substance Misuse in Young People in Ireland - A Focus on Benzodiazepines

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Declaration

I declare that this thesis has not been previously submitted for a degree at this, or any other university. It is entirely my own work, apart from due acknowledgement. The library may lend or copy this thesis upon request.

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Table of Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
CBT	Cognitive Behavioural Therapy
CINAHL	Cumulative Index to Nursing and Allied Health Literature
COREQ	Consolidated criteria for reporting qualitative research
CREC	Cork Ethics Research Committee
CSO	Central Statistics Office
DA	Dopamine
DAT	Dopamine Active Transporter
DDD	Defined Daily Dose
DPS	Drug Payment Scheme
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders 4, Text Revision
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
ERIC	Education Resources Information Centre
ESPAD	European School Survey Project on Alcohol and Other Drugs
EU	European Union
GABA	gamma-aminobutyric acid
GMS	General Medical Services
GP	General Practitioner
HII	Health Intelligence Ireland
HRB	Health Research Board
HSE	Health Service Executive
ICD	International Classification of Diseases
IQR	Interquartile Range
JLO	Juvenile Liaison Officer
LSD	Lysergic Acid
LTI	Long Term Illness
MDMA	methylenedioxymethamphetamine
MeSH	Medical Subject Headings
MINORS	Methodological Index of Non-Randomised Studies

MOR	Mu Opioid Receptors
MTS	Matt Talbot Services
NAc	Nucleus Accumbens
NACD	National Advisory Council on Drugs
NDTRS	National Drug Treatment Reporting System
NHS	National Health Service
NICE	National Institute of Clinical Excellence
NMDA	N-methyl-D-aspartate
PCRS	Primary Care Reimbursement Service
PFC	Prefrontal Cortex
PKC	Protein Kinase C
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses
RCT	Randomised Control Trial
SAMSHA	Substance Abuse and Mental Health Services Administration
SD	Standard Deviation
SPC	Summary of Product Characteristics
SPHE	Social Personal and Health Education
SUDS	Substance Use Disorder Syndrome
THC	Tetrahydrocannabinol
UNICEF	United Nations Children's Fund
USA	United States of America
VTA	Ventral Tegmental Area
WHO	World Health Organisation
WHO-ATC	World Health Organisation - Anatomical Therapeutic Chemical Classification System
YC	Youth Counsellor

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Poster: Substance Use in Young Persons in Ireland, a Systematic Review

Murphy, K., Sahm, L., Lambert, S., Byrne, S.

Poster: Analysis of service-users attending Matt Talbot Services (MTS) from 2007-2010

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- Health Services Research & Pharmacy Practice 2012

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Thesis Abstract

Introduction

Substance misuse in Ireland has a long history. Alcohol was recognised as the main concern, but it was not until the 1960s that other dependence-forming substances have been recognised as problematic in Ireland. Since then, the number of misused substances has risen sharply to include novel synthetic compounds and prescription-only medicines. Many attempts have been made to reduce the misuse of these substances: restricting growth and manufacture of substances, criminalising possession, increasing prescribing requirements, and using treatment centres to assist those who wish to stop misusing. Despite enormous expense and effort, substance misuse is still a problem. The mechanism by which these substances excite the brain's natural reward pathways means it can be difficult for misusers to stop desiring the effects of the substances. Much has been discovered about how misused substances create their dependence-forming effect, but there is still much unsolved in such a complex area.

Methods

A systematic review was undertaken on the prevalence of substance misuse amongst young people in Ireland between 2000 and 2012 to create a context in which later research among substance misusers can be compared, and to put benzodiazepine misuse in the context of other misused substances.

Data from national reimbursement claims were analysed to examine trends in: (i) the prescribing of benzodiazepines nationally and internationally and (ii) the prescribing of benzodiazepines to patients younger than 18 years between 2009 and 2012, to monitor adherence to benzodiazepine prescribing guidelines and to highlight areas in prescribing where the potential for misuse could be decreased.

The differences between urban and rural attendees of a substance misuse treatment centre in Cork were compared to examine whether there were differences in substance misuse between the groups. This was followed by a comparison of regular and non-regular benzodiazepine misusers from the substance misuse treatment centre and their self-reported misuse-related symptoms.

The next stage involved qualitative research using semi-structured interviews with young people who had misused benzodiazepines in their adolescence. This approach was used to describe the experiences and causes of youth benzodiazepine misuse in Cork and to guide future interventions to reduce misuse. This approach was also utilised for interviews conducted with youth counsellors (YCs) and general practitioners (GPs). As substance misuse in adolescence can lead to damaged brain development, which may result in a lack of insight into their behaviours, it was important to gain this information from those who have worked with young benzodiazepine misusers.

Results

The systematic review returned 18 articles that matched the inclusion criteria for the study. The review showed that tobacco, alcohol and cannabis use levels in Ireland have reduced in the period between 2000 and 2012. Lifetime tobacco use reported at the beginning of the review period ranged from approximately 61-67%, and decreased to 43-48% at the end of the study period. Lifetime alcohol levels similarly decreased from 71-92% at the beginning of the review period to 58-81%. Lifetime cannabis misuse decreased from 29-39% to approximately 18%. Lifetime benzodiazepine misuse was the only parameter which did not decrease over the study period. Research conducted into the comparison of Irish prescribing data relative to European counterparts found that Ireland had the fourth highest level of benzodiazepine prescribing among those countries surveyed between 2009 and 2012. However Irish prescribing did decrease by 16% over this time. Approximately 15% of Irish people aged 17 and under were prescribed benzodiazepines for greater than four weeks, whilst approximately 40% were prescribed hypnotics, both in contravention of the Good Practice Guideline for Clinicians.

Data comparing urban and rural treatment centre attendees showed that a greater percentage of rural service-users were employed ($p = 0.015$), more urban service-users were unemployed ($p = 0.015$), while there were similar levels of students from urban and rural areas. A greater proportion of urban service-users had taken multiple substances in their lifetime (73.7% vs.

52.2%, p = 0.001) and continued to use multiple substances regularly (49.3% vs. 31.3%, p = 0.003) compared with their rural counterparts. The study comparing regular and non-regular benzodiazepine usage showed that benzodiazepines had ever been used by 51.0% treatment centre attendees, and of these, 55.8% were regular benzodiazepine users. The mean age of first use was 14.9 ± 1.4 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 reported 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.

Interviews with benzodiazepine misusers highlighted that benzodiazepines are used by young people coping with the pressures of life, and its use is encouraged and/or normalised by those around them. Participants said that they took benzodiazepines to escape negative feelings, to *“not feel anything at all”*, and that they were taken in a group setting. The majority of participants indicated that they had no knowledge of benzodiazepines when they started taking them.

The YC/GP interviews confirmed these findings and added the importance of family and community attitudes on the potential for young people to misuse benzodiazepines. GPs and YCs felt that doctors were more aware of the

risks of prescribing to young people and prescribed less than in the past. Participants suggested that public awareness campaigns and stricter prescribing regulations could reduce the levels of misuse.

Conclusion

This thesis provides a comprehensive overview of the issues of benzodiazepine misuse by young people in Ireland. Quantitative analysis has demonstrated that while prescribing of benzodiazepines to young people has decreased over the last number of years, approximately 15% of those aged 17 and under were prescribed benzodiazepines for greater than four weeks, whilst approximately 40% were prescribed hypnotics. Qualitative research with young people, GPs and substance misuse counsellors has highlighted the many factors that can influence misuse and makes recommendations on what can be done to reduce it, which ultimately will benefit the individual and society.

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1. Thesis Introduction

1.1 Drugs Policy in Ireland

The beginning of drug policies in Ireland originates with legislation enacted before Irish independence. Prior to the first legislation in 1851, all substances were relatively freely available in Ireland. The Arsenic Act, 1851 controlled the supply of arsenic to the public (1). Following this was the introduction of the Pharmacy Act (Ireland), 1875 which made changes such that the preparation or sale of opium could only be performed by a registered pharmacist, and medicines containing opium were required to be labelled "Poison" (1). The next significant legislation was the Poisons and Pharmacy Act, 1908 which added coca and its derivatives to the list of pharmacist-controlled substances. The Dangerous Drugs Act, 1920 put these substances under stricter control. The Act required those in possession of the above substances and the synthetic opioid heroin to have a prescription from a doctor or dentist. It also restricted their importation and exportation (2) The first legislation drafted by the Irish Free State was the Dangerous Drugs Act, 1934, which replaced the Dangerous Drugs Act, 1920. It included other legislation to comply with the International Convention for Limiting the Manufacture and Regulating the Distribution of Narcotic Drugs in 1931. The commencement order for the act [Dangerous Drugs Act, 1934 (Commencement) Order, 1937] was not enacted until the 1st April 1937. From this time, there was a prohibition of the possession of the above substances, cannabis, and other natural or synthetic opioids that were known at the time. Exceptions to this were provided for specified medicinal products that contained morphine.

The Misuse of Drugs Act, 1977 which was commenced on 1st May 1979, created four schedules into which prohibited substances were placed (updated schedules Appendix I). A person may only legally possess a Schedule 1 substance if they have been licenced by the Minister of Health. Substances in Schedule 1 are deemed to have little medicinal use and high abuse potential, and contained substances such as cannabis, coca leaf (from which cocaine is obtained), lysergic acid diethylamide (LSD), psilocin (the psychoactive chemical in magic mushrooms derived from the prodrug, psilocybin), and raw opium. Schedules 2 and 3 contained substances that were controlled less strictly than Schedule 1 as they were deemed to have greater medicinal properties. They may be prescribed in some circumstances by registered prescribers. Cocaine, codeine, heroin, methadone, and morphine were part of Schedule 2. The Act also updated the list of substances that were regulated to include novel substances such as amphetamines, and other synthetic opioids such as fentanyl.

The next significant update was provided by the Misuse of Drugs Regulations, 1988. A further schedule was added to the regulations which were mostly populated by benzodiazepines. Schedule 4 from the previous Act was renamed Schedule 5 and the restrictions on benzodiazepines occupied the new Schedule 4. This schedule had minimal restrictions similar to Schedule 5, but the disposal and destruction of Schedule 4 substances were regulated. Amendments have been made to the schedules as set out in the Misuse of Drugs Act to include novel substances such as midazolam (Schedule 4) in 1993, or substances that were becoming more widely used in

Ireland such as khat (the leaves of *Catha edulis*) (Schedule 1) in 1993, magic mushrooms (Schedule 1) in 2006, zolpidem (Schedule 4) in 2010. The most significant of these changes was from the Misuse of Drugs (Amendment) Regulations 2007, which permitted nurses to prescribe medicines such as opioids from Schedules 2 or 3 in limited circumstances. Another significant piece of legislation enacted was the Criminal Justice (Psychoactive Substances) Act 2010. The act forced the closure of head shops i.e. premises where unregulated novel psychoactive substances were sold.

In the near future, there are plans to more strictly regulate the prescription of all benzodiazepines due to the increase in illicit trading. A draft of the regulations include requirements for those in possession of benzodiazepines to have a prescription, benzodiazepine quantities to be stated in words and figures, and that pharmacies must notify the government of privately dispensed benzodiazepines as well as medicines in Schedules 1, 2 and 3 (Appendix II) (3). It is hoped that these regulations may reduce the current high availability of illicit benzodiazepines.

In parallel to evolution of laws to regulate substance use, there has also been the evolution of other methods to prevent and treat substance misuse. The first organised attempt to reduce substance misuse on a large scale in Ireland was the Cork Total Abstinence Society founded in 1835 by a Quaker named William Martin. The organisation, which promoted abstention from alcohol, became widespread when Father Theobald Mathew joined the

organisation in 1938 (4). The organisation spread across the country and by 1843, 250,000 Irish people had pledged lifelong abstinence from alcohol. The organisation declined during the Great Famine and never recovered. The tradition of abstention in Ireland was continued by Fr. James Cullen when he founded the Pioneer Total Abstinence Association of the Sacred Heart in 1889 which is still in existence today (5).

During this period, there was no government involvement in dealing with substance misuse and it was only in 1945, with the enactment of the Mental Treatment Act, that the government put forward legislation regarding mental health (6). This act provided for voluntary and/or compulsory admission of addicts to psychiatric hospitals. This was mainly intended for the treatment of alcoholism, as the 1966 Report of the Commission of Inquiry on Mental Illness stated that Ireland had avoided serious drug use (7). The problem of rising misuse was recognised soon thereafter however, and the first Irish statutory outpatient treatment facility was established at Jervis Street Hospital in 1969 (7). The government commissioned a report entitled: Report of the Working Party on Drug Abuse, which was published in 1971, and it was the first report to present recommendations for the prevention and treatment of substance misuse (6). Some of its recommendations such as differentiating between possession and possession with intent to supply, and penalties based on the drug possessed are still enforced to this day.

There was a dramatic rise in opiate use in Dublin at the beginning of the 1980s, but it was not until 1985 that the National Co-ordinating Committee on Drug Abuse was set-up to monitor and advise on drug misuse (7). The drug treatment approach changed because of fears of an Acquired Immune Deficiency Syndrome (AIDS) epidemic in the late 1980s to incorporate a harm reduction approach to reduce the risk of drug misusers becoming infected with the disease. Examples of harm reduction approaches that were pursued were (i) use of a prescribed medicine; methadone, to replace the use of heroin from 1987, and (ii) needle exchange schemes from 1989 (6). It was not until 1991 that the harm reduction approach received official backing from the National Co-ordinating Committee on Drug Abuse in the Government Strategy to prevent Drug Misuse report (8). This was the first drugs policy that had been used in a national drugs strategy. The report recommended a decentralised approach to prevention and treatment, such as the development of community drug services and a greater role for general practitioners (GPs) for treatment of dependence (6).

In 1998, the methadone treatment protocol was rolled out nationally. It created the two-tier system for methadone treatment, where Level 1 doctors could not initiate methadone prescriptions, but rather this could only be done by the specifically-trained Level 2 doctors. A new drugs strategy document was published in 2001 called; “Building on experience: national drugs strategy 2001-2008” (8). This report stratified drugs policy around four pillars, (i) supply reduction, (ii) prevention, (iii) treatment, and (iv) research. Regional drugs task forces were created to tackle alcohol and drug issues at a local

level. The strategy sought to increase the availability of treatment places in communities and prisons to reduce waiting times. The latest National Drugs Strategy, covering the period 2009-2016, reported that alcohol would be included as a substance that would be monitored in a new policy called the National Substance Misuse Strategy (9). Some of the initiatives suggested to reduce alcohol misuse include the introduction of minimum pricing and the phasing out of alcohol advertising at large sporting and other public events by 2016 (10).

To understand what challenges may lay ahead, and what strategies can be used to prevent them, it is important to understand the source of the problem with all these drugs i.e. dependence.

1.2 Defining addiction and dependence

In layman's terms "addiction" and "dependence" have essentially the same meaning. It becomes clear however that as more is learned about the field that these concepts refer to different things. Addiction is the older term and referred to intense liking of any activity, e.g. addicted to reading. It was only in the beginning of the 20th century that this word took on the specialised drug meaning (11). Such was the confusion that the World Health Organisation (WHO) abandoned the word and instead used the word "dependence" (12). The use of the word addiction however, has not diminished and today there are a myriad of definitions for the word, with different yet overlapping features. A report by the European Monitoring

Centre for Drugs and Drug Addiction (EMCDDA) highlighted this by presenting a sample of nine varying definitions of addiction in their Models of Addiction report (13). The EMCDDA report created a definition that aggregated the concepts suggested by these definitions and defined addiction as (8):

"*A repeated powerful motivation to engage in a purposeful behaviour that has no survival value, acquired as a result of engaging in that behaviour, with significant potential for unintended harm."*

It can be seen that this definition is not restricted to legal and illegal substance use but can potentially include activities such as gambling and internet use.

As stated earlier, the term 'dependence' was first formally used in a drug use context by the Expert Committee on Addiction-producing Drugs of the WHO in 1964 in an attempt to replace the ambiguous terms of addiction and habituation. The report defined dependence as *"a state arising from repeated administration of a drug on a periodic or continuous basis"* (14). The definition has changed subsequently and the present definition of dependence given by:

> *"As a general term, the state of needing or depending on something or someone for support or to function or survive. As applied to alcohol and*

other drugs, the term implies a need for repeated doses of the drug to feel good or to avoid feeling bad" (15).

On its own, the term refers to the concept of dependence, but it can be qualified to confer greater specificity. Dependence can be divided into two types; (i) psychological and (ii) physiological dependence. Both of these terms will be explained in detail later. Dependence can also be qualified to include reference to a class of substances or to an individual substance, e.g. opioid dependence, morphine dependence.

1.3 Diagnosing dependence

The broad definitions of dependence available can make diagnosis of dependence more difficult in a clinical setting. To aid diagnosis, criteria have been developed to support mental health professionals in their diagnosis and treatment of those with dependence. There are two primary diagnostic criteria used internationally:

The first of these is the Tenth Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) (16). Section F10-F19 covers *"Mental and behavioural disorders due to psychoactive substance use"*. Dependence in this classification falls under F1x.2, where 'x' is a digit that differs depending on the substance that the patient is using. The diagnostic guidelines for dependence for any

dependence-forming substances in general are listed in Table 1.1. The Beta Draft of the updated ICD criteria, ICD-11, put substance dependence at section 5C1.Since it is a beta draft, no criteria were described (17). The full diagnostic criteria are expected to be released in 2015.

Table 1.1. ICD-10 diagnostic criteria for substance dependence

A definite diagnosis of dependence should usually be made only if three or more of the following have been present together at some time during the previous year:
(a) a strong desire or sense of compulsion to take the substance;
(b) difficulties in controlling substance-taking behaviour in terms of its onset, termination, or levels of use;
(c) a physiological withdrawal state (see F1x.3 and F1x.4) when substance use has ceased or been reduced, as evidenced by: the characteristic withdrawal syndrome for the substance; or use of the same (or a closely related) substance with the intention of relieving or avoiding withdrawal symptoms;
(d) evidence of tolerance, such that increased doses of the psychoactive substances are required in order to achieve effects originally produced by lower doses (clear examples of this are found in alcohol-and opiate-dependent individuals who may take daily doses sufficient to incapacitate or kill non-tolerant users);
(e) progressive neglect of alternative pleasures or interests because of psychoactive substance use, increased amount of time necessary to obtain or take the substance or to recover from its effects;
(f) persisting with substance use despite clear evidence of overtly harmful consequences, such as harm to the liver through excessive drinking, depressive mood states consequent to periods of heavy substance use, or drug-related impairment of cognitive functioning; efforts should be made to determine that the user was actually, or could be expected to be, aware of the nature and extent of the harm;

An intermediate stage between non-use and substance dependence is described in the ICD-10; harmful use. Diagnosis of harmful use is made based on whether *"…actual damage should have been caused to the mental*

or physical health of the user", without the diagnosis of substance dependence (16).

The second commonly used criteria comes from the American Psychiatric Association's Text revision of the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV-TR) (18). The diagnostic guidelines for substance dependence are listed in Table 1.2.

Table 1.2. DSM-IV-TR diagnostic criteria for substance dependence

A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period:
1 Tolerance, as defined by either of the following:
a A need for markedly increased amounts of the substance to achieve intoxication or desired effect
or
b Markedly diminished effect with continued use of the same amount of the substance
2 Withdrawal, as manifested by either of the following:
a The characteristic withdrawal syndrome for the substance
or
b The same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms
3 The substance is often taken in larger amounts or over a longer period than was intended
4 There is a persistent desire or unsuccessful efforts to cut down or control substance use
5 A great deal of time is spent on activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances), use the substance (e.g., chain-smoking), or recover from its effects

6	Important social, occupational, or recreational activities are given up or reduced because of substance use
7	The substance use is continued despite knowledge of having a persistent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was made worse by alcohol consumption)

Much like the harmful use criteria used in the ICD-10, DSM-IV-TR has a stage of substance use that occurs before substance dependence; substance abuse. The criteria for substance abuse are listed in Table 1.3.

Table 1.3. DSM-IV-TR diagnostic criteria for substance abuse

A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12-month period:

1	Recurrent substance use resulting in a failure to fulfil major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household
2	Recurrent substance use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by substance use)
3	Recurrent substance-related legal problems (e.g., arrests for substance-related disorderly conduct)
4	Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g., arguments with spouse about consequence of intoxication, physical fights)

The symptoms have never met the criteria for Substance Dependence for this class of substance.

A newer version of the DSM was released in May 2013 (DSM-5) and contains some changes from the previous iteration (19). Substance use is no longer a dichotomous choice between Substance Abuse and Substance Dependence, each with differing criteria. Instead, both have been merged into a single condition called Substance Use Disorder, which ranges from mild to severe. Substance Use Disorder comprises of a list of 11 statements. The list is generally the same as the items in the previous list except that item 3 in Substance Abuse was removed, due to *"cultural considerations that make the criteria difficult to apply internationally"*. Additionally, drug craving was added to the list. A diagnosis of Mild Substance Use Disorder requires the presence of two to three symptoms on the list, Moderate Substance Use Disorder requires the presence of four to five symptoms, while Severe Substance Use Disorder signifies the patient having six or more symptoms (20). The DSM-5 is less than a year old and has yet to become widely referenced in scientific literature so for the purposes of this introduction the criteria of DSM-IV-TR are still used. Because these criteria were developed and are to be used by psychiatric assessment, they assume a top-down view of dependence; dependence at the level of the individual, their beliefs, view and their interactions with others. The basis for this view is discussed in the next section.

1.4 Psychological dependence

Psychological dependence is a state of dependence that occurs purely at the psychological or mental level, as opposed to the physiological level. As with many terms in the area of substance use, there is no single agreed definition

of psychological dependence, however the definitions used do overlap. Psychological dependence is defined by the WHO as *"the experience of impaired control over drug use"* (15). The definition used by the American Psychiatric Association is *"dependence on a psychoactive substance for the reinforcement it provides"* (21). Examples of alternative definitions include *"The emotional state of craving a drug either for its positive effect or to avoid negative effects associated with its absence"* (22), and *"A non-physiological attachment to the availability of the prescribed medication that may be a natural response to effective relief of distressing symptoms"* (23). Smith, *et al.* 2013 performed a systematic review of definitions of common terms used in substance abuse, and examined common features of definitions of these definitions (24). For psychological dependence, the features were: *compulsive use and impaired control*, *craving*, *characterised by drug use to obtain psychotropic or euphoric effects*, *avoidance of negative effects and symptoms associated with drug absence*, *unpleasant emotional and motivational effects*, and *non-physiological attachment to availability of a drug*. The main features studied in the literature were craving and compulsion.

Craving, like addiction, is a term with many definitions and no consensus. The WHO definition of craving is a *"very strong desire for a psychoactive substance or for the intoxicating effects of that substance"* (15). A recent definition of craving came from a review of models of craving published in 2010 (25). Craving was defined as *"a desire of any intensity to consume a substance"*. There are also perspectives on craving that are generalised

beyond substance use. One study wrote that *"craving is the 'grasping' quality of the mind as it attempts to pursue its attachments"* (26). Just as there are many definitions of craving there are also many explanations for it. The review by Skinner and Aubin in 2010 found many attempts to explain craving, and some are presented below (27):

- Conditioning models work on the assumption that *"craving is an automatic, unconscious reaction to a stimulus"*.
- Cognitive models use the principle that *"craving arises from the operation of information processing systems"*. This differs from conditioning models in that conscious, higher functions such as expectancies and concentration influence cravings (28).
- Psychobiological models work on the premise that cravings are due to a combination of both physical and psychological factors.
- Motivation models see craving as one of many factors that influence motivation to use a substance. Level of motivation to use a substance decides whether a person will actually use that substance.

Each of these models has its strengths and weaknesses so it is difficult to prioritise any one of the models.

Compulsion is defined by the WHO as *"…a powerful urge - attributed to internal feelings rather than external influences - to take the substance (or substances) in question. The substance user may recognize the urge as detrimental to well-being and may have a conscious intent to refrain"* (15), and as *"repetitive, purposeful acts performed according to certain rules or in*

a ritualized manner" (29). There are conflicting opinions among researchers as to whether cravings and compulsions are separate factors in psychological dependence. Some view craving as the cause of the compulsion to misuse substances, while others view compulsion as an automatised behaviour (30). The latter view craving as a conscious process while compulsion is an unconscious process (31).

1.5 Physiology of psychological dependence

While the previous section described psychological dependence from a top-down approach, this section uses a bottom-up approach to describe psychological dependence in a neurophysiological manner. The primary location for the rewarding effects of dependence-forming substances is the *nucleus accumbens* (NAc) (Figure 1.1) (32). An increase in the level of dopamine (DA) in this area results in increased reward. Increased levels of DA in the NAc has also been linked with other non-substance related activities such as seeking social approval from others (33). All substances which have the potential to cause psychological dependence increase DA in the NAc (34).

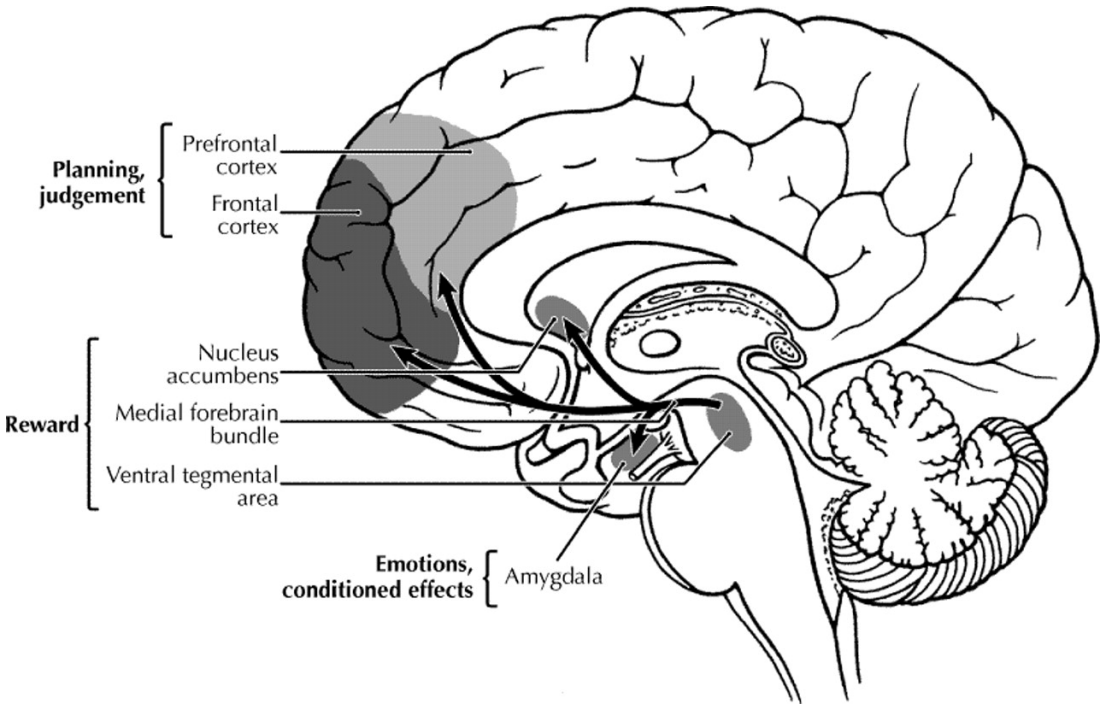

Figure 1.1. Schematic diagram of the human brain that highlights some of the main brain areas and neurotransmitter pathways implicated in reward processes (35)

Mesolimbic neurons that reach the NAc from the ventral tegmental area (VTA) are recognised as the main neurons responsible for stimulation of the NAc (36). Dopaminergic (DAergic) neurons from the VTA also innervate areas of the prefrontal cortex (PFC) (Figure 1.2) (37).

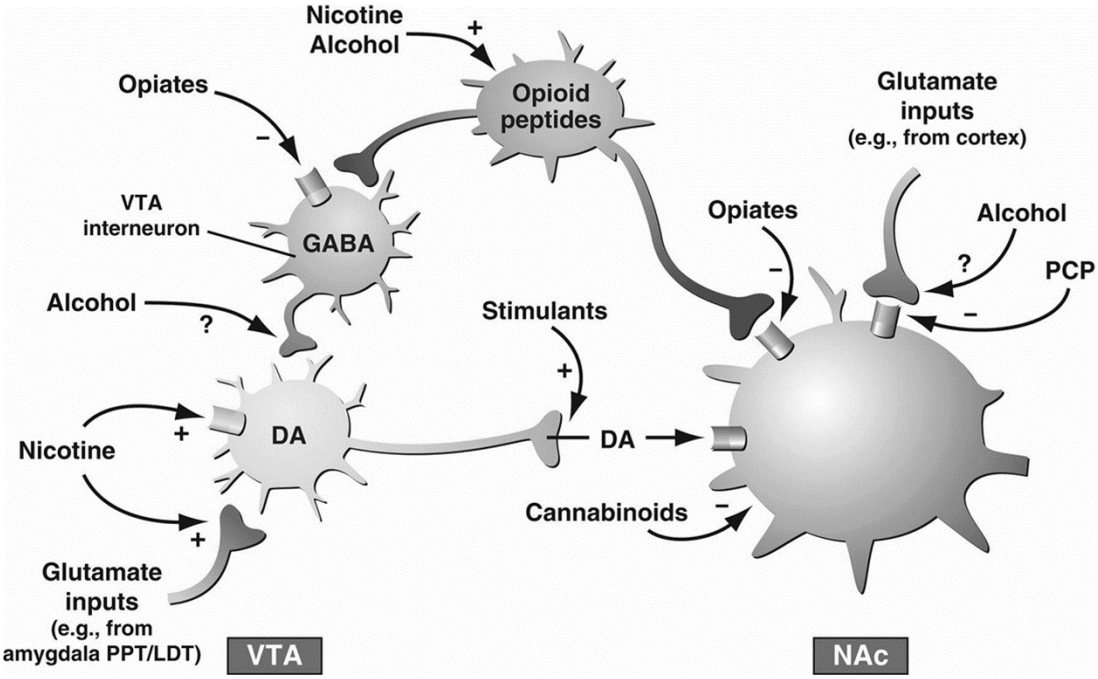

Figure 1.2. Action of selected dependence-forming substances in the mesolimbic system (38)

Stimulation of some of these areas is thought to be responsible for other features of psychological dependence. Other areas include; conditioning to cues, executive function and motivation (32). Effects on misusers' memories can result in the sensation of craving when exposed to drug cues, such as watching others use the substance. This powerful effect is thought to be due to the presence of DA in the dorsal striatum, as a correlation has been observed between cue-induced DA increases and high scores on addiction severity tests (39). Indeed, in one study of cocaine addicts, the DA increase appeared greater for the cues than the DA increase produced by the drug itself (40). This suggests that at the beginning of substance misuse the DA increases may be linked to the effect of the substance, however after repeated use, the increases in DA appear to be primarily due to cues such as drug administration equipment or watching others use. Executive function

in physiology refers to cognitive processes such as planning, decision-making and self-monitoring, and it is the PFC that is primarily responsible for executive function (41). Impairments in this area of the brain are thought to lead to reduced self-control. This was shown in a study where lateral PFC activity in cigarette smokers predicted smoking behaviour over a three-week period (42). This is thought to occur due to damage to the PFC which increases subjects' desires for immediate gratification compared with larger, delayed rewards (43, 44). This would suggest that a misuser would prefer drug use over the benefits of staying clean.

Motivation to procure a substance is a defining feature of substance dependence; misusers are often willing to engage risky behaviour with severe consequences to obtain the drug they seek (45). In a dependent misuser, substance-seeking and substance-taking can be the biggest motivator in that person's life and, in comparison, the person can lack motivation to pursue non-substance-related activities (46). The PFC and NAc are both involved in regulating motivation behaviour. Increased DA activity in the PFC is associated with motivation and has been observed when dependent subjects are exposed to substance-conditioned cues in comparison to the levels when exposed to non-substance-conditioned cues (47). Another study showed that dependent subjects showed more activity in the same region than nondependent subjects when administered a stimulant (48). The conclusion of both of these studies is that substance dependence can result in higher motivation to take the substance.

1.6 Physical dependence

Physical dependence is the counterpart to psychological dependence. Both forms of dependence can have deleterious effects on the substance misuser if they cannot access their drug. Psychological and physical dependence to a substance do not always occur together, and those who are dependent can experience both types of dependence with differing severities. Examples of substances which can result in physical dependence with little-to-no psychological dependence are caffeine, (49) β-blockers (50) and some antidepressants (51). To understand how this can be, it is helpful to look at definitions of physical dependence. Physical dependence as defined by the WHO *"…refers to tolerance and withdrawal symptoms…is also used in the psychopharmacological context in a still narrower sense, referring solely to the development of withdrawal symptoms on cessation of use"* (15). The systematic review by Smith *et al.* 2013, found that definitions of physical dependence had the following elements, "*associated with withdrawal symptoms or a withdrawal syndrome, adaptive physiologic process, occurs when the drug is rapidly withdrawn, tolerance to substance effects"* (24). Both of these highlight that tolerance and withdrawal are the essential features of physical dependence. Tolerance is defined as *"a decrease in response to a drug dose that occurs with continued use"* (15), while a withdrawal syndrome is,

> *"a group of symptoms of variable clustering and degree of severity which occur on cessation or reduction of use of a psychoactive*

substance that has been taken repeatedly, usually for a prolonged period and/ or in high doses" (15)

The difficulty in defining the effects of withdrawal exist because withdrawal symptoms differ based on the substance in question. A brief description of withdrawal symptoms for different classes of misused substances will now be provided.

Withdrawal symptoms to opioids can begin as soon as 8-12 hours for short-acting substances such as morphine or heroin, while onset may not start until 1-3 days after cessation of use for longer-acting opioids such as methadone (52). Withdrawal symptoms are generally milder for longer-acting opioids but can last for several weeks, while the withdrawal symptoms of short-acting opioid may be more severe but subside after 7-10 days. The typical symptoms experienced include; craving, anxiety, dysphoria, yawning, sweating, piloerection, lacrimation, rhinorrhoea, insomnia, nausea or vomiting, diarrhoea, cramps, muscle aches and fever (52). Alcohol withdrawal symptoms can appear within 6-12 hours. In mild cases of withdrawal the symptoms include insomnia, tremor, mild anxiety, gastrointestinal upset, headache, perspiration, while severe withdrawal can lead to seizures and delirium tremens; which involves hallucinations and disorientation. Symptoms can persist for up to five days (53). Unsurprisingly as benzodiazepines have a similar mechanism of action to alcohol, benzodiazepine withdrawal symptoms share similar features to alcohol

withdrawal. Symptoms include all symptoms listed above and others including formication (skin crawling), tingling and numbness, and depersonalisation (54).

Psychostimulants are a class of substances that includes amphetamines, cocaine, methamphetamine, and ecstasy (55). These substances have different mechanisms of action but all produce similar effects and likewise have similar withdrawal symptoms. These symptoms include; dysphoria, depression, poor concentration, agitation, insomnia, craving, irritability. The duration of withdrawals differs between psychostimulants, for example amphetamine withdrawal can last up to four weeks while methamphetamine withdrawal can last months (55). Nicotine is another substance that is classed as a stimulant (56), and thus the withdrawal symptoms of nicotine misuse are similar; irritability, anxiety, difficulty concentrating, restlessness, bradycardia, weight change, dysphoria and insomnia (57). The onset of withdrawal symptoms from cannabis misuse can begin from 1-4 days after cessation (58). Common withdrawal symptoms include craving, sleep difficulties, irritability, aggression, anxiety, and change in appetite (58). Withdrawal symptoms from inhalants such as acetone and toluene are not widely recognised because they are claimed not to be clinically significant, however this may be due to a paucity of research in the area (59). Examples of symptoms experienced as a consequence of withdrawal from inhalant use are headaches, nausea, hallucinations, rhinorrhoea, tachycardia, dysphoria and anxiety. Further research into the area could uncover further symptoms or re-prioritise the existing ones.

The final category of misused substances is the hallucinogens. Hallucinogens comprise of substances that produce changes in mood and perception (60). Substances included in this category include LSD, peyote (whose active substance is mescaline), and magic mushrooms (18). There is conflict about whether withdrawal symptoms are a feature of hallucinogen misuse, as DSM-IV-TR states that withdrawal is not necessary for a diagnosis of hallucinogen dependence (18), while others doubt whether hallucinogens cause dependence (61). Others suggest that such symptoms exist and describe them as craving, fatigue, irritability, reduced ability to experience pleasure (62).

1.7 Mechanisms of action of misused substances

To understand how these substances cause their withdrawal effects and how they have their acute effects, it is necessary to understand how these substances affect the body. As described in the psychological dependence above, all dependence-forming psychoactive substances interact with DAergic neurons in the NAc and the VTA. This section will describe how this occurs in the human body.

Opioids bind to G-protein-coupled opioid receptors in the body, of which there are four types: mu (μ), delta (δ), kappa (κ), and opioid receptor-like 1 (ORL_1)(61). The μ opioid receptor (MOR) is the primary opioid receptor responsible for substance dependence and euphoria (63). The MOR is

distributed throughout the central nervous system with the greatest densities occurring at the thalamus, dorsal striatum, and NAc (64). The dependence-forming effects of opioids are thought to be due to the presence of MOR on gamma-aminobutyric acid (GABA) interneurons that project from VTA to NAc (65). MOR-mediated hyperpolarisation of these GABAergic interneurons decreases their inhibitory effect on mesolimbic DAergic neurons, and so causes an indirect increase in the DA levels in the reward area of the brain. Tolerance to the effects of opioids such as morphine generally occurs through desensitisation of the MOR (66). Side effects of opioid use can be associated with the MOR in the case of pupil constriction, other opioid receptors such as in the case of hallucinations (κ receptor), or through multiple receptors in the case of spinal analgesia (MOR, δ, and κ receptors) (61).

As alcohol and benzodiazepines have similar pharmacological action, they will be described together. They have action on the $GABA_A$ receptor, and for benzodiazepines it is the only site of action but alcohol binds to multiple receptors (61). $GABA_A$ receptors are pentamer ligand-gated ion channels that are predominantly located on postsynaptic neurons and activation of the receptor allows movement of chloride (Cl^-) ions so benzodiazepines act as an allosteric modulator of the $GABA_A$ receptor. Benzodiazepines bind to their allosteric site causing the receptor to change shape to make the receptor sensitive to GABA (61). This leads to an increased frequency of opening of the receptor's Cl^- channels and subsequent hyperpolarisation of the postsynaptic neuron. Alcohol binds to the $GABA_A$ receptor also, however its

exact mechanism of action is not clear (67). It is thought that it has actions on the δ subunit which is found in extrasynaptic $GABA_A$ receptors and that it may potentiate the effect of neurosteroids (68). It is also thought that alcohol can act presynaptically to cause the release of GABA, potentially involving $GABA_B$ receptors (69). The dependence-forming ability of benzodiazepines derive from the presence of $GABA_A$ receptors on GABAergic interneurons in the VTA (70). Benzodiazepines binding to the receptors lead to hyperpolarisation of the interneurons, which decrease the release of GABA, and hence decrease the inhibition of DAergic cells in the VTA. Alcohol appears to decrease GABA release in the VTA (Figure 1.3), as opposed to increase GABA release as is in other areas (71). This paradoxical effect is thought to be due to alcohol-activated endogenous opioid release and alcohol-mediated N-methyl-D-aspartate (NMDA) channel inhibition, which cause decreased GABA transmission in the VTA.

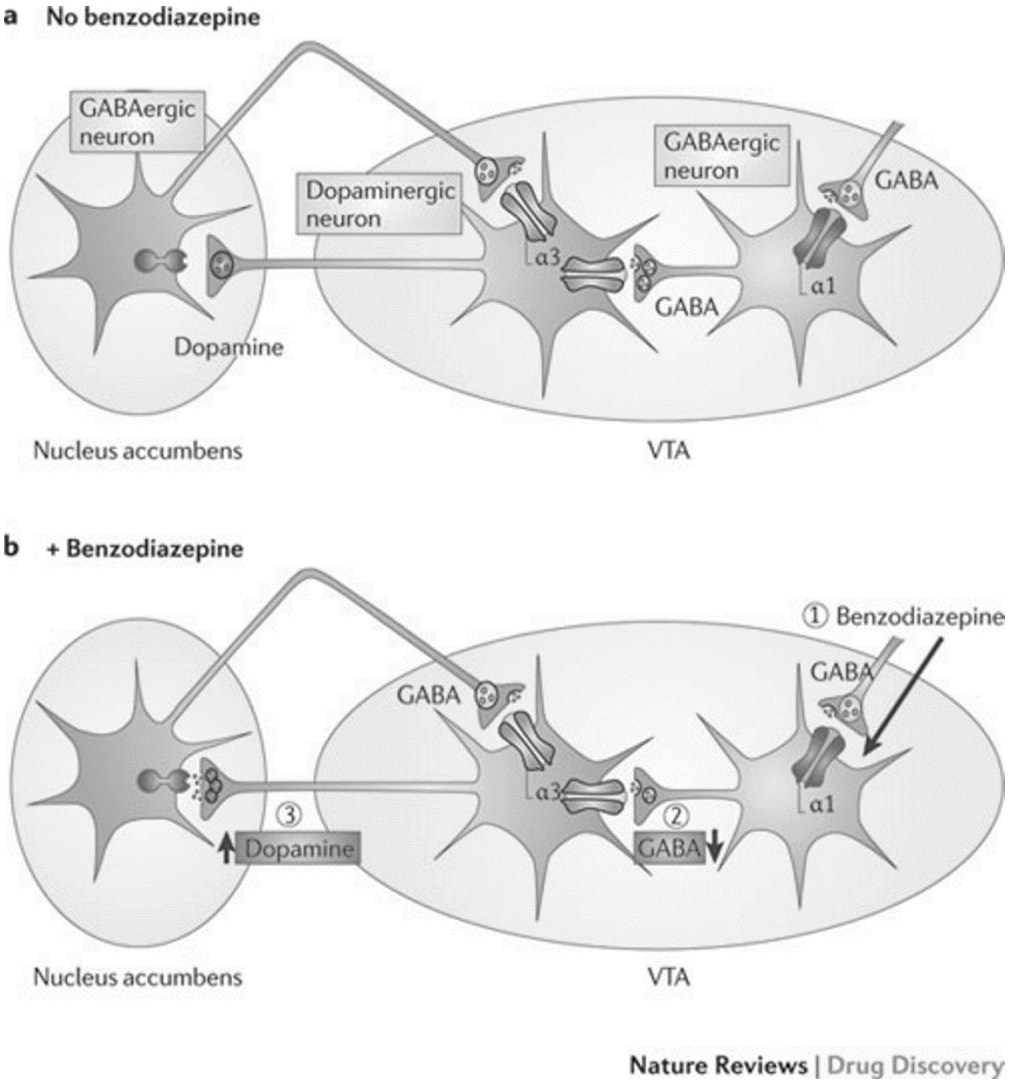

Figure 1.3. GABA receptors in the mesolimbic dopaminergic systems involved in addiction (70)

Inhalants are a class of substance that are categorised by their method of administration, and include glue, shoe polish, nail varnish remover, and butane lighter fluid (72). Exposure of some $GABA_A$ receptors have recorded increased activation in the presence of inhalants (73). Activation of the MOR by inhalants has also been noted in the literature (74). The mechanism by which each of these interact with the VTA has been described already, and thus give an indication of how dependence to inhalants can be formed,

however inhalants also have a direct, excitatory effect on DAergic neurons in VTA (75).

Psychostimulants are a class of substances that are defined by their subjective effects of wakefulness and alertness. Cocaine, amphetamines, methamphetamine, and methylenedioxymethamphetamine (MDMA, ecstasy) are psychostimulants. Their effects are achieved by increasing the activity of monoamine neurotransmitters, however psychostimulants achieve this by different mechanisms (76). Cocaine's primary mechanism is blocking the DA reuptake channel, DAT 1, which recycles DA from the synapse. This leads to apparent higher concentrations of DA in the synapse (77). Amphetamine, methamphetamine, and ecstasy have a more complex mechanism and stimulate DA release in multiple ways (78). These substances can be taken into a neuron by DAT and this increases the likelihood of efflux of cytosolic DA by DAT down its concentration gradient into the synapse. Amphetamines can promote DA efflux by DAT through protein kinase C (PKC). Amphetamines can activate PKC which phosphorylates DAT and the result is that DA efflux is increased, without modifying its DA neuronal-uptake activity (78). The amphetamine-family of substances make efflux more effective by disrupting the formation of vesicles, which leaves a greater concentration of DA in the cytosol to be effluxed by DAT. Overall the effect is to increase the activity of DAergic neurons, and this activity in the VTA can lead to dependence (76). Tolerance to the effects of psychostimulants is due to down-regulation of neurotransmitters. Side effects of psychostimulant use are derived not only from their DAergic effects, but also from their adrenergic

effects (hypertension and tachycardia) and serotonergic effects (hyperlocomotion) (79, 80).

Hallucinogens include LSD, peyote, and magic mushrooms. Like the psychostimulants, the hallucinogens act on many receptor types but their hallucinogenic activity is due to their agonist activity on the 5-HT_{2A} receptor (81, 82). As described above, hallucinogens are not described as having dependence-forming ability in the majority of scientific literature, however excitation of 5-HT_{2A} receptors in the medial PFC can cause DA release in the VTA (83), and this could possibly be a mechanism for dependence.

The pharmacological effects of cannabis are primarily due to Δ^9-tetrahydrocannabinol (THC), but also Δ^8-tetrahydrocannabinol, cannabinol, and cannabidiol (84). Cannabis elicits its psychological effects through the cannabinoid 1 (CB_1) receptor, a G protein-coupled receptor (85). CB_1 receptors reside primarily on GABAergic but also on glutamatergic neurons (86), and activation causes increased DA levels in the NAc (87). THC has also been shown to increase DA levels in the NAc through its actions on the MOR (88), and both of these may account for its dependence-forming action (89). Tolerance to the effects of cannabis after prolonged use occurs through the down regulation of CB_1 receptor levels and impaired G protein coupling (85).

1.8 Summary

Substance misuse has a long history in Ireland and has evolved from alcohol misuse in the 1800s to the plethora of substances misused at present. Drug policies in Ireland have reacted to the changing nature of substance misuse with ever-changing laws regarding substance misuse and approaches to the prevention and treatment of substance misuse and dependence, but they have not succeeded in eliminating the problem. This is because these substances stimulate natural reward pathways in the brain and so create a desire to continue taking the substance. It is a desire that can be powerful and difficult to resist. Much has been learned about the mechanism of action of misused substances, but because of the complexity of the interactions with the brain, there is still more to learn.

2. Substance use in young persons in Ireland, a systematic review

The work of this chapter has been published as Murphy, K., Sahm, L., McCarthy, S., Lambert, S., & Byrne, S. (2013). Substance use in young persons in Ireland, a systematic review. Addictive Behaviors, 38(8), 2392-2401. doi: http://dx.doi.org/10.1016/j.addbeh.2013.03.016 (Appendix III)

2.1 Introduction

Adolescence is a time of discovery and experimentation. It is also a period of physical and mental development when small changes can impact on the rest of a person's life. Adolescence is also the time when a large proportion of teenagers try alcohol (90, 91), tobacco (92), and cannabis (91) for the first time. Use of these substances during this period can often be detrimental to normal adult growth (93, 94) and may result in chronic use leading to long-term health problems and early death (95). The number of deaths attributable to addictive substances worldwide in 2004 was estimated to be over seven and a half million people (96). The same report showed that in Europe, 22.5% of all deaths in the region were directly caused by addictive substances, the highest percentage in any World Health Organisation (WHO) region in the world. There were 65,087 recorded drug-induced deaths due to illicit drugs alone in European Union (EU) member states between 2000 and 2008; with approximately 16% of those deaths occurring in under 25s (97).

Ireland is similarly affected by substance use. Approximately 287 adolescents under the age of 19 years died in Ireland between 1998 and 2009, due to or as a consequence of substance use (98-100). These statistics highlight the magnitude of substance use amongst the adolescent population in Ireland. Substance use in Ireland has been on the rise over the past decade; lifetime use of any illegal substance has risen by nearly 10% in the 15-34 years age category. Increased use of cannabis (up 9.6% to 33.4%) and cocaine (doubled to 9.4%) are the most concerning trends identified from a recent report from the National Advisory Committee on Drugs (NACD)

(101). A recent survey from United Nations International Children's Emergency Fund (UNICEF) reported that 38% of Irish 18-year-olds have taken drugs (defined in this survey as any substance except alcohol or tobacco) at some stage in their lives, and it rose to 44% for 20 year-olds (102). In the same survey, when asked if they were currently taking drugs, 28% admitted that they were.

This widespread substance use in Irish society is placing an undeniably large burden on resources. Between 2005 and 2010, there were 2,295 recorded cases of adolescents under the age of 18, who utilised a drug treatment centre for the first time (103). This reflects an increase of over 50% in treatment demand over this five-year period. Large amounts of public funds and manpower have been invested in reducing availability of illegal substances in our society. Figures from the Central Statistics Office (CSO) show that the number of cases of *"possession of drugs for personal use"* in 2010 was 14,523, which is more than double the figure for 2004 (104). This database also shows a similar rise in the recorded number of cases of *"possession of drugs with intent to supply"*; 4,159 reported in 2010, almost twice the level recorded in 2004. There appears also to be a sharp increase in the domestic production of these substances to supply the high level of demand. In the same period of time as above, there was a 14-fold increase in the number of cases of *"cultivation or manufacture of drugs"*. This is a substantial challenge to the resources of An Garda Síochána, (Irish national police force). There are presently over 400 Gardaí involved in the Garda

National Drugs Unit and in divisional units solely working to combat drug crime (105).

Persons who start experimenting with substances at an early age are more likely (i) to engage in polysubstance use (106), (ii) to have problem use later in life (107, 108), (iii) to suffer from health problems (109), and (iv) to experience psychological problems (94). Preventing or delaying the onset of experimentation could reduce the number of persons requiring medical treatment; thus potentially reducing the burden on the public health-care system, and related health-care expenditure. Furthermore, it would likely lead to a decrease in polysubstance use, which has been associated with increased mortality (110) and has been implicated in approximately 50% of all substance-related deaths in Ireland between 2004 and 2009 (100).

The prevalence of substance use and the harm that is caused by young people is an area of concern for policy makers, health workers, the criminal justice system, youth workers, teachers and parents. It is therefore important to have a clear understanding of the extent of the problem. Whilst there have been studies which have examined this issue, there has not been a comprehensive review of the literature relating to substance use by young people in Ireland.Therefore a systematic review was conducted to identify, synthesise and summarise the existing literature on the prevalence of substance use among adolescents and young adults in Ireland. The review will look at prevalence figures for the four most-used substances across the

Republic of Ireland for persons between the age of 13 and 24, and compare usage across the years studied, 2000-2012.

2.2 Methods

This review was produced according to Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews and meta-analyses (111). These guidelines are primarily used for the reporting of controlled randomised trials (RCTs) or intervention studies, and so while not all items were applicable to this review of prevalence studies, the guidelines were adhered to as closely as possible. The articles were compiled from a large number of databases to ensure that as many relevant articles were included. The review was limited to articles reporting the use of cannabis, alcohol, nicotine, and benzodiazepines. These four substances were identified as the most widely-used substances in two recent large-scale studies (112, 113). An age range of 13-24 years was used as the criteria for searching as it encompasses the National Library of Medicine's Medical Subject Headings (MeSH) definitions of an 'adolescent' (13-18 years) and 'young adult' (19-24 years) (114). The following inclusion criteria were applied to the searches: English language, full-text access, and published since 2000. The databases searched with a Boolean string were: PubMed, Scopus, Web of Knowledge, Google Scholar, ERIC, Embase and CINAHL. The PubMed database was searched using the keywords as follows: *adolescent* or *young adult*, *marijuana smoking*, *benzodiazepines*, *smoking*, *ethanol*, *Ireland*. A search of the remaining databases was performed including the search terms: *adolescent* or *young adult*, *cannabis*

or *marijuana* or *benzodiazepine* or *alcohol* or *nicotine* or *tobacco* or *cigarette,* and *Ireland*. These searches were conducted in December 2011 and updated thereafter to include relevant studies that were published after December 2011. An additional manual search of the National Documentation Centre on Drug Use was necessary as it did not allow searches using Boolean operators (115). This website is controlled by the Health Research Board (HRB) in Ireland and is a *"database of Irish drug and alcohol research – an electronic library of full-text reports, journal articles, theses, and conference papers"* (116). This database has links to grey literature published by the government, national and international bodies. Personal contact was made with authors of some articles to obtain additional information.

The eligibility of articles found by the database search was checked by searching the title and abstract of the articles. Duplicates and records that were found to be not relevant were excluded. Reasons for exclusion included: multiple papers publishing data from the same dataset, articles which were commentaries and not original research, articles which covered a range of ages but were not divided into age categories, and articles which were part of a multi-national study, but did not provide country-specific information for Ireland. If there was still doubt about the eligibility of a paper, it was included so that a detailed inspection could be done at the next stage. The next stage was to obtain full-text copies of the remaining articles, and do a further assessment for eligibility and relevance. The data points of interest were extracted from the full-text reports and compiled into summary tables

(see Tables 2.1-2.5). The data points assessed were divided into two categories: study characteristics (sample size, sampling method, age range, region of sampling, and any other information that might influence the analysis of the survey), and study results (details of alcohol, tobacco, cannabis, and benzodiazepines). These study results would be the outcomes of interest for the review.

Quality of the final articles was assessed using the Methodological Index for NOn-Randomised Studies (MINORS) tool (117). The tool was customised for use in this review, and all the articles retrieved were assessed in a scale of 0-10 based on their methodological quality. The scoring of the studies can be seen in Table 2.1 and Appendix IV.

Table 2.1. Summary of study characteristics

Study	n	Region	Age	Gender (%)	Substance(s) surveyed	Sampling method	MINORS score	Notes
Currie *et al.*, 2008	4840	Republic of Ireland	11-15	**M: 50.6**, F: 49.4	Alcohol, Cannabis, Tobacco	Stratified random	10	*a*
Curtin, 2004	248	County Cork	15-16	**F: 100**	Tobacco, Alcohol	*Unable to identify*	4	*a*
Flanagan *et al.*, 2003	1426	Cavan, Louth, Meath & Monaghan	12-19	**M: 59.7**, F:39.3[1]	Alcohol, Cannabis, Tobacco	Stratified random	8	*a*
Hibell *et al.*, 2004	2407	Republic of Ireland	15-16	**M: 50.6**, F: 49.4	Alcohol, BZDs, Cannabis, Tobacco	Stratified random	10	*a*
Hibell *et al.*, 2009	2221	Republic of Ireland	15-16	M: 45.2, **F: 54.8**	Alcohol, BZDs, Cannabis, Tobacco	Stratified random	10	*a*
Hibell *et al.*, 2012	2207	Republic of Ireland	15-16	**M: 50.3**, F: 49.7	Alcohol, BZDs, Cannabis, Tobacco	Stratified random	10	*a*
Kabir *et al.*, 2010	2805	Republic of Ireland	13-14	M: 40.4, **F: 59.6**	Tobacco	Stratified random	8	*a*
Kelleher *et al.*, 2003	2297	Clare, Limerick & Tipperary	13-19	M: 44.8, **F: 53.3**	Alcohol, BZDs, Cannabis, Tobacco	Stratified random	6	*a*
Manning *et al.*, 2002	2580	Republic of Ireland	13-14	M: 45.2, **F:54.8**	Tobacco	Stratified random	8	*a*
McNeill *et al.*, 2011	214	Republic of Ireland	13-15	*Unable to identify*	Tobacco	Stratified random	7	b
Moran *et al.*, 2000	1070	Louth	12-19	**M: 100**	Tobacco	*Unable to identify*	4	*a*
Morgan *et al*, 2008	1048	Republic of Ireland	18-24	M: 45.9, **F: 54.1**	Alcohol, BZDs, Cannabis, Tobacco	Cluster sampling	10	
O' Cathail *et al.*,	370	Cork city	15-17	M: 38.4, **F: 61.6**	Tobacco	Convenience	8	*a*

Study	n	Region	Age	Gender (%)	Substance(s) surveyed	Sampling method	MINORS score	Notes
2011								
Office of Tobacco Control, 2006	777	Republic of Ireland	8-24	*Unable to identify*	Tobacco	Stratified random	6	
Palmer *et al.*, 2008	462	South-east Ireland & Cork city	14-19	M: 45, **F: 55**	Alcohol, BZDs, Cannabis	Convenience	10	*a*
Share *et al.*, 2004	620	Leitrim	14-15	M: 49.2, **F: 50.5**[1]	Tobacco	Randomised control trial	5	*a*, c
Smyth *et al.*, 2011	133	Republic of Ireland	15-16	M:43.6, **F: 56.4**	Alcohol	Simple randomisation	8	
UNICEF, 2011	508	Republic of Ireland	16-20	*Unable to identify*	Alcohol, Cannabis, Tobacco	Convenience	6	d

M = Male, F = Female, DNS = Did not specify, BZDs = benzodiazepines, Notes: a – school(s) survey, b – in-home interviews, c – intervention study, d – online survey 1 – some participants did not answer the question

2.3 Results

A total of 2,562 articles were found in the database search, and 11 were found in additional searches. The titles and abstracts for each article were reviewed and duplicates were removed. This reduced the number of remaining articles to 1,773. The next stage was to examine the title and abstracts of the remaining articles and eliminate those which did not match the eligibility criteria. 1,702 articles were discarded; 360 were excluded because the study was not investigating Irish young people, 1309 were excluded because they were not measuring drug prevalence, 10 were excluded because they measured prevalence in a different age group, 18 were excluded because they were not original research i.e. editorials, literature reviews etc., and 5 were excluded because they were studies that were based on data used from previous studies. After the excluded articles were discarded, 71 remained. The full-text articles were then obtained and assessed for suitability. Fifty-three articles were excluded; 8 had no Ireland-specific data, 36 were not substance use prevalence studies, 7 had data from studies with age ranges that included ages over 24, 2 had data based on previous research, and 1 was not a research article. There were 18 articles included in the review. A PRISMA flow diagram (Figure 2.1) provides a summary of the stages, and the number of studies in each stage (111). The study characteristics for the papers included in the review are summarised in Table 2.1. One of the included studies was a randomised control trial (RCT) that measured the effect of a smoking prevention initiative (118). There were eleven observational studies that had partial or full

randomisation in the sampling process (90, 112, 113, 119-126), and one study employed cluster

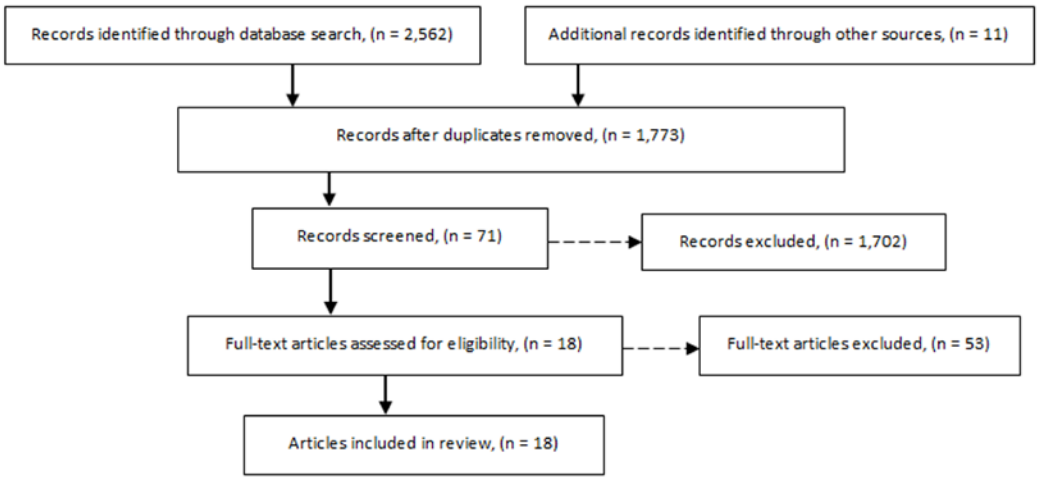

Figure 2.1. Adapted from the PRISMA flow diagram

Sampling (127). Convenience sampling was used by three of the studies (102, 128, 129), and the method of sample selection could not be identified in two studies (130, 131). Half of the studies surveyed the use of a single substance while the majority of the remaining studies investigated the use of three or more substances. Sixteen studies had tobacco as a substance studied, eleven studies investigated alcohol consumption, nine studies looked into cannabis use, and six investigated benzodiazepine use.

To facilitate observation of trends over time, the studies are presented according to three time periods: Period 1 (2000-2006), Period 2 (2007-2009), and Period 3 (2010-2012). As fewer studies were published in the earlier

years, Period 1 encompasses a longer timeframe of 7 years. Period 2 and 3 have equal timeframes of 3 years. These groupings provided approximately equal-sized groups, in terms of numbers of publications thereby avoiding issues such as diluting the group size to one or two articles.

2.3.1 Tobacco Usage

There were sixteen studies which collected data on tobacco usage, and a summary of the data can be seen in Table 2.2. One study was a RCT (118), eleven were observational studies with randomly-selected participants (112, 113, 119-126), one study used cluster sampling (127), two used convenience sampling (102, 128) and two did not describe how participants were selected (130, 131).

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Table 2.2. Summary of smoking prevalence rates

Study name	n	Age range (yrs)	Lifetime use of tobacco	First cigarette by 13 years	Tobacco use in the previous month	Daily tobacco use
Currie *et al.*, 2008	4840	11-15	26% (13 y.o.), 50% (15 y.o.)	33% (female), 29% (male)	-	3% (13 y.o.), 15% (15 y.o.)
Curtin, 2004	248	15-16	50%	-	31%	19%
Flanagan *et al.*, 2003	1426	12-19	50.8%	30.2%	-	18.2%
Hibell *et al.*, 2004	2407	15-16	67%	45%	33%	-
Hibell *et al.*, 2009	2221	15-16	52%	32%	23%	-
Hibell *et al.*, 2012	2207	15-16	43%	21%	21%	-
Kabir *et al.*, 2010	2805	13-14	-	-	10.6%[1]	-
Kelleher *et al.*,2003	2297	14-18	61.3%	49.7%	30.0%	-
Manning *et al.*, 2002	2580	13-14	-	-	19.0%[1]	-
McNeill *et al.*, 2011	214	13-15	-	-	10.5-13.5%	-
Moran *et al.*, 2000	1070	12-19	-	-	39%	22.5%
Morgan *et al.*, 2008	1048	18-24	-	-	29% (18-19 y.o.), 40% (20-24 y.o.)	23% (18-19 y.o.), 31% (20-24 y.o.)
O' Cathail *et al.*, 2011	370	15-17	48.4%	-	18.1%	-
Office of Tobacco Control, 2006	777	8-24	-	-	16%[2] (12-17 y.o.), 42%[2] (18-24 y.o.)	
Share *et al.*, 2004	620	14-15	57%	38%	21%[1]	11%

Study name	n	Age range (yrs)	Lifetime use of tobacco	First cigarette by 13 years	Tobacco use in the previous month	Daily tobacco use
UNICEF, 2011	508	16-20	-	-	23%	-

Notes: Dash – No data reported, 1 – Answer positively when asked if they are currently smoking, 2 - Figure represents current smokers that smoke greater than once a week or more, 3 - y.o = year-olds

2.3.1.1 Lifetime use of tobacco

This was reported in over half of the studies.

Period 1 (2000-2006): The levels from five studies in Period 1 ranged between 50-67% (118-120, 122, 130). The variation in the levels may exist because four of the five studies were measuring regional populations. The only national study reported a lifetime usage level of 67% (120). The largest of the regional studies reported a similar figure at the high end of the range, 61%, and so the true estimate probably lies in the somewhere in this region (122).

Period 2 (2007-2009): Two studies in Period 2 surveyed lifetime use: one of the studies measured usage in 13 year-olds and 15 year-olds and reported 26% and 50% respectively (112), while the second study reported 52% in a survey of 15-16 year-olds (113). Both of these studies were on a large scale and encompass national populations so their estimates would be close to the true figure.

Period 3 (2010-2012): There were two studies from Period 3, and these studies estimated lifetime tobacco usage at 48% and 43% respectively. There were differences between the two studies however, the former study

was conducted in Cork City (128) while the latter was a nation-wide study (126).

2.3.1.2 Smoking a cigarette by age 13 years

The second category examined was smoking a cigarette by age 13 years. It has been shown that initiation of substance use prior to 13 years of age is associated with chronic substance use (132). There were seven studies that collected data on this.

Period 1 (2000-2006): Four studies were published with results which ranged from 30-50% (118-120, 122).

Period 2 (2007-2009): Two studies were published which both had similar levels of approximately 30% (112, 113). These studies had good study designs and used a national sample so the true level is likely to be close to this.

Period 3 (2010-2012): A single study published reported a level of 21% (126).

2.3.1.3 Smoking in the previous month.

The third category examined was smoking in the previous month. This is considered a good indicator of regular use.

Period 1 (2000-2006): The studies from Period 1 ranged from 19-39% (118, 120, 122, 123, 125, 130, 131). Some of the variation in this can be explained thus: the two studies with the lowest percentages, 19% and 21%, were phrased in a different manner (118, 123). They measured positive responses to a question relating to whether they were currently smoking. This is not a clearly defined question and may account for the lower percentage. Two of the studies did not clearly indicate how samples were picked (130, 131), and so caution is advised when generalising the results from these studies. The final two studies gave estimates of smoking in the previous month to be 33% and 30% respectively, so the true level is likely to be near this figure (120, 122).

Period 2 (2007-2009): The level of smoking in the previous month in Period 2 was measured in two studies, and was estimated to be 23% (113) for one and between 29 and 40% for the other (127). The study was a large-scale, nationwide survey, and it is likely that the result is indicative of the true figure.

Period 3 (2010-2012): Five studies were found from Period 3; it is difficult to make a direct comparison between them due to significant heterogeneity in

the studies. Two studies recorded levels of 10.6% and 10.5% for 13-14 year-olds (121) and 13-15 year-olds (124) respectively, even though the former study measured the percentage of young persons currently smoking, and the latter measured the percentage of young persons that smoke greater than once a week or more. Two studies measured the level in older adolescents, 15-17 year-olds and 16-20 year-olds and reported levels of 18% (128) and 23% (102) respectively. Both of these studies however used convenience sampling to select their participants. The remaining study from Period 3 looked at 15-16 year-olds, and showed a level of 21% (126).

2.3.1.4 Daily tobacco use

The final category examined was daily tobacco use.

Period 1 (2000-2006): The range in data from Period 1 was 11-23% (118, 119, 130, 131). However, caution should be exercised when interpreting results of the studies reporting the two highest levels, 23% (131) and 19% (130), as the method of sample selection was not specified in the paper. The remaining two studies had good design; however they were both regional studies and so may not give a good indication of the national estimate.

Period 2 (2007-2009): There were two studies from Period 2 and both studies reported two levels; the first study reported one for 13 year-olds, 3%, and one for 15 year-olds, 15% (112). The second study reported on levels of

18-19 year-olds, 23%, and 20-24 year-olds, 31% (127). These are nationally representative studies and have good design so it is likely that they approximate the national level closely.

Period 3 (2010-2012): None of the studies from Period 3 reported levels of daily smoking.

2.3.2 Alcohol Usage

There were eleven studies that looked into alcohol usage and a summary is provided in Table 2.3. Randomised sample selection was used in seven of the studies (90, 112, 113, 119, 120, 122, 126), convenience sampling was used for two (102, 129), cluster sampling in one study (127), and the method of sample selection was not described in one of the studies (130).

2.3.2.1 Lifetime use of alcohol

For lifetime use of alcohol, the figures varied both between and within these periods.

Period 1 (2000-2006): There were four studies published in Period 1, and their levels ranged from 71-92% (119, 120, 122, 130). Differences in levels in these studies can in part be attributed to the age range of the participants. The studies with the lowest figure had a participant age ranging from 12-19 years, while each of the others studies had a

Table 2.3. Summary of alcohol prevalence rates

Study name	n	Age range (yrs)	Lifetime use of alcohol	First alcohol consumption before 13 years	Alcohol use in the previous 12 months	Alcohol use in the previous month
Currie *et al.*, 2008	4840	11-15	-	38%[1]	-	-
Curtin, 2004	248	15-16	82%	-	-	59%
Flanagan *et al.*, 2003	1426	12-19	71.3%	-	-	-
Hibell *et al.*, 2004	2407	15-16	92%	47% (beer), 45% (wine), 32% (spirits)	88%	73%
Hibell *et al.*, 2009	2221	15-16	86%	33% (beer), 31% (wine), 21% (spirits)	78%	56%
Hibell *et al.*, 2012	2207	15-16	81%	40% (beer), 18% (wine), 35% (spirits)	73%	50%
Kelleher *et al.*,2003	2297	14-18	90.2%	50.2%	83.4%	62.4%
Morgan *et al.*, 2008	1048	18-24	84% (18-19 y.o.), 93% (20-24 y.o.)	-	-	78.3% (18-19 y.o.), 84.5% (20-24y.o.)
Palmer *et al.*, 2008	462	14-19	86.10%	-	82.6%[2]	61.6%[3]
Smyth *et al.*, 2011	133	15-16	58%	-	-	-
UNICEF, 2011	508	16-20	77%	-	-	-

Notes: Dash – No data reported, 1 - only 15 y.o. reported, 2 – those who drank alcohol once a year or more often, 3 – those who drank once a month or more often, 3 - y.o = year-olds

minimum age of 14 or 15 years. One of the studies reported a lifetime level of 82%, but this study was conducted in County Cork with an unknown method of sampling, so it is difficult to extrapolate from it (130). Two studies demonstrated close agreement at 92% and 90% levels for lifetime usage and the true level is likely to be close to this (120, 133).

Period 2 (2007-2009): Only two of the three studies in Period 2 had data relating to lifetime alcohol usage and both of those studies reported similar results: 86.1% and 86% (113, 129).

Period 3 (2010-2012): There were three studies published in Period 3 and they reported 77%, 58% and 81% usage (90, 102, 126). The wide discrepancy between these figures may be due to the age of participants; up to 20 years in one study (102) and up to 16 years for the latter 2 studies. Another reason could be the nature of the studies: one was an internet poll and this may be a source of bias in the study (102). This contrasts with the third study which was a national study with randomised sampling (126).

2.3.2.2 Consumption of alcohol before 13 years of age

Period 1 (2000-2006): This examined the percentage of young persons who first consumed alcohol before 13 years of age. A limitation with this category was that it was reported in only two studies. Unfortunately, one of the studies quoted percentages for three types of alcohol (beer, wine, and spirits) which

ranged from 32-47%, so it was not possible to get an overall figure (120). The remaining study reported an overall consumption level of 50% (122).

Period 2 (2007-2009): two studies from Period 2 reported on this category. One of the studies differentiated between alcohol types, which ranged from 21-33% (113). The other study, Currie *et al.*, reported a level of 38% (112). Both of the studies were well-designed and were probably an accurate reflection of the actual population level.

Period 3 (2010-2012): A single study from Period 3 reported levels of first consumption prior to 13 years of age at between 18% and 40% for the three types of alcohol mentioned above (126).

2.3.2.3 Alcohol use in previous 12 months

Alcohol use in the previous 12 months was used as a measure of occasional use. Five studies (two from Period 1, two from Period 2, and one from Period 3) included data on 12 month usage (113, 120, 122, 126, 129).

Period 1 (2000-2006): Both studies reported similar values, 88% and 83% (120, 122). Both studies were large scale and had good design, so it probably reflects an estimate of the population figure.

Period 2 (2007-2009): The two studies from Period 2 were in broad agreement with each other. Hibell *et al.* and Palmer *et al.* reported levels of 78% and 83% respectively (113)‘(129). The result from Palmer is a percentage of positive responses to the question if they drank once a year or more.

Period 3 (2010-2012): The single study from Period 3 reported a level of 73% for alcohol use in the previous year (126).

2.3.2.4 Alcohol use in the previous month

The final category related to alcohol use in the previous month. Only one of the most recent studies reported data, but there were data from six older papers (three from Period 1, two from Period 2, and one from Period 3) (113, 120, 122, 126, 127, 129, 130).

Period 1 (2000-2006): The studies from Period 1 reported a range of levels from 59-73%. The 59% figure comes from the paper by Curtin, which was a small County Cork study and the study design was unknown (130). This affects the ability to generalise with its data and gives precedence to the results from the other studies which were 73% and 62% (120, 122).

Period 2 (2007-2009): Hibell *et al.*, 2008 had a level of 56% for the alcohol use in the previous month (113), while Palmer *et al.* gave a level of 62%

(129). This final figure was the percentage of those that responded positively when asked if they drank alcohol once a month or more often.

Period 3 (2010-2012): The study from Period 3 reported a level of 50% in this category (126).

2.3.3 Cannabis Usage

A summary of the studies reviewed that included surveyed cannabis usage is displayed in Table 2.4. There were nine studies that reported cannabis use amongst adolescents and young adults in Ireland (102, 112, 113, 119, 120, 122, 126, 127, 129). The studies were mostly randomised school surveys, while the remaining two studies were convenience studies (102, 129). All of the studies measured lifetime use of cannabis and there was a wide variation between levels, 20-80%. The two highest usage levels, 80% and 41%, were reported by two studies that used convenience sampling, so the true level may differ (102, 129). A pattern was seen in the other studies based on their year of publishing.

Table 2.4. Summary of cannabis prevalence rates

Study name	n	Age range (yrs)	Lifetime use of cannabis	Cannabis use in the previous 12 months	Cannabis use in the previous month
Currie *et al.*, 2008	4840	11-15	20%[1]	17%[1]	7% (female)[1], 11% (male)[1]
Flanagan *et al.*, 2003	1426	12-19	31.0%	-	12.8%
Hibell *et al.*, 2004	2407	15-16	39%	31%	16%
Hibell *et al.*, 2009	2221	15-16	20%	15%	9%
Hibell *et al.*, 2012	2207	15-16	18%	14%	7%
Kelleher *et al.*,2003	2297	14-18[2]	28.6%	24.2%%	15.4%
Morgan *et al.*, 2008	1048	18-24	-	12% (18-19 y.o.), 14% (20-24 y.o.)	-
Palmer *et al.*, 2008	462	14-19	41.1%	32.5%	13.62%[3]
UNICEF, 2011	508	16-20	>80% (weed)[4], 46% (hash)	-	-

Notes: Dash – No data reported, 1 – only 15 y.o. reported, 2 – 13 and 19 y.o. excluded due to lack of data, 3 – cannabis use once a month or more frequently, 4 – precise percentage could not be determined

2.3.3.1 Lifetime use of cannabis

Period 1 (2000-2006): Earlier studies from Period 1 showed a usage level of between 29 and 39% (119, 120, 122).

Period 2 (2007-2009): There were three studies in this period. Two of the studies had a level of 20% (112, 113), and the third study had a level of 41.1% (129).

Period 3 (2010-2012): There were two studies from Period 3 that reported on lifetime cannabis use. The most recent European School Project on Alcohol and Other Drugs (ESPAD) study reported a level of 18% (126), while the second report gave separate levels for the dried plant form (weed), >80%, and the extracted resin (hash), 46% (102). These levels are largely different from levels reported at any time throughout the entire time range, and so their use as a representative figure must be cautioned. Overall, the levels are suggestive of a decreasing experimentation with cannabis amongst young people.

2.3.3.2 Cannabis use in the previous 12 months

A similar pattern was observed in the reporting of cannabis use in the previous 12 months.

Period 1 (2000-2006): Higher levels were observed amongst the earlier studies, 25-31% (120, 122) than in subsequent periods.

Period 2 (2007-2009): There were four studies in period two and these studies showed a decrease compared to earlier studies to 12-17% (112, 113, 127). The exception to this is the study carried out by Palmer *et al.*, which gives a level of 33% for 12 month usage (129). A possible explanation for this higher figure may be that the study covers a broader age range (14-19 years), and the level of use generally increases with age. Owing to problems with generalisation of this study, the true level is likely to be closer to Currie *et al.* and Hibell *et al.* (112, 113).

Period 3 (2010-2012): A single study from Period 3 reported a level of 14% (126).

2.3.3.3 Cannabis use in the previous month

Period 1 (2000-2006): The trends in cannabis use in the previous month paralleled those in use in the previous 12 months. The three studies from period one showed high levels of use, 13-16% (119, 120, 122).

Period 2 (2007-2009): There were three studies ranged from 7-14% (112, 113, 129). The highest of the more recent figures, (14%) is from Palmer *et*

al., which as mentioned already suggests that the true level may be lower than this (129).

Period 3 (2010-2012): There was one study in Period 3 that reported this data and the level was 7% (126).

2.3.4 Benzodiazepine Usage

A summary of the studies reporting benzodiazepine usage can be found in Table 2.5. Four of the six studies had sample sizes greater than 2,000 and participants were randomly selected, so there is a high degree of confidence in the figures reported from these studies (113, 120, 126, 127). One study reported an overall prevalence level for benzodiazepine usage, and the remaining studies categorised usage into prescription use and non-prescription use. The percentage of subjects who have tried benzodiazepines without the advice of a doctor was consistently higher than prescription use in each of the studies.

2.3.4.1 Lifetime benzodiazepine use on prescription

Period 1 (2000-2006): There were similar levels for the prevalence of lifetime prescription benzodiazepine use at 9.2% and 10.0% (120, 122). Variation in the figure can be attributed in part to the difference in participant age with one study carried out by Kelleher *et al.* ranging from 13-19 years (122) while the other had a narrower age range. Another contributing factor to the

difference was that the participants in the Kelleher *et al.* study were recruited from three counties in the west of Ireland only, while the other study selected participants nationwide. This suggests that the higher end of the range is closer to the actual prevalence of non-prescription benzodiazepine use.

Period 2 (2007-2009): There were two studies in this period (113, 127). There was a wide discrepancy between the values in these two studies.

Period 3 (2010-2012): There was only one study in the third period, and this reported a level of use 9.0% (126).

Table 2.5. Summary of benzodiazepine prevalence rates

Study name	n	Age range (yrs)	Lifetime use of benzodiazepines	Lifetime use of benzodiazepines without prescription	Lifetime use of benzodiazepines on prescription
Hibell *et al.*, 2004	2407	15-16	-	2.0%	10.0%
Hibell *et al.*, 2009	2221	15-16	-	3.0%	10.0%
Hibell *et al.*, 2012	2207	15-16	-	3.0%	9.0%
Kelleher *et al*., 2003	2297	13-19	-	5.6%	9.2%
Morgan *et al.*, 2008	1048	18-24	-	0% (18-19 y.o.), 1.4% (20-24 y.o.)	1.0% (18-19 y.o.), 1.1 (20-24 y.o.)
Palmer *et al.*, 2008	492	14-19	10.8%	-	-

Notes: Dash – No data reported

2.3.4.2 Lifetime benzodiazepine use without prescription

Period 1 (2000-2006): The levels ranged 2.0% to 5.6%, with the Kelleher *et al.* study reporting a level of 5.6% and the Hibell *et al.*, 2004 study reporting 2% (120, 122).

Period 2 (2007-2009): There were three benzodiazepine studies that measured lifetime non-prescription benzodiazepine use. Two of the studies had reported differing levels of usage. One of the studies reported a level of 3.0% (113), while the other reports between 0 and 1.4% usage (127). One of the studies reported both prescription and non-prescription benzodiazepine use at 10.8% (129). This level appears to be in agreement with the rest of the studies; however the study cohort was not a national sample nor were the participants randomly selected. Both of these factors mean that generalisation of the results is not possible.

Period 3 (2010-2012): There was a single study in Period 3, and it reported a level of 3.0% (126).

2.4 Discussion

2.4.1 Summary of Evidence

This review examined available peer-reviewed research and other available reports on substance use in Irish young people since the year 2000. The review found a variety of studies that ranged from RCTs to online surveys

and from small-scale rural studies to national studies. This allowed for a wide perspective on substance use. Some overall trends were observed in the literature. The clearest pattern that was elucidated was a trend towards a decrease in all substance use over time between Period 1, Period 2 and Period 3. This decrease in use was consistent between the first period and the most recent period. An explanation for this trend is not suggested by the majority of authors, though something may be learnt from their observations. One author suggests that the fall in tobacco usage levels may be attributed in part to tighter government restrictions on the sale, display, and usage of tobacco products (124). A likely significant factor to contribute to Ireland's decreasing substance use rates is the creation and publication of Ireland's first National Drug Strategy document in 2000 (134). It was the first time that a comprehensive and national approach to substance use was examined. There had been a report previous to this, Government Strategy to Prevent Drug Misuse 1991 (135), but this had separate strategies for Dublin and the rest of the country. The National Drug Strategy paper introduced for the first time in Ireland the four pillar system. These pillars are (i) supply, (ii) prevention, (iii) treatment, and (iv) research. This allowed resources to be allocated to areas where they are needed. It allowed *"the bringing together of key agencies, in a planned and co-ordinated manner, to develop a range of appropriate responses to tackle drug misuse…"* (134).

The report resulted in the creation of a National Awareness Campaign which used traditional media such as brochures and radio, and newer forms of promotion i.e. Facebook, Twitter and Drugs.ie website to increase

awareness of the effects and consequences of substance use. The most recent National Drug Strategy document (9) builds on the determination to lower substance use. The biggest change in this report is the inclusion of alcohol as a drug of abuse. The high level of alcohol use nationally amongst adults and young people, and the cost to the public health system warranted its inclusion. Another stated reason for its inclusion was *"For many, alcohol is also seen as a gateway to illicit drug use, particularly for young people, while poly -drug use - which very often includes alcohol - is now the norm among illicit drug users"*. A recommendation in the report aimed at school students was the delivery of drug education to primary and post-primary students in schools through the Social, Physical, and Health Education (SPHE) curriculum.

It would appear that the combination of more harsh sales restrictions and increased education and awareness has had its intended effect on drug levels. The efforts of those involved should be applauded, and their support should be continued to maintain this positive trend. This work should be augmented by international good practice such as the WHO's guidelines on reducing harmful alcohol use (136). These recommend implementing various strategies should as pricing changes, closely regulating the advertisement of alcoholic drinks, and modifying the system of selling alcohol, such as reducing the hours of retail sales, and regulating the number and location of businesses that can sell alcohol. Further reduction in illicit substance use may come from educational interventions as outlined by Faggiano *et al.* 2005

(137) and 2010 (138). By continuing efforts such as these, the burden of substance use on young people can be reduced.

As stated above, tobacco and alcohol use followed the trend of decreasing use across all measures of use, experimental, occasional, or regular. The fall in levels of use are a positive step in the reduction in the burden caused by *"the single most preventable cause of death in the world today"*; cigarettes (139), and reducing the level of total alcohol consumption amongst the Irish, who rank second highest in the EU and 15th highest in the world (140). Sustaining these trends could result in reduced burden on the health-care system due to chronic treatment for preventable diseases, and on the justice system owing to reduced public order violations. The trend in decreasing tobacco use in Ireland mirrors that of Europe. The average lifetime use of tobacco for 15/16 year-olds across the 34 countries included in the ESPAD study fell from 67% to 60% between 2003 and 2007 (113). The same report gave a similar description for tobacco use in the previous month, and daily smoking; the former falling from 32% to 28%, while the latter fell from 10% to 8%. An opposite trend was observed in relation to alcohol use. There was no change in the average lifetime use of alcohol from 2003 to 2007 (113), and the percentage of 15/16 year-olds who consumed alcohol in the previous month fell from 65% to 62% over the same four-year period. When looking broadly, it is positive to see a reduction of the levels of both experimental and regular use of these widely-available substances when compared to our European counterparts (113).

There was a trend, amongst Irish adolescents, of decreased lifetime cannabis use, use in the previous 12 months, and use in the previous month over the length of the study period (113, 120, 126). The pan-European levels indicated by the latter report were similar to the levels of use in Ireland in 2007 (113). Ireland differs from the European average however as the level of Irish use decreased while the European level increased from 12% in 2003 to 19% in 2007. Most of this increase can be attributed to countries in the east of Europe, as the United Kingdom, France, Italy, Germany, Norway, Sweden, and Austria also had decreased lifetime cannabis use between 2003 and 2007. A similar pattern was observed in the category of cannabis use in the previous month (113).

Benzodiazepine usage was unchanged across the time periods studied. European levels appear to vary from Irish levels according to the most recent survey of benzodiazepine usage (126). The estimated average level of illicit benzodiazepine use was 6%, compared to 3% in Ireland. The level of prescribed use of benzodiazepines in Ireland was 1% higher than the European average of 8%. The levels of prescription and non-prescription use in Ireland did not appear to have changed significantly throughout the years of reference of this review. An explanation that may account for the steady level of benzodiazepine use in Ireland is that no campaign on the dangers of inappropriate benzodiazepine usage has been active in the country in the last ten years, since the launch of the Benzodiazepine: Good Practice

Guidelines for Clinicians document in 2002 (53). Such a campaign could encourage a young person or their parents to ensure that prescription usage is within safe limits, and deter its illicit use.

2.4.2 Limitations

A limitation to this systematic review is that the conclusions are only as accurate as the studies it returns. This is a limitation with every systematic review and literature review. To minimise the impact of low quality studies on the review, it was decided to quantify the quality of the studies using the Methodological Index for NOn-Randomised Studies (MINORS) tool (117).

An important limitation in the studies in this review was the lack of consistency in survey design. An example of this is evident in Table 2.2 under the column *"Tobacco use in the previous month"*. It is a standard, internationally-used question used to estimate regular use of a substance. Some studies chose to survey regular use with questions such as *"Are you currently smoking?"* and *"Do you smoke one or more cigarettes each week?"* Each question is attempting to measure the same outcome but because of the differences in the actual questions, it makes cross-study comparisons inappropriate and difficult. This limitation affected the ability to make comparisons between studies surveying tobacco, alcohol, cannabis, and benzodiazepine use.

There were few papers found in the literature search that surveyed benzodiazepine usage. A comprehensive search of scientific databases and grey literature could only find six relevant papers. Each of these studies measured usage superficially; one or two questions were asked as part of a section dealing with illicit substance use. It is difficult to get a clear understanding of benzodiazepine usage from these papers. It is important at present to look closer for patterns in benzodiazepine use because it was the only substance in this review whose usage did not appear to be decreasing. This could be the first stage in the development of a targeted educational campaign highlighting the dangers of inappropriate benzodiazepine usage.

There is a category of young person that is excluded from most of the studies in this review. As can be seen in the 'Notes' column in Table 2.1, twelve of the seventeen studies chose participants from pupils attending the schooling system in Ireland. This method of selection has many advantages; it is more efficient to randomly select young persons around the country, and it saves time because the students are all in the same place at the same time. However, this misses out on early school-leavers, who account for up to 14.1% of school-leavers in total(141). This cohort of young persons is a significant absence from any study reporting on substance use. International studies have shown that early school-leavers are more likely to use both legal and illegal substances(142). Excluding this group has the potential to underreport the true level of substance use in young persons.

2.4.3 Conclusions

This review has shown that substance use is still occurring in Ireland. Much of the research that is being undertaken on this topic in Ireland is of high quality and it indicates that the level of use is declining across many substances. However, there is still further work that can be done by policy-makers to ensure that this positive trend will continue. However, the fall in use is not evident with some substances and efforts must be increased to inform the public on their risks. Future work should redress the imbalance in substance use research that sees the majority of researchers looking at a few substances while little work is done on the others. Knowledge derived from these papers and reports, and from future work should guide the development of targeted drug prevention programs that are directed at the sections of population that will benefit the most from them.

3. Benzodiazepine prescribing guideline adherence and misuse potential in Irish minors

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3.1 Introduction

3.1.1 Background

Benzodiazepines are a commonly used substance worldwide. Data from the International Narcotics Control Board for 2011 estimate that between 26 and 26.5 billion defined daily doses (DDD), which is the average dose of a drug used in adults (143), were prescribed globally (144). The same study reported that European consumption of benzodiazepines, between the years 2009 and 2011, was the highest in the world at approximately 64 DDD/1,000 (persons)/day. Oceania, including Australia, had the second highest consumption at approximately 53 DDD/1,000/day, while the consumption of the remaining regions was below 36 DDD/1,000/day. While the majority of benzodiazepines are prescribed by doctors, benzodiazepines are also obtained illegally for recreational use. Recreational use amongst young people (under 18 years) in Europe has been studied and it is important to understand the pattern of recreational use in this group to understand potential benzodiazepine misuse in the future. Whilst benzodiazepine misuse without prescription amongst European 15-16 year olds decreased from 7% in 1999 to 6% 2003, the levels remained stable from 2003-2011 (113, 126, 145, 146). This pattern is also reflective of the situation in Ireland as demonstrated in a review of studies surveying benzodiazepine misuse between 2000 and 2012, which found that levels remained stable at 3% (147).

Recreational benzodiazepine misuse as well as prescribed benzodiazepine use can have adverse lifelong consequences if used on a long-term basis.

The acute effects of benzodiazepine use can include; muscle weakness, episodic memory impairment, and paradoxical disinhibition (148). Chronic benzodiazepine use is associated with visuospatial and verbal learning impairment, depressive symptoms and increased suicide risk (148-151). The consequences of benzodiazepine misuse are not restricted solely to the person misusing but also affect the community around them. Regular benzodiazepine misuse in Ireland has been associated with crime such as robbery, vehicle theft, fraud (152) and violent behaviour (153, 154). The consequences of benzodiazepine misuse at society level and the burden on the justice system and the health-care system are also worth noting. In 2011 in Ireland, the Garda Síochána (police force of Ireland) seized approximately 287,000 benzodiazepine tablets. This corresponded to a 6.4% increase on the number of tablets seized in 2010 (155). In 2010, benzodiazepines were the second most common substance involved in poisoning deaths. Of the 94 cases where benzodiazepines were involved, approximately 20% involved the consumption of multiple benzodiazepines (156).

Problematic misuse of benzodiazepines was known before this and in 2000 the Minister for Health and Children in Ireland established the Benzodiazepine Committee. The Committee sought to establish good practice guidelines to guide prescribers who prescribe benzodiazepines. The Committee published their Good Practice Guidelines for Clinicians in August 2002 (157). The guidelines sought to promote safe benzodiazepine prescribing. The guidelines provided recommendations on prescribing benzodiazepines for the first time to patients, prescribing for benzodiazepine-

dependent patients, prescribing to children and prescribing in nursing homes. This study analyses the implementation of these guidelines in young people under the age of 18 years.

3.1.2 Aims

The aims of this study are:

1. to examine Ireland's benzodiazepine consumption within a European context,
2. to evaluate the prescribing of benzodiazepines in under-18's in Ireland relative to guidance issued in the Good Prescribing Practice for Clinicians guidelines,
3. to highlight areas in prescribing where the potential for under-18's to misuse benzodiazepines can occur.

3.2 Methods

Ethical approval was sought and granted for this study from the Clinical Research Committee of the Cork Teaching Hospitals (see Appendix V). Data for this study came from Primary Care Reimbursement Service (PCRS); these data are collected by the Health Service Executive (HSE) and accessed using the Health Intelligence Ireland (HII) database (158). Access to the database was granted for information relating to medicines dispensed between January 2009 and December 2012. The HSE collects information about community-pharmacy-dispensed medicines in Ireland that are subsided fully or in part by the Irish government. The database includes

information on patient details such as gender, age, and area of residence (however this did not include whether the patient lived in an urban or rural area). Prescription details available on the database include (i) the World Health Organisation's Anatomical Therapeutic Chemical (WHO-ATC) classification, (ii) brand name, (iii) strength, (iv) quantity, (v) reimbursement price, (vi) the prescribing physician and (vii) the dispensing pharmacy. As the database is based on pharmacy reimbursement claims, there is no information regarding clinical diagnosis. The database contained information on three reimbursement schemes operating in Ireland (159).

Every Irish citizen is entitled to participate in the Drug Payment Scheme (DPS). An individual or family pays a maximum of €144 per month for approved medicines. DPS uptake was 35.8% of the Irish population in 2011. The General Medical Scheme (GMS) requires patients to pay a small fee for each approved medicine up to maximum ceiling. The fee was first introduced in October 2010 and between October 2010 and the end of the study period, the charge was €0.50 per item up to a maximum of €10 per person. Participation in the GMS is restricted to people who have a low income, have high medical costs, or are over the age of 65. GMS uptake was 37.0% in 2011. The Long-Term Illness scheme (LTI) is available to patients who have certain chronic illnesses such as epilepsy, diabetes, cystic fibrosis, and mental illness in patients less than 16 years. Patients on this scheme are entitled to free medicines for the treatment of their chronic condition. The HSE must give written approval for any medicine before it may be dispensed

under the LTI scheme. Uptake of the LTI scheme in 2011 was 1.3%. The remaining 25.9% of the population did not participate in these schemes.

For the purposes of this study, benzodiazepines are defined as any drug that has a benzodiazepine structure or acts in a similar pharmacological manner to benzodiazepines, *i.e.* zolpidem, zopiclone and zaleplon. Therefore benzodiazepines in this study were defined as drugs with WHO-ATC codes in groups N05BA for anxiolytics, and N05CD and N05CF for hypnotics.

In this study, dispensing data are used as a surrogate for consumption data. Irish national consumption data could not be calculated directly as some (25.9% of population in 2011) are not enrolled in government reimbursement schemes. The level of benzodiazepine consumption amongst those who are dispensed benzodiazepines privately could not be identified directly and so an estimate of private benzodiazepine consumption was calculated based on DPS consumption levels. This estimate was chosen because those patients receiving private prescriptions are entitled to enrol in the DPS, and so private patients and DPS patients are likely to be more similar to each other.

Comparative national benzodiazepine consumption data between 2009 and 2012 were obtained from publicly-accessible information published by:

- the Danish Medicines Agency (160),
- the State Agency of Medicines of Latvia (161),

- the French Agency for the Safety of Health Products (162),
- the Finnish Medicine Agency/Social Insurance Institution (163, 164),
- the Health-care Insurance Board of the Netherlands(165),
- the Family Practitioner Service section of Business Services Organisation in Northern Ireland (166),
- the Norwegian Institute of Public Health (167),
- the Information Services Division of the NHS in Scotland(168),
- and the Swedish National Board of Health and Welfare (169).

Data sources for some countries (Finland, Ireland, Scotland and the Netherlands) did not include 2012 information and therefore 2009-2011 information only, is provided. Although data were also available for Spain (170), Italy (171), and Portugal (172), it was decided not to include them as some of the benzodiazepines e.g. bentazepam, delorazepam, and mexazolam respectively, used in these countries, did not have an official WHO-ATC designation.

Benzodiazepine prescribing was compared against guidelines published by the Department of Health and Children in 2002. Guidance which relates specifically to under-18's are given below (157):

1) Benzodiazepines should be prescribed only for as long as is necessary, aiming for the shortest possible time but no longer than 4 weeks,
2) The long-term risks of using benzodiazepines need to be balanced against the benefits. If a decision to prescribe maintenance

benzodiazepines is made then the following recommendation is suggested;

Issue small quantities at a time (usually not more than one-week),

3) They are contraindicated for use as hypnotics in children.

3.2.1 Analysis

Consumption of benzodiazepines in this study was quantified in terms of the Defined Daily Dose (DDD). DDD is a term created by the World Health Organisation (WHO), and is defined as *"the assumed average maintenance dose per day for a drug used for its main indication in adults"* (173). This definition highlights both the strengths and the weaknesses of the system. Its major strength is that it allows researchers to measure the consumption of drugs in a similar class, as it accounts for the fact that drugs within a class have different potency. This allows for the comparison between drugs in a class, age groups, and countries. The disadvantages of DDD are that it is defined by (i) the maintenance dose of a drug, (ii) only includes a drug's main indication, and (iii) includes the recommended adult dose. These weaknesses can have an impact on measurement of DDD, but these weaknesses are inherent in any system for measuring drug consumption. The DDD system is the most recognised system used internationally. Irish benzodiazepine consumption was calculated as DDD/1000/day as recommended by the WHO to allow for comparison with other countries (174). It is generally calculated annually for each benzodiazepine as per Equation 3.1 (174).

Equation 3.1. DDD/1,000/day calculation

$$DDD/1{,}000/day = \sum \left(\frac{n_d * s_d}{DDD_d}\right) * \left(\frac{1000}{\sigma * 365}\right)$$

Where n_d = number of dosages of the dispensed benzodiazepine,

s_d = strength of the dispensed benzodiazepine dosage,

DDD_d = the defined daily dose of the dispensed benzodiazepine, and

σ = population of group being measured.

The sum of consumptions for all benzodiazepines was calculated to give the national consumption estimate.

The calculation of receiving greater than four weeks treatment was based on a patient receiving greater than 28 DDD in a month. Some patients may not have received their prescription at the start of the month, so patients who cumulatively received greater than 28 DDD over two consecutive months were also included as having receiving greater than four weeks of benzodiazepines.

For comparisons the Mann-Whitney U test was performed on non-normally-distributed continuous/interval data. For categorical data, Pearson's chi-square analysis was performed. A significance level of α=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.

Sensitivity analyses were performed on the main results to determine if excluding patients who were not taking benzodiazepines for their anxiolytic or hypnotic properties would significantly alter the results of the study. The PCRS database does not provide a diagnosis of the patient's illness or an indication for which the medicine is being used, so an alternative means of doing this was required. It was suspected that benzodiazepines prescribed on the LTI scheme would be for the treatment of clinically-diagnosed mental illness and/or epilepsy as they are the only indications of benzodiazepines covered by the LTI scheme. A separate sensitivity analysis was performed for all patients who received benzodiazepines by non-oral routes as these benzodiazepines are not likely to be misused.

3.3 Results

3.3.1 All-age benzodiazepine use in a European context

Firstly, an overview of benzodiazepine prescribing in Ireland will be placed in the context of international patterns of benzodiazepine prescribing. Figure 3.1 represents benzodiazepine consumption between 2009 and 2012 for selected countries where consumption data were publicly available. Benzodiazepine consumption in Ireland decreased from 59.3 DDD/1,000/year in 2009 to 49.8 DDD/1,000/year in 2011. This 16.0% decrease was the largest decrease among the countries surveyed. This is in contrast to the 16.1% increase in the Netherlands to 11.5 DDD/1,000/year over the same period. There were four countries with increased consumption, Latvia, Netherlands, Sweden and France, by 2.3, 1.6, 1.0 and 0.9 DDD/1,000/year respectively. The consumption of the remaining

countries, Finland, Norway, Denmark, Northern Ireland, and Scotland, decreased by, 7.6, 6.4, 5.1, 2.8, and 1.3 DDD/1,000/year respectively.

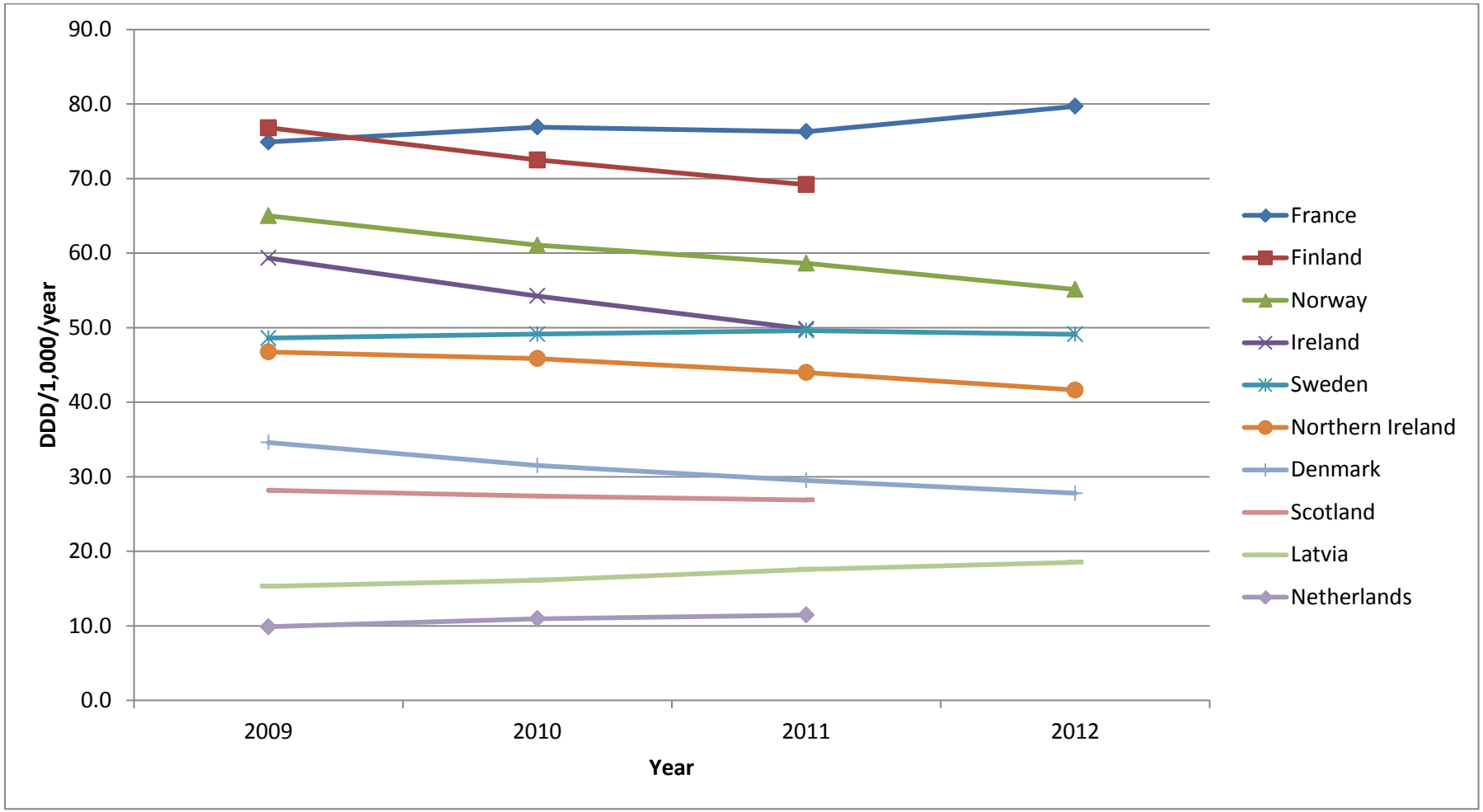

Figure 3.1.Benzodiazepine consumption in selected European countries between 2009 and 2012

3.3.2 Benzodiazepine use among young people in Ireland

3.3.2.1 Patient and benzodiazepines consumption data

There were 14,916 individuals aged less than 18 years who were dispensed 51,222 items on 46,208 prescriptions over the period from 2009 to 2012 inclusive. The majority of prescriptions (90.0%) had a single benzodiazepine dispensed, while 9.4% had two benzodiazepine items on their prescriptions. The remaining 0.6% of prescriptions contained three or four benzodiazepine items. Patients who received a single benzodiazepine prescription accounted for 63.9% (9,535) of all patients. The median consumption of benzodiazepines per patient was 5.3 DDD (IQR = 2.5 - 17.9). Diazepam was the benzodiazepine with the highest consumption between 2009 and 2011, while in 2012, clobazam had the highest consumption. Table 3.1 displays the characteristics of patients who received prescriptions for benzodiazepines between 2009 and 2012.

Table 3.1. Background statistics of patients issued benzodiazepines between 2009 and 2012

Measure	Year			
	2009	2010	2011	2012
Patients	4876	4597	4534	4727
Male	49.1%	50.3%	50.3%	51.0%
Age group				
0-4 years	15.5%	14.8%	16.3%	15.7%
5-9 years	18.0%	17.8%	15.5%	17.2%
10-14 years	24.8%	23.9%	25.2%	25.0%
15-17 years	41.7%	43.5%	43.0%	42.1%
Scheme				
GMS	64.1%	67.5%	70.7%	70.0%
LTI	9.7%	14.0%	14.0%	16.2%
DPS	26.2%	18.5%	15.3%	13.8%

The percentage of male patients was similar during the years 2009-2012 ($\chi^2 = 3.487$, $p = 0.359$). The percentage of 5-9 year olds decreased in 2011

compared with 2009 and 2010 ($\chi^2 = 17.851$, $p = 0.037$). No other significant differences were found. Likewise, there was an association between scheme and the year the patient received benzodiazepines ($\chi^2 = 337.109$, $p < 0.001$). There was a decrease in the percentage of DPS patients issued benzodiazepines in the time period, while the percentage of GMS and LTI patients issued benzodiazepines increased.

Total benzodiazepine prescribing increased by 4.7% between 2009 and 2012 in contrast to hypnotic consumption which decreased 9.2% during the same period (Table 3.2).

Table 3.2. Benzodiazepine prescribing between 2009 and 2012

Measure	Year			
	2009	2010	2011	2012
Total benzodiazepine consumption (DDD)	181,264.6	178,607.9	190,316.5	199,689.2
Total hypnotic consumption (DDD)	74,856.8	63,969.5	69,972.0	67,933.7

Figure 3.2 shows benzodiazepine prescribing in patients ranging between 5073.0 DDD (0 years) and 125,930.9 DDD (17 years) over the study period. Prescribing increased with age with an increase of 56.4% in prescribing between 15 and 16 year olds and an increase of 72.8% between 16 and 17 year olds.

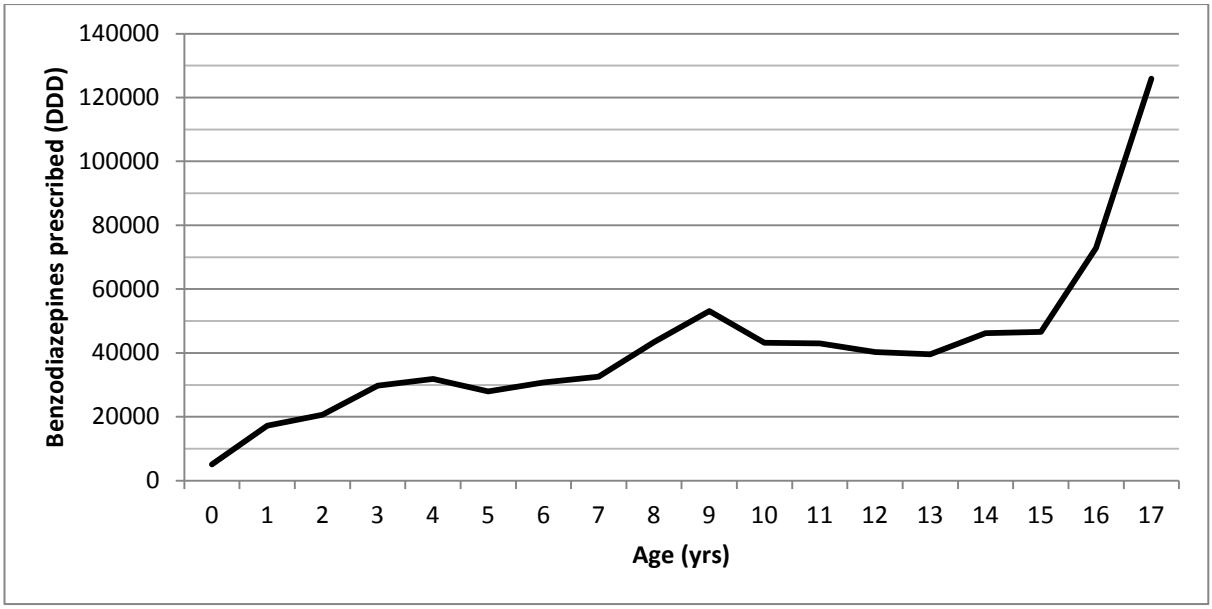

Figure 3.2. Benzodiazepine prescribing between 2009 and 2012 by age

3.3.2.2 Benzodiazepine guideline 1: "Benzodiazepines should be prescribed only for as long as is necessary, aiming for the shortest possible time but no longer than 4 weeks"

Almost 15% of patients were prescribed benzodiazepines for greater than four weeks and thus were outside guideline 1; of these, there were a greater percentage of males (16.0%) than females (13.4%) ($\chi^2 = 19.237$, $p < 0.001$). A greater percentage of DPS prescriptions were not compliant with guideline 1 (16.6%) compared to GMS (14.6%) or LTI (14.2%) prescriptions ($\chi^2 = 10.317$, $p = 0.006$). A greater percentage of those who had been prescribed a hypnotic (23.5%) had received over four weeks of benzodiazepines than those who had not been prescribed a hypnotic (9.0%) ($\chi^2 = 594.035$, $p < 0.001$) (Table 3.3).

3.3.2.3 Benzodiazepine guideline 2: “Issue small quantities at a time (usually not more than one-week)”

Over half (51.4%) of those who were in breach of guideline 1 were issued in quantities all greater than one week, contravening benzodiazepine prescribing guideline 2, while there were 15 patients (0.7%) whose prescribing was completely within guideline 2 (Table 3.4). There was no difference in the percentage of males and females who were issued benzodiazepines for greater than 7 days ($\chi^2 = 2.022$, $p = 0.568$). More than half of patients (58.5%) who were issued a hypnotic had received all their benzodiazepines in contravention to guideline 2, compared with less than half of those not prescribed hypnotics (47.2%) ($\chi^2 = 32.546$, $p < 0.001$) (Table 3.4).

Table 3.3. Compliance to benzodiazepine guideline 1

	≤ 4 weeks (compliant)	**> 4 weeks (non-compliant)**	**Chi-square analysis**
Patients, n (%)	12723 (85.3%)	2193 (14.7%)	
Gender			
Male, n (%)	6168 (84.0%)	1175 (16.0%)	$\chi^2 = 19.237$, $p < 0.001$
Female, n (%)	7972 (86.4%)	1253 (13.6%)	
Reimbursement scheme			
GMS, n (%)	9133 (85.8%)	1512 (14.2%)	
DPS, n (%)	2376 (83.4%)	473 (16.6%)	$\chi^2 = 10.317$, $p = 0.006$
LTI, n (%)	1214 (85.4%)	208 (14.6%)	
Hypnotic prescription			
Not prescribed, n (%)	8265 (91.0%)	821 (9.0%)	$\chi^2 = 595.035$, $p < 0.001$
Prescribed, n (%)	4458 (76.5%)	1372 (23.5%)	

Table 3.4. Compliance to benzodiazepine guideline 2

	100% of dispensings ≤ 7 days	**1% - 50% of dispensings > 7 days**	**51% - 99% of dispensings > 7 days**	**100% of dispensings > 7 days**	**Chi-square analysis**
	(compliant)	(----------non-compliant----------)			
Patients, n (%)	15 (0.7%)	258 (11.8%)	792 (36.1%)	1128 (51.4%)	
Gender					
Male, n (%)	8 (0.7%)	128 (10.9%)	433 (36.9%)	606 (51.6%)	$\chi^2 = 2.022$, $p = 0.568$
Female, n (%)	7 (0.7%)	130 (12.8%)	359 (35.3%)	522 (51.3%)	
Reimbursement scheme					
GMS, n (%)	11 (0.7%)	183 (12.1%)	525 (34.7%)	793 (52.5%)	
DPS, n (%)	1 (0.2%)	45 (9.5%)	146 (30.9%)	281 (59.4%)	$\chi^2 = 71.598$, $p < 0.001$
LTI, n (%)	3 (1.4%)	30 (14.4%)	121 (58.2%)	54 (26.0%)	
Hypnotic prescription					
Prescribed, n (%)	3 (0.4%)	67 (8.2%)	271 (33.0%)	480 (58.5%)	$\chi^2 = 32.546$, $p < 0.001$
Not prescribed, n (%)	12 (0.9%)	191 (13.9%)	521 (38.0%)	648 (47.2%)	

3.3.2.4 Benzodiazepine guideline 3: "They are contraindicated for use as hypnotics in children"

Hypnotics were prescribed to 5,829 people (39.1%). The hypnotic with the highest level of consumption between 2009 and 2011 was zopiclone, while nitrazepam consumption was greatest in 2012, increasing to 22,371 DDD from 9,722 DDD in 2009. Hypnotic use by males and females was similar at 39.7% and 38.5% respectively ($\chi^2 = 2.307$, $p = 0.129$). There were differences in the schemes of those who received hypnotics, with LTI patients (85.6%) receiving more than DPS patients (39.3%), who in turn received more than GMS patients (32.8%) ($\chi^2 = 1466.721$, $p < 0.001$) (Table 3.5). Patients who were issued hypnotics consumed greater median amounts of benzodiazepines (14.0, IQR = 5.3 - 35.0) than those who did not (3.5, IQR = 1.8 - 9.2) ($Z = -53.963$, $p < 0.001$).

Table 3.5. Compliance to benzodiazepine guideline 3

	Not prescribed hypnotic (compliant)	**Prescribed hypnotic (non-compliant)**	**Chi-square analysis**
Patients, n (%)	9086 (60.9%)	5829 (39.1%)	
Gender			
Male, n (%)	4428 (60.3%)	2915 (39.7%)	$\chi^2 = 2.307$, $p = 0.129$
Female, n (%)	4658 (61.5%)	2914 (38.5%)	
Reimbursement scheme			
GMS	7151 (67.2%)	3494 (32.8%)	
DPS	1730 (60.7%)	1119 (39.3%)	$\chi^2 = 1466.721$, $p < 0.001$
LTI	205 (14.4%)	1217 (85.6%)	

3.3.2.5 Sensitivity analysis

Sensitivity analyses were performed to examine the effect of the inclusion of those not likely to misuse benzodiazepines; LTI patients and those prescribed non-oral-route benzodiazepines. When patients receiving non-

oral benzodiazepines were removed from the analysis, a small change was detected. Where there had been a similar percentage of males (34.4%) and females (34.0%) prescribed hypnotics ($\chi^2 = 0.254$, $p = 0.652$) in the full analysis, a statistically significant difference between males (43.9%) and females (41.1%) emerged ($\chi^2 = 9.400$, $p = 0.002$).

3.4 Discussion

This study examined benzodiazepine prescribing in patients of all ages in Ireland in the context of benzodiazepine prescribing across a number of European countries and also examined benzodiazepine prescribing to people under the age of 18 years in Ireland from 2009-2012 in the context of the Good Practice Guidelines for Clinicians published in 2002 (157).

Benzodiazepine consumption among the entire population of Ireland was compared with nine other countries between 2009 and 2012. Irish benzodiazepine consumption had the largest decline in prescribing, decreasing 16.0% between 2009 and 2011 and was following the trend of decreasing consumption in most of the countries surveyed. The decrease in overall consumption should lead to an overall reduction in the supply of benzodiazepines to young people who wish to misuse. Access to family medications and dealers are some of the main ways that young people are supplied with benzodiazepines (175). Dealers themselves often get their benzodiazepines from visiting multiple doctors or buying them from people who are prescribed them (176). Thus it can be seen how reducing the

consumption of the entire population can have a positive effect on the illicit supply of benzodiazepines to young people.

There was a decrease in estimated global benzodiazepine consumption between 2009 and 2011 from 30 billion DDD to 26.25 billion DDD, respectively (144). All of the countries included in this study had levels above the average global benzodiazepine consumption for 2011, 10.4 DDD/1,000/year. This figure was calculated using the above estimated benzodiazepine consumption and a population estimate for 2011 (6.974 billion) from the United Nations Population Fund (177). The Netherlands was close to this level but its increases are indicating that the country will not stay at the low level in the future.

Approximately one in every seven young people who were prescribed benzodiazepines was prescribed them for greater than four weeks. Of those who were prescribed benzodiazepines for greater than four weeks, over half of them were given more than a week's supply per dispensing. In terms of prescribed hypnotics, there was a difference where the majority of those on the LTI scheme who were prescribed benzodiazepines (85.6%) were prescribed hypnotics compared with those prescribed hypnotics on GMS (32.8%) and DPS (39.3%). In contrast to the decreasing consumption nationally, there was a 4.7% increase in consumption among under-18s between 2009 and 2012, while hypnotic consumption fell by 9.2%. This decrease is welcome as the Good Practice Guidelines contraindicates

hypnotic use in under-18s (157). The rise in overall consumption is worrying because of the long-term potential side effects of regular benzodiazepine use. There was an increase in median benzodiazepine dispensing among Norwegian 15-16 year olds between 2006 and 2010, while in Australians aged 15-24 years, dispensing decreased by approximately half between 2003 and 2006 (178, 179). Neither study suggested reasons for their change in dispensing.

In the current study, prescribing of the study drugs was similar between males and females, but there was a significant difference in prescribing based on scheme. GMS and LTI scheme patients' percentage prescribing increased while DPS prescribing decreased to such levels that there were less DPS patients than LTI patients in 2012. The greater consumption of the study drugs by GMS patients compared to DPS patients may be explained in terms of income as evidence from the literature, albeit from adult data, suggests that benzodiazepine consumption is generally greater in patients with lower income and unemployment (180, 181). The increase in the number of LTI patients may be related to the increase in clobazam consumption, as clobazam and diazepam are the only benzodiazepines licenced in the treatment of epilepsy in Ireland (182).

Approximately one in every seven patients were prescribed benzodiazepines for greater than four weeks against the recommendations of the Good Practice Guidelines (157). There was a difference with overprescribing in

males. This result is unexpected as anxiety, for which benzodiazepines are most commonly prescribed, affects women to a greater degree than men (183). A possible explanation for this difference is prescribing for epilepsy in males, as there is a higher prevalence of epilepsy among males, but this would imply a higher percentage of LTI patients receiving greater than four weeks which is not reflected in the data (184). Another possibility is that more males are misusing benzodiazepines for nonmedical use but this finding is not unanimous (185, 186).

The potential for iatrogenic benzodiazepine dependence to develop in a short period of time should not be underestimated. One study reported that a moderately-high daily dose of diazepam (15mg/70kg/day) in healthy volunteers produced observable withdrawal symptoms after seven days of treatment (187). The results of that study also show that even at lower doses, dependence may develop after four weeks of treatment. This dependence would make patients hesitant to discontinue use of benzodiazepines and could lead to chronic benzodiazepine therapy. The higher levels of hypnotic prescribing in those prescribed benzodiazepines for greater than four weeks (23.5% v. 9.0%) is an issue as benzodiazepines with shorter half-lives carry a greater dependence potential (188). Benzodiazepine guideline number 2 recommends that those who are prescribed benzodiazepines for greater than a month should have their prescriptions issued in quantities of not greater than one week. Over half of patients (51.4%) were prescribed all their medicines in quantities greater than one week while 0.7% had their benzodiazepines prescribed according

to the guideline. GMS and DPS scheme patients appeared to have similar patterns of prescribing but LTI patients were prescribed their benzodiazepines in smaller quantities (Table 3.4). Smaller issue quantities in LTI may be common where benzodiazepines such as midazolam and diazepam can often be given in small quantities irregularly for the cessation of *status epilepticus*.

Hypnotics were prescribed to 39.1% of patients, in contravention of the prescriber's guidelines. Due to their short half-lives, hypnotics have the highest potential for tolerance and dependence (148), and this is part of the reason why the guideline states that hypnotics are contraindicated in this group. This is also the reason why the two most commonly consumed benzodiazepines, zopiclone and nitrazepam, state on their manufacturer's licence that they are 'contraindicated' and 'not recommended' in children, respectively (189, 190). Prescribing levels among males and females were similar but LTI patients were prescribed hypnotics at a level more than double that of GMS or DPS patient (Table 3.5). A probable reason for this high level is that midazolam is classified as a hypnotic (N05CD08), but it is also indicated for use in epilepsy. Between 2009 and 2011, midazolam was recommended as second-line treatment to diazepam for prolonged or repeated seizures in the community by the National Institute for Health and Clinical Excellence (NICE) (191) and the updated guidelines in January 2012 recommended midazolam as the first-line treatment (192). The recommendation for the use of midazolam in the updated guidelines is likely

to cause an increase in midazolam, and as a consequence hypnotic, prescribing in under-18s.

There were two sensitivity analyses performed, one which excluded LTI patients and one which excluded patients who received non-oral-route benzodiazepines. The first analysis showed no significant change in any of the results, while there was one change in the second sensitivity analysis. The chi-square analysis of prescription of a hypnotic to boys (43.9%) and girls (41.1%) returned a value of $\chi^2 = 9.400$ with a $p = 0.002$. The 1.8% difference between the sexes may have been statistically significant but prior to sensitivity analysis the difference was 1.2%. It was deemed that the sensitivity analyses showed no major difference because none of the significant results were nullified. The exclusion of those patients who were not suspected of misusing benzodiazepines did not meaningfully change results so including their data was appropriate.

3.4.1 Limitations

The main weakness of this study is that the HII database did not provide diagnoses for patients so the reseacher was unable to differentiate between those taking benzodiazepines for psychologically-based illnesses, with potential misuse, and those who were not. Our sensitivity analysis attempted to eliminate the effect of patients who are less likely to misuse benzodiazepines however; the changes that resulted were not large. Another limitation was the lack of data on adherence to the prescribed medicines. It is

not possible to know whether a prescribed medicine has been taken by the patient at the time of dispensing or stockpiled, with the unintentional possibility of misuse by family members, or has been diverted for commercial gain, which can occur (193). Notwithstanding these points, the data were derived from a nationwide reimbursement database and so would not be subject to errors in patient memory compared with a study based on patient recollection of prescribed benzodiazepines.

3.4.2 Conclusion

Benzodiazepine consumption levels to patients of all ages in Ireland had the largest decrease of the nine countries surveyed. This finding is contrasted by the increase in consumption by under-18s. Prescribing of benzodiazepines to young people is often not in adherence with the benzodiazepine guidelines for safe prescribing, with at least 40% of patients prescribed benzodiazepines outside of the guidelines. The consequences of this can include lifelong benzodiazepine usage and increased burden upon the Irish health-care system. It would be prudent to further investigate the reasons for not adhering to the guidelines so that inventions may be developed to improve adherence in the future.

4. Use of addiction treatment services by Irish youth: does place of residence matter?

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4.1 Introduction

4.1.1 Background

Substance use is a global public health issue. Approximately 7.4 million people died worldwide in 2004 due to alcohol and tobacco use; this accounted for 12.6% of all deaths worldwide according to the World Health Organisation (WHO) (96). The same report highlighted substance use as the cause of approximately 245,000 deaths and the loss of over 13 million disability-adjusted life years (DALYs) (96). The impact of substance use was more pronounced in Europe. The WHO European region accounted for 13.7% of the world's population in 2004, yet 28.1% of deaths attributed to addictive substances occurred there (96).

Most experimentation with substances of potential misuse begins in adolescence (91, 194). Early experimentation (less than 13 years of age) can be problematic and can progress to misuse (132, 195). There are long-term problems associated with early initiation of substance use, such as greater likelihood of multiple substance use (106) and increased incidence of psychosocial problems (94, 196). Geographical location is a factor that influences substance use. Living in an urban area has traditionally been associated with increased substance use while rurality was a protective factor (197, 198). This situation is changing as the gap between the patterns of substance use in urban and rural setting becomes narrower. Two reviews examined urbanisation as a risk factor for substance misuse found no conclusive evidence that it led to higher levels of substance misuse in urban areas compared with rural areas (199, 200). Another review examined the

impact of substance abuse on rural areas found that there was *"a convergence in substance use patterns between metropolitan and non-metropolitan areas"* (201). These papers suggest that it is too simplistic to discuss which area has a higher level of substance misuse.

It is more appropriate to examine individual substance use patterns; one review noted that though overall levels were similar, cocaine and cannabis levels were higher in urban areas while alcohol, methamphetamine and inhalant use levels were higher in rural areas (201). Other international studies concur with these findings and conclude that the differences are now to be found at the level of the individual substance (202-208). There are scarce data relating to urban/rural comparisons of substance use in Ireland. In a study of approximately 3,400 young people in Ireland urban and rural alcohol use was examined and a marked difference was observed (209). The study found that young people from rural areas reported having their first alcoholic drink at an older age and had the lower percentage for having drunk alcohol in the last 30 days. This report focussed solely on one substance thereby making it impossible to generalise the findings.

There is also literature on the perceptions of parents who reside in rural areas that suggests that differences in urban and rural drug use may be narrowing (210). In the Cork/Kerry region of Ireland, where this study took place, a single study comparing urban and rural substance use levels in the general population was published (211). Substance use was compared in

Cork city, Cork county, and Kerry. Lifetime use of any substance was highest in Cork city (41%), compared to Cork county (31%) and Kerry (29%). The study also listed the lifetime use of individual substances. Cork city was highest in each substance listed except for over-the-counter codeine, where Kerry (4.4%) was greater than Cork city or county, with 3.0% and 1.8% respectively. There were no statistical analyses of these differences so no definite conclusions can be drawn. A recent review of Irish substance use has shown that substance use levels have changed since the report was published in 2004, so these patterns may have changed (147).

Two studies were conducted in substance misuse treatment centres in Ireland in the past (212, 213). The treatment centres were almost exclusively urban populations in Dublin. Both of the studies omitted location from their studies, so it was not possible to use these data as a comparator. Another limitation to these studies is that they focussed on one or two substances. One of the studies examined concurrent alcohol and cocaine use (212) while the other performed an in-depth analysis of alcohol consumption (213). It is often difficult to include rural substance users in studies such as these, as services are less prominent than in urban areas and substance users may not be captured by the system. However, the treatment centre in this study has attendees from the counties of Cork and Kerry and thus serves a larger population from rural areas; therefore this study will attempt to redress this issue. The Cork/Kerry area of Ireland has the third highest level of substance treatment uptake in the country (103) . The level increased from 74.2 per 100,000 to 110.1 per 100,000 in period between 2005-2007 and 2008-2010

respectively. This increase highlights the need for more information about those who are entering these services. The review of the literature highlighted gaps in the knowledge of substance use in urban and rural areas in the general population which has not been updated in nearly a decade. The lack of research into the nature of rural substance use was also highlighted by the literature review. There is also a need for research regarding those attending treatment centres, and how having urban or rural residence can affect the nature and success of treatment. Finally, it is important that an emphasis is placed on adolescents in each of these areas, as substance misuse can harm adolescents immensely.

4.1.2 Aims

The aims of this study were to examine the data of young service-users (up to 21 years old) attending a substance treatment centre, and compare attendees from urban and rural areas, between 2007 and 2011.

4.2 Methods

4.2.1 Design

Ethical approval for this research was obtained by the Clinical Research Ethics Committee (CREC) of the Cork Teaching Hospitals and University College Cork (Appendix VI). Matt Talbot Services (MTS) is substance misuse treatment centre for young people under the age of 21 years. It is the only Tier 3 substance misuse treatment centre in the Cork/Kerry region that will admit young people under the age of 18 years (211). Before 2010, MTS

exclusively treated males, but a policy change resulted in the admission of females. Young people must provide written informed consent to allow their data to be used for research as part of the requirements for admission.

Between 2007 and 2011, 684 young people requested treatment from MTS. Of these, 457 (66.8%) of the young people received a place. Seven of these service-users were omitted from analysis because they were over the age of 21 years, and 14 were excluded because there were no data on their location of residence. A total of 436 service-users were included for analysis. The Health Research Board (HRB) requires all treatment services receiving public funding to complete the National Drug Treatment Reporting System (NDTRS) form to collect information such as demographic information, treatment history, and substance use history (excluding tobacco use). Electronic copies of the NDTRS forms submitted by MTS from the years 2007 to 2011 were obtained from the HRB for the purposes of this study (Appendix VII). In the Cork/Kerry region, there is a single city, Cork city, so for the purposes of this study, urban service-users were those who resided in Cork city, while rural service-users resided outside Cork city.

4.2.2 Analyses

Descriptive analysis of demographic and recent substance use data was performed. The highest level of education was taken directly from the National Drug Treatment Reporting System (NDTRS) survey, so some of the terms may be unfamiliar to those outside of Ireland. A brief description of

these options given follows: (i) did not complete primary education (age approximately less than 12 years), (ii) completed primary education (age approximately 12 years), (iii) completed the Junior Certificate (the first national examination; age approximately 15 years), (iv) received the Leaving Certificate (the final examination of secondary level education; age approximately 18 years). International readers may be unfamiliar with the term *"head shop drugs"*. It is the term used in Ireland for novel psychoactive compounds not restricted by law such as mephradone. Sale of head shop drugs was made illegal on 23rd August 2010.

An independent t-test was performed to measure the difference in age at admission and the age of first substance use between urban and rural service-users, while the Mann-Whitney U test was used to test for significance in the differences between lifetime/previous month/daily use of multiple substances. For the remaining categorical 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. If contingency tables yielded significant differences, then a column proportion test with Bonferroni correction was applied to identify the items that contributed to the significant value. 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.

4.3 Results

There has been a steady increase in the number of individuals who were accepted for treatment from 2007-2011. Of the total number of cases recorded during this period: 26 were in 2007, 70 in 2008, 90 in 2009, 101 in 2010, and 163 in 2011. The percentage gap between the urban and rural has lessened in the same period, with urban service-users accounting for 73.1% in 2007, 35.7% in 2008, 52.3% in 2009, 53.7% in 2010, and 45.3% in 2011. The regional breakdown of these service-users was 212 from Cork city, 223 from Cork County and a single person from Kerry, so further analysis using these categories was not performed.

Table 4.1 presents data on urban and rural service-users. There were more service-users from rural areas (51.3%) than from urban areas (48.7%). Both groups were similar in mean age, urban (16.7 ± 1.39 years) and rural service-users (16.8 ± 1.48 years). Males accounted for most users from both urban and rural settings. The percentage of service-users that resided with their parents was also similar for urban (93.3%) and rural (92.2%). The highest level of education was found to be similar between urban and rural service-users. The service-users current work/educational status was examined also; significant differences were observed between urban service-users and rural service-users. More urban service-users were unemployed when compared to rural service-users.

Table 4.1. Comparison of demographics between urban and rural service-users

Measure	Urban (n=212)	Rural (n=224)	Significance
Mean age ± standard deviation (years)	16.69 ± 1.39	16.78 ± 1.48	t=-0.640, p=0.523
Gender			
Male (%)	98.6%	96.8%	p=0.341
Female (%)	1.4%	3.2%	
Living situation (%)			
Resides with parents (%)	93.3%	92.2%	χ^2=0.067, dF=1, p=0.795
Does not reside with parents (%)	6.7%	7.8%	
Nationality			
Irish	98.2%	98.6%	p=1.000
Other European	1.8%	1.4%	
Highest level of education (%)			
Primary level incomplete	1.0%	1.1%	
Primary level	29.1%	43.8%	p=0.153
Junior Certificate	62.1%	48.3%	
Leaving Certificate	7.8%	6.7%	
Current status (%)			
In paid employment	4.1% †	10.3% ¶	
Unemployed	33.3% †	22.2% ¶	
Adult training course	22.2%	17.0%	χ^2=12.287, dF=4, p=0.015*
Student	37.4%	47.4%	
Other	2.9%	3.1%	

Subscript † and ¶ indicate that the difference in a measure was due to the items with the subscript. *p < 0.05

An examination of the source of referrals between urban and rural service-users showed that the distribution in the source of referrals was similar (p = 0.158). However, when the drug of referral was examined, there was a difference observed between the urban and rural service-users (p < 0.001). More benzodiazepine and head shop drug referrals were associated with

urban service-users while more alcohol referrals were associated with rural service-users. Age of first substance use was also examined. Both groups had similar mean ages of first substance use (12.4 years for urban service-users and 12.7 years for rural service-users) ($p = 0.058$). The percentage of urban service-users who had ever used three or more substances was significantly higher ($p = 0.001$). A more detailed examination of their substance use histories revealed that usage was greater for urban service-users for the number of substances used monthly ($p = 0.003$) and daily use ($p= 0.004$). There was a significant difference between the two groups when the first substance used was examined ($p < 0.001$). A more detailed analysis found that first use of inhalants by urban service-users was significantly more frequent while alcohol use was more common in rural service-users. See Table 4.2 for detailed descriptions.

Table 4.2. Comparison of substance use between urban and rural service-users

Measure	Urban	Rural	Significance
Source of referral (%)			
Self	7.1%	10.4%	
Family/friends	30.0%	25.9%	
Social/Community Services	20.0%	17.5%	p=0.158
Medical services	1.9%	1.4%	
Irish legal system	37.1%	44.3%	
Education sector	2.9%	0.5%	
Employer	1.0%	0.0%	
Drug of referral (%)			
Opioids	1.4%	0.4%	
Cocaine	1.9%	2.2%	
Ecstasy	0.9%	0.4%	
Benzodiazepines	16.0%†	4.0% ¶	
Inhalants	0.9%	0.0%	p < 0.001***
Cannabis	54.0%	59.6%	
Alcohol	22.5%†	32.3% ¶	
Head shop drugs	4.2%†	0.9% ¶	
Age of 1st substance use (years)	12.4	12.7	t=1.899, p=0.058
Percentage that have lifetime use of at least 3 substances	73.7%	52.2%	Z=-3.203, p=0.001**
Percentage that have last month use of at least 3 substances	49.3%	31.3%	Z=-2.998, p=0.003**
Percentage using at least 2 substances daily	11.3%	4.9%	Z=-2.882, p=0.004**
First drug used (%)			
Cocaine	0.0%	0.5%	
Ecstasy	0.0%	0.5%	
Benzodiazepines	4.1%	1.5%	
Inhalants	6.1%†	0.5% ¶	p < 0.001***
Cannabis	81.7%	80.9%	
Alcohol	7.6%†	16.1%¶	
Head shop drugs	0.5%	0.0%	

Subscript † and ¶ indicate that the difference in a measure was due to the items with the subscript. **p < 0.01, ***p < 0.001

4.4 Discussion

4.4.1 Summary

For both urban and rural service-users, the typical service-user was an Irish male aged between 16 and 17, who resided with his parents. Service-user characteristics were analysed to examine for differences between urban and rural service-users. In terms of employment, there were a greater percentage of rural service-users who were employed, while there were a significantly greater percentage of urban service-users who were unemployed. There were differences in the drug of referral between urban and rural service-users, particularly for alcohol and benzodiazepines. A greater proportion of urban service-users had tried multiple substances in their lifetime and continued to use more substances regularly. A significant difference in the first substance used by service-users was also highlighted. More urban service-users' first substance was inhalants while their rural counterparts tried alcohol first. This differs from a study found on Irish alcohol use (209), which saw that alcohol use was greater in urban adolescents. Greater rural use of alcohol was detected elsewhere, such as Scotland (214) and the United States (201).

The results also showed that benzodiazepine referrals were greater in urban areas. A possible explanation for this is the trend of greater levels of prescribing in urban areas (215, 216) could result in more opportunities to access benzodiazepines. Early initiation of substance use has been linked with developing a substance use disorder or dependence (217), mental health problems (218), educational under-achievement (219), suicidal

ideation (220), and suicide attempts (221). A report from the Substance Abuse and Mental Health Services Administration (SAMHSA) compared urban and rural attendees of treatment centres in the United States of America in 2012 (222). The report concluded that rural admissions were more likely to be in full-time employment, and report alcohol as their main substance of abuse, while urban admissions were more likely to not be in the labour force, and report cocaine or heroin as their main substance of abuse. These results correspond with the findings in this study. It was not possible to compare results from the current study with research in Ireland or the United Kingdom, as there is a lack of research examining associations between attendees' residence and treatment centre attendance.

4.4.2 Limitations

A limitation to this study is that there were a limited number of characteristics to analyse, and so confounding factors may be present, such as parental substance use (223), romantic partner use (224), physical abuse at a young age (225), level of exercise (226), and sexual preference (227). Another limitation on this study is that tobacco was not included as a substance of abuse. Tobacco and alcohol are often the first substances that preadolescents and adolescents will use (228); excluding tobacco may raise the age of first substance use. It should be noted when interpreting this result.

A further limitation is that service-users of a treatment centre were examined, so differences in substance use are not generalisable to the Irish population. Service-users form a sub-section of the population that misuses substances. However the substance use of these young people may suggest the patterns of substance use in their peer group and their locality. This could be a reasonable explanation as MTS is the only Tier 3 centre for under-18's in the region, thus limiting the choice of centre. This means that a particular group of urban or rural substance users are not self-selecting, and therefore this bias is not introduced into the study.

4.4.3 Conclusions

Urban and rural service-users showed differences in their patterns of use. Policy in Ireland needs to take these differences into account. Policies are often formulated with urban service-users in mind and this can result in suboptimal preventative and treatment strategies for rural service-users. This is the first study in Ireland to compare service-users from an urban and rural setting and further work needs to be done to fully describe the differences between service-users, so that effective strategies to prevent and reduce substance use nationwide can be implemented.

5. Benzodiazepine use amongst young attendees of an Irish substance treatment centre

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5.1 Introduction

5.1.1 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 (229). This is similar to the estimate of treatment uptake in 2005, which was around 3.7 million people (230). 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% (231, 232). 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 (231, 233). 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 (103). 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 (234). 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% (101). The most commonly used drugs in the year previous (2010/2011) in this age group 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 (147). 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. Between 1995 and 2011, the percentage of 15/16 year olds that had used benzodiazepines without a prescription decreased from 7% (145) to 3% (126), although this is greater than 2003 levels of 2% (120). This is in contrast to the percentage of young people who are prescribed benzodiazepines in Ireland which has decreased from 11% in 1999 (146) to 9% in 2011 (126). 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 examine 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 (235).

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 impaired risk, which can lead to high-risk sexual behaviour and reckless driving (28, 236). Benzodiazepines can also lead to paradoxical reactions and can result in restlessness, agitation, anxiety and aggressive behaviour (237). There is evidence that these reactions are more likely to occur to those at either extremes of age, that is, at younger or older ages (238), and that combining with alcohol can increase the occurrence of violent behaviour (154). Cognitive impairment is a well-documented side-effect of benzodiazepine use (239-241), both short-term and long-term. There is evidence that these effects can remain even after treatment with benzodiazepines has ceased (25, 242), although this is not without dispute (26). 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 (243). The significance of benzodiazepines in self-harm is such that the report views restricting access to benzodiazepines as a priority.

5.1.2 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.

5.2 Methods

5.2.1 Design

Ethical Approval for this research was gained from the Clinical Research Ethics Committee of the Cork Teaching Hospitals (Appendix VI). The study used data collected from service-users who entered treatment with MTS between 2005 and August 2011. Applicants were initially interviewed by 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 (244). 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 (Appendix VIII). 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.

5.2.2 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 (101, 245). 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.

5.3 Results

5.3.1 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 1.3 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 5.1.

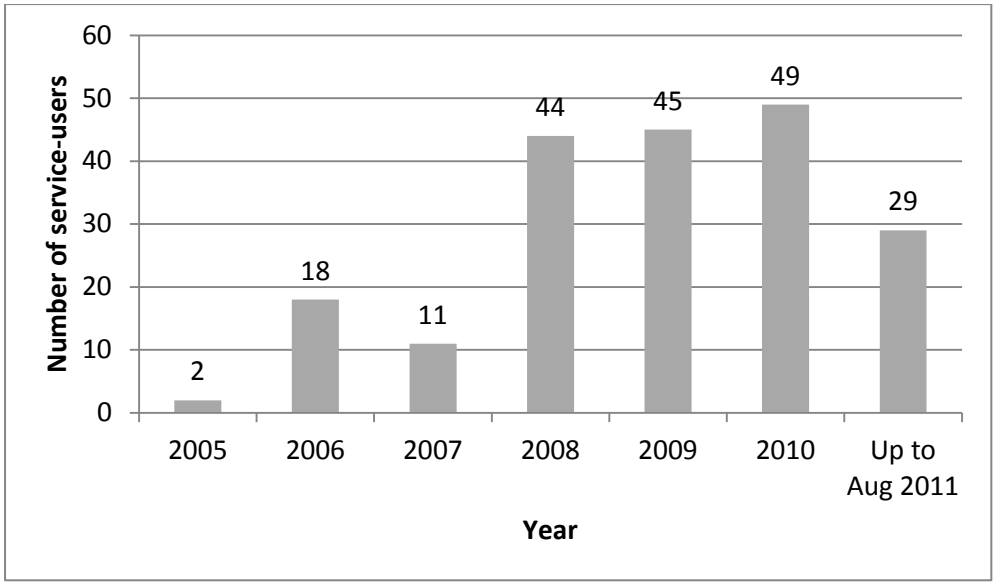

Figure 5.1. Number of service-user forms filled out by year

Table 5.1. Breakdown of referrals of service users by source of referral

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)

A breakdown of referral sources can be seen in Table 5.1. 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 (Table 5.2). 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).

Table 5.2. Service-users who 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)

5.3.2 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 ± 1.4 years. Characteristics of service-users entering treatment and their substance use history, as it relates to benzodiazepines, are examined in Table 5.3.

Table 5.3. 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 ± 1.0	16.7 ±1.2	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	p=0.776
Social Worker (%)	10.0	21.4	
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

Bold highlight signifies significance ≤ 0.05

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 5.4. 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 Table 5.4).

Table 5.4. Comparison of physical and behavioural symptoms experienced by benzodiazepine users

Measure	Regular users	Non-regular users	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%	χ^2=0.859, p=0.354	47.7 (73)
Changing friends and moving away from old friends	79.5%	72.4%	χ^2=0.153, p=0.696	68.9 (111)
Dramatic attention-seeking behaviour	**81.3%**	**50.0%**	**χ^2=5.232, p=0.022**	65.2 (101)
Extreme apathy	80.6%	60.7%	χ^2=1.960, p=0.161	60.0 (87)
Hyperactivity	83.8%	76.7%	χ^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%	χ^2=1.947, p=0.163	78.9 (131)
Increased time spent alone in room/withdrawn behaviour	88.9%	69.0%	χ^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%	χ^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%	χ^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%	χ^2=0.008, p=0.930	28.0 (44)
Suicide attempts	22.9%	20.7%	χ^2=0.000, p=1.000	15.7 (24)

Measure	Regular users	Non-regular users	Significance	Total, % (n)
Temper outbursts	92.3%	80.0%	p=0.163	79.8 (134)
Median physical signs	**8**	**6**	**Z=-1.969, p=0.049**	
Physical signs				
Blackouts	83.8%	83.3%	p=1.000	71.4 (115)
Bloodshot eyes that appear glassy or vague	85.7%	71.4%	χ^2=1.164, p=0.281	61.3 (93)
Change in appetite	86.1%	67.9%	χ^2=2.096, p=0.148	61.3 (95)
Change in weight	81.6%	60.0%	χ^2=2.880, p=0.090	62.0 (103)
Deterioration in appearance	74.3%	48.3%	χ^2=3.535, p=0.060	54.8 (86)
Excessive sleeping	59.5%	55.6%	χ^2=0.003, p=0.955	49.0 (77)
Insomnia	79.5%	60.7%	χ^2=1.979, p=0.160	59.9 (97)
Loss of fine motor co-ordination e.g. holding a glass	75.0%	60.7%	χ^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%**	**χ^2=4.702, p=0.030**	44.1 (67)
White or pale face	**86.8%**	**60.7%**	**χ^2=4.654, p=0.031**	65.9 (108)

Bold highlight signifies significance ≤ 0.05

5.4 Discussion

5.4.1 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' backgrounds 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. Over 90% of attendees reported lifetime use of alcohol, cannabis, and tobacco.

Over half of the attendees reported lifetime use of benzodiazepines, while over a quarter of attendees used 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 was 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 (246). 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 (247). The Summary of Product Characteristics (SPC) for Valium states that delusions occur in response to using benzodiazepines predominantly in the elderly and in children (247). Attention-seeking behaviour is often a symptom of borderline personality disorder (248) and histrionic disorder (249), and both of these disorders have been associated with benzodiazepine dependence, possibly because those the two disorders mentioned above are prone to depression and anxiety (250). 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 (16). Specifically for benzodiazepines taken at clinical doses can lead to fatigue, drowsiness, decreased alertness, and depression (247). All of these side effects can lead to 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 (251). There does not appear to be a link between benzodiazepine use and vomiting according to SPCs. There was a weak link in the literature that described benzodiazepines as a potential anti-emetic (252). This suggests that vomiting may be a benzodiazepine withdrawal symptom, and there are cases reports that would support this hypothesis (253), as well as evidence from primate research (254), and reviews (255).

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.

5.4.2 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 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 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.

5.4.3 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 health-care 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 could indicate regular benzodiazepine use. Regular benzodiazepine users often are polysubstance users and raising awareness of polysubstance use amongst this group is important. 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.

6. “You Don’t Feel” – The Experience Of Youth Benzodiazepine Misuse

6.1 Introduction

6.1.1 Background

The most recent worldwide benzodiazepine usage estimate was that approximately 8.4 people per 1000 were consuming benzodiazepines daily in 2009 (256). Within this worldwide context, Europe had the highest level of benzodiazepine consumption for both anxiolytic benzodiazepines and sedative/hypnotic benzodiazepines between 2007 and 2009, according to a report by the International Narcotic Control Board (257). Anxiolytics in Europe were consumed by approximately 42 people per 1000, which contrasts with consumption levels of approximately 25 people per 1000 in the Americas and approximately 5 people per 1000 in Africa.

The increase in benzodiazepine consumption in Europe has been mirrored by an increase in the number of individuals seeking treatment for benzodiazepine misuse. Between 2004 and 2011, there were a 2.5 times increase in the number of users seeking outpatient treatment for benzodiazepine misuse (258). During the same time period, there was an increase in the percentage of cases where benzodiazepines were the primary substance of abuse from 1.8% to 3.0%. This highlights that problem benzodiazepine use has become a greater burden on the addiction services system in Europe. Similarly, Ireland has seen a sharp increase in the number of benzodiazepine users seeking treatment; there was an almost threefold increase in numbers between 2004 and 2010 (103, 259). The percentage of cases where benzodiazepines were the main substance of abuse increased in the same time period from 2.6% to 4.4%. The increase in demand was

largely due to an increase in the number of younger users seeking treatment. The median age of first use (by new users of benzodiazepines) has fallen from 20 years (2003-2008) to 18 years (2005-2010) (103, 235).

This trend of earlier admission for treatment of benzodiazepine misuse corresponded to the trend for increased use by young people. The percentage of 15-16 year-olds in Ireland who had experimented with benzodiazepines without a prescription between 2003 and 2011 increased from 2% to 3% (120, 126). There has been little research into the motivations behind this trend. Three studies in this area are: (a) an American study that looked into alprazolam consumption in 15-18 year-olds who were attending a treatment facility (260), (b) an Irish study that examined substance use in 15-19 year-olds (261), and (c) another Irish study that conducted interviews and focus groups with a wide variety of members of the local community about benzodiazepine use (262). These studies have strengths and weaknesses in relation to this topic. The first study was well conducted and gave a good description of adolescent benzodiazepine use; however it focussed on a single benzodiazepine, alprazolam, and might not fully reflect different experiences of different benzodiazepine types. The second study gives a thick description of substance use, however it did not focus on any individual substance and so it would difficult to determine if particular findings are relevant to benzodiazepines. The third study was extensive; it involved interviews and focus groups with health-care professionals, people who had been prescribed benzodiazepines, polysubstance misusers, and, *"Young people who are likely to include benzodiazepines in their drug repertoire"*

which is of relevance to our study (262). This indicated that the young people interviewed might not have first-hand experience with benzodiazepines. These studies are important as they point to the issues that might affect young people who consume benzodiazepines.

6.1.2 Aims

This study aims to give a thick description (as described by Lincoln and Guba as *"…a sufficient base to permit a person contemplating application in another receiving setting to make the needed comparisons of similarity"* (263) of the experiences of young people who have used benzodiazepines without being prescribed them. This will be done by conducting semi-structured interviews with young people who consumed benzodiazepines as adolescents.

6.2 Method

6.2.1 Approach

The reseacher sought and obtained ethical approval from the Clinical Research Ethics Committee (CREC) of the Cork Teaching Hospitals (Appendix IX). Semi-structured interviews were chosen as the data collection method of choice as it allowed data collection to be focussed on topics surrounding benzodiazepine misuse in young people, whilst allowing freedom to explore new topics that emerged from interviews. The qualitative descriptive approach as described by Sandelowski was used (264, 265). This approach is favoured where prior qualitative research is scarce and

established theories are absent, as *"there is no pre-selection of variables to study, no manipulation of variables, and no a priori commitment to any one theoretical view of the target phenomenon"* (264). This allowed the results of this study to be determined entirely by the data. Quality assurance was achieved by following the recommendations of authors in this subject area (266, 267). These authors recommend that credibility and dependability can be maintained at a high quality by having a clear audit trail, where a record is kept of decisions made at every stage of the research process. The authors of this study wanted to maintain the highest standard of reporting, so the reseacher wrote the report as suggested by the Consolidated Criteria for Reporting Qualitative Studies (COREQ) guidelines (268). The guidelines were compiled from 22 existing checklists for qualitative reporting.

6.2.2 Sampling

A purposive sampling strategy was chosen as it allowed us to focus on obtaining data from data-rich sources. The reseacher asked substance misuse treatment centre and community drugs workers in Cork city, Ireland, to act as gatekeepers for the recruitment of young people. The inclusion criteria used in the selection of participants was that the interviewees used benzodiazepines when they were younger than 21 years of age. Candidates were excluded if they were vulnerable subjects or had an intellectually disability, as assessed by their gatekeeper. Participants were told by their counsellor/drugs worker that a pharmacy PhD student (the primary researcher and interviewer, the researcher) from the local university was interested in knowing more about their benzodiazepine use and were invited

to participate in the study. If the participant agreed to be interviewed, then they met with the interviewer who explained the purpose of the study and to establish rapport with the interviewee; the interviewer told of his personal motivation for studying this topic, which was the researcher's regular contact with benzodiazepine-dependent patients in community pharmacy. The reseacher then gave the participant an information sheet with frequently asked questions about the interview process and contact details in the event that the participant wished to contact the researcher afterwards. Participants were asked to sign a consent form if they agreed to do an interview, and were asked to tick a box if they allowed quotes from the interview to be used in an anonymous manner in the study's report (Appendix X). Of the 14 people who were asked, 13 people agreed to participate and one person declined to be interviewed because they did not wish to talk about their benzodiazepine use.

6.2.3 Interview

In line with COREQ guidelines, for the purposes of reflexivity a description of the interviewer is provided. The reseacher was the interviewer, and is a male qualified pharmacist who is in the 3rd year of his Doctoral studies. The interviewer had no formal qualitative interviewing experience, but had received training in interview techniques and in qualitative research methods. Single semi-structured interviews were conducted in the treatment centre/community centre that the interviewees were attending, as this would be a safe, familiar environment that would encourage free speech. Interviewees had the option of conducting the interviews in the presence of

their counsellor/drugs worker. This option was chosen by three of the interviewees. The interviewees composed of a mix of men and women, over the age of 18 years from Cork city in Ireland. The reseacher asked interviewees questions from a topic guide that was produced from the topic guide of previous research into recreational benzodiazepine use (260). Additional topics, such as family history of benzodiazepine use and benzodiazepine in their social environment were included to get a more comprehensive view of benzodiazepine use. The reseacher and PhD supervisors reviewed the topics and changes were made based on their comments. The topic guide was then shown to an attendee of the treatment centre and changes were made to ensure that the language used in the interview was suitable and could be understood easily. All interviews were recorded by a dictaphone (Sony ICD-P620), and interviews lasted between 6 minutes and 41 minutes (median = 16 minutes). Notes were written as appropriate after the interviews had concluded.

6.2.4 Analysis

The researcher decided to use the method suggested by Francis *et al*. to determine when informational redundancy had been reached (269). The authors suggest that a minimum of 10 interviews be conducted and that the stopping criterion for interviews is when there are three consecutive interviews without any new themes. Another study suggests that the vast majority of themes emerge from the first 12 interviews (270). Sandelowski states that informational redundancy is attained when a researcher has *"seen and heard the same thing over and over again"* (271). The reseacher

transcribed the recordings and after transcription was completed, the transcript was checked against the original recording to ensure fidelity and also to familiarise the researcher with the sense of the interview. NVivo® software was used in the coding phase of analysis.

Inductive content analysis was chosen as the method of analysis because it allows the data to guide the results and is more appropriate in situations where previous studies in the area are lacking (272). Content analysis was performed as suggested by Berg (273). The basic unit of analysis used in coding the data was themes. These first level codes were then organised into higher level categories, and the categories were then organised into themes, which were more abstract. In this process, codes were constantly re-examined to ensure their appropriateness to the higher level categories and themes. If a code was not appropriate, then it was reassigned to a more appropriate category/theme or if there were none appropriate, then the code was given a separate category/theme. To ensure the high credibility of the research, peer-debriefing was performed. The reseacher performed the initial coding and one fo the PhD supervisors independently coded four randomly selected transcripts. Both researchers met and minor discrepancies were discussed to reach consensus. Additionally, negative case analysis was incorporated into the reporting of the study as suggested by Creswell as *"real life is composed of different perspectives that do not always coalesce, discussing contrary information adds to the credibility of the account"* (274).

6.3 Results

6.3.1 Benzodiazepine terminology

Table 6.1 is a description of the commonly used street names for benzodiazepines mentioned in the interviews. It shows the wide variety of benzodiazepines that were used by the interviewees. They are presented here to aid comprehension of quotes used in the findings.

Table 6.1. Street names for benzodiazepines

Street name	Brand Name	Strength	Generic Name	Clinical Indication
D10's	Anxicalm	10mg	Diazepam	Anxiolytic
D5's	Anxicalm	5mg	Diazepam	Anxiolytic
D2's	Anxicalm	2mg	Diazepam	Anxiolytic
Duck eggs	Tenox	10mg/20mg	Temazepam	Hypnotic
Purple hearts	Rohypnol	1mg	Flunitrazepam	Hypnotic
Roche 1.5's	Lexotan	1.5mg	Bromazepam	Anxiolytic
Roche 10's	Valium	10mg	Diazepam	Anxiolytic
Roche 2's	Rivotril	2mg	Clonazepam	Anxiolytic
Roche 5's	Valium	5mg	Diazepam	Anxiolytic
Sleepers	*General name for hypnotics*			Hypnotic
Smarties	*General name for benzodiazepines*			Anxiolytic/Hypnotic
Sweets	*General name for benzodiazepines*			Anxiolytic/Hypnotic
Upjohn 10's	Halcion	0.125mg	Triazolam	Hypnotic
Upjohn 17's	Halcion	0.25mg	Triazolam	Hypnotic
Upjohn 29's	Xanax	0.25mg	Alprazolam	Anxiolytic
Upjohn 55's	Xanax	0.5mg	Alprazolam	Anxiolytic
Upjohn 90's	Xanax	1mg	Alprazolam	Anxiolytic
Zimo’s	Zimovane	7.5mg	Zopiclone	Hypnotic
Zok's	Zopitan	7.5mg	Zopiclone	Hypnotic

6.3.2 Coding Tree

The coding tree of themes developed from the interviews can be seen in Table 6.2. There were six main themes uncovered from the interviews, with a total of 14 categories within the themes. The themes are presented in chronological order as the interviewee would experience them, to aid reader comprehension.

Table 6.2. Themes and categories discussed in interviews

Themes	Categories
1. 1st benzodiazepine misuse	a) Prior knowledge of benzodiazepines
	b) Circumstances of first misuse
2. Motivation to take benzodiazepines	a) Barrier against the world
	b) Social group using them
3. Taking benzodiazepines	a) Benzodiazepine sources
	b) Positives of benzodiazepine misuse
	c) Negatives of benzodiazepine misuse
	d) Compulsive nature of benzodiazepines
4. Consequences of benzodiazepine misuse	a) Effects on personal life
	b) Effects on family life
5. Associated substance use	a) Alcohol and benzodiazepines
	b) Cannabis and benzodiazepines
	c) Associated substance misuse
6. Withdrawal effects	a) Short-term withdrawal effects
	b) Long-term withdrawal effects

6.3.3 1st benzodiazepine misuse.

6.3.3.1 Prior knowledge of benzodiazepines

The young people interviewed had mixed knowledge of benzodiazepines prior to taking them for the first time. There were three interviewees who had indicated that they had knowledge of benzodiazepines and six that said that they had no knowledge. Knowledge of benzodiazepines mostly came from seeing others in their peer group taking them. The interviewees learned about the acute effects of benzodiazepines from seeing the behaviour of their friends, *"I knew what to expect cos I've seen people out of their heads, I've been in company of people out of their heads, and I didn't take them."* (YP10)

Some of those who did not indicate any knowledge of benzodiazepines said that they had expectations based on hearsay or friends' descriptions. These expectations were often false,

> *"It was when I started taking yokes around the same time, you know, and I saw them, I saw them as any kind of drug, you know, and I was like I'll take them, might as well, you know."* (YP8),

> *"And I'd never actually heard of them, never heard of them before and it was just like, the first was actually a friend of mine brought them up and goes, these are like a party drug, everybody takes them."* (YP12)

As can be seen above, each of the interviewees knew, or thought they knew, what to expect when they took benzodiazepines. A negative case for this category was from Interviewee 11, who took a benzodiazepine tablet that they had found on the street, without any expectation of what its effects would be,

> *"You'd rarely see tablets on the ground like, and I just said, what are these. I just said, I don't know like. It was kind of stupid too, I was 13 years old ... It could've been anything to me. I just went away and took it like, just being stupid. And then my brother told me what it was after kicking in like."* (YP11).

6.3.3.2 Circumstances of first misuse

The majority of young people interviewed described that their first experience of benzodiazepines was as part of a group. These young people said that they were curious about their effects or that they took them because they were available. The availability of benzodiazepines as a reason for taking them seemed to be linked to a culture of trying substances in the young person's peer group. Taking other substances in the past appears to have lowered their internal resistance to taking benzodiazepines. They perceived it as being one more substance to try. Some of the interviewees also mentioned that they were intoxicated at the time of their first benzodiazepine use, *"just to see what it was like ..."* (YP1),

> *"I was already after taking other different drugs right, so I was after stepping into that kind, that kind of network or whatever, so then*

someone pulled out these, these smarties, and I just took them for the sake of ... " (YP3)

"... one of my buddies robbed them off his, his Mam or Dad or something, do you know. I was after drinking a naggin and 4 cans, I swallowed 10 of them, and just couldn't remember the night". (YP13)*

*Naggin = 200ml measurement of spirits commonly sold in Ireland

There were two interviewees who defied this pattern, and the quote from interviewee 11 in the section above applies to this section also,

"I found a stash of them in my Mum's room of them and it said Upjohn on them, you know, on the pouch for them anyway, so I took a rake of them anyway." (YP8).

6.3.4 Motivation to take benzodiazepines

6.3.4.1 Barrier against the world

A common description of their reason for taking benzodiazepines involves two words, feeling and caring. The interviewees wished to avoid these two emotions, *"You don't feel, it's the best way to describe it. You don't feel anything at all…"* (YP2),

"... they give you, do you know they make you really stoned, when you first start out on them, you're stoned, and when you're stoned, you just don't really care what goes on around you, do you know?" (YP3)

Conflict in the young person's personal life was noted as a common reason for taking benzodiazepines. It helped the young person to cope with the negative emotions, *"I think that's one of the reasons as well why I take them, cos they get rid of every single problem you have."* (YP10), *"I started taking them when my Mam and Dad broke up. I started taking them and I was taking them f**king everyday"* (YP13).

6.3.4.2 Social group using them

The majority of young people interviewed have a peer group that was supportive of benzodiazepine misuse and of substance misuse in general. The young people acknowledged that substance taking was expected in group settings, *"... then I started hanging around with this other fella, this other friend of mine, and I started to take them ferocious amounts of them."* (YP3), *"We did them together. We all did it together."* (YP8), *"... the whole lot of us did, it was about, it was, would've been between 10 and 15 of us I'd say like. It would've been a big gang ..."* (YP9). A small number of young people indicated that their friends were not taking benzodiazepines or were actively trying to dissuade them from taking benzodiazepines. Their friends' attempts at dissuasion did not succeed, *"... before when I used take them now, none of my friends were taking benzos ..."* (YP1),

> *"... my proper friends would have said it to me like. Friends I grew up my whole life with were saying like what the f**k you doing, that's not you at all like do you know. You're just being stupid like." (YP13)*

6.3.5 Taking benzodiazepines

6.3.5.1 Benzodiazepine sources

Multiple sources were mentioned for obtaining benzodiazepines, and the most common ones were general practitioners (GPs), dealers, friends, and family. GPs were mentioned as a source by ten interviewees. They spoke about attempting to get them directly from the GP and others acknowledged that it can be indirectly obtained *"off people that get prescriptions of it that would be selling it." (YP5)*. For some, getting benzodiazepines from a doctor would not be sufficient for their consumption, and they would need to be *"hitting three or four doctors in a week" (YP6)*. Most of the interviewees described methods they had used, or methods they had heard others use. One interviewee declined to discuss the subject. The usual methods involved feigning an illness to elicit sympathy from the GP and get a prescription,

> *"Most people would say they're after coming out of prison and they were taking heroin in prison. And that they're f**ked now. They're paranoid, owe a load of money, and they just used get it like." (YP9)*

> *"To be honest like they'd go in, and be faking crying and s**t like that, telling haven't been sleeping in weeks and s**t like that, and can't relax and stuff, you know. And even at that like, the doctor could still say no like." (YP7)*

> *"Back pain, that was the big one. Back pain. They knew full well you can't, like prove proper back pain like. They can test for whether it's*

muscles or spine. But they can't really prove there's something wrong with your back like." (YP12)

A variation of the feigning illness strategy was to initially reject treatment with benzodiazepines to allay any suspicions of misuse that the doctor might have,

"For months he'd say he couldn't sleep anyway and getting headaches and all that kind of craic. The doctor was offering him this and that but he kept refusing it, refusing it and then eventually by the end of it he said it was getting too much and he started taking it. So by the end of it, the doctor was giving him a large amount of them like."* (YP6)

**and all that kind of craic = and other similar symptoms*

The reactions of the GPs to these attempts varied. The young people interviewed were able to get benzodiazepine prescriptions themselves or knew of people who were able to get prescriptions. Some refused to supply a prescription for benzodiazepines because of knowledge of past use or suspicions of misuse, *"I tried going to the doctors but they said no because of my history of substance abuse, you know."* (YP8),

"Now my doctor is, he's kind of younger and he kind of got it, here's some paracetamol like and out the door… He was no fool like, I tried it once or twice to go in and try them off him." (YP12)

One interviewee noted that there was a doctor that knowingly prescribed benzodiazepines for non-medical purposes for personal reward,

> "*I've often heard of a doctor now boy that you give him a bottle of whiskey and he'll prescribe you anything, €50 now and he'll prescribe you what you want ...*" (YP9)

It was perceived that after getting the initial prescription, *"they hand them out to you like the new time" (YP7)*, and being stopped was unlikely.

Dealers were another source of benzodiazepines. The interviewees thought that dealers get access to benzodiazepines because they *"go to the chemist and don't take them" (YP4) or "they get prescribed them" (YP11)*. One interviewee thought that dealers were responsible for most of the supply of benzodiazepines to users.

> *"... if it was a normal fella, then it would say from dealers, but the fellas who seem to be copping on are going, they're hitting three or four doctors in a week, getting them off like their parents, finding them round the place."* (YP6)

The description provided by interviewees about the availability of benzodiazepines was mixed. Some spoke of how easy it was to get benzodiazepines, whereas some spoke about how demand for them was never satisfied,

“Like just 1 year that it was everywhere. And you could get them every street corner, every time you turned the corner you'd see someone who had them.” (YP12)

“... people are putting up the price because they can do it. They can sell them for this price. That’s exactly why, they’re so addictive as well that people put up the price and you are going to buy them. Because then you’re addicted to them, when you’re told there’s sweets there, they’re gone out the door. No matter who sends them, no matter, no matter what, if there’s sweets there, you will always have a buyer.” (YP10)

*“... they'd be coming in hundreds and thousands as well, they wouldn't come in no packaging now or nothing. They'd just be f**king there in a bag or something like but, you can get them f**king piss easy like.”* (YP13)

There appeared to be discrepancies between the cost of benzodiazepines in different areas and for different benzodiazepines. Consequentially there are differing opinions about benzodiazepine prices, *“Sometimes I find I’ve been able to get them for 50c a tablet. That’s brilliant like.”* (YP6),

*“They’re expensive to buy on the street, if, like that’s one of them. Do you know, you could pay top price there now for f**king, you’d pay €1.50 for a D10, you’d pay €3 for a Purple Heart, maybe €3.50.“* (YP10)

There seems to be consensus that although the price might vary, it is cheaper than cannabis, which has similar effects,

> "*... the fellas we hang around with, they were mad on the grass like. They liked it like but it was always the grass like. They only went with them because they were cheaper.*" (YP6)

> *"You go away and spend €50 on a 50-bag, a 50-bag could be gone in 2 hours, and do you know, the stone is gone after 4 or 5 hours like, do you know what I mean. But it's like paying a tenner or €15 you're stoned for the rest of the day like. So that's why people'd be taking them I'd say like."* (YP13)

A strategy that one of the interviewees used to reduce the price further was to buy benzodiazepines in bulk, which allowed them to get a discount off the price per tablet,

> *Yeah, they were dear enough like, but like I would have been buying them in bulk like, you know, that kind of way. And like f**king, see f**king, you'd end up ordering a load because you end up taking the bulk of them, like. It'd be about €1.20 like, and that's what you'd be paying if you're buying, you know, if you're buying 5 of them or something like.* (YP7)

Friends were another source of benzodiazepines. The difference between friends and dealers was that they were a member of the interviewee's peer

group and so would usually be present when they were consumed. This resulted in one of the friends acquiring benzodiazepines and that person would *“end up sharing stuff with everyone” (YP2).* For some of these interviewees, their friends would have obtained the benzodiazepines by stealing them from their parents, *“And my friend eh…one of his parents was, eh, on lots of Xanax but she never used to take them because she didn’t like to take medication.”* (YP8), *“... one of my buddies robbed them off his, his Mam or Dad or something, do you know. He got a box of 30 ...“* (YP13). Friends who had access to larger quantities of benzodiazepines usually obtained them from other sources, *“And then as I said there was places being robbed, there was literally about, I remember there was like 20,000 Upjohn 17’s like, between all of us like ...”* (YP9).

There was an impression amongst the interviewees that taking benzodiazepines from family members occurred, *“Em, they get like Xanax and stuff off their families. They wouldn’t really like get D10s and stuff off them. That’s what I think anyway.”* (YP5),

> *“There's old people there that have months and months scripts packed in a f**king Dunnes* bag, thousands of sweets like…Just go around and take f**king 500 of them. Sure Nan's not going to notice that like. She'd have a bin bag full of them like.”* (YP7)
>
> *Dunnes = Supermarket chain in Ireland

Generally, the benzodiazepines would be taken without the parents' knowledge. There was an exception; a single interviewee said that some parents give benzodiazepines to help their child's sleep, *"A lot of people like, their parents give them sleeping tablets and stuff ..."* (YP5). Other sources mentioned were the internet and stealing. The impression is that benzodiazepines from the internet were not genuine benzodiazepines, *"I tried the internet but I said that that's probably risky like, the Xanax might be just some kind of dope junk ripoff ..."* (YP8), *"They're fake, there's no, they buy them for nothing on the internet. F**King €1.50 a pop and they're fake sweets."* (YP10).

There was one reference to theft of large quantities of benzodiazepines from a place *"that makes the tablets" (YP9)*.The interviewee did not know anything about how or where this was being done, but there was *"about 20,000" (YP9)* tablets stolen from there.

6.3.5.2 Positives of benzodiazepine misuse

A common description of the effects of benzodiazepines is that it makes them stoned. Some use different words to describe the same effect: buzz, bang or chilled. There was usually no further description of being stoned, except that it involved a sense of intense relaxation, *"It was a good buzz like."* (YP1), *"If I wasn't smoking or drinking, just take sweets to get a bang off it."* (YP4), *"It kind of like being stoned really. Really relaxed, really calm."* (YP8),

"I used to take them, handfuls of them and I'd get whatever kind of buzz I'd get off them. Different kind of buzz I used to get years ago. A handful I used to get stoned out of my head, but as time went on, handfuls of them wasn't doing much." (YP3)

Another commonly described positive effect of benzodiazepines is the increase in self-confidence it gives the users,

"I don't know, it's hard to explain like, but you feel very good on them when you're taking them, do you know, you feel very good about yourself, and you feel like you could talk to anyone." (YP13)

In some cases, the increase in confidence can lead to excessive levels of confidence. It can lead to a sense of separateness from things around them. This separateness could be emotional, where the user does not feel a connection to any other person, or it can be physical where a user is immune to physical pain, *"... you don't really feel on them. Like I've punched walls, I've punched in windows and not felt it."* (YP2), *"You think you're invincible, you don't care about anyone or anything."* (YP3), *"You're untouchable, you can do what you want when you want."* (YP9), *"It's just like, I was the king of the world like, I was made of steel."* (YP12).

6.3.5.3 Negatives of benzodiazepine misuse

There were numerous negative effects that the users associated with benzodiazepine. The most prominently discussed negative effect was

blacking out/memory loss because of benzodiazepine use, *"I've woke up on days, em, I've had people call me going just, yeah did you realise you were doing this last night, and I'm like going em what day's today."* (YP2*), "... you could stab a fella and you don't know it the next day. You could wake and as I said your head is clear, you don't know what you're after doing."* (YP10),

> *"... everyone would be passing out at random times. Just no sleeping pattern whatsoever. And people passing out for like 14 hours straight, and not waking up at all and stuff."* (YP5)

> *"They were just telling me the next day what was going on, but I can't even remember. I don't know, I can remember falling into a bonfire, you know what I mean <laughing>."* (YP13)

Even though memory loss was acknowledged as a negative effect, more than one young person claimed to enjoy this negative aspect, *"... I think I like that side though, the whole messy side to it, you know."* (YP8),

> *"I just thought it was funny really I couldn't remember or nothing, just the way I was walking around doing s**t all day like and I couldn't remember a thing. I just thought it was funny like."* (YP9)

The second most commonly talked about negative effect was lack of motor co-ordination. This came in two general forms. These forms were physical co-ordination and speech difficulties. The interviewees described their inability to keep upright after taking benzodiazepines, even in circumstances

that involved significant risk to themselves, *"You're sloppy and you're stumbling."* (YP3), *"... nearly every time they took it their legs feel like jelly that they'd get fierce dizzy afterwards and stuff."* (YP6), *"Apparently I was roll, I fell down the stairs when I was trying to leave the house and I was getting sick everywhere, so he kicked me out of the house."* (YP8), *"... I couldn't stand, I fell, I was falling, I fell into the bonfire 2 or 3 times ..."* (YP13). Slurred speech was seen as a signature of benzodiazepine use. It can be described as rambling or incoherent, and slow and slurred, *"I live across the road from a fella and he's chronically on them like, and he'd come out like, his speech would be always slow."* (YP7), *"You're, you're slurring words, whereas when you're drunk, you, can get them out, when you're stoned, <imitation of slurring of speech>, do you know."* (YP10),

> *"... if I take a few of them I just get, I just be walking around the place, I could talk different. I'd be like <imitation of slurred speech>, and then my face looks different ..."* (YP11)

Some interviewees spoke about how benzodiazepines would have the opposite effect to what has been described previously. The benzodiazepines can make a person more agitated, and prone to reacting in a more extreme manner. The young people associated this behaviour with the mix of alcohol and benzodiazepines, *"There's, there's a lot of bad things about smarties. You know, they could, you could go in home and start breaking up your house."* (YP10),

*"If he was drinking, he would have whacked around the gaff with a golf club, or something, might have whacked him around the gaff with his fists. He'd only give him a beating like. But a big f**king kitchen blade like, the kitchen blade was bigger than a bottle of coke like. It was the drug, the sweets you know, f**king, you know."* (YP7)

Other less frequently commented on negatives associated with benzodiazepines were weight loss, takes away motivation, clouded-thinking and being indoors for long periods of time.

6.3.5.4 Compulsive nature of use

Nearly every person interviewed spoke about the compulsion to take more benzodiazepines. Benzodiazepine consumption would begin with small quantities and would build up to larger quantities,

"Em, when I first started taking them, then I'd only take a few of them, like but, they got very addictive, you know. And I ended then taking kind of 30 or 40 a day like you know." (YP7).

In many cases, the limit on benzodiazepine use was imposed on the user because of their inability to purchase more or the scarcity of supply in the area, *"They'd be kind of, they'd want them every day, they mightn't get them every day, but they'd want them, they would never refuse them."* (YP3),

*“But like, due to his past like, if they give him a month's script [prescription] like, month'd be f**king gone in one-go like. And they come back in thinking it's next month, the next day.”* (YP7)

The compulsion to take benzodiazepines would overpower the interviewees’ self-control, leading one interviewee to take medication, *“... don’t even know if there was a stone off them, you just take them in desperation I swear.“* (YP9),

> *“And like you try, you'd say you going to buy 100, you say, I'll keep these 50 for myself and I'll give these 50 to sell, at double the price. That is not going to happen like. As soon as you take one, then another one, then another one, another one, they're very addictive like.” (YP12)*

In other cases the emotional drive to take them appeared to be absent, and interviewees described taking them as a habit, *“It was more habit than anything else when I was taking them, because I was so used taking them. I was taking them every day ...”* (YP13).

6.3.6 Consequences of benzodiazepine misuse

6.3.6.1 Effects on personal life

Benzodiazepines had effects on interviewees’ education and hobbies. The motivation to learn disappeared and the amnesiac effect caused

interviewees to forget lessons, *"I gave up completely, I prefer to stay at home now and get stoned."* (YP9), *"Like when I was in school, I can't even kind of remember it. But in work, yeah with machines and all that definitely. You're just not, everything is pure slow."* (YP11), *"I'd just, I didn't know what was on the board like. I was after doing it yesterday but I still don't remember what was on the board ..."* (YP12),

> *"I went to school, I just, depended on smoking joints at lunch, and looking at books was never on, never the case where, I'm looking at the book and I'm saying, I don't give a f**k about this, I just want to, I just want to smoke my joint and I want to take my sweets."* (YP10)

Benzodiazepines also affected the ability of interviewees to concentrate while in school or at work, which led to accidents or near-misses,

> *"... I was doing an apprenticeship in a mechanics, and I remember I went up, I fell into the engine of a car that was running, the timing belt was flying and all the cam belts were flying. My boss caught me and just pulled me up ..."* (YP7)

> *"You're just not even thinking like properly like. I often nearly took off my finger there, and there's people in my class who took out eyes, with chisels getting stabbed in the eye. Another fella nearly took off his finger there over them."* (YP11)

Benzodiazepines had an effect on interviewees' after-school hobbies. Students who played sports spent less time playing sports,

> *"Played every match, Friday, Saturday, and Sunday. Training twice a day like, the weed kind of took the drive and the sweets just f**king blew it out of the park. Just dropped it into touch, I couldn't run as far as the bus stop now these days, or put a squad car behind me anyway and I might."* (YP7)

A negative case for this came from an interviewee who said that benzodiazepine use had not affected their personal life, but this interviewee used benzodiazepines *"once or twice a month." (YP8),*

> *"It didn't have much because I only used them at the weekend, I really didn't use them during the week. But impact during school, nothing really. I wasn't really addicted properly to them, I wasn't taking them as often as I could. I just enjoy taking them every once in a while. I'd take a lot when I took them."* (YP8)

6.3.6.2 Effects on family life

The interviewees tried to hide their benzodiazepine use from their parents. Alcohol would often be a cover for their use, *"... I might drink when I'm taking them which is even worse again. That would be my excuse, that would be my way for my Dad not to catch me."* (YP10), *"They had a hint like but I never got caught, never got caught like. When I got caught, they thought I was drinking."* (YP11). For one interviewee, hiding their benzodiazepines

around the house did not work out as intended as after taking some, they forgot that they were trying to hide their use.

> *"Oh yeah, 100% trying to hide it from my family yeah. Now and again it would come to the, like after that month when I started doing like hiding in the kitchen, sure after I took the 1st four or five of them hiding, I was too, in a way, spaced out and I didn't even realise, I was like going into the front room and doing this and drinking and they were like saying it to me the next morning, you were doing stuff right in front of us."* (YP12)

Benzodiazepine-taking often created conflict in the family. This could be as a result of the effects of the benzodiazepines themselves or from the parents' attempts to reduce their children's use,

> *"My Mum was really mad. My parents are split up so my Dad doesn't really know too much like, but my Mum was really upset because she couldn't get any more of them for a month. She was pretty upset with that. And she was saying it was a bit stupid to be taking them for no reason like."* (YP8)

> *"Just being kicked out of home. Just getting arrested out of my house all the time. My Mam would ring the Guards on me and s**t like that. Stupid things now boy, I suppose it wasn't stupid, but on my part it was stupid, and I didn't want to do them."* (YP9)

"I was telling people made me cups of tea, and then when they made me a cup of tea, I didn't want it, and why did you make me a cup of tea. I can do it myself. I was just creating war for myself like." (YP12)

6.3.7 Associated substance misuse

6.3.7.1 Alcohol and benzodiazepines

Alcohol and benzodiazepines were commonly taken together by interviewees. Some of the interviewees called the combination a *"charge sheet" (YP11)* because mixing the two substances led to aggression. They thought that benzodiazepines would not cause such behaviour by itself, *"... when you drink with them, it's different, you go mad. They're dangerous."* (YP4),

"... once you mix sweets with drink as well like, it just goes, you might as well just walk into the Bridewell like and just tell them to put you in a cell like." (YP7)*

**Bridewell = Garda station in Cork*

*"Like I've yet to come across someone anyway who can f**king drink and take, take a load of sweets and go drinking. Because it's just a recipe for disaster like."* (YP13)

The main effect associated with combining the two substances was memory loss. This deterred many from taking both substances together, or the young people to take lower doses of the substances, *"I wouldn't go drinking when I*

was taking them because that's just, a bad combination because you're going to black out like." (YP13),

> *"Ah yeah, charge sheets boy, that's all they are. You'd have one the length of your f**king arm boy in a week and you won't f**king know what you're after doing."* (YP7)

6.3.7.2 Cannabis and benzodiazepines

Many interviewees compared cannabis and benzodiazepines. They had some similarities but they also had differences. Both substances gave the user a stoned feeling, but benzodiazepines gave the interviewees a *"bigger, better stone" (YP10)*, *"It kind of like being stoned really. Really relaxed, really calm. You could punch yourself in the arm and you wouldn't feel it, you know."* (YP8), *"... it's probably just like smoking weed, they are really."* (YP11),

> *"It's, it's a bit like weed, you're chilled out, you're a bit tuned out. But it's like a lot stronger version of that like, what you'd smoke a gram of weed for, you get in 1 tablet."* (YP12)

Even though benzodiazepines had a greater effect, some of the interviewees preferred cannabis, whereas others preferred to take them together. The interviewees did not explain their preferences,

> *"... with the fellas we hang around with, they were mad on the grass like. They liked it like but it was always the grass like. They only went with them because they were cheaper."* (YP6)

"... if you're smoking weed like, you'd always want be craving the tablets for that extra stone." (YP9), *"If I can't get smarties then I'm getting f**king weed."* (YP10), *"They go hand-in-hand like do you know. If you're chilling out having a few sweets, you may as well have a few smokes like."* (YP13)

Even though the interviewees said both made them stoned, there appeared to be other differences between them. Benzodiazepine had additional physical and psychological effects compared with cannabis, *"It's similar like to grass or hash, but a lot of my friends say that their legs feel like jelly and all that kind of craic."* (YP6),

> *"... you could go away and smoke f**king 20 joints a week and you'd still have, mentally, or whatever, you'd still have the, what way of saying it, the, still have the head about you to not do something like you know, whereas if you took f**king 20 sweets like, you walk out there and like f**king do anything, you won't know what you're doing… "(YP7)*

6.3.7.3 Associated substance misuse

Three of the interviewees talked about using benzodiazepines to minimise the effects of withdrawal symptoms of other substances. The substance most commonly mentioned in this regard was cocaine, *"... I take it to come down off like, uppers to bring me down easy. I'm relaxed so I won't have a comedown really as such."* (YP5),

*"... when we were coming down off something, do you know, you're in pain and your stomach's in s**t you know and you want to take something to get away."* (YP8)

Some of the interviewees also took unknown substances in the hope of obtaining benzodiazepine-like effects,

"I took tablets that I knew I shouldn't have been taking. Weird things. Aww god, don't even know if there was a stone off them, you just take them in desperation I swear." (YP9)

"So I started liking them and started taking them. Found the rest of her medication. I found Lexapros, you know, the antidepressants, I was taking them but jeez, they had no real effect. They made me feel like crap really, you know." (YP8)

6.3.8 Withdrawal effects

6.3.8.1 Short-term withdrawal effects

Short-term withdrawal effects were those that happened within the first few days of not using benzodiazepines. It was acknowledged as being *"rotten" (YP3)*. Specific symptoms experienced by interviewees while dealing with withdrawal were irritability, sweating, sleep disturbances, perceptual changes, and craving, *"you'd be just craving them and craving them at the start."* (YP1), *"The sleeping patterns, coming off them, you've some weird dreams. Very weird dreams. Disturbing dreams, disturbing like. You wouldn't wish on your worst enemy."* (YP2), *"If I was coming down then I'd be very f**king like agitated, just be snapping at my Mam and fighting ..."* (YP9),

*“Ah f**k it, you’re a wreck, because anytime I come off them it feels like…do you know that little tap <taps chair to imitate sound>, everything’s a lot louder, in your face.”* (YP2)

“I'd wake up and I would be in absolutely pools of sweat. And this is soaking the blankets, as if someone wet the bed, but it's sweat, and it's all over you and you really need to get into the shower.” (YP12)

6.3.8.2 Long-term withdrawal effects

Long-term effects were those that interviewees experienced after the acute withdrawal symptoms had dissipated. There were three interviewees who described their experiences of chronic withdrawal symptoms. Cognitive impairment was the main effect described in the interviews, *“You know it takes you a while to pick back up after taking a load of them. You’d be a bit slow for weeks as well.”* (YP5),

“I dropped the remote, and I picked up the remote. And the batteries were in my hands. And I was sitting there with the batteries in one hand and the remote in the other hand. And I completely could not figure out, I was looking at the plus and the minus, and the plus and the minus on the remote and I couldn't completely figure out why, how did they come out. And there was people, my Mam was actually sitting there talking to me, going <interviewee's name repeated three times>, and it was like, I was tuned out. I just, and I, she said when my Mam told me about this, I sat there for like 20 minutes. Just sitting there

going <silence>, completely scared, that how, this should not happen." (YP12)

Craving never disappeared completely in the abstinence period after withdrawal, *"You still get cravings now but I know now that even if I took them now, in a minute I'd be looking for more and tomorrow it's more and more."* (YP9).

6.4 Discussion

This study investigated the experiences of young benzodiazepine users in a treatment centre in the south of Ireland. Interviewees talked about a wide variety of experiences concerning benzodiazepine use. In general it can be seen there were push and pull factors that encouraged benzodiazepine use by the interviewees. These have been described as factors in other studies (260, 262). The push factor involved the stress of daily life. The interviewees turned to benzodiazepines as a means of escape from these pressures. The main pull factor that interviewees experienced was peer influence. Peer influence was also mentioned in one of the above studies (260), and in other studies (261, 275, 276). Interviewees described how everyone in the group took them, and that benzodiazepines were taken in a group setting. Not taking benzodiazepines in a situation like this could lead to being different from the rest of the group. This might cause stress to the young person and as shown above, the interviewees want to avoid stresses in their lives. This suggests that the provision of alternative means of stress-reduction or the

improvement of coping skills could be helpful to benzodiazepine users. There is some support for this approach in the literature (277, 278).

Another possible means of reducing or preventing the use of benzodiazepines by an adolescent, based on the findings of this study, would be to encourage and facilitate new friendships with non-users. For the majority of interviewees, the description of the benzodiazepine use appears to be in accordance with social cognitive theory as outlined by Bandura (279, 280). Social cognitive theory as it applies to adolescent substance use posits that the decision to experiment with a substance is influenced by several factors. The main factors are the imitation of substance use behaviour by role models/peers, positive reinforcement by role models/peers, positive expectation of social and physical consequences of the substance use, and use self-efficacy. The first two of these factors was highlighted in the interviews when the first exposure to benzodiazepines was described at peer gatherings. This follows another study in Ireland which reported that *"first drug experiences took place in the company of friends and were rarely, if ever, embarked upon alone"* (261).

The positive reinforcement was offered when the interviewees were offered and recommended benzodiazepines. Use by peers in group settings built up positive expectations. The interviewees were told of the positive effects by the friends, that they were a *"party drug"*. This expectation was further enhanced by the fact that taking this substance allowed the interviewee to be

part of the social group, and diminishing the potential for social exclusion. The final main factor, use self-efficacy, is the *"ability to successfully obtain and use substances"* (279). Use self-efficacy is can be high for benzodiazepines because they are readily available and are in tablet form, which means that they do not need to be mixed or prepared to be consumed as heroin and cannabis commonly must be.

The interviews suggested that levels of benzodiazepine use can vary with the levels of benzodiazepine supply in their area. This suggestion is reinforced by two studies that reported that the interviewees thought that to discontinue benzodiazepines, a person would have to leave the area (262), whereas another study reported that environmental accessibility was quoted as a barrier to abstaining from benzodiazepines (260). From this suggestion, the harm to users could be reduced if their ability to procure benzodiazepines was reduced. One of the main sources of benzodiazepine prescriptions appears to be GPs. Although they might not usually supply the user, the proximal sources appear to obtain their benzodiazepines from GPs. The main proximal sources documented in this study were dealers, friends, and family members.

Dealers and friends of users targeted GPs by feigning illness to procure benzodiazepines. Various methods of deceiving GPs are described in the results section. There were a variety of situations described and it would be difficult for GPs to discern between genuine and feigned cases. Methods of

procuring benzodiazepines such as these are described in the literature, such as feigning back pain (281), being unable to sleep (262), requiring symptom control for opiate dependence (282), and *"gaining sympathy"* from GPs (282). These strategies could be used on individual GPs, but they can also be used on multiple GPs in an area. This is often known as *"doctor-shopping"* and appears to be a common strategy (262, 281, 282). Another issue that was mentioned in relation to GPs was the ease with which repeat prescriptions were written. There was the impression that the initial prescription was the main hurdle and that once the first prescription was written, then they *"hand out"* repeat prescriptions. This perception of the ease of getting repeat prescriptions mirrored the view in another study conducted in Ireland (262).

This prescribing behaviour contravenes guidelines published in 2002 by the Department of Health and Children (157). The report states that *"benzodiazepines should be prescribed only for as long as necessary, aiming for the shortest possible time but no longer than 4 weeks."* The report also recommended that for patients receiving long-term prescriptions, they should *"issue small quantities at a time (usually not more than one week)"*, and that prescribers should *"review regularly (usually monthly)"*. The interviewees suggest that this practice is not being performed by some GPs. Adherence to these guidelines published in 2002 by all medical professionals would be important to reduce the amount of benzodiazepines prescribed.

The guidelines would also be useful for decreasing benzodiazepine prescribing for misusers, but they would also be beneficial for reducing unnecessary benzodiazepine prescribing in therapeutically-indicated cases. The interviewees in this study commented on how they acquired benzodiazepines from their family, mostly unknown to the family members. Parents giving their children benzodiazepines to help them sleep has been reported in other studies but was not discussed in this study (260, 262). It is evident from the interviews that this occurs because family members hoard their benzodiazepines. Regular reviews of benzodiazepine therapy and prescriptions of small quantities, as recommended by the guidelines should reduce stockpiling behaviour. Educating the public on the risks of stockpiling medicines and sharing medicines in general could reduce the acquisition of benzodiazepine by these means. It could also reduce the potentially harmful effects of experimentation with other medications at home, as described in the Associated substance misuse category, for example anti-depressants.

Another area where public education would have beneficial effects is by increasing awareness of the effects of benzodiazepines. The interviews highlighted that many young people who take benzodiazepines for the first time were not aware of their effects. This was also highlighted in another study (262). In fact, some were told that they were *"party drugs"*, which would have misled them about their depressive effects. Such an educational campaign could publicise the negative effects as described by the interviewees. Memory loss, bodily clumsiness, speech difficulties, weight changes, and decreased motivation could all show the unattractive side of

benzodiazepine misuse. The longer-term consequences of benzodiazepine misuse can have life-long effects.

The interviewees described how benzodiazepine misuse resulted in decreased motivation. In the sample quotes above, interviewees described how their school performance deteriorated as a result and that preferred “to stay at home and get stoned”. This is not to suggest that benzodiazepine use was the only reason for reduced school performance, however it can have a noticeable impact. This could result in a lower level of educational achievement, and there are many negative results from this. *Level of education is positively related to physical health* (283, 284)*, mental health* (285, 286)*, and employment* (287)*, and social support* (288)*. Benzodiazepine use was one the factors that led some interviewees to stop their extra-curricular hobbies and sports.*

The public could also be made aware of the compulsive nature of benzodiazepine misuse; how it can lead to use of larger quantities and loss of control of behaviour. This is mirrored in other studies that benzodiazepines cause the users to behave out of character (262)*.* Some of the effects described as positive by interviewees could be described in an educational initiative as they are acute, short-term effects but they can have consequences over the longer term. Interviewees described how they “*punched in windows*” and did not feel it. Such immunity to pain finishes when the substance leaves their body. The user will feel the pain and injury

that results from their actions in the following days. The consequences can be social as well as physical and emotional. Nearly all of the young people interviewed lived in the family home, so changes in behaviour were noticed by their parents. This resulted in conflict in the household between the young person and their parents. In one case, the conflict reached a level where the young person's mother needed the assistance of An Garda Síochána to remove the young person from their house. This action could be explained by the parent fearing their own safety in her house, and was likely done out of necessity rather than by choice. This shows that the damaging effects of benzodiazepines spread beyond the user and, in the case of death by overdose, to the community.

The severity of damage to the individual and the community was increased when alcohol was consumed with benzodiazepines. The use of both substances together was reported in other studies (260, 262). The tendency to increased aggressive behaviour was so well known amongst the interviewees in this study that their combination was known as a charge sheet. This paradoxical reaction to benzodiazepines is well-documented and is thought to occur to 1% of benzodiazepine users (247). The likelihood of a paradoxical reaction is increased for those at the extremes of age, and when alcohol is consumed with it (247). Another substance that was commonly associated with benzodiazepines was cannabis. Many interviewees commented that both substances have many of the same effects, and that both substances help them feel stoned. The consensus amongst the interviewees was that benzodiazepines were stronger than cannabis. Even

though they had different potencies, some users preferred the weaker cannabis to benzodiazepines. This suggests that though similar, either cannabis can have other favourable effects, or that benzodiazepines can have other unfavourable effects. There is physiological evidence for the comparison of cannabis and benzodiazepines (289, 290).

Some interviewees mentioned benzodiazepine use in conjunction with other substances. Benzodiazepines were taken to minimise the withdrawal effects of stimulant substances that they took. This was mirrored in another study where it was reported that benzodiazepines were *"used to come down off stimulants, particularly ecstasy and cocaine"* (262). These reports have a physiological basis, as it has been shown in animal models that anxiety induced by cocaine withdrawal can be alleviated by a benzodiazepine (291). For the withdrawal effects of benzodiazepines, the interviewees did not report taking anything, and so they experienced the full withdrawal effects. Many interviewees spoke about the short-term withdrawal effects that occurred in the days after taking benzodiazepines. The withdrawal effects experienced by interviewees could be divided into psychological effects such as irritability, and perceptual changes, and cravings, and physical effects such as sweating and sleep disturbances. Some of these symptoms, such as sweating and sleep disturbances were similarly reported in another qualitative study and in a review of benzodiazepine withdrawal symptoms (262, 292). Nearly all of these disturbances subsided after an extended period with the exception of craving, which continued months after benzodiazepine use had stopped. One of the interviewees described

experience of cognitive impairment that continued for months after benzodiazepine abstinence. Though not a common occurrence, prolonged benzodiazepine withdrawal syndrome does occur, and might persist greater than six months after withdrawal (242, 293). It is important to give support to those who desire to withdraw from benzodiazepines. Support can come in many forms from pharmacological to psychological supports. Pharmacological substitution using flumenazil, carbamazepine, and valproate can reduce the severity of withdrawal symptoms from benzodiazepines (294). An example of a psychological support that can be effective for benzodiazepine withdrawal is cognitive behavioural therapy (CBT) (294). The beneficial effects of CBT continued for up to a year after therapy.

6.4.1 Limitations

This research allows an insight into the experiences of young people who consume benzodiazepines; however there were limitations to the study. The data collected were semi-structured interview data collected from a purposively sampled population. Generalisation of this data is not possible, however the authors have attempted to maximise the transferability of this research by using thick description in the findings. It could be seen in the discussion, that much of what was reported in the findings were corroborated by independent qualitative and quantitative studies. A topic guide was used to maximise the coverage of the interviews. An inductive approach was used in analysis, and while the topic guide was not used in framing the analysis, it is a limitation of the study that the topic guide would influence the analysis.

The ‘Barrier against the world’ and ‘Cannabis and benzodiazepines’ categories arose entirely from the interviewees, and shows that the inductive approach revealed categories that were not part of the topic guide.

6.4.2 Conclusions

Benzodiazepine use by young people is a complex, multi-faceted experience. This study captured descriptions of this experience that could aid understanding of the experience. Benzodiazepines are used by young people coping with the pressures of life, and its use is encouraged and normalised by those around them. This short-term remedy has long-term consequences of which they are unaware. Education about benzodiazepines and their risks to young people, to families, and to the public can raise awareness and might reduce benzodiazepine misuse. Improvement in services to support young people who want to withdraw from benzodiazepines is vital.

7. “They’re too good” - Health-care worker views on youth benzodiazepine misuse

7.1 Introduction

Benzodiazepine misuse by young people is growing problem. In Europe, the misuse of benzodiazepines by 15-16 year olds has increased by 50% to an estimated 6% between 2003 and 2011 (120, 126). In the USA, the level of benzodiazepine misuse amongst 10th graders (15-16 years old) was comparable at 6.3% in 2012 (295). The level of benzodiazepine misuse amongst this age group in Ireland in 2011 was 3%, and a recent systematic review revealed that this has not changed in the past 10 years (147).

Benzodiazepines are dependence-forming medicines which produce withdrawal symptoms if stopped suddenly (54). Even at therapeutic doses, tolerance to their effects can require escalating doses to achieve a comparable effect (296). Other features of dependence include a compulsion to take the benzodiazepines and continuing use despite harmful consequences (16). The acute effects of benzodiazepine use can include muscle weakness, episodic memory impairment, and paradoxical disinhibition (148). Chronic benzodiazepine use is associated with visuospatial and verbal learning impairment, depressive symptoms and increased suicide risk (148-151). These effects can be long-lasting especially if substance misuse occurs in adolescence as major development of the frontal cortex occurs at this time (297). Substance misuse can interfere with the normal development of this area which is responsible for impulse control and motivation. A study found adolescent decision-making processes differ from adult processes as they encourage risky behaviour (298), and this study suggested that although adolescents are aware of the risks, perception of the

benefits were stronger determinants of whether they would engage in this behaviour.

As the perceptions, knowledge and views of those taking benzodiazepines may be influenced by their substance misuse and their age, we sought the observations of those involved in their care. The aim of this study was to describe the experiences of youth counsellors (YC) and general practitioners (GPs) in their work with young people who have taken benzodiazepines. These health-care workers would have experience with numerous benzodiazepine-misusing young people and so could provide additional insight into commonalities in benzodiazepine misuse

7.2 Method

7.2.1 Approach

Ethical approval for the study was sought and obtained from the Clinical Research Ethics Committee (CREC) of the Cork Teaching Hospitals. Data were gathered for the study using semi-structured interviews to allow for the full exploration of themes. Qualitative description was chosen as the methodology for this study (264, 265). Qualitative description assumes no prior qualitative research or theories, as *"there is no pre-selection of variables to study, no manipulation of variables, and no a priori commitment to any one theoretical view of the target phenomenon"* (264). The results of this study would originate wholly from the data. The authors of this study wanted to maintain the highest standard of reporting, so this was achieved

by following the Consolidated Criteria for Reporting Qualitative Studies (COREQ) guidelines (268).

7.2.2 Sampling

Purposive sampling was used as it allowed researchers to collect data from a wide variety of appropriate sources. The area of recruitment for YCs and GPs was chosen as counties Cork and Kerry in the Republic of Ireland, as YCs from these counties are under the control of the South-Western Drugs Task Force, and it would allow for wider recruitment potential. Recruitment letters were sent via the Health Service Executive to every GP working in the counties of Cork and Kerry. Extra GP participants were recruited to address gaps in demographics of GPs not represented in the framework. The inclusion criteria were that the GPs had to be actively working in general practice, and that they are practicing in Cork or Kerry. Recruitment letters were sent to YCs in Cork and Kerry. Their email addresses were obtained from Cork City Partnership Directory (299). The inclusion criteria for YCs were that they worked with young people aged between 13 and 21 years who had a history of benzodiazepine misuse and worked in Cork or Kerry.

7.2.3 Interview

In line with COREQ guidelines, for the purposes of reflexivity a description of the interviewer is provided. The interviewer for these interviews is the author of this thesis. The interviewer had previous interviewing experience and had received training in interview techniques and in qualitative research methods.

Single semi-structured interviews were conducted in a location of the interviewee's choosing, as this would be a safe, familiar environment that would encourage free speech. The interviewees comprised of both males and females over the age of 18 years and worked in either Cork or Kerry. The purpose of the study was explained and rapport was established with the interviewee; the interviewer told of his personal motivation for studying this topic; the researcher's regular contact with benzodiazepine-dependent patients in community pharmacy. Participants were then given an information sheet with frequently asked questions about the interview process and contact details in the event that the participant wished to contact the researcher afterwards.

Participants were asked to sign a consent form if they agreed to do an interview, and were asked to tick a box if they allowed quotes from the interview to be used in an anonymous fashion in the study's report. Of the 17 people who replied to the recruitment letter, all agreed to do the interview, though one participant declined to allow extracts from their interview to be quoted. Interviewees were asked questions from the topic guide that was produced from the topic guide of a previous study conducted by the researchers, which looked at youth benzodiazepine misuse (Appendix XI). The topics were modified and reviewed by the researcher and his supervisors to ensure that the language used in the interview was suitable and could be understood easily. All interviews were recorded by a dictaphone (Sony ICD-P620). Notes were written as appropriate after the interviews had concluded.

7.2.4 Analysis

The method suggested by Francis *et al*. was employed to determine when informational redundancy had been reached (269). The authors suggest that a minimum of 10 interviews be conducted and that the criterion for interviews to stop is when there are three consecutive interviews without any new themes. Sandelowski states that *"…informational redundancy is attained when a researcher has seen and heard the same thing over and over again"* (271). Due to the nature of the study with two sets of health-care workers, the authors decided to use a more conservative baseline. It was decided to use 14 interviews initially instead of 10 as either group could have varying viewpoints.

The recordings were transcribed by the researcher, the transcript was checked against the original recording to familiarise the researcher with the sense of the interview. Nvivo® Version 10 software was used in the coding phase of analysis by the researcher. Inductive content analysis was chosen as the method of analysis because it allows the data to guide the results and is more appropriate in situations where previous studies in the area are lacking (272). The basic unit of analysis used in coding the data was the individual theme. These first level codes were then organised into higher level categories, and the categories were then organised into themes, which were more abstract. In this process, codes were constantly re-examined to ensure their appropriateness to the higher level categories and themes. To

ensure the high credibility of the research, peer-debriefing was performed. Initial coding by the researcher and independent coding of three randomly selected transcripts was performed by a supervisor. Both researchers met and minor discrepancies were discussed to reach consensus. Negative case analysis was incorporated.

7.3 Results

The 17 participants comprised of seven GPs and 10 YCs; nine of the respondents were male. Seven of the participants were aged less than 40 years. Eleven participants were involved in the care of benzodiazepine misusers from urban areas, two participants were involved the care of misusers from rural areas and four participants were involved in the care of misusers from both urban and rural areas. Interviews lasted between 11 minutes and 74 minutes (median = 31 minutes).

7.3.1 Coding Tree

The themes and categories which arose from the data are displayed in Table 7.1.

Table 7.1. Themes and categories discussed in interviews

1. Factors affecting likelihood of benzodiazepine misuse	a) Family and benzodiazepine misuse
	b) Friends and benzodiazepine misuse
	c) Triggers for misuse
	d) Culture of acceptable use
2. Benzodiazepine misusers	a) Past and present
	b) User differences
3. Benzodiazepine effects on personal life	a) Effects on school/work
	b) The Gardaí* and benzodiazepines
4. GP prescribing of benzodiazepines	a) GPs as a source of benzodiazepines
	b) Decision to prescribe benzodiazepines
	c) Doctor-patient relationship
5. Measures to reduce benzodiazepine misuse	a) Limiting sources of benzodiazepines
	b) Education
	c) Alternative therapies

*Gardaí are the national police force of Ireland

7.3.2 Factors affecting likelihood of benzodiazepine misuse

7.3.2.1 Family and benzodiazepine misuse

A suggestion which was common to many of the interviews was that adolescent benzodiazepine misusers come from unstable families,

> *"It'd be fairly chaotic at home maybe as well. They wouldn't be kind of the usual boring morning and night routines you know. The boring things keep the kids on the straight and narrow." (YC07)*

Families with dysfunctional relationships and *"where the family structure has broke [sic] down" (YC06)*, have an increased likelihood of misuse occurring.

This can be explained by parents not guiding their child's development and *"…a lack of intervention earlier on when they're smoking weed at 14" (YC04)*. This relative lack of parental involvement would increase the *"likelihood that the substance use will get more and more…serious" (YC04)*. Parental substance misuse would be a complicating factor in this for two reasons. The first was that their own substance misuse can shape their attitude to the issue and can lead to a parent not seeking treatment for their child,

> *"…where there's a lot of drug use in the family as it is, then it's minimised. It's not really seen as a big deal as such because it's like drug use is, that's what's familiar and that's what's normal. So it's not seen as anything out of the ordinary. It's what people do…" (YC04)*

The second issue that can arise is that children can subconsciously see their parents' substance-misusing behaviour and internalise it as a normal behaviour. Seeing it as normal in the home can become self-reinforcing when they are outside the home,

> *"…you'll have Mum using them prescribed by her GP for anxiety and that's perfectly ok in their attitude. And I think that's what's passed on to the kids. Sure I'm anxious, so I'll use what Mum is using." (YC05)*

> *"...you hear the same names, the same family names turning up over and over again, you realise it's a very small subset of the population, I think, who are actually doing this. And again I know when they go out on the street, they are looking for the person like themselves and*

therefore they group together. And it becomes normal in that group." (GP04)

This behaviour is not indicative of all parents of children misusing benzodiazepines; parents can also have *"a heart attack" (YC09)* when they find out. Families at this extreme may also suffer due to benzodiazepine misuse and they attempt to hide it because *"…there's shame and they don't want Mary next door to know"* or because they aren't *"…sure what to do, or they think that'll just pass, that it's just a phase" (YC06)*.

7.3.2.2 Friends and benzodiazepine misuse

Friends were seen as *"hugely influential" (YC03)* in a young person's benzodiazepine use. The strongest influence was *"peer group…more so than family" (YC01)*. It was thought that this was because *"…they're taking their guidelines from peers now. Not necessary [sic] from family anymore" (YC07).* It was commonly perceived that for *"…anyone with a problem, all of their friends would be using drugs…" (YC09)*, and *"…usually their friends are taking benzos as well" (YC08)*.

Young benzodiazepine misusers may have sets of friends who use and friends who do not use. It was perceived that the young person would identify more with one of the groups, *"so if they're gravitating towards their group of friends who are using then it's going to be more difficult" (YC04)*. It can place a strain on the young person's friendships with those that who do not use so

that *"the person gives up from nagging them or else they kind of pull away from them because they don't want to hear it" (YC06)*.

7.3.2.3 Triggers for misuse

There can also be acute triggers of benzodiazepine use for young people. There was an acceptance that *"…everyone's triggers are different…I wouldn't say there's one common reason…" (YC09)*, and that triggers *"…could be anything" (YC01)*. Other participants observed broad triggers of misuse, *"anything that happens out of the normal will probably require most usage to manage it" (YC06).* Triggers were generally seen as events that had *"the potential to cause…hurt and pain…" (YC04).* Examples of situations that may trigger benzodiazepine misuse are *"when something happens at home" (YC07)* and *"breakup with a girlfriend" (YC04)*. Benzodiazepine can also be triggered by *"…an event coming up…it's this idea of I kind of have to build myself up" (YC06)*.

Alternatively triggers of benzodiazepine misuse can be unrelated to the young person's state of mind. An increased availability of benzodiazepines on the street will lead to increased use, *"…if there's a glut of tablets onto the street…they'll keep using them" (YC05)*. Being intoxicated with alcohol can increase the susceptibility of benzodiazepine misusers to take benzodiazepines, *"…they've been off them a while, but often if they go out drinking and if they are offered the benzos, they're more inclined to say yes if they have been drinking" (YC08).* One participant gave details of the

unpredictability of use, *"it can be as simple as it's a group of young lads and just to…get out of it for a couple of days… (YC02).*

7.3.2.4 Culture of acceptable use

The culture of the local community can contribute to its young people using benzodiazepines when *"we…come from a society that has become very drug-orientated" (GP04)* and when it is acceptable for neighbours to be,

> *"pooling all their tablets and putting them in a basin in the middle of the table. And literally that you would take a handful of tablets, and you would probably having a beer or wine or something"* (YC06)

In some communities there is an *"expectation of a pill to cure everything" (GP05)*. There is the often an assumption that tablets will solve the problem,

> *"The 13 year old wasn't sleeping. So he was up all night. And the mother was saying, I'll bring him down to the doctor to get some sleepers for him…the problem with him was like, she was leaving him up all night on the Xbox…" (YC09)*

There is no hesitation in these communities because *"…there's no illegality about it, it's an ok drug to be on" (YC03)* and *"the doctor's prescribing these, so it must be ok" (YC02)*. All of these factors can combine to give a sense to normality to benzodiazepine use, especially where alternative messages about benzodiazepines are not picked up by young people.

7.3.3 Benzodiazepine misusers

7.3.3.1 Past and present

The participants often spoke about differences in relation to misuse at present and those that they had experience with in the past. A commonly mentioned difference was that *"…GPs are becoming more aware and they're not giving them to young people" (YC08)*. This was because *"there wasn't the same awareness of habituation" (GP04)* and *"that the thinking 30 or 40 years ago was somebody's depressed, give them some benzos" (GP03).* This is not the case now, as *"there's been a bit of tightening up in GPs…" (YC01)* and *"…we have finally gotten to the point where the psychiatry services aren't prescribing benzodiazepines" (GP01)*.

Another change from the past was that more young people *"…are no longer saying oh I'm satisfied having a drink and taking a weed" (YC07),* and *"if I was to look back 5 years ago…they would have come in relation to their alcohol and maybe use of cannabis…now benzos are involved" (YC08)*. Others disagreed with this saying, *"the only thing I would have seen was…the price would have gone up…that's the only thing I would have seen" (YC03)*.

7.3.3.2 Benzodiazepine misusers

Participants spoke about the differences between benzodiazepine users at present. The areas where differences were observed were in gender,

educational/social background, and in age. There was a consensus that *"the problem is just as big with young girls and women as what it is with, men" (YC01).* The difference between the sexes was in terms of outcome,

> *"there was use with girls and they'd slip the net a little bit. You know they didn't tend to get into as much trouble as boys. Em, because maybe there was a bit of drinking at home you know, and their friend would come in and they'd drink" (YC07)*

This has the consequence that *"fellas are…directed to services because…they're in trouble more" (YC01)*. Another area where differences were apparent to the participants was in terms of social class. Participants thought that young people from *"…more disadvantaged backgrounds…" (GP07)* were more likely to misuse. This view is reinforced by other participants commenting on third level students that *"…it does not appear to be a recreational drug of use in…the student population" (GP05)*. However this was not universally acknowledged with some commenting that benzodiazepine users come from *"…all walks of life…we've had some right sort of posh kids as much as we've had lower socioeconomic groups coming in here using benzos" (YC05)*.

It was suggested that benzodiazepine misuse is,

> *"…across the board. That is also scary in itself, in the fact that there's no one particular group that is concentrating on benzodiazepine use.*

Cos usually with drugs, you could nearly categorise them into, you know you've got your party drugs, and you've got your alcohol and cannabis for the younger ones…it's really across the board" (YC02)

The age of the user plays a significant part in the pattern of benzodiazepine misuse. Those in early adolescence who take benzodiazepines would be *"…getting them on the street…" (YC08)* or *"…that they're stealing Mum's tablets or Nan's tablets…" (YC06).* Another feature of benzodiazepine use at a younger age is that they are *"…taking a pill here or a pill there…they're not saying they're taking them regular" (YC07)* and *"they're using them…because they're being handed out" (YC06)*. Because of this behaviour, benzodiazepine use is *"much more in group than it is individually in a home setting…usually in a party out at night" (YC06)*. Benzodiazepines are not the only substance misused by this group, *"with the younger ones more so, it's benzos, cannabis, you know, alcohol" (YC02)* and *"you're not looking at one usage, rarely in my experience is one substance on its own. Particularly in the younger age group" (YC06)*.

Those in late adolescence would have a different attitude to benzodiazepines. It is at this stage *"when they get to be kind of 18, up to 20, 25, that they're recognising that the tablets, that they actually need them to cope" (YC07).* They have moved from taking benzodiazepines sporadically with friends and,

"It becomes a little more sophisticated as they get older…they actually then have a system. So they take so many maybe to get them up in the morning. Then there's, there's a program to the day around usage. So then there might be something to get you up, something to what I call lose time. So they want to remove x number of hours in the day, and then a certain amount again to sedate you to put you to sleep. Because without it, they won't sleep…" (YC06)

Heavy episodic (binge) benzodiazepine use would not disappear as the misuser got older but it would be less extreme, for example a person could be *"taking 3 or 4 a day, and then some days if they felt they wanted more they'd take more" (YC08)*. They would not get their benzodiazepines on the street, *"…definitely the 18 to 25 year old, seem to get prescriptions from doctors, easy enough…they would have told me that they were going to different doctors" (YC07)*. For those starting at a very young age, often a level of tolerance can build up such that benzodiazepine users *"move on to the heroin when they're 19 or 20. The benzos stop working for them then" (YC05)*. Even then benzodiazepines can be

"a managing tool…so if you are using heroin and there's a drought…or there's a problem with supply, or they have no money. They would mostly move to benzodiazepines" (YC06)

7.3.4 Benzodiazepine effects on personal life

7.3.4.1 Effects on school/work

Awareness of the deleterious effects of benzodiazepines on school or work varied between participants. The GPs gave a common type of response when asked about their awareness of effects on school or work, *"not that I'm aware of" (GP01).* Some GPs were not able to give an answer because they *"…don't hear them commenting on adverse effects cos we actually don't prescribe that much" (GP05)*. One GP offered an explanation for why they do not hear about effects on schooling, *"they wouldn't have that insight. If it was, that wouldn't be their worry" (GP03)*. YCs had differing views from GPs, they believed that poor school/work performance was *"probably a combination of factors, but benzos would probably be one of the more predominant factors" (YC04).* Young benzodiazepine misusers *"might be going to school, but few would have jobs…missing days, not getting up. In bed all day type of thing" (YC09).* If they do attend school/work, *"…they're kind of not…mentally present…meaningful work through school or their work would be very difficult to achieve…" (YC02*). This can eventually lead to getting *"…pretty much expelled or they would leave themselves…most of my guys are on the dole now…" (YC02)*. Others would have doubts about *"…whether there's other psychosocial issues going on previous to their use that would have them out of school anyway" (YC05)*.

7.3.4.2 The Gardaí and benzodiazepines

GPs and YCs were mostly in agreement that *"…anybody I've had put on my list, who are on benzodiazepine have big legal issues. All of them, or more or*

less all of them" (GP04). Some participants thought that young people's interactions with the Gardaí were due to *"…using illegal drugs rather than prescribed drugs" (GP02)*. Others suspected that compared with benzodiazepines alone, mixing alcohol with benzodiazepines made users *"…more visible, sometimes very equal in lifestyle and everything but just in more trouble with the law" (YC03).* Some thought that *"where they might get involved with the Guards, not through their behaviours while stoned, but from either stealing or...dealing" (YC05)* or from *"stealing usually…not a lot of violence now" (GP02)*. In contrast to these views, one participant believed that involvement with the Gardaí was as common among non-drug users,

> *"…that's the area we're in. That wouldn't set them out in the practice…involvement with the Guards…probation officers, and social workers and all that. That doesn't set them apart from drug users" (GP03)*

7.3.5 GP prescribing of benzodiazepines

7.3.5.1 GPs as a source of benzodiazepines

GPs can be a common source of benzodiazepines for misusers. As shown above, those in early adolescence tend not to get benzodiazepines from GPs. The older adolescent misusers would be *"…comparing notes, who's the best doctor to go…just tell him…you're feeling depressed or feeling suicidal, you can't sleep. Just tell him that and he'll…write you the script" (YC09)*. The success of this strategy *"…depends on the GP. There's certain GPs in the area that won't give them out" (YC08)*, conversely *"…there were very large*

prescriptions available because we had an issue with a practitioner…" (YC06).

Benzodiazepines prescribed are sometimes not enough and patients can *"…supplement whatever the doctor will give them with extras" (YC02).* Another strategy used to increase the number of benzodiazepines prescribed is to have *"3 or 4 doctors…what we find here is that you'll have a gang, say 4 or 5 people like. They'll all have scripts" (YC09)*.

7.3.5.2 Decision to prescribe benzodiazepines

GPs appeared to have conflicting views on prescribing benzodiazepines. Some admit that *"…they're very effective" (GP03)* and *"they work" (GP04)*. While holding this positive view, GPs simultaneously *"…wish they didn't exist on the market…in many ways, they're too good" (GP01),* and *"because they're so effective, they've become very popular" (GP04).* GP participants spoke of benzodiazepines being useful for *"…severe short-term anxiety…measured in matters of hours to days…" (GP02)*. The temporary nature of their use was reiterated by other GPs who thought of their use *"…where somebody needs fast-acting medications such as a panic attack or a specific phobia maybe of flights…" (GP07)*, and they *"…would not give more than 4 to 5 days [supply]" (GP05)*. Some participants would offer *"…beta-blockade as a way of symptomatic relief of physical signs of anxiety…" (GP05)* first line. Other uses of prescribed benzodiazepine would be as a *"…muscle relaxants in situations…like whiplash and torticollis, where*

they have acute muscle spasm…" (YC07), *"…in the treatment of epileptic seizures" (GP02)*, *"…and for hypnotic treatment…" (GP05)*.

The views of GPs about prescribing benzodiazepines to under 18s ranged from *"…I don't think I could justify giving a minor a benzodiazepine…" (GP04)* to *"…I would almost never prescribe to an under-18…I would take psychiatric advice" (GP01)* to *"If I was going to prescribe…it would really be with extreme caution…starting off with the lowest dose possible" (GP03)*. All of the GPs who offered an opinion did not like prescribing benzodiazepines in under 18s. GPs were also cautious in prescribing benzodiazepines where *"…there's a history of addiction there" (GP03)* or even outside of the individual where there was a *"…history of benzodiazepine use in the family" (GP01)*.

Some GPs accepted that patients were using benzodiazepines prescribed by GPs but had to focus more on *"…damage limitation" (GP04)*. They would continue to prescribe benzodiazepines in some circumstances where *"…patients who initiate benzodiazepines, do so from outside the practice" (GP02)*, but the approach to potentially new patients was,

> *"…just don't let the new generation get hung up on them like the older generation did…cos it's much easier to not do it in the first place, than to try and stop once it's started already" (GP07)*

7.3.5.3 Doctor-patient relationship

GPs noted several ways that they could recognise new patients who were misusing benzodiazepines. The main pattern was that patients would tell the GP that they had received benzodiazepines previously and that they want to get them now, for example some would say *"…they got it elsewhere and it's the only thing that works…they always get it from their previous doctor…" (GP05)*. Variations on this theme can be that the patient had misused benzodiazepines in prison *"and they've just been released and they need a supply otherwise they're going to withdraw" (GP01)* or that *"…they've been up the country but normally they'll say they've been in the UK" (GP03)*. Some patients would be offered *"…other treatments like psychological treatments…beta-blockers they'd usually say neither of those work for them" (GP05)*. Some patients try an alternative strategy of threatening self-destructive behaviour unless the GP prescribes them benzodiazepines. Examples of such threats are that *"…if I didn't give him "Valium"™ that he would be forced to go on booze and other illegal drugs. That would be at my door" (GP07)* or *"I'll go out of here and I'll have a seizure and it'll be on your head doctor" (GP03)*.

In contrast to deceitful attempts to get prescribed benzodiazepines, some patients will be *"…straight up and say that they've got an addiction problem and…they want to enter into a program to wean off them" (GP01)*. These interactions with patients appear to influence GPs opinions, *"…I think what they do is they find the soft touches. The soft touches being single-handed practitioners, often people with problems themselves…" (GP04)*. Some

practitioners believe that the behaviour described above is typical, *"they're normally deceitful…they are very rarely actually looking for help. They're just looking for prescriptions" (GP01)*, and that *"…they don't really want to come clean" (GP07)*. Other GPs have a more positive opinion of *"…people who'd have genuine serious social problems…it's hard to blame them for wanting something to blot it out" (GP04)* and seek *"…concordance, or a shared understanding of what…the patient's problem is" (GP02)*. One GP expressed the view that *"it's not for me to blame them. It's for me to show them that there's possibly another way of living your life" (GP04).*

GPs were united in their reticence to prescribe and generally did not want to give patients the impression that *"…by multiple re-presenting that they will be able to get a meaningful sustained…prescription of any benzos" (GP05)*. Adherence to this belief could affect relationships with their patients, *"…who have left the practice because I just won't prescribe" (GP02)*. GPs deter benzodiazepine prescribing in a variety of ways from warning of side-effects like *"…this will make you sleepy…" (GP07)* to *"…repeat prescriptions with benzodiazepines must be reviewed every 3 months" (GP04)*. One GP's differing approach to deterring prescribing was that

> *"…if you're going to deny something that they feel is the only thing that's going to work, it's important to have another reasonable evidence-based alternative…psychological treatments…more appropriate pharmacological approaches like the SSRIs…" (GP05)*

Even though a GP may try to dissuade a young person, often using the strategies mentioned above, patients may still try to manipulate GPs resulting in an inner conflict between their desire to help and *"…knowing that you shouldn't really be prescribing in a person in their 20s, long-term Valium… (GP07)*. This can occur because *"…in the real world of general practice the pressure on a general practitioner to prescribe is almost always driven…by the lack of alternative support therapies" (GP05)*. GPs can also feel pressure from long-term benzodiazepine patients who, *"…if the subject is raised…about possibly discontinuing their benzodiazepines, get quite agitated" (GP02)*. When a GP takes over from an existing practice and decides to change benzodiazepine prescribing practices, there can be resistance from the patients who think *"…my other doctor gave me these and there was no problem and they were great and what are you talking about now" (GP07)*. This means that new GPs can often continue

> *"…the prescription because, new doctor, new face, new system. Patients already have their back up about that. I didn't initially want it to be new treatment as well. You have to win their trust." (GP03)*

Some GPs accepted that they cannot get all of their patients to discontinue benzodiazepines and accept that they will have patients on benzodiazepines,

> *"…we're beating ourselves up trying to achieve this ideal…one of the things of maturing is to understand what you can't change...it would be easiest thing in the world for me to write to the PCRS* and say I want*

the following 20 people taken off my list...all I'd be doing is transferring the patients to some other poor bugger." (GP04)

**Primary Care Reimbursement Service (PCRS) is responsible for the administration of government-subsidised medical aid in Ireland*

7.3.6 Measures to reduce benzodiazepine misuse

Faced with the problems described in the previous themes, participants gave suggestions about how benzodiazepine misuse could be reduced.

7.3.6.1 Limiting sources of benzodiazepines

Participants had a variety of ideas about how to *"…make the availability of benzodiazepines…much harder" (GP02)*. Suggestions for changing GP practice ranged from *"…training through postgraduate bodies to ensure that they have the confidence to em, say no…" (GP05)* to *"…enforcement is the way to go…I think there should be a traffic light system out there…" (GP04)*. Other suggestions were in the area of *"…regulation of benzos….it's not a controlled substance" (YC05)*. Some were advocating severe regulation of benzodiazepines *"…where we could not prescribe for longer than a month…where people are told that they would get perhaps say six weeks supply of benzodiazepines in their lifetime…" (GP02)*, and one participant supported banning them outright. Another participant thought that strategies to reduce prescribing to young benzodiazepine misusers will have problems as *"…swapping of drugs amongst all age groups has always gone on and will probably continue to go on" (GP05)*.

7.3.6.2 Education

Education was another suggestion that was popular among participants to reduce benzodiazepine misuse. Participants thought that educating doctors *"…how to speak to patients, how to relay the information is very clear how addictive these substances can be…" (YC02)* and about *"…guidelines as to the maximum duration, maximum dosage… (GP05)*. Some GPs saw *"…the big challenge is to educate the patient…how we can use them effectively" (GP03)*. GPs should be *"informing of side-effects. Informing of the possibility of addiction. Most people are afraid of getting addicted to things…" (GP07)*. Another participant thought that Patient Information Leaflets were too confusing,

> *"…datasheets need to be…simplistic not legalistic…this is designed for short term use only, if you are using it long-term please ask your doctor why…this is a habit-forming drug…this drug will…work less every time you use it. Why not talk to your pharmacist or your doctor about it" (GP04)*

Finally, increased public awareness by *"…running campaigns about the dangers of benzodiazepine use or excessive benzo use" (YC02)* was identified as important.

7.3.6.3 Alternative therapies

There was a view among some participants that *"…prescribing them for long periods of time…doesn't get to the root of the problem" (YC05)* and that

"...when we look at addiction we need to look beyond the physical and get into the psychological" (GP04). This view was common among both health-care workers, that GPs are *"…under pressure and prescribe. I think if there was a therapist within each practice, it might prevent the…high level of prescribing of benzos" (YC03)*.

7.4 Discussion

This study explored the views of the health-care workers who would be in frequent contact with young benzodiazepine misusers. Participants discussed their views on a range of topics from the factors which can make a young person more prone to substance misuse to measures which could help to reduce youth substance misuse. To the authors' knowledge, this is the first qualitative study to use the views of trained health-care workers, GPs and YCs, to describe the patterns of behaviour of young people who misuse benzodiazepines. One of the main findings of interest was that participants perceived that benzodiazepine prescribing had reduced greatly compared to levels in the past. Both groups also agreed that extra controls should be placed on the prescription of benzodiazepines of all age groups, not just young people. Most participants felt that many of the factors that influenced young people's misuse were outside of the young people's control. Family structure, parental attitude to substance misuse, and acceptability of substance use within the local community were identified as having an influence on young people.

The large influence of family on a young person's benzodiazepine misuse was indicated by participants in this study. Parental substance misuse or attitude to misuse, and absence of proper parental supervision can lead to positive expectancies and the opportunities to misuse benzodiazepines respectively. Study of adolescent benzodiazepine misuse found an inverse association between misuse and parental bond (300, 301). This association is not unique to benzodiazepine misuse, as there were studies showing that maternal neglect is associated with the development of substance use disorders (SUDS) (302, 303). An Irish study in 2010 found that use of alcohol and cannabis was *"linked with an increase in consumption of various kinds of substances by young people"* (304). This finding has been supported by other studies (305, 306). The influence of the community's perceived acceptance of benzodiazepine was highlighted by participants as influencing the misuse of benzodiazepines. Although no studies relating to this were retrieved from the literature, studies relating to alcohol misuse highlighted that perceived community disapproval of underage drinking was inversely associated with youth alcohol misuse (307, 308). These findings highlight that the community in which a young person grows up in has an enormous influence on a young person's substance misuse progression.

Participants held views that GPs were now more aware of benzodiazepine prescribing than in the past and that benzodiazepine prescribing decreased in recent years. There corroborates with evidence from Chapter 3, which showed all-age benzodiazepine prescribing decreased by 16% between 2009 and 2011 (section 3.3.1). Another difference highlighted between the

past and the present was that young people are experimenting with benzodiazepines at a younger age. The European School Project on Alcohol and Other Drugs (ESPAD) study investigated the percentage of 15-16 year-olds who had ever misused benzodiazepines at any time between 1995 and 2011, and found that the level decreased from 9% to 3% (126, 145). The same studies found that the percentage of those who first used benzodiazepines under the age of 13 years decreased from 2% to 1%. These studies suggest that early misuse of benzodiazepines appears to be decreasing, contrary to the opinion of participants. Analysis of the referrals to substance misuse treatment centres in Ireland however shows that the median age of benzodiazepine misuse initiation among new cases has been decreasing. The median fell from 20 years between 2003 and 2008, to 18 between 2005 and 2010 (103, 235). This indicates that while fewer young people may have been misusing benzodiazepines, those who were misusing them were beginning at a younger age.

Participants opined that there was no gender preponderance regarding substance misuse, a finding which is corroborated by the 2011 ESPAD survey indicating a 3% prevalence of misuse in male and females (126). The participants noted that males accessed more treatment than females. Between 2005 and 2010, the majority (60.8%) of new cases of benzodiazepine misuse treatment were males, in line with the findings of this study (103). Study participants suggested that benzodiazepine misusers originate from disadvantaged backgrounds and obtained lower levels of education and this is supported in the literature (309, 310).

One of the themes which arose from the interviews was the effect of benzodiazepines. One of the categories within this theme was the effect that benzodiazepines have on school and work. There is clear evidence in the literature that benzodiazepines can affect cognitive performance in long-term users (25, 239), and there is some evidence that prescription misuse is linked with dropping out of school (311). Some participants also spoke about young people staying in bed all day, and this could be due to the hangover effect of long-acting benzodiazepines (312). Overall the views expressed by the participants are in agreement with findings in the scientific literature. Another consequence of benzodiazepine misuse was interaction with the legal system. It has been noted that taking benzodiazepines can result in violent behaviour (313, 314). It is posited that violence from an anxiolytic is due to irritability caused by withdrawal effects or due to taking unusually high doses. This is in contrast to the views of some of the participants that the benzodiazepine use did not lead to violent crime but to theft or drug dealing. A search of the literature returned a single study that reported an association between regular benzodiazepine use and acquisitive crime in Ireland (152). The participants also noted that mixing benzodiazepines with alcohol can result in more violent behaviour. This has been called a paradoxical reaction to benzodiazepines (238). It has been reported in several studies that mixing alcohol and a benzodiazepine will lead to increased aggression (154, 315). These studies support the views of the participants.

The study included GPs decision-making regarding prescribing benzodiazepines to young people under 18 years. The overall view of benzodiazepines was quite negative although participants conceded that there were circumstances in which benzodiazepines are effective and appropriate. They felt that only short-term prescribing of benzodiazepines was acceptable. Guidelines for benzodiazepine prescribing recommend that benzodiazepines be prescribed for the shortest period possible but no longer than four weeks (157, 316, 317).

Participants reported that young people misused prescriptions from GPs. Participants reported that there was a view among misusers that it was easier to obtain prescriptions from some GPs than others. Some participants mentioned that benzodiazepine misusers would attempt to get benzodiazepine prescriptions from multiple GPs as another means of increasing their supply of benzodiazepines. The idea of “doctor shopping”, the simultaneous use of several physicians by a patient, is a topic that appears in the literature (318). In one study doctor shopping allowed for the greatest number of benzodiazepines to be obtained (193). The same study also mentioned obtaining benzodiazepines from a single doctor and from “script doctors”, physicians who sell prescriptions illegally. No reference to such behaviour was discussed in these interviews, but it may be a feature of benzodiazepine acquisition in Ireland.

The nature of the GP-patient consultation was discussed by both sets of participants. Their opinions about the strategies used by young substance misusers differed. YCs described how misusers would feign the appropriate mental illnesses to acquire benzodiazepines. GPs spoke about misusers telling them of moving from elsewhere and wishing to continue their prescription with this GP. Another approach used by misusers was to threaten greater self-destructive behaviour if they did not get benzodiazepines. From studies of GP-patient consultations, some of these approaches are common among the general population. The most frequent reason for a benzodiazepine request among all patients in one study was the *"initiation and continuation of treatment for anxiety, depression, or side effects"* (319). The approaches suggested by participants of the current study are in line with approaches used by the general population, although threatening self-destructive behaviour was not observed in the literature.

GPs were generally suspicious of young people looking for benzodiazepines. Some GPs opined that young misusers did not come for help but for prescriptions to continue their benzodiazepine habit. A recent study found that GPs labelled drug addicts as undeserving patients (320). The same study did note that in some cases, a GP's empathy for the suffering of some patients may lead the GP to prescribe to a patient with substance issues. These exceptions were noted in some participants who felt conflicted between helping patients who are in need of help and feeling guilty about prescribing benzodiazepines to a young person where there is a chance that they might be risking a lifetime of benzodiazepine use. Another source of

conflict amongst the GPs was starting in a new practice or when doing GP locum work. Their training put pressure on them to change the chronic benzodiazepine prescribing pattern that the patient was used to. There is an awareness of the conflict between old and new prescribing practices, and between older and more recently trained doctors in the literature (320). Some GPs resigned themselves to the fact that some patients will not ever come off benzodiazepine but just saw it as something they had to live with.

The participants did make suggestions to reduce the misuse of benzodiazepines. One of the suggestions was to limit the prescribing of benzodiazepines by GPs. Limiting the prescribing programs such as the triplicate prescription program in New York State show that benzodiazepine prescribing can be reduced (321, 322). Another form of limitation was pursued in the Netherlands where in 2009, the government excluded benzodiazepines from their reimbursement list when used as an anxiolytic, hypnotic or sedative. This policy change resulted in a dramatic decrease in the number of long-term and short-term prescriptions issued (323, 324). Changes to benzodiazepine-prescribing laws and reimbursement policies must be carefully examined as there can often be unintended consequences, such as substitution to other potentially unsuitable medicines (325).

Education was another area that participants thought was important. Both patient and public education could play a role in reducing the demand for benzodiazepines. A simple educational strategy described in the literature

was to send benzodiazepine patients letters that advised gradual reduction in benzodiazepines. This strategy was most successful in short-term users, however it had a poor success rate among long-term users (326). A higher level of success was obtained when the letter sent to each patient was customised with details of the patient and their benzodiazepine history (327). There have also been educational strategies aimed at GPs with conflicting results. Some studies reporting a lasting improvement while other studies describing no change (328, 329). A recent Cochrane review of educational visits to change health-care professional care reported that education can make small but potentially important changes to practice (330). Further exploration of professional education in relation to benzodiazepine prescribing is warranted. The other form of education suggested by participants was public health campaigns. Scientific literature in the area of public campaigns to modify health behaviours suggests that they can have a small-to-moderate impact (331). Research indicates that public health campaigns to modify addictive behaviours are more effective when run as preventative campaigns before the behaviour begins compared with cessation campaigns (331). Thus, a campaign directed at young people who have never used benzodiazepines may be more effective than those that take them regularly.

The third suggestion that participants recommended was to offer benzodiazepine patients and potential patients non-pharmacological alternatives to benzodiazepines. Some participants used CBT as an example of an evidence-based alternative. CBT has been shown to be effective for

anxiety and depressive disorders in children and adolescents (332, 333). A meta-analysis of randomised control trials showed that CBT was an effective treatment for adult anxiety disorders (334). The other indication for which benzodiazepines are commonly prescribed, insomnia, can also be treated effectively by CBT (335, 336). Indeed, the results of two randomised direct comparison trials between CBT and nonbenzodiazepines with controls indicated that CBT was superior in treating chronic insomnia and should be recommended as first-line therapy (337, 338). Although there is a small body of evidence supporting this, more research is needed before it can replace hypnotics, however it does highlight the potential power of CBT in the treatment of these serious conditions. A practical consideration that may stifle the introduction of CBT as a means of treatment is the relative expense of counselling therapies in comparison to benzodiazepines.

7.4.1 Limitations

This study gives an insight into the experiences of YCs and GPs dealing with adolescent benzodiazepine misusers. A limitation of this study was that the population was purposively-sampled population, and whilst the study cannot be generalised to the larger population, the authors have attempted to maximise the transferability of this research by using thick description in the findings. The discussion section of this paper relates the findings of this study to existing literature. Another possible limitation could be due to the fact that the interviewer was a pharmacist, GPs may have felt pressure to give a socially desirable response when asked about their attitude to prescribing to young people. It would be difficult to verify this without

examining their prescribing data, however as some of the GPs mentioned in their interviews that they had prescribed to under 18s, the effect of this bias is thought to be limited.

7.4.2 Conclusion

Young people may have poor insight into their substance misuse so working with health care workers who encounter them on a regular basis serves to give further understanding into their behaviour. Many of the factors which can influence whether they will misuse are outside of their control. Measures which seek to reduce youth benzodiazepine misuse should be multi-faceted. Restrictions on benzodiazepine prescriptions can reduce the supply of benzodiazepine to patients and to the communities for whom the patients can be dealers. Measures to reduce misuse should also reduce the desire to misuse. Educating patients and the public about the long-term effects of benzodiazepines can reduce their attractiveness. The provision of psychologically-based therapies such as CBT can simultaneously provide GPs with an evidence-based alternative for patients afflicted with mental illness, and reduce both the burden of the cost of medicines and on the substance misuse treatment services. Due to the cost of such therapies, further research should be conducted on their economic feasibility.

8. Thesis Discussion

8.1 Discussion

Substance misuse has been a documented problem in Ireland for over 150 years. Until the late 1960s, alcohol misuse was perceived as the sole problem by the Irish government (6). It was not until the rising opiate misuse problems in the 1980s that the government seriously invested in substance prevention and treatment (7). This lead to the decentralisation of treatment and the creation of the methadone scheme and regional drugs task forces (6). The rise in cases of misuse of prescribed medicines led to increasingly stricter regulations from the 1990s onwards, whilst the increasing availability of unregulated novel psychoactive compounds in the late 2000s resulted in the ban on these substances and the premises where they were sold (head shops) (339). The history of substance misuse in Ireland came full circle with the release of the National Substance Misuse Strategy in 2012 (10). This report made reduction in alcohol misuse a priority. Similar to goals of the earliest alcohol misuse prevention campaigns, the National Substance Misuse Strategy aims to reduce not only alcohol dependence, but alcohol misuse amongst the general population.

Substance misuse amongst young people was the focus of a systematic review conducted (Chapter 2); youth and adolescence tend to be the times when substance misuse most frequently starts (5) and so it is important to appraise the evidence available. Including studies from the period 2000-2012 allowed a retrospective analysis of whether misuse of the four most-used substances: alcohol, tobacco, cannabis, and benzodiazepines (126) was increasing or decreasing. The studies included in the review had varying

quality, as highlighted by their Methodological Index for Non-randomised Studies (MINORS) score (see Table 2.1). The results of the review concluded that alcohol has still the highest level of misuse, followed by tobacco, cannabis and benzodiazepines. This corresponds to European data which also cites the same four substances in 2011, with alcohol lifetime misuse at 87%, tobacco at 54%, cannabis at 17%, and benzodiazepines at 6% (126). A novel finding from the systematic review was that substance misuse levels, in general, were decreasing over the period studied (see section 2.4), however; lifetime benzodiazepine misuse levels were stable over the same period. The ESPAD studies published in 2000 or 2004 did not give average European levels of substance misuse, however data collected in 2007 did show that alcohol, tobacco and cannabis misuse decreased by 2% between the 2007 and 2011 study (113).

Benzodiazepine misuse did not change across the various time points. Differences were observed when data on European substance misuse was compared to data from the USA. The Monitoring the Future survey (MTF) was similar to the ESPAD survey, but it surveyed students of 8th, 10th and 12th grade in the USA (340). Comparisons between data from the 10th grade students (approximately 15 years old) are most applicable to the ESPAD survey. Alcohol was still the substance with the highest lifetime misuse, but at 56% it is at least 30% lower than European counterparts. Cannabis misuse at 34.5% made it the second-most-misused substance at a level double of Europe's. Tobacco and benzodiazepine misuse was at 30% and 7%, respectively. Comparing misuse levels in 2007 and 2011, cannabis was

the only substance which did not show a decline. Differences between European and American cannabis misuse levels could be due to the more relaxed attitude towards cannabis in the USA (341). Examples of this relaxed attitude can be seen in the use of medical cannabis in 18 states, and the decriminalisation of cannabis for recreational use in the states of Washington and Colorado (342). The disparity in alcohol misuse levels may be due to the differing minimum drinking ages in the USA (21 years) and Europe (16-20 years depending on country) (343). Benzodiazepine misuse levels were similar in both areas, but misuse has fallen in the USA while European levels were static (340). Future work should focus on the reasons for the decline in the USA and how European countries reduce their levels.

Since benzodiazepines can only legally be obtained on foot of a prescription, an investigation into benzodiazepine prescribing in young people was performed to examine if excessive prescribing could be a contributing factor to their availability. Chapter 3 examined benzodiazepine prescribing in Ireland using pharmacy claims data. National prescribing data was presented firstly to put the youth prescribing in context. Ireland had the largest decrease (16%) in benzodiazepine prescribing between 2009 and 2011, as shown in section 3.3.1, although it was still the fourth highest level of those countries surveyed. The decrease is welcome but further reductions must continue if Ireland's prescribing level is to match the global average of 10.4 DDD/1,000/day in 2011 as calculated in section 3.4. This average however is likely to increase as developing countries get better access to clinical diagnoses (344). The low level of prescribing in some countries may be due

to underdiagnosis, and increasing diagnosis may result in increased prescribing. The decrease in Irish prescribing levels could lead to a reduction in the supply of benzodiazepines to young people via family and/or dealers. These can be the sources of benzodiazepines when misusers are at a young age (175, 176). The decreasing overall prescribing is counteracted by the ≈5% increase in benzodiazepine prescribing to those aged under-18. This may be due to increased prevalence of mental health disorders in young people (345), and increased misuse of these benzodiazepines.

Adherence to the national Good Practice Guidelines for Clinicians varied. Approximately 40% of patients had been prescribed hypnotics, while approximately 15% of those had been prescribed benzodiazepines for a period of more than four weeks, either of which would constitute non-compliance to Guidelines (157). Adherence to these guidelines in particular is important because hypnotics can cause rebound insomnia which may be mistaken as a return of the original complaint and may result in the patient continuing to take the medication (346). Withdrawal effects can develop within a short period (3-14 days) of taking benzodiazepines, which is the reason that the benzodiazepine manufacturers' licences limit use to four weeks (190, 247). Such can be the speed of tolerance development that one review recommended tapering the dose of benzodiazepines for children who have received benzodiazepines for more than 5-7 days (347). The development of tolerance to the effects of benzodiazepines can, in some circumstances, lead to 'topping up', as described in Chapter 7; a phenomenon whereby young patients can supplement benzodiazepines

prescribed from their doctor with benzodiazepines bought on the street (section 7.3.5.1). This may not occur after a single month's benzodiazepine use, but the longer duration of use will increase the likelihood of it occurring. Apart from iatrogenic dependence to benzodiazepines, the results of Chapter 7 in this study shows that it is possible for intentional misusers to feign illness to supplement and/or feed their addiction (section 7.3.5.1). The findings in Chapters 6 and 7 showed that young misusers seek prescribers who will prescribe them benzodiazepines. Reducing the number of patients who receive prescriptions for greater than four weeks could help reduce the availability of benzodiazepines to misusers.

Chapters 4 and 5 examined substance misuse amongst young people attending a substance misuse treatment centre in Cork city, Ireland. Firstly, an examination of the differences between attendees from urban and rural areas was examined (Tables 4.1 and 4.2). Secondly, a comparison of regular and non-regular benzodiazepine misusers with respect to substance-related symptoms recorded at admission was conducted (Tables 5.3 and 5.4). The results of these studies showed that the percentage of benzodiazepine and head shop referrals was higher in urban attendees ($P < 0.001$). Benzodiazepine referrals may be higher due to the higher levels of prescribing in urban areas (215). Another Irish study supported this finding in relation to urban preference for head shops (348). The similar levels of lifetime use in the majority of substances showed further evidence for the convergence of urban and rural substance misuse as described in other studies (210, 349). If this convergence continues then it could result in similar

admission levels for benzodiazepine misuse for both urban and rural misusers. Another interesting result was that urban misusers used more substances on a regular basis than rural misusers (Table 4.2). This may appear contradictory however as regular substance misuse can be influenced by other factors such as income; evidence suggests that urban dwellers are at a disadvantage *i.e.* urban areas have a higher level of poverty in comparison to rural areas of Ireland (155).

Chapter 5 illustrates that regular benzodiazepine misusers tend to misuse higher numbers of substances on a regular basis compared with those classified as non-regular misusers. This was to be expected, however the results show that regular benzodiazepine misusers misused two more substances than non-regular misusers (Table 4.2). An explanation for the higher level of regular misuse may be evident from the findings of the interviews in Chapter 7 *i.e.* the participants spoke about two types of benzodiazepines misusers; those who were at an early stage in their misuse and those who were more advanced. The former were described as taking benzodiazepines sporadically whereas the advanced misusers had settled into a pattern of daily benzodiazepine misuse (section 7.3.3.2). It was also described by participants of the interview study how some of those at the advanced stage will have a high level of tolerance which may lead to the progression to other substances such as heroin.

Other interesting results from Chapter 5 include the behavioural signs and physical symptoms that were experienced by regular misusers compared with non-regular misusers (Table 5.4). Loss of interest in sports was one such sign, and participants (Chapter 6) spoke about their decreased motivation and how their school performance was adversely affected. One participant commented that the only thing he wished to do was to stay at home and use drugs (section 6.3.6.1). For misusers experiencing this level of decreased motivation, involvement in sport or other hobbies can be non-existent. Paranoia was also a feature of regular benzodiazepine misuse and according to interviews (Chapter 6) perceptual changes were listed as withdrawal effects experienced by misusers. Paranoia is also a paradoxical side effect of benzodiazepines (247).

Chapter 6 focused on young people who had misused benzodiazepines and their experiences of misuse while in Chapter 7 YCs and GPs were interviewed to give their perspective as trained health-care workers. Common themes emerged from both studies, however the individual studies provided unique insights into youth benzodiazepine misuse. There were shared opinions about the awareness of benzodiazepine's effects. In Chapter 6 participants stated that younger doctors were more aware of misuse and would offer alternatives (section 6.3.5.1) while in Chapter 7, some participants noted that GPs had become more aware of the potential for benzodiazepine misuse (section 7.3.3.1). Reasons given for this included the feeling that older doctors were not aware of the habituation effects of benzodiazepines or that prescribing of benzodiazepines had started in the

treatment of depression (section 7.3.3.1). This gave evidence that newly-trained GPs were taught about the misuse potential of benzodiazepines while it was not known at the time of the predecessors' education.

In relation to misuse of prescribed benzodiazepines, both YCs and young people mentioned that feigning illness was a common strategy used to procure a prescription for benzodiazepines (sections 6.3.5.1 and 7.3.5.1). The GPs did not mention this strategy. They instead spoke about stories from the patient about recently relocating, and wanting to renew their prescription (section 7.3.5.3). This suggests that GPs may not be aware of some of the strategies used by young benzodiazepine misusers. All participants discussed the adverse effects of benzodiazepines on the young person's schooling and education (sections 6.3.6.1 and 7.3.4.1). Participants spoke about how benzodiazepine misuse led to deterioration in school attendance, and if in school, the inability to concentrate. This correlates with evidence on the long-term consequences of benzodiazepine misuse on brain development and on the lower level of educational attainment by those who misuse benzodiazepines (219). Although some misusers may successfully withdraw from benzodiazepines, the many disadvantages associated with a low level of education such as; (i) poorer health, (ii) higher likelihood of unemployment and (iii) poorer social support, remain (286-288).

Chapter 6 participants spoke about the use of benzodiazepines to minimise the severity of the withdrawal effects from stimulants such as cocaine

(section 6.3.7.3). The fact that regular benzodiazepine misuse can occur in conjunction with regular cocaine misuse could provide another explanation for the higher number of regularly misused substances amongst regular benzodiazepine misusers noted in Chapter 4. A contribution to the understanding of benzodiazepine misuse that came from Chapter 7 was the effect that both the family and the community had on the individual's benzodiazepine misuse (section 7.3.2). Parents can influence their children subconsciously by implicitly promoting substance misuse by (i) misusing substances in front of their children or (ii) by their attitude to misuse as described in Chapter 7. Outside of the family, participants thought that the community's perceived attitude to substance misuse could also either promote or dissuade substance misuse. The young people interviewed in Chapter 6 did not mention these as influencing factors but it is possible that their experiences of life outside of their home or outside of their community may be restricted. In their immediate surroundings, their friends and neighbours would have held similar attitudes and so the young people would normalise the acceptance of misuse. This can be contrasted with the participants in Chapter 7 who would have received substance misuse training, but more importantly they would be in regular contact with people from different communities and recognise that different attitudes can exist in communities.

There were suggestions from the interviews on how to reduce the level of misuse. This is important because the results from Chapters 2 and 3 show that benzodiazepine use and misuse are not decreasing among adolescents

less than 18 years. Changes suggested were to tighten restrictions on benzodiazepine prescribing, educating the public on the dangers of benzodiazepine misuse, and to offer patients non-pharmacological alternatives such as CBT (section 7.3.6.3). The first of these suggestions has been proposed by the Irish government as described in Chapter 1 (3). Proposals include making possession of benzodiazepines without a prescription illegal, a requirement for benzodiazepine quantities to be written in words and figures on prescriptions, and monitoring of benzodiazepines not prescribed under a government-subsidised scheme. Examination of the scientific literature failed to find research on the effect of benzodiazepine awareness campaign on levels of prescribing or misuse; however two reviews indicated that public awareness campaigns were capable of reducing prescribing levels (350, 351). Campaigns have also been successful in reducing the use of dependence-forming substances such as alcohol and cigarettes, but one review states that the negative effects of substance use must be prominent (352).

The benefit of alternative therapies such as CBT have been shown in economic evaluations in insomnia and anxiety (353, 354), however these studies compared CBT against standard treatment and so further research should be performed to compare CBT with benzodiazepine treatment. Future work in this area should investigate the utility of these, and implement them if they are found to be beneficial.

8.2 Limitations

There are limitations to the work presented here. Descriptions of the limitations of individual chapters are provided already (sections 2.4.2, 3.4.1, 4.4.2, 5.4.2, 6.4.2, and 7.4.1) so general limitations will be discussed here.

The studies from Chapters 4 and 5 were conducted using data from clients attending a substance misuse centre, while the studies from Chapters 6 and 7 were interview-based, so for different reasons they were not generalisable to all young people in Ireland. The treatment centre clients represent a section of the general population; those who have been referred for substance misuse. This means that the results of these chapters cannot represent substance misuse nationally; however they can provide a means of monitoring trends in substance misuse. For example, the top five misused substances reported were alcohol, tobacco, cannabis, benzodiazepines, and cocaine while the top five misused substance amongst clients in Table 5.2 were the same.

As is the nature with qualitative studies, the interviews in Chapters 6 and 7 cannot be generalised externally to the national population. However, thick description was used to maximise the transferability of the work. The findings of the chapters were also compared with scientific literature to validate the findings.

8.3 Future Work

Future work from this thesis would focus on testing interventions suggested by the work of this thesis that could reduce benzodiazepine and other misuse in young people. A public awareness campaign to highlight the dangers of misusing benzodiazepines could be developed and implemented. Research into the effectiveness of such a campaign would involve surveying adolescents before the campaign and after the campaign about their knowledge of benzodiazepines. Such a survey would ask participants about their perceptions of benzodiazepine misuse in their community, benzodiazepines' dependence-forming ability, and the uses of prescribed benzodiazepines and the side effects associated with prescribed benzodiazepines. Such a survey should capture if a campaign changed the perception of benzodiazepines by adolescents.

The Good Practice Guidelines for Clinicians are 12 years old, and updating the guidelines to reflect recent insights into best practice in benzodiazepine prescribing and the treatment of benzodiazepine dependence is important. The production of new guidelines would remind GPs of the potential dangers associated with benzodiazepine prescribing and would also help them to confidently treat patients with iatrogenic dependence and dependence from other source of benzodiazepines.

Further research needs to be conducted into the applicability of CBT in assisting benzodiazepine treatment. CBT can be used for insomnia and

anxiety but the effectiveness of CBT for these conditions in adolescence needs to be clarified. The potential for CBT to reduce relapse levels in those undergoing treatment for benzodiazepine treatment should be explored.

8.3.1 Conclusion

This thesis has added to the understanding of youth substance misuse in Ireland. Substance misuse has decreased for the three most commonly misused substances, but the fourth, benzodiazepines has not changed in the 12 year period from 2000 to 2012. Benzodiazepine prescribing to young people has increased and a large minority of those patients are prescribed hypnotics which is not in line with national benzodiazepine guidelines. Benzodiazepine misusers attending a treatment centre in Cork are more likely to come from urban areas, and regular misusers are more likely to regularly misuse multiple substances than those that do not regularly misuse. It has contextualised the problems as seen by the client and those who are trying to help them. Family attitude and community perception can influence the level of youth benzodiazepine misuse. It has also highlighted the recommendations favoured by those intimately involved in youth benzodiazepine misuse to reduce benzodiazepine misuse amongst young people but which may also reduce benzodiazepine prescribing nationwide.

9. References

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10. Appendices

10.1 Appendix I - Controlled drugs schedules in Ireland

Schedule 1

- 1-(1,3-Benzodioxol-5-yl)-2-(1-pyrrolidinyl)-pentanone
- 1-Benzylpiperazine
- Bufotenine
- Cannabinol (except where contained in cannabis or cannabis resin)
- Cannabinol derivatives
- Cannabis and cannabis resin (hashish)
- Cathinone
- Coca leaf
- Concentrate of poppy-straw
- [2,3–Dihydro–5–methyl–3–(4–morpholinylmethyl)pyrrolo[1, 2, 3–de]–1,4–benzoxazin–6–yl]–1–naphthalenylmethanone
- 3–Dimethylheptyl–11–hydroxyhexahydrocannabinol
- Eticyclidine
- Etryptamine
- 1-(2-Fluorophenyl)-2-methylaminopropan-1-one
- 1-(3-Fluorophenyl)-2-methylaminopropan-1-one
- 1-(4-Fluorophenyl)-2-methylaminopropan-1-one
- 9-(Hydroxymethyl)–6, 6–dimethyl–3–(2–methyloctan–2–yl)–6a, 7, 10, 10a–tetrahydrobenzo[c]chromen–1–ol
- [9–Hydroxy–6–methyl–3–[5–phenylpentan–2–yl] oxy–5, 6, 6a, 7, 8, 9, 10, 10a octahydrophenanthridin–1–yl] acetate
- Khat (being the leaves of *Catha edulis* (Celastraceae))
- Lysergamide
- Lysergide (and other N-alkyl derivatives of lysergamide)
- Mescaline
- Methcathinone (added by 2010 Regulations)
- 1-(4-Methoxyphenyl)-2-(methylamino)propan-1-one
- 2-Methylamino-1-(3,4-methylenedioxyphenyl)butan-1-one
- 2-Methylamino-1-(3,4-methylenedioxyphenyl)propan-1-one
- -Methyl-4-(methylthio)phenethylamine
- 1-(4-Methylphenyl)-2-methylaminopropan-1-one
- Psilocin

- Raw opium
- Rolicyclidine
- Tenocyclidine
- N,N-Diethyltryptamine
- N.N-Dimethyltryptamine
- N-(1-Benzyl-4-piperidyl) propionanilide
- N-[1(2-Thenyl)- 4-piperidyl] propionanilide
- 2.5-Dimethoxy-∝, 4-dimethylphenethylamine
- N-Hydroxytenamphetamine
- 4-Methyl-aminorex

Schedule 2

- Acetorphine
- Acetylmethadol
- Alfentanil
- Allylprodine
- Alphacetylmethadol
- Alphameprodine
- Alphamethadol
- Alphaprodine
- Anileridine
- Benzethidine
- Benzylmorphine
- Betacetylmethadol
- Betameprodine
- Betamethadol
- Betaprodine
- Bezitramide
- Carfentanil
- Clonitazene
- Cocaine
- Codoxime

- Desomorphine
- Dextromoramide
- Diampromide
- Diethylthiambutene
- Difenoxin
- Dihydroetorphine
- Dihydromorphine
- Dimenoxadole
- Dimepheptanol
- Dimethylthiambutene
- Dioxaphetyl butyrate
- Diphenoxylate
- Dipipanone
- Drotebanol
- Ecgonine
- Ethylmethylthiambutene
- Etonitazene
- Etorphine
- Etoxeridine
- Fentanyl
- Furethidine
- Heroin
- Hydrocodone
- Hydromorphinol
- Hydromorphone
- Hydroxypethidine
- Isomethadone
- Ketobemidone
- Levomethorphan
- Levomoramide
- Levophenacylmorphan
- Levorphanol
- Lofentanil
- Medicinal opium

- Metazocine
- Methadone
- Methyldesorphine
- Methyldihydromorphine
- Metopon
- Morpheridine
- Morpine
- Morphine methobromide
- Myrophine
- Nabilone
- Nicomorphine
- Noracymethadol
- Norlevorphanol
- Normethadone
- Normorphine
- Norpipanone
- Oripavine
- Oxycodone
- Oxymorphone
- Pethidine
- Phenadoxone
- Phenampromide
- Phenazocine
- Phencyclidine
- Phenomorphan
- Phenoperidine
- Piminodine
- Piritramide
- Proheptazine
- Properidine
- Racemethorphan
- Racemoramide
- Racemorphan
- Remifentanil

- Sufentanil
- Tapentadol
- Thebacon
- Thebaine
- Tilidine
- Trimeperidine
- 4-Cyano-2-dimethylamino-4,4-diphenylbutane
- 4-Cyano-1-methyl-4-phenylpiperidine
- 2- Methyl-3-morpholino-1, 1-diphenylpropanecarboxylic acid
- 1-Methyl-4-phenylpiperidine-4-carboxylic acid
- 1-Phenylcyclohexylamine
- 4 Phenylpiperidine-4-carboxylic acid ethyl ester
- 4-(1-Phenylcyclohexyl) morpholine
- 1-Piperidinocyclohexanecarbonitrile
- 1-[1-(2-Thienyl)cyclohexyl] pyrrolidine
- 4-[1-(-2-Thienyl)cyclohexyl]morpholine
- Substances
- Acetyldihydrocodeine
- Amineptine
- Amphetamine
- Amphetaminil
- Benzphetamine
- Buprenorphine
- Butorphanol
- Codeine
- Dexamphetamine
- Dextropropoxyphene
- Dihydrocodeine
- Ethylmorphine (3-ethylmorphine)
- Fenethylline
- Glutethimide
- Lefetamine
- Mecloqualone
- Methaqualone

- Methylamphetamine
- Methylphenidate
- Nalbuphine
- Nicocodine
- Nicodicodine (6-nicotinoyldihydrocodeine)
- Norcodeine
- Phendimetrazine
- Phenmetrazine
- Pholcodine
- Propiram
- Quinalbarbitone
- N-Ethylamphetamine
- Zipeprol

Schedule 3

- Cathine
- 1-(3-Chlorophenyl)-4-(3-chloropropyl)piperazine
- 1-(3-Chlorophenyl)piperazine
- Chlorphentermine
- Diethylpropion
- Ethchlorvnol
- Ethinamate
- Flunitrazepam
- 4-Hydroxybutanoic acid
- Ketamine
- Mazindol
- Mephentermine
- Meprobamate
- Methyprylone
- Pemoline
- Pentazocine
- Phentermine

- Pipradrol
- Temazepam

Schedule 4

- Alprazolam
- Aminorex
- Bromazepam
- Brotizolam
- Camazepam
- Chlordiazepoxide
- Clobazam
- Clonazepam
- Clorazepic Acid
- Clotiazepam
- Cloxazolam
- Delorazepam
- Diazepam
- Estazolam
- Ethyl loflazepate
- Fencamfamin
- Fenproporex
- Fludiazepam
- Flurazepam
- Halazepam
- Haloxazolam
- Ketazolam
- Loprazolam
- Lorazepam
- Lormetazepam
- Medazepam
- Mefenorex
- Mesocarb

- Midazolam
- Nimetazepam
- Nitrazepam
- Nordazepam
- Oxazepam
- Oxazolam
- Pinazepam
- Prazepam
- Propylhexedrine
- Pyrovalerone
- Selegiline
- Tetrazepam
- Triazolam
- Zolpidem

Schedule 5

- (a) Any preparation of one or more of the substances to which this paragraph applies (not being a preparation designed for administration by injection) when compounded with one or more other ingredients and which contains a total of not more than 100 milligrammes of the substance or substances (calculated as base) per dosage unit and which in the case of an undivided preparation has a total concentration of not more than 2.5 per cent of the substance or substances (calculated as base).

  (b) The substances to which this paragraph applies are acetyldihydrocodeine, codeine, ethylmorphine (3-ethylmorphine), nicocodine, nicodicodine (6-nicotinoyldihydrocodeine), norcodeine, pholcodine and their respective salts.

- Any preparation of dihydrocodeine (not being a preparation designed for administration by injection) containing, per dosage unit, not more than 10 milligrammes of dihydrocodeine (calculated as base) and which in the case of an undivided preparation has a concentration of not more than 1.5 per cent of dihydrocodeine (calculated as base).

- Any preparation of cocaine containing not more than 0.1 per cent of cocaine calculated as cocaine base, being a preparation which is compounded with one or more other ingredients in such a way that the cocaine cannot be readily recovered.

- Any preparation of medicinal opium or of morphine containing, in either case, not more than 0.2 per cent of morphine calculated as anhydrous morphine base, being a preparation which is compounded with one or more other ingredients in such a way that the opium or morphine cannot be readily recovered.

- Any preparation of dextropropoxyphene, being a preparation designed for oral administration, containing not more than 135 milligrammes of dextropropoxyphene (calculated as base) per dosage unit or with a total concentration of not more than 2.5 per cent, (calculated as base) in undivided preparations.

- Any preparation of difenoxin containing, per dosage unit, not more than 0.5 milligrammes of difenoxin and a quantity of atropine sulphate equivalent to at least 5 per cent of the dose of difenoxin.

- Any preparation of diphenoxylate containing, per dosage unit, not more than 2.5 milligrammes of diphenoxylate calculated as base, and a quantity of atropine sulphate equivalent to at least 1 per cent of the dose of diphenoxylate.

- Any preparation of propiram containing, per dosage unit, not more than 100 milligrammes of propiram calculated as base and which is compounded with at least the same amount, by weight, of methylcellulose.

- Any powder of ipecacuanha and opium comprising 10 per cent powdered opium, 10 per cent powdered ipecacuanha root, both well mixed with the remaining 80 per cent consisting of any other powdered ingredient which contains no controlled drug.

- Any mixture containing one or more of the preparations specified in this Schedule, being a mixture of which none of the other ingredients is a controlled drug.

Schedule 8

Part 1 - Drugs for pain relief in hospital

- Morphine sulphate
- Codeine phosphate

Part 2 - Drugs for palliative care

- Morphine sulphate
- Hydromorphone
- Oxycodone

- Buprenorphine
- Fentanyl
- Methylphenidate
- Codeine phosphate

Part 3 - Drugs for purposes of midwifery

- Pethidine

Part 4 - Drugs for neonatal care in hospital

- Morphine sulphate Fentanyl
- Fentanyl

10.2 Appendix II - Draft Misuse of Drugs (Amendment) Regulations, 2013

An Roinn Sláinte
DEPARTMENT OF HEALTH

Tús Áite do Shábháilteacht Othar
Patient Safety First

CONSULTATION

DRAFT Misuse of Drugs (Amendment) Regulations, 2013

to amend the Misuse of Drugs Regulations, 1988 as amended

August 2013

INTRODUCTION

What is the purpose of this consultation?

The purpose of this consultation is to seek input from stakeholders and interested parties on the text of Draft Misuse of Drugs (Amendment) Regulations 2013 which will amend the Misuse of Drugs Regulations 1988. The text of the Draft Misuse of Drugs (Amendment) Regulations is enclosed. The purpose of this document is to explain the changes in law proposed to be made by means of the Draft Misuse of Drugs (Amendment) Regulations.

Interested organisations, stakeholders and individuals are invited to make a written submission containing their comments on the Draft Misuse of Drugs (Amendment) Regulations 2013 to Controlled_Drugs@health.gov.ie by 30 August 2013.

What is the background to this consultation?

This consultation on the text of Draft Misuse of Drugs (Amendment) Regulations follows on from a scoping consultation which took place with stakeholders during late Summer/Autumn 2012 regarding the introduction of measures to address the problem of the illicit trading and supply of certain prescription medicines, such benzodiazepines[1] and z-drugs[2], and other updates to the Misuse of Drugs Regulations.

During the scoping consultation in Summer/Autumn 2012, the Department engaged with a wide range of organisations including: medical, pharmacy and nursing organisations; patient organisations; representatives of the pharmaceutical industry; representatives of pharmaceutical wholesalers; other relevant Government Departments and statutory bodies. Consultations also took place with an Garda Siochána, the Customs Service of the Revenue Commissioners, the Irish Medicines Board and the Forensic Science Laboratory on issues specific to the illicit supply of benzodiazepines and z-drugs.

[1] Benzodiazepines are a group of prescription medicines commonly used to treat anxiety, sleep disturbance and insomnia. Inappropriate use of benzodiazepines medicines can be associated with dependence and withdrawal symptoms.

[2] "Z drugs" refers to a group of prescription medicines (zopiclone, zolpidem and zaleplon) which are used to treat insomnia. There are reports of dependence to these medicines when inappropriately used. Only one of the three z-drugs, zolpidem, is currently controlled under the Misuse of Drugs Regulations.

Arising from the scoping consultation process, draft Regulations to amend the Misuse of Drugs Regulations, 1988 were prepared. The purpose of this second phase consultation is to seek input from stakeholders and interested parties on the Draft Misuse of Drugs (Amendment) Regulations 2013 which are enclosed.

What are the Misuse of Drugs Regulations, 1988?

All medicines are categorised as either prescription medicines or non-prescription medicines. Prescription medicines are supplied by a pharmacist from a pharmacy on foot of a prescription written by a medical practitioner, a nurse prescriber in certain circumstances or a dentist in the case a dental treatment.

Some substances and medicines have a high potential for misuse and these substances are subject to additional and stricter controls under the Misuse of Drugs legislation. The Misuse of Drugs Act 1977 as amended, is the legislation under which substances deemed to have potential for misuse are subject to control. The Schedule to the Act lists the substances controlled as "controlled drugs" in Ireland, and under section 2 of the Act, the Government may, from time to time, update this list of controlled drugs by declaring new substances to be controlled.

Once a substance is declared a "controlled drug" by the Government, the Minister for Health makes Regulations setting out in detail the level of control which will apply to each controlled drug, depending on the drug in question, its medicinal value and its potential for misuse.

The Misuse of Drugs Regulations, 1988 are the regulations made by the Minister for Health which specify the levels of control that apply to different "controlled drugs". These Regulations categorise controlled drug substances into five schedules (ranging from the most strictly controlled in Schedule 1 to the least strictly controlled in Schedule 5) and apply controls on the manufacture, production, importation, exportation, supply and possession of listed controlled drugs, depending on the extent to which these drugs are used for medical or scientific purposes and the potential of the substances to be misused.

The Regulations also set out the rules governing: the prescribing, supply and administration of controlled drugs within the health system; the keeping of records; arrangements for destruction or disposal of these drugs; and provisions regarding possession of forged prescriptions.

The Misuse of Drugs Regulations 1988 have been amended on nine occasions since 1988 (i.e. in 1993, 1999, 2006, 2007, twice in 2009, twice in 2010, and in 2011). An unofficial consolidated version of the Misuse of Drugs Regulations 1988 containing all of the amendments made to those Regulations is provided for ease of reference as part of this consultation.

What is the purpose of the Draft Misuse of Drugs (Amendment) Regulations?

The Draft Misuse of Drugs (Amendment) Regulations 2013 contain a number of amendments to the Misuse of Drugs Regulations 1988 which will, in summary:

- Strengthen controls on the import, export and possession of benzodiazepines and z-drugs to address the problem of illicit trading in these products by:

- introducing a requirement to obtain a **licence to import or export** benzodiazepine and z-drug substances, thus making it an offence to import or export without a licence (this is in compliance with Ireland's obligations under UN Resolutions[3]),
- introducing an **offence of unauthorised possession** of benzodiazepine and z-drug substances,
- introducing **stricter prescribing and dispensing rules** on benzodiazepines and z-drugs,
- **controlling additional benzodiazepines** (phenazepam) and z-drugs (zopiclone and zaleplon).

- Improve and update the rules governing the **prescribing and supply of benzodiazepines** and z-drugs within the health system.

- Amend the Regulations to allow a **newly authorised medicinal product containing cannabis extract** to be prescribed, supplied and used by patients. The product Sativex® (nabiximols) has been authorised in other EU Member States for the relief of symptoms of spasticity in multiple sclerosis.

- Apply new **controls** or update the level of controls under the Misuse of Drugs Regulations in relation to the following substances:
  - apply controls to 36 Phenylethylamine derivatives (Pihkals),
  - apply controls to approximately 60 anabolic steroids,
  - apply controls to the new psychoactive substance – 5-IT,
  - apply controls to the new medicinal product lisdexamfetamine,
  - increase the level of control on Gamma-hydroxybutanoic acid in accordance with international guidance.

- Update the list of controlled drugs and the clinical situations in which those controlled drugs may be prescribed by **nurse prescribers**.

- Introduce a requirement for community pharmacies to **notify all controlled drug prescriptions (both public and private) to the Minister or body nominated by him,** for public health reasons to provide a full picture of the extent of controlled drug prescribing and dispensing.

- Update the **prescription-writing rules for methadone prescriptions** to remove the requirement for methadone prescriptions to be handwritten, in line with the recommendation of the *Introduction of the Opioid Treatment Protocol Report*[4].

[3] UN ECOSOC Resolutions 1987/30 and 1991/44
[4] http://www.drugs.ie/resourcesfiles/reports/Opioid_Treatment_Protocol.pdf

Enclosed with this explanatory document is the text of a Draft Misuse of Drugs (Amendment) Regulations 2013. The draft Misuse of Drugs (Amendment) Regulations will amend the Misuse of Drugs Regulations 1988. The purpose of this document is to provide an explanation of the proposed amendments to the Misuse of Drugs Regulations 1988 set out in the draft Misuse of Drugs (Amendment) Regulations.

Throughout this explanatory document:

- the term "Principal Regulations" refers to the Misuse of Drugs Regulations 1988 including all of its amendments since 1988,
- the term "Draft Regulations" is used to refer to the Draft Misuse of Drugs (Amendment) Regulations which are the subject of the current consultation.

In the following sections, an explanation is provided of the purpose of each Regulation of the draft Misuse of Drugs (Amendment) Regulations.

Regulation 1: *Collective Citation*

The Misuse of Drugs Regulations were made in 1988 but have been amended nine times since then, most recently in 2010 and 2011 to introduce controls on new psychoactive substances, commonly called "legal highs". Regulation 1(1) specifies that the name of these amending regulations is to be the Misuse of Drugs (Amendment) Regulations, 2013. Regulation 1(2) creates the collective citation "Misuse of Drugs Regulations 1988 to 2013" to refer to the Misuse of Drugs Regulations 1988 and all its amending Regulations.

Regulation 2*: Commencement*

While it is intended that most of the provisions of the Regulation will enter into force as soon as the Regulations are signed by the Minister, it is proposed that the commencement of certain provisions will be deferred to allow sufficient time to put in place the necessary implementation measures.

Provisions which will come into force **6 months after signing** of the Regulations:

- the **new Article 13** (other than Article 13(2)(a)) and **the amendments to Article 14** which set out the new prescribing and dispensing rules applicable to Schedule 4 Part 1 controlled drugs i.e. benzodiazepines and z-drugs.

Provisions which will come into force **1 year after signing** of the Regulations:

- the **new Article 13(2)(a)** (amended by Regulation 10 of the Draft Regulations) which provides for a pro-forma prescription for Schedule 2, 3 and 4 Part 1 controlled drugs, and

- the **new Article 16A** (inserted by Regulation 13 of the Draft Regulations) which provides for notification of all Schedule 2, Schedule 3 and Part 1 of Schedule 4 prescriptions to the HSE.

Regulation 3: *Interpretation*

Regulation 3 entitled *Interpretation* clarifies that the term "Principal Regulations" used throughout the Draft Regulations is intended to cover the Misuse of Drugs Regulations 1988 and all of its amending Regulations.

Regulation 4: *Amendment of Article 3 of the Principal Regulations (Interpretation)*

Article 3 of the Principal Regulations deals with *Interpretation* in those Regulations and sets out the key definitions applicable throughout those Regulations.

Regulation 4 of the Draft Regulations inserts a **new definition of "marketing authorisation**" into the Principal Regulations. This new definition is relevant to Regulations 16 and 17 of the Draft Regulations (which amend Schedule 1 and Schedule 2 to the Principal Regulations respectively) dealing with the controls on **medicinal products containing cannabis extract**.

Only medicinal products containing cannabis extract which have been granted a marketing authorisation by the Irish Medicines Board, by the European Commission, or by a medicines agency of an EEA country including the Swiss Confederation, may be prescribed and supplied to patients in Ireland.

Regulation 5: *Amendment of Article 3A of the Principal Regulations (Provisions applicable to Practitioners who are registered nurses)*

Regulation 5 and Regulation 21 of the Draft Regulations, when read together, **expand the list of controlled drugs and the clinical settings in which those drugs may be prescribed by nurse and midwife prescribers**.

By way of background, in 2007 the Principal Regulations were amended to provide for prescribing by nurses of specified controlled drugs via specified routes of administration and in a limited number of settings.

Article 3A of the Principal Regulations sets out the rules governing nurse-prescribing of controlled drugs, and Schedule 8 to those Regulations lists the controlled drugs which may be prescribed by nurses. In 2009 a *National Independent Evaluation of the Nurse and Prescribing Initiative in Ireland*[5] was published and it recommended that the rules governing nurse prescribing of controlled drugs should be updated to provide for additional clinical settings in which nurse prescribers may prescribe Schedule 2 and 3 controlled drugs. A consultation process took place with nurse and medical prescribers during the Summer of 2012 in relation to this.

Regulation 5 of the Draft Regulations will amend Article 3A(2)(d) of the Principal Regulations to expand the clinical settings in which nurse prescribers may prescribe listed controlled drugs. In addition, Regulation 21 of the Draft Regulations amends Schedule 8 to the Principal Regulations to expand the list of controlled drugs which may be prescribed by nurse prescribers in specified settings.

[5] http://www.hse.ie/eng/services/Publications/services/Hospitals/prescribing_initiative.pdf

Regulation 6: *Amendment of Article 4 of the Principal Regulations (General prohibitions)*

Article 4 of the Principal Regulations entitled "General Prohibitions" provides that a person may not produce, supply or offer to supply, import or export a controlled drug except where permitted under the Regulations.

Regulation 6 of the Draft Regulations will amend Article 4(2) of the Principal Regulations. The effect of this amendment will be that **it will be prohibited to import or export substances listed in:**

- **Schedule 2,**
- **Schedule 3 (including flunitrazepam and temazepam), and**
- **Part 1 of Schedule 4 (including benzodiazepines and z-drugs)**

except in accordance with a licence.

This amendment will now mean that anyone wishing to import or export benzodiazepines or z-drugs may only do so in accordance with a licence. Persons importing such substances without licence will be guilty of an offence. This amendment will assist the Revenue Commissioner's Customs Service in fighting the illicit importation of these drugs. In addition, by implementing a licensing requirement for the import or export benzodiazepines, Ireland is fulfilling its obligations under UN ECOSOC Resolutions 1987/30 and 1991/44.

Regulation 7: *Amendment of Article 9 of the Principal Regulations (General exemptions)*

Regulation 7 of the Draft Regulations will amend Article 9 of the Principal Regulations entitled "General Exemptions". Article 9 when read with Article 11 of the Principal Regulations allows certain categories of people to have controlled drugs in their possession for the purposes of their professions e.g.:

- Health professionals such as medical practitioners, pharmacists, nurses, and other prescribers,
- Persons with a general authority to have a controlled drug in their possession in the course of their duties e.g. members of the Gardaí, Customs officials, postal workers, prison officers etc.
- Patients or carers in possession of controlled drugs on foot of a prescription written by a practitioner.

The effect of this amendment to Article 9 is that it will become **an offence for anyone to possess a benzodiazepine or a z-drug**, unless the person is expressly permitted to do so under the Regulations e.g. on foot of a prescription or on foot of a legal authority by virtue of the person's profession.

Regulation 8: *Amendment of Article 11 of the Principal Regulations (General Authorities)*

Article 11(2) of the Principal Regulations deals with the return of unused controlled drugs and allows a person to return a controlled drug to the person from whom he obtained it.

The proposed new Art 11(3) will **allow a person to return out-of-date or unused / unwanted controlled drugs to a pharmacist *other* than the pharmacist or practitioner who originally supplied the controlled drug.** In relation to veterinary medicines which are controlled drugs, the proposed new Art 11(4) is intended to allow controlled drugs be returned to either a pharmacist or a veterinary surgeon.

It should be noted that references to "keeping open shop" in the Principal Regulation are, under section 75(2) of the Pharmacy Act 2007, to be construed as a reference to a retail pharmacy business registered under the Pharmacy Act 2007.

Regulation 9: *Amendment of Article 12 of the Principal Regulations (Documents to be obtained by a supplier)*

Article 12 of the Principal Regulations deals with the documentation which must be received by persons supplying controlled drugs (e.g. pharmacists, pharmaceutical wholesalers etc.). This Article specifies: the contents of requisitions; the persons that may issue requisitions; the obligations on wholesalers to provide receipts with consignments of controlled drugs; and the responsibilities of pharmacists to check consignments of controlled drugs received.

Article 12(9) of the Principal Regulations currently states that these controls do not apply to any drug specified in Schedule 4 or 5, which would include benzodiazepines and z-drugs. In order to impose additional controls on benzodiazepines and z-drugs to counter illicit trade in these medicines, it is proposed that Regulation 9 of the Draft Regulations will amend Article 12(9) of the Principal Regulations to have the effect that the **documentation requirements will apply also to drugs in Schedule 4 Part 1** (ie benzodiazepines and z-drugs).

Regulation 10: *Amendment of Article 13 of the Principal Regulations (Forms of prescriptions)*

Regulation 10 of the Draft Regulations will replace Article 13 of the Principal Regulations in its entirety. It is proposed to replace Art 13 in order to:

- simplify and clarify the existing provisions,
- provide for stricter controls on the prescribing benzodiazepines and z-drugs, and
- introduce a new pro-forma or template prescription form for controlled drugs in Schedules 2, 3 and 4 Part 1.

Article 13 currently provides that a prescriber shall not issue a prescription for a controlled drug in Schedules 2 or 3 unless:

- he or she is satisfied as to the identity of the patient,
- certain provisions of the prescription are in the prescriber's own handwriting,
- instructions regarding dosage and how the medicine is to be dispensed are handwritten, and
- directions are given if the medicine is to be dispensed in instalments.

By substituting a new Article 13 into the Principal Regulations the main changes to Art 13 will be as follows:

- Prescriptions for Schedule 2, 3 and 4 Part 1 drugs will be required to be written on a **pro-forma or template prescription form** issued by the Minister or on the Minister's behalf. This will come into effect 1 year after signing of the Regulations. The proforma prescription will not be required to be used in public hospitals or nursing homes.

- The **controlled drug prescription-writing requirements** (other than the controlled drug prescription handwriting-requirements) **will now apply to benzodiazepines and z-drugs**, in order to better protect against the misuse potential of these substances.

- The **total quantity** of Schedules 2, 3 and 4 Part 1 controlled drugs that may be prescribed on a controlled drug prescription will be limited to what is reasonably required by the patient for **3 months** treatment. However, an exemption will apply to Schedule 4 Part 1 drugs, where the prescriber indicates in his or her own handwriting that a greater quantity (up to a maximum of 6 months' supply) is necessary for the treatment of the patient. This exemption is to provide for the treatment of persons with certain long-term conditions in line with views expressed during the consultation.

- An exemption from the **controlled drug prescription handwriting requirements** will also be provided for prescriptions **for methadone**. This is in line with the recommendation of the *Introduction of the Opioid Treatment Protocol Report*[6]. It is considered that the other precautionary regulatory measures which apply to methadone prescriptions (i.e. prescribing by specified prescribers, dispensing from specified pharmacies and registration of the patient on the Central Treatment List) are sufficient safeguards against forged prescriptions.

Regulation 11: *Amendment of Article 14 of the Principal Regulations (Supply on prescription)*

Article 14 of the Principal Regulations sets out the requirements applicable to pharmacists or other persons engaged in supplying and dispensing controlled drugs.

Regulation 11 of the Draft Regulations will amend Article 14 of the Principal Regulations to apply the controlled drug dispensing rules to Schedule 4 Part 1 controlled drugs also (i.e. benzodiazepines and z-drugs). These amendments apply stricter rules to the dispensing of Schedule 4 Part 1 prescriptions, which mirror the stricter prescribing rules provided for in the amendment of Article 13. The obligations on pharmacists which exist for Schedule 2 and 3 controlled drugs will be extended to benzodizepines and z-drugs, i.e. the prescriber must be known to the pharmacist, and the pharmacist must be satisfied as to the identity of the patient.

Most importantly, like prescriptions for Schedule 2 and Schedule 3 controlled drugs, benzodiazepine prescriptions will no longer ordinarily be of 6 months' duration, but instead will be valid for 14 days (unless there are instalments in which case the prescription will be ordinarily valid for up to 2 months).

However, it is recognised that there are some medical conditions that require ongoing treatment with benzodiazepines and therefore it is necessary to provide an exception to allow certain benzodiazepine prescriptions be valid for up to 6 months. The exception is intended only to apply where the prescriber has indicated in his/her own handwriting on the prescription that treatment of longer than 2 months' duration is necessary for the patient.

Regulation 12: *Amendment of Article 15 of the Principal Regulations (Marking of containers)*

Article 15 of the Principal Regulations sets out the rules governing the labelling of containers containing controlled drugs. Regulation 12 will amend Art 15 so that the rules governing labelling of containers will also apply to drugs in Schedule 4 Part 1 (i.e. benzodiazepines and z-drugs).

Regulation 13: *Amendment of the Principal Regulations by insertion of Article 16A (Furnishing particulars in relation to drugs in Schedules 2, 3 and Part 1 of Schedule 4)*

[6] http://www.drugs.ie/resourcesfiles/reports/Opioid_Treatment_Protocol.pdf

Regulation 13 of the Draft Regulations proposes to insert a new Article 16A into the Principal Regulations. The purpose of the new Article 16A is to require that all prescriptions for Schedule 2, 3 or 4 Part 1 drugs must be notified to the Minister or a body designated by the Minister, other than veterinary prescriptions and prescriptions dispensed in public hospitals or public nursing homes or dispensed in a prison.

Currently, only prescriptions which are reimbursed under the State schemes are notified to the Primary Care Reimbursement Service (PCRS) of the HSE. This means that the State has no information on private prescribing of controlled drugs.

The draft Regulation 13 proposes that the notification will be done by means of monthly returns to the Minister (or other body designated by the Minister, such as the HSE) of all Schedule 2, 3 or 4 Part 1 controlled drugs dispensed or supplied for the purposes of human health.

A recent initiative undertaken by the HSE using data on the frequency of supply of benzodiazepines, provided prescribers with useful information on prescribing and usage trends in comparison with weighted average prescribing rates, thus allowing prescribers to review their prescribing practice.

Increased visibility of controlled drug prescribing, both funded under the Community Drugs Schemes and paid for privately, is in line with the recently-adopted EU Action Plan on Drugs (2013 -2016)[7], in accordance with which EU Member States are to collect and collate data on levels and patterns of prescribing of psychoactive medicines as a mean of addressing the misuse of prescribed opioids and other psychoactive medicines. This is also in line with the National Drugs Strategy 2009-2016[8], which states that the monitoring of private prescribing needs to be addressed.

Regulation 14: *Amendment of Article 18 of the Principal Regulations (Keeping of records for drugs in Schedules 3 and 4)*

Regulation 14 of the Draft Regulations will amend Article 18 of the Principal Regulations to require persons holding a licence under section 14 of the Misuse of Drugs Act to additionally retain records of all Schedule 4 Part 1 drugs imported or exported. Also, a person authorised under Article 8(5) of the Principal Regulations will now also be required to retain records of any Schedule 4 Part 2 imported or exported.

Regulation 15: *Amendment of Article 20 of the Principal Regulations (Preservation of records for drugs in Schedules 3, 4 and 5)*

Regulation 15 of the Draft Regulations replaces Article 20 of the Principal Regulations. Article 20 of the Principal Regulations provides for a range of records to be kept by the different players involved in the supply of controlled drugs contained in Schedules 3 and 5. These records are required to be kept for a minimum of 2 years.

The purpose of this amendment is to **extend and clarify the record-keeping requirements relating to Schedule 4 drugs.**

Article 20 will now provide that:

[7] http://register.consilium.europa.eu/pdf/en/13/st09/st09963.en13.pdf, Action 1.4

- producers and wholesalers must keep all relevant records (eg invoices) relating to quantities of Schedule 3, 4 or 5 controlled drugs obtained or supplied,

- pharmacists or matrons in hospitals, persons authorised under Art 8(5), and persons in charge of a laboratory must keep all relevant records relating to quantities of Schedule 3 or Schedule 4 Part 1 controlled drugs obtained or supplied, and

- pharmacists in a community pharmacy must keep all relevant records relating to:
  - quantities of Schedule 3 or Schedule 4 Part 1 controlled drugs obtained or supplied, and
  - quantities of Schedule 4 Part 2 and Schedule 5 controlled drugs obtained.

Regulation 16: *Amendment of Schedule 1 to the Principal Regulations*

The Misuse of Drugs Regulations classify substances which have been declared controlled drugs into five schedules, permitting different levels of control to apply to the different categories of controlled drugs.

Schedule 1 includes raw opium, coca leaf and major hallucinogenic drugs (eg LSD, mescaline, etc) which have little, if any therapeutic value but which have a strong potential for misuse. Substances listed in Schedule 1 are utterly prohibited, meaning that it is an offence to manufacture, produce, import, export, supply and possess these substances. A special licence is required for any activity in respect of these drugs.

Regulation 16 of the Draft Regulations amends Schedule 1 to the Principal Regulations in two main ways:

a) Regulation 16, paragraphs (a) and (b) amend the terms "cannabinol derviatives" and "cannabis and cannabis resin" to exclude from Schedule 1 certain medicinal products containing cannabis extract,

In order to enable medicinal products containing cannabis extract to be prescribed and dispensed in Ireland, it is necessary to amend Schedule 1 in order to exclude specific medicinal products containing cannabis extract from Schedule 1 while retaining existing controls on cannabis, in line with Government policy. The product Sativex® (nabiximols) which contains cannabis extract has been authorised in some EU Member States for the relief of symptoms of spasticity in multiple sclerosis.

b) Regulation 16 paragraph (c) inserts a list of 36 phenethylamine ("Pihkals") psychoactive substances into Schedule 1, as well as the substance 5-IT.

The additional substances listed, so-called Pihkals, have hallucinogenic properties similar to Ecstasy. They have been controlled in other countries but have not, as yet, been controlled in Ireland.

The substance 5-IT (also known as 5-(2-aminopropyl)indole) has been associated with a number of deaths within the EU and the EU Commission has recently published a Proposal for a Council Decision to control this substance at EU level[9].

[8] http://www.dohc.ie/publications/pdf/nds_2009-16.pdf?direct=1, Recommendation 4.37
[9] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2013:0436:FIN:EN:PDF

Regulation 17: *Amendment of Schedule 2 to the Principal Regulations*

Schedule 2 of the Misuse of Drugs Regulations contains substances with known therapeutic value but the high potential to be misused. Schedule 2 includes opiates, such as morphine and heroin, major stimulants such as the amphetamines, and synthetic narcotics such as pethidine, hydromorphone and buprenorphine.

Regulation 17 of the Draft Regulations amends Schedule 2 of the Principal Regulations to:

- insert certain **medicinal products containing cannabis extract** so that such products may be prescribed and dispensed and used in Ireland, thus applying the strictest level of control to this product until further information is available as to its profile of use and potential for abuse,

- move the substance 4-Hydroxybutanoic acid (commonly known as gamma-hydroxybutyric acid, GHB) from Schedule 3 to Schedule 2 in line with the decision taken at the 56th session of the United Nations Commission on Narcotic Drugs in March 2013[10], based on a recommendation by the World Health Organisation, to increase the level of control on to GHB by moving it to Schedule II of the UN Convention on Psychotropic Substances,

- insert the substance lisdexamfetamine, a new amphetamine-type medicine, which has been authorised in some EU countries for the treatment of ADHD in children.

Regulation 18: *Amendment of Schedule 3 to the Principal Regulations*

Schedule 3 of the Misuse of Drugs Regulations includes most barbiturates, some potent analgesics, minor stimulants, as well as benzodiazepines flunitrazepam and temazepam.

When read with Regulation 17 of the Draft Regulations as explained above, Regulation 18 deletes 4-Hydroxybutanoic acid (commonly known as gamma-hydroxybutyric acid, GHB) from Schedule 3.

Regulation 19: *Amendment of Schedule 4 to the Principal Regulations*

Schedule 4 includes benzodiazepines (other than flunitrazepam and temazepam) and low strength phenobarbitone preparations.

In line with policy to control the illicit trade in benzodiazepines and z-drugs and strengthen applicable prescribing and dispensing rules, Regulation 19 of the Draft Regulations proposes to divide Schedule 4 into two parts: Part 1 and Part 2, thus allowing different controls to be applied to benzodiazepines listed in Schedule 4 Part 1 and the other substances listed in Schedule 4 Part 2.

In addition, 3 new substances are proposed to be inserted into Schedule 4 Part 1, namely phenazepam, zaleplon and zopiclone.

A range of new anabolic steroids will be inserted into the new Part 2 of Schedule 4.

[10] http://www.unodc.org/documents/commissions/CND-Res-2011to2019/CND-Res-2013/CND-DEC-56-1.pdf

Regulation 20: *Amendment of Schedule 5 to the Principal Regulations*

Schedule 5 of the Principal Regulations lists low-strength preparations exempt from most of restrictions under the Regulations which would normally be applicable to Schedule 2 substances.

In Regulation 20 of the Draft Regulations it is proposed that Schedule 5 should be divided into two parts: Schedule 5 Part 1 and a new Schedule 5 Part 2. In Schedule 5 Part 1, paragraph 4 is to be amended to restrict the exemption to preparations of **medicinal opium or morphine not for injection**.

Regulation 20 of the Draft Regulations proposes to move the low strength non-injectable **barbiturate** products from Schedule 4 Part 2 to the new Schedule 5 Part 2 and **selegiline** from Schedule 4 Part 1 to Schedule 5 Part 2.

Regulation 21: *Amendment of Schedule 8 to the Principal Regulations (Drugs which practitioners who are registered nurses may prescribe within Schedules 2 and 3)*

As explained under Regulation 5 above, Regulation 21 of the Draft Regulations amends Schedule 8 to the Principal Regulations to update the list of controlled drug substances that may be prescribed by **nurse prescribers**.

Regulation 22: *Transitional provision*

The amendments to Article 13 and 14 of the Principal Regulations introduce new controlled drug prescription and dispensing rules. Regulation 22 is intended to set out the transitional arrangements applicable to prescriptions for Schedule 2, 3 and Schedule 4 Part 1 drugs, written before the date of coming into force of the new controlled drug prescription and dispensing rules but which are still valid for a period of time after that date.

Prescriptions for Schedule 2, 3 and 4 Part 1 drugs issued before the date of coming into force of the new prescribing and dispensing rules but which do not comply with the new controlled drug prescription-writing requirements, may be dispensed up until the date of expiry of those prescriptions and in any event no later than six months after the coming into force of the changes to Articles 13 and 14 of the Principal Regulations which introduce new controlled drug prescription-writing and dispensing rules.

10.3 Appendix III – Substance use in young persons in Ireland

Addictive Behaviors 38 (2013) 2392–2401

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Addictive Behaviors

Substance use in young persons in Ireland, a systematic review

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HIGHLIGHTS

- Systematic review of the levels of drug use in Irish 13–24year olds from 2000.
- Drugs included in the review are tobacco, alcohol, cannabis and benzodiazepines.
- Tobacco, alcohol and cannabis levels have mostly fallen over the review period.
- Benzodiazepine levels have been generally static over the review period.

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ABSTRACT

Adolescence is a time of physical and mental development when small changes can impact on the rest of a person's life. Substance use in this crucial period can have long-lasting consequences for the individual and for society. The prevalence of substance use in young people is an area of concern for policy makers and health workers. This systematic review looked at prevalence for four substances: alcohol, tobacco, cannabis, and benzodiazepines, across the Republic of Ireland for persons between the ages of 13 and 24, and compared usage between 2000 and 2012. Eighteen articles were included in the review. It was seen that tobacco, alcohol, and cannabis use has fallen in the lifetime and previous month use. The level of benzodiazepine use has remained similar in the period of study. Future work should redress the imbalance in substance use research that sees the majority of researchers looking at a few substances while little work is done on the others.

1. Introduction

Adolescence is a time of discovery and experimentation. It is also a period of physical and mental development when small changes can impact on the rest of a person's life. Adolescence is also the time when a large proportion of teenagers try alcohol (Smyth, Kelly, & Cox, 2011; Vega et al., 2002), tobacco (2002), and cannabis (Vega et al., 2002) for the first time. Use of these substances during this period can often be detrimental to normal adult growth (Gruber, Sagar, Dahlgren, Racine, & Lukas, 2011; Tucker, 2009) and may result in chronic use leading to long-term health problems and early death (Schuppan & Afdhal, 2008). The number of deaths attributable to addictive substances worldwide in 2004 was estimated to be over seven and a half million people (World Health Organisation, 2009). The same report showed that in Europe, 22.5% of all deaths in the region were directly caused by addictive substances, the highest percentage in any World Health Organisation (WHO) region in the world. There were 65,087 recorded drug-induced deaths due to illicit drugs alone in European Union (EU) member states between 2000 and 2008; with approximately 16% of those deaths occurring in under 25s (EMCDDA, 2011).

Ireland is similarly affected by substance use. Approximately 287 adolescents under the age of 19 years died in Ireland between 1998 and 2009, due to or as a consequence of substance use (Health Research Board, 2010, 2011a, 2011b). These statistics highlight the magnitude of substance use amongst the adolescent population in Ireland. Substance use in Ireland has been on the rise over the past decade; lifetime use of any illegal substance has risen by nearly 10% in the 15–34 years age category. Increased use of cannabis (up 9.6% to 33.4%) and cocaine (doubled to 9.4%) is the most concerning trends identified from a recent report from the National Advisory Committee on Drugs (NACD) (National Advisory Committee on Drugs, 2011). A recent survey from United Nations International Children's Emergency Fund (UNICEF) reported that 38% of Irish 18-year-olds have taken drugs (defined in this survey as any substance except alcohol or tobacco) at some stage in their lives, and it rose to 44% for 20 year-olds (UNICEF Ireland, 2011). In the same survey, when asked if they were currently taking drugs, 28% admitted that they were.

This widespread substance use in Irish society is placing an undeniably large burden on resources. Between 2005 and 2010, there were

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2295 recorded cases of adolescents under the age of 18, who utilised a drug treatment centre for the first time (Bellerose, Carew, & Lyons, 2011). This reflects an increase of over 50% in treatment demand over this five-year period. Large amounts of public funds and manpower have been invested in reducing availability of illegal substances in our society. Figures from the Central Statistics Office (CSO) show that the number of cases of "possession of drugs for personal use" in 2010 was 14,523, which is more than double the figure for 2004 (Central Statistics Office, 2011). This database also shows a similar rise in the recorded number of cases of "possession of drugs with intent to supply"; 4159 reported in 2010, almost twice the level recorded in 2004. There appears also to be a sharp increase in the domestic production of these substances to supply the high level of demand. In the same period of time as above, there was a 14-fold increase in the number of cases of "cultivation or manufacture of drugs". This is a substantial challenge to the resources of An Garda Síochána (Irish national police force). There are presently over 400 Gardaí involved in the Garda National Drugs Unit and in divisional units solely working to combat drug crime (Byrne, 2011).

Persons who start experimenting with substances at an early age are more likely (i) to engage in polysubstance use (Lewinsohn, Rohde, & Brown, 1999), (ii) to have problem use later in life (Chen, Storr, & Anthony, 2009; Dawson, Goldstein, Chou, Ruan, & Grant, 2008), (iii) to suffer from health problems (Hart, Morrison, Batty, Mitchell, & Davey Smith, 2010), and (iv) to experience psychological problems (Tucker, 2009). Preventing or delaying the onset of experimentation could reduce the number of persons requiring medical treatment; thus potentially reducing the burden on the public health care system, and related healthcare expenditure. Furthermore, it would likely lead to a decrease in polysubstance use, which has been associated with increased mortality (Gossop, Stewart, Treacy, & Marsden, 2002) and has been implicated in approximately 50% of all substance-related deaths in Ireland between 2004 and 2009 (Health Research Board, 2011a).

The prevalence of substance use and the harm that is caused by young people is an area of concern for policy makers, health workers, the criminal justice system, youth workers, teachers and parents. It is therefore important to have a clear understanding of the extent of the problem. While there have been studies which have examined this issue, there has not been a comprehensive review of the literature relating to substance use by young people in Ireland. We have therefore conducted a systematic review, to identify, synthesise and summarise the existing literature on the prevalence of substance use amongst adolescents and young adults in Ireland. The review will look at prevalence figures for the four most-used substances across the Republic of Ireland for persons between the age of 13 and 24, and compare usage across the years studied, 2000–2012.

2. Methods

This review was produced according to Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews and meta-analyses (Moher, Liberati, Tetzlaff, Altman, & The, 2009). These guidelines are primarily used for the reporting of controlled randomised trials (RCTs) or intervention studies, and so while not all items were applicable to this review of prevalence studies, the guidelines were adhered to as closely as possible. The articles were compiled from a large number of databases to ensure that as many relevant articles were included. The review was limited to articles reporting the use of cannabis, alcohol, nicotine, and benzodiazepines. These four substances were identified as the most widely-used substances in two recent large-scale studies (Currie et al., 2008; Hibell et al., 2009). An age range of 13–24 years was used as the criteria for searching as it encompasses the National Library of Medicine's Medical Subject Headings (MeSH) definitions of an 'adolescent' (13–18 years) and 'young adult' (19–24 years) (National Center for Biotechnology Information, 2011). The following inclusion criteria were applied to the searches: English language, full-text access, and published since 2000. The databases searched with a Boolean string were: PubMed, Scopus, Web of Knowledge, Google Scholar, ERIC, Embase and CINAHL. The PubMed database was searched using the keywords as follows: *adolescent* or *young adult*, *marijuana smoking*, *benzodiazepines*, *smoking*, *ethanol*, and *Ireland*. A search of the remaining databases was performed including the search terms: *adolescent* or *young adult*, *cannabis* or *marijuana* or *benzodiazepine* or *alcohol* or *nicotine* or *tobacco* or *cigarette*, and *Ireland*. These searches were conducted in December 2011 and updated thereafter to include relevant studies that were published after December 2011. An additional manual search of the National Documentation Centre on Drug Use was necessary as it did not allow searches using Boolean operators (Health Research Board, 2011c). This website is controlled by the Health Research Board (HRB) in Ireland and is a "database of Irish drug and alcohol research – an electronic library of full-text reports, journal articles, theses, and conference papers" (National Documentation Centre on Drug Use, 2012). This database has links to grey literature published by the government, national and international bodies. Personal contact was made with authors of some articles to obtain additional information.

The eligibility of articles found by the database search was checked by searching the title and abstract of the articles. Duplicates and records that were found to be not relevant were excluded. Reasons for exclusion included: multiple papers publishing data from the same dataset, articles which were commentaries and not original research, articles which covered a range of ages but were not divided into age categories, and articles which were part of a multi-national study, but did not provide country-specific information for Ireland. If there was still doubt about the eligibility of a paper, it was included so that a detailed inspection could be done at the next stage. The next stage was to obtain full-text copies of the remaining articles, and do a further assessment for eligibility and relevance. The data points of interest were extracted from the full-text reports and compiled into summary tables (see Tables 1–5). The data points assessed were divided into two categories: study characteristics (sample size, sampling method, age range, region of sampling, and any other information that might influence the analysis of the survey), and study results (details of alcohol, tobacco, cannabis, and benzodiazepines). These study results would be the outcomes of interest for the review.

Quality of the final articles was assessed using the Methodological Index for NOn-Randomised Studies (MINORS) tool (Slim et al., 2003). The tool was customised for use in this review, and all the articles retrieved were assessed in a scale of 0–10 based on their methodological quality. The scoring of the studies can be seen in Table 1.

3. Results

A total of 2562 articles were found in the database search, and 11 were found in additional searches. The titles and abstracts for each article were reviewed and duplicates were removed. This reduced the number of remaining articles to 1773. The next stage was to examine the title and abstracts of the remaining articles and eliminate those which did not match the eligibility criteria. 1702 articles were discarded; 360 were excluded because the study wasn't investigating Irish young people, 1309 were excluded because they were not measuring drug prevalence, 10 were excluded because they measured prevalence in a different age group, 18 were excluded because they weren't original research i.e. editorials, literature reviews etc., and 5 were excluded because they were studies that were based on data used from previous studies. After the excluded articles were discarded, 71 remained. The full-text articles were then obtained and assessed for suitability. Fifty-four articles were excluded; 8 had no Ireland-specific data, 36 weren't substance use prevalence studies, 7 had data from studies with age ranges that included ages over 24, 2 had data based

Table 1
Summary of study characteristics.

Study	n	Region	Age (yr)	Gender (%)	Substance(s) surveyed	Sampling method	MINORS score	Notes
Currie et al. (2008)	4840	Republic of Ireland	11–15	M: 50.6, F: 49.4	Alcohol, Cannabis, Tobacco	Stratified random	10	a
Curtin (2004)	248	County Cork	15–16	F: 100	Tobacco, Alcohol	*Unable to identify*	4	a
Flanagan et al. (2003)	1426	Counties Cavan, Louth, Meath & Monaghan	12–19	M: 59.7, F: 39.3[a]	Alcohol, Cannabis, Tobacco	Stratified random	8	a
Hibell et al. (2004)	2407	Republic of Ireland	15–16	M: 50.6, F: 49.4	Alcohol, BZDs, Cannabis, Tobacco	Stratified random	10	a
Hibell et al. (2009)	2221	Republic of Ireland	15–16	M: 45.2, F: 54.8	Alcohol, BZDs, Cannabis, Tobacco	Stratified random	10	a
Hibell et al. (2012)	2207	Republic of Ireland	15–16	M: 50.3. F: 49.7	Alcohol, BZDs, Cannabis, Tobacco	Stratified random	10	a
Kabir et al. (2010)	2805	Republic of Ireland	13–14	M: 40.4, F: 59.6	Tobacco	Stratified random	8	a
Kelleher et al. (2003)	2297	Counties Clare, Limerick & Tipperary	13–19	M: 44.8. F: 53.3	Alcohol, BZDs, Cannabis, Tobacco	Stratified random	6	a
Manning et al. (2002)	2580	Republic of Ireland	13–14	M: 45.2, F:54.8	Tobacco	Stratified random	8	a
McNeill et al. (2011)	214	Republic of Ireland	13–15	Unable to identify	Tobacco	Stratified random	7	In-home interviews
Moran et al. (2000)	1070	County Louth	12–19	M: 100	Tobacco	*Unable to identify*	4	a
Morgan et al. (2008)	1048	Republic of Ireland	18–24	M: 45.9, F: 54.1	Alcohol, BZDs, Cannabis, Tobacco	Cluster sampling	10	
O'Cathail et al. (2011)	370	Cork city	15–17	M: 38.4, F: 61.6	Tobacco	Convenience	8	a
Office of Tobacco Control (2006)	777	Republic of Ireland	8–24	*Unable to identify*	Tobacco	Stratified random	6	
Palmer and O' Reilly (2008)	462	South-east Ireland & Cork city	14–19	M: 45, F: 55	Alcohol, BZDs, Cannabis	Convenience	10	a
Share et al. (2004)	620	County Leitrim	14–15	M: 49.2, F: 50.5[a]	Tobacco	Randomised control trial	5	a, intervention study
Smyth et al. (2011)	133	Republic of Ireland	15–16	M:43.6, F: 56.4	Alcohol	Simple randomisation	8	
UNICEF (2011)	508	Republic of Ireland	16–20	*Unable to identify*	Alcohol, Cannabis, Tobacco	Convenience	6	Online survey

M = Male. F = Female, DNS = Did not specify, BZDs = benzodiazepines, notes: a – school(s) survey.
[a] Some participants did not answer the question.

on previous research, and 1 wasn't a research article. There were 18 articles included in the review. A PRISMA flow diagram (Fig. 1) provides a summary of the stages, and the number of studies in each stage (Moher et al., 2009). The study characteristics for the papers included in the review are summarised in Table 1. One of the included studies was a randomised control trial (RCT) that measured the effect of a smoking prevention initiative (Share, Quinn, & Ryan, 2004). There were eleven observational studies that had partial or full randomisation in the sampling process (Currie et al., 2008; Flanagan, Bedford, O' Farrel, & Howell, 2003; Hibell et al., 2004, 2009, 2012; Kabir, Manning, Holohan, Goodman, & Clancy, 2010; Kelleher, Cowley, & Houghton, 2003; Manning et al., 2002; McNeill et al., 2011; Office of Tobacco Control, 2006; Smyth et al., 2011), and one study employed cluster sampling (Morgan et al., 2008). Convenience sampling was used by three of the studies (O'Cathail et al., 2011; Palmer & O' Reilly, 2008; UNICEF Ireland, 2011), and the method of sample selection could not be identified in two studies (Curtin, 2004; Moran, Maguire, & Howell, 2000). Half of the studies surveyed the use of a single substance while

Table 2
Summary of smoking prevalence rates.

Study name	n	Age range (years)	Lifetime use of tobacco	First cigarette by 13 years	Tobacco use in the previous month	Daily tobacco use
Currie et al. (2008)	4840	11–15	26% (13 y.o.), 50% (15 y.o.)	33% (female), 29% (male)	–	3% (13 y.o.), 15% (15 y.o.)
Curtin (2004)	248	15–16	50%	–	31%	19%
Flanagan et al. (2003)	1426	12–19	50.8%	30.2%	–	18.2%
Hibell et al. (2004)	2407	15–16	67%	45%	33%	–
Hibell et al. (2009)	2221	15–16	52%	32%	23%	–
Hibell et al. (2012)	2207	15–16	43%	21%	21%	–
Kabir et al. (2010)	2805	13–14	–	–	10.6%[a]	–
Kelleher et al. (2003)	2297	14–18	61.3%	49.7%	30.0%	–
Manning et al. (2002)	2580	13–14	–	–	19.0%[a]	–
McNeill et al. (2011)	214	13–15	–	–	10. 5–13. 5%	–
Moran et al. (2000)	1070	12–19	–	–	39%	22.5%
Morgan et al. (2008)	1048	18–24	–	–	29% (18–19 y.o.), 40% (20–24 y.o.)	23% (18–19 y.o.), 31% (20–24 y.o.)
O'Cathail et al. (2011)	370	15–17	48.4%	–	18.1%	–
Office of Tobacco Control (2006)	777	8–24	–	–	16%[b] (12–17 y.o.), 42%[b] (18–24 y.o.)	
Share et al. (2004)	620	14–15	57%	38%	21%[a]	11%
UNICEF (2011)	508	16–20	–	–	23%	–

y.o = year-olds.
[a] Answer positively when asked if they are currently smoking.
[b] Figure represents current smokers that smoke greater than once a week or more.

Table 3
Summary of alcohol prevalence rates.

Study name	n	Age range (years)	Lifetime use of alcohol	First alcohol consumption before 13 years	Alcohol use in the previous 12 months	Alcohol use in the previous months
Currie et al. (2008)	4840	11–15	–	38%[a]	–	–
Curtin (2004)	248	15–16	82%	–	–	59%
Flanagan et al. (2003)	1426	12–19	71.3%	–	–	–
Hibell et al. (2004)	2407	15–16	92%	47% (beer), 45% (wine), 32% (spirits)	88%	73%
Hibell et al. (2009)	2221	15–16	86%	33% (beer), 31% (wine), 21% (spirits)	78%	56%
Hibell et al. (2012)	2207	15–16	81%	40% (beer), 18% (wine), 35% (spirits)	73%	50%
Kelleher et al. (2003)	2297	14–18	90.2%	50.2%	83.4%	62.4%
Morgan et al. (2008)	1048	18–24	84% (18–19 y.o.), 93% (20–24 y.o.)	–	–	78.3% (18–19 y.o.), 84.5% (20–24 y.o.)
Palmer and O' Reilly (2008)	462	14–19	86.10%	–	82.6%[b]	61.6%[c]
Smyth et al. (2011)	133	15–16	58%	–	–	–
UNICEF (2011)	508	16–20	77%	–	–	–

y.o = year-olds.
[a] Only 15 y.o. reported.
[b] Those who drank alcohol once a year or more often.
[c] Those who drank once a month or more often.

the majority of the remaining studies investigated the use of three or more substances. Sixteen studies had tobacco as a substance studied, eleven studies investigated alcohol consumption, nine studies looked into cannabis use, and six investigated benzodiazepine use.

To facilitate observation of trends over time, the studies are presented according to three time periods: Period 1 (2000–2006), Period 2 (2007–2009), and Period 3 (2010–2012). As fewer studies were published in the earlier years, Period 1 encompasses a longer timeframe of 7 years. Period 2 and Period 3 have equal timeframes of 3 years. These groupings provided approximately equal-sized groups, in terms of numbers of publications thereby avoiding issues such as diluting the group size to one or two articles.

3.1. Tobacco usage

There were sixteen studies which collected data on tobacco usage, and a summary of the data can be seen in Table 2. One study was a RCT (Share et al., 2004), eleven were observational studies with randomly selected participants (Currie et al., 2008; Flanagan et al., 2003; Hibell et al., 2004, 2009, 2012; Kabir et al., 2010; Kelleher et al., 2003; Manning et al., 2002; McNeill et al., 2011; Office of Tobacco Control, 2006), one study used cluster sampling (Morgan et al., 2008), two used convenience sampling (O'Cathail et al., 2011; UNICEF Ireland, 2011) and two did not describe how participants were selected (Curtin, 2004; Moran et al., 2000).

3.1.1. Lifetime use of tobacco

This was reported in over half of the studies.

Period 1 (2000–2006): The levels from five studies in Period 1 ranged between 50 and 67% (Curtin, 2004; Flanagan et al., 2003; Hibell et al., 2004; Kelleher et al., 2003; Share et al., 2004). The variation in the levels may exist because four of the five studies were measuring regional populations. The only national study reported a lifetime usage level of 67% (Hibell et al., 2004). The largest of the regional studies reported a similar figure at the high end of the range, 61%, and so the true estimate probably lies somewhere in this region (Kelleher et al., 2003).

Period 2 (2007–2009): Two studies in Period 2 surveyed lifetime use: one of the studies measured usage in 13 year-olds and 15 year-olds and reported 26% and 50% respectively (Currie et al., 2008), while the second study reported 52% in a survey of 15–16 year-olds (Hibell et al., 2009) Both of these studies were on a large scale and encompass national populations so their estimates would be close to the true figure.

Table 4
Summary of cannabis prevalence rates.

Study name	n	Age range (years)	Lifetime use of cannabis	Cannabis use in the previous 12 months	Cannabis use in the previous month
Currie et al. (2008)	4840	11–15	20%[a]	17%[a]	7% (female)[a], 11% (male)[a]
Flanagan et al. (2003)	1426	12–19	31.0%	–	12.8%
Hibell et al. (2004)	2407	15–16	39%	31%	16%
Hibell et al. (2009)	2221	15–16	20%	15%	9%
Hibell et al. (2012)	2207	15–16	18%	14%	7%
Kelleher et al. (2003)	2297	14–18[b]	28.6%	24.2%	15.4%
Morgan et al. (2008)	1048	18–24	–	12% (18–19 y.o.), 14% (20–24 y.o.)	–
Palmer and O' Reilly (2008)	462	14–19	41.1%	32.5%	13.62%[b]
UNICEF (2011)	508	16–20	>80% (weed)[c], 46% (hash)	–	–

y.o = year-olds.
[a] Only 15 y.o. reported, 2–13 and 19 y.o. were excluded due to lack of data.
[b] Cannabis use once a month or more frequently.
[c] Precise percentage could not be determined.

Table 5
Summary of benzodiazepine prevalence rates.

Study name	n	Age range (years)	Lifetime use of benzodiazepines	Lifetime use of benzodiazepines without prescription	Lifetime use of benzodiazepines on prescription
Hibell et al. (2004)	2407	15–16	–	2.0%	10.0%
Hibell et al. (2009)	2221	15–16	–	3.0%	10.0%
Hibell et al. (2012)	2207	15–16	–	3.0%	9.0%
Kelleher et al. (2003)	2297	13–19	–	5.6%	9.2%
Morgan et al. (2008)	1048	18–24	–	0% (18–19 y.o), 1.4% (20–24 y.o.)	1.0% (18–19 y.o.), 1.1 (20–24 y.o.)
Palmer and O' Reilly (2008)	492	14–19	10.8%	–	–

y.o = year-olds.

Period 3 (2010–2012): There were two studies from Period 3, and these studies estimated lifetime tobacco usage at 48% and 43% respectively. There were differences between the two studies however, the former study was conducted in Cork City (O'Cathail et al., 2011) while the latter was a nation-wide study (Hibell et al., 2012).

3.1.2. Smoking a cigarette by age 13 years

The second category examined was smoking a cigarette by age 13 years. It has been shown that initiation of substance use prior to 13 years of age is associated with chronic substance use (Hawkins et al., 1997). There were seven studies that collected data on this.

Period 1 (2000–2006): Four studies were published with results which ranged from 30 to 50% (Flanagan et al., 2003; Hibell et al., 2004; Kelleher et al., 2003; Share et al., 2004).

Period 2 (2007–2009): Two studies were published which both had similar levels of approximately 30% (Currie et al., 2008; Hibell et al., 2009). These studies had good study designs and used a national sample so the true level is likely to be close to this.

Period 3 (2010–2012): A single study published reported a level of 21% (Hibell et al., 2012).

3.1.3. Smoking in the previous month

The third category examined was smoking in the previous month. This is considered a good indicator of regular use.

Period 1 (2000–2006): The studies from Period 1 ranged from 19 to 39% (Curtin, 2004; Hibell et al., 2004; Kelleher et al., 2003; Manning et al., 2002; Moran et al., 2000; Office of Tobacco Control, 2006; Share et al., 2004). Some of the variation in this can be explained thus: the two studies with the lowest percentages, 19% and 21%, were phrased in a different manner (Manning et al., 2002; Share et al., 2004). They measured positive responses to a question relating to whether they were currently smoking. This is not a clearly defined question and may account for the lower percentage. Two of the studies did not clearly indicate how samples were picked (Curtin, 2004; Moran et al., 2000), and so caution is advised when generalising the results from these studies. The final two studies gave estimates of smoking in the previous month to be 33% and 30% respectively, so the true level is likely to be near this figure (Hibell et al., 2004; Kelleher et al., 2003).

Period 2 (2007–2009): The level of smoking in the previous month in Period 2 was measured in two studies, and was estimated to be 23% (Hibell et al., 2009) for one and between 29 and 40% for the other (Morgan et al., 2008). The study was a large-scale, nationwide survey, and it is likely that the result is indicative of the true figure.

Period 3 (2010–2012): Five studies were found from Period 3; it is difficult to make a direct comparison between them due to significant heterogeneity in the studies. Two studies recorded levels of 10.6% and 10.5% for 13–14 year-olds (Kabir et al., 2010) and 13–15 year-olds (McNeill et al., 2011) respectively, even though the former study measured the percentage of young persons currently smoking, and the latter measured the percentage of young persons that smoke greater than once a week or more. Two studies measured the level in older adolescents, 15–17 year-olds and 16–20 year-olds and reported levels of 18% (O'Cathail et al., 2011) and 23% (UNICEF Ireland, 2011) respectively. Both of these studies however used convenience sampling to select their participants. The remaining study from Period 3 looked at 15–16 year-olds, and showed a level of 21% (Hibell et al., 2012).

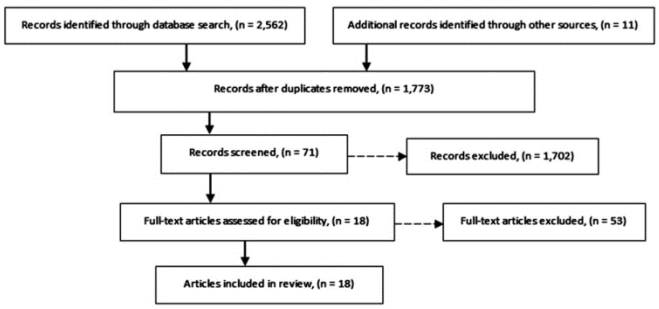

Fig. 1. Adapted from the PRISMA flow diagram.

3.1.4. Daily tobacco use

The final category examined was daily tobacco use.

Period 1 (2000–2006): The range in data from Period 1 was 11–23% (Curtin, 2004; Flanagan et al., 2003; Moran et al., 2000; Share et al., 2004). However, caution should be exercised when interpreting results of the studies reporting the two highest levels, 23% (Moran et al., 2000) and 19% (Curtin, 2004), as the method of sample selection was not specified in the paper. The remaining two studies had good design; however they were both regional studies and so may not give a good indication of the national estimate.

Period 2 (2007–2009): There were two studies from Period 2 and both studies reported two levels; the first study reported one for 13 year-olds, 3%, and one for 15 year-olds, 15% (Currie et al., 2008). The second study reported on levels of 18–19 year-olds, 23%, and 20–24 year-olds, 31% (Morgan et al., 2008). These are nationally representative studies and have good design so it is likely that they approximate the national level closely.

Period 3 (2010–2012): None of the studies from Period 3 reported levels of daily smoking.

3.2. Alcohol usage

There were eleven studies that looked into alcohol usage and a summary is provided in Table 3. Randomised sample selection was used in seven of the studies (Currie et al., 2008; Flanagan et al., 2003; Hibell et al., 2004, 2009, 2012; Kelleher et al., 2003; Smyth et al., 2011), convenience sampling was used for two (Palmer & O' Reilly, 2008; UNICEF Ireland, 2011), cluster sampling in one study (Morgan et al., 2008), and the method of sample selection was not described in one of the studies (Curtin, 2004).

3.2.1. Lifetime use of alcohol

For lifetime use of alcohol, the figures varied both between and within these periods.

Period 1 (2000–2006): There were four studies published in Period 1, and their levels ranged from 71 to 92% (Curtin, 2004; Flanagan et al., 2003; Hibell et al., 2004; Kelleher et al., 2003). Differences in levels in these studies can in part be attributed to the age range of the participants. The studies with the lowest figure had a participant age ranging from 12 to 19 years, while each of the others studies had a minimum age of 14 or 15 years. One of the studies reported a lifetime level of 82%, but this study was conducted in County Cork with an unknown method of sampling, so it is difficult to extrapolate from it (Curtin, 2004). Two studies demonstrated close agreement at 92% and 90% levels for lifetime usage and the true level is likely to be close to this (Bould et al., 2007; Hibell et al., 2004).

Period 2 (2007–2009): Only two of the three studies in Period 2 had data relating to lifetime alcohol usage and both of those studies reported similar results: 86.1% and 86% (Hibell et al., 2009; Palmer & O' Reilly, 2008).

Period 3 (2010–2012): There were three studies published in Period 3 and they reported 77%, 58% and 81% usage (Hibell et al., 2012; Smyth et al., 2011; UNICEF Ireland, 2011). The wide discrepancy between these figures may be due to the age of participants; up to 20 years in one study (UNICEF Ireland, 2011) and up to 16 years for the latter 2 studies. Another reason could be the nature of the studies: one was an internet poll and this may be a source of bias in the study (UNICEF Ireland, 2011). This contrasts with the third study which was a national study with randomised sampling (Hibell et al., 2012).

3.2.2. Consumption of alcohol before 13 years of age

Period 1 (2000–2006): This examined the percentage of young persons who first consumed alcohol before 13 years of age. A limitation with this category was that it was reported in only two studies. Unfortunately, one of the studies quoted percentages for three types of alcohol (beer, wine, and spirits) which ranged from 32 to 47%, so it was not possible to get an overall figure (Hibell et al., 2004). The remaining study reported an overall consumption level of 50% (Kelleher et al., 2003).

Period 2 (2007–2009): two studies from Period 2 reported on this category. One of the studies differentiated between alcohol types, which ranged from 21 to 33% (Hibell et al., 2009). The other study, Currie et al., reported a level of 38% (Currie et al., 2008). Both of the studies were well-designed and were probably an accurate reflection of the actual population level.

Period 3 (2010–2012): A single study from Period 3 reported levels of first consumption prior to 13 years of age at between 18% and 40% for the three types of alcohol mentioned above (Hibell et al., 2012).

3.2.3. Alcohol use in previous 12 months

Alcohol use in the previous 12 months was used as a measure of occasional use. Five studies (two from Period 1, two from Period 2, and one from Period 3) included data on 12 month usage (Hibell et al., 2004, 2009, 2012; Kelleher et al., 2003; Palmer & O' Reilly, 2008).

Period 1 (2000–2006): Both studies reported similar values, 88% and 83% (Hibell et al., 2004; Kelleher et al., 2003). Both studies were large scale and had good design, so it probably reflects an estimate of the population figure.

Period 2 (2007–2009): The two studies from Period 2 were in broad agreement with each other. Hibell et al. and Palmer & O' Reilly reported levels of 78% and 83% respectively (Hibell et al., 2009; Palmer & O' Reilly, 2008). The result from Palmer & O' Reilly is a percentage of positive responses to the question if they drank once a year or more.

Period 3 (2010–2012): The single study from Period 3 reported a level of 73% for alcohol use in the previous year (Hibell et al., 2012).

3.2.4. Alcohol use in the previous month

The final category related to alcohol use in the previous month. Only one of the most recent studies reported data, but there were data from six older papers (three from Period 1, two from Period 2, and one form Period 3) (Curtin, 2004; Hibell et al., 2004, 2009, 2012; Kelleher et al., 2003; Morgan et al., 2008; Palmer & O' Reilly, 2008).

Period 1 (2000–2006): The studies from Period 1 reported a range of levels from 59 to 73%. The 59% figure comes from the paper by Curtin, which was a small County Cork study and the study design was unknown (Curtin, 2004). This affects the ability to generalise with its data and gives precedence to the results from the other studies which were 73% and 62% (Hibell et al., 2004; Kelleher et al., 2003).

Period 2 (2007–2009): Hibell et al., 2008 had a level of 56% for the alcohol use in the previous month (Hibell et al., 2009), while Palmer & O' Reilly gave a level of 62% (Palmer & O' Reilly, 2008). This final figure was the percentage of those that responded positively when asked if they drank alcohol once a month or more often.

Period 3 (2010–2012): The study from Period 3 reported a level of 50% in this category (Hibell et al., 2012).

3.3. Cannabis usage

A summary of the studies reviewed that included surveyed cannabis usage is displayed in Table 4. There were nine studies that reported

cannabis use amongst adolescents and young adults in Ireland (Currie et al., 2008; Flanagan et al., 2003; Hibell et al., 2004, 2009, 2012; Morgan et al., 2008; Palmer & O' Reilly, 2008; UNICEF Ireland, 2011). The studies were mostly randomised school surveys, while the remaining two studies were convenience studies (Palmer & O' Reilly, 2008; UNICEF Ireland, 2011). All of the studies measured lifetime use of cannabis and there was a wide variation between levels, 20 and 80%. The two highest usage levels, 80% and 41%, were reported by two studies that used convenience sampling, so the true level may differ (Palmer & O' Reilly, 2008; UNICEF Ireland, 2011). A pattern was seen in the other studies based on their year of publishing.

3.3.1. Lifetime use of cannabis

Period 1 (2000–2006): Earlier studies from Period 1 showed a usage level of between 29 and 39% (Flanagan et al., 2003; Hibell et al., 2004; Kelleher et al., 2003).

Period 2 (2007–2009): There were three studies in this period. Two of the studies had a level of 20% (Currie et al., 2008; Hibell et al., 2009), and the third study had a level of 41.1% (Palmer & O' Reilly, 2008).

Period 3 (2010–2012): There were two studies from Period 3 that reported on lifetime cannabis use. The most recent European School Project on Alcohol and Other Drugs (ESPAD) study reported a level of 18% (Hibell et al., 2012), while the second report gave separate levels for the dried plant form (weed), >80%, and the extracted resin (hash), 46% (UNICEF Ireland, 2011). These levels are largely different from levels reported at any time throughout the entire time range, and so their use as a representative figure must be cautioned. Overall, the levels are suggestive of a decreasing experimentation with cannabis amongst young people.

3.3.2. Cannabis use in the previous 12 months

A similar pattern was observed in the reporting of cannabis use in the previous 12 months.

Period 1 (2000–2006): Higher levels were observed amongst the earlier studies, 25–31% (Hibell et al., 2004; Kelleher et al., 2003) than in subsequent periods.

Period 2 (2007–2009): There were four studies in period two and these studies showed a decrease compared to earlier studies to 12–17% (Currie et al., 2008; Hibell et al., 2009; Morgan et al., 2008). The exception to this is the study carried out by Palmer & O' Reilly, which gives a level of 33% for 12 month usage (Palmer & O' Reilly, 2008). A possible explanation for this higher figure may be that the study covers a broader age range (14–19 years), and the level of use generally increases with age. Owing to problems with generalisation of this study, the true level is likely to be closer to Currie et al. (2008) and Hibell et al. (2009).

Period 3 (2010–2012): A single study from Period 3 reported a level of 14% (Hibell et al., 2012).

3.3.3. Cannabis use in the previous month

Period 1 (2000–2006): The trends in cannabis use in the previous month paralleled those in use in the previous 12 months. The three studies from period one showed high levels of use, 13–16% (Flanagan et al., 2003; Hibell et al., 2004; Kelleher et al., 2003).

Period 2 (2007–2009): There were three studies compared with 7–14% respectively (Currie et al., 2008; Hibell et al., 2009; Palmer & O' Reilly, 2008). The highest of the more recent figures (14%) is from Palmer & O' Reilly, which as mentioned already suggests that the true level may be lower than this (Palmer & O' Reilly, 2008).

Period 3 (2010–2012): There was one study in Period 3 that reported this data and the level was 7% (Hibell et al., 2012).

3.4. Benzodiazepine usage

A summary of the studies reporting benzodiazepine usage can be found in Table 5. Four of the six studies had sample sizes greater than 2000 and participants were randomly selected, so there is a high degree of confidence in the figures reported from these studies (Hibell et al., 2004, 2009, 2012; Morgan et al., 2008). None of these studies reported an overall prevalence level for benzodiazepine usage but instead categorised usage into prescription use and non-prescription use. The percentage of subjects who have tried benzodiazepines without the advice of a doctor was consistently higher than prescription use in each of the studies.

3.4.1. Lifetime benzodiazepine use on prescription

Period 1 (2000–2006): There were similar levels for the prevalence of lifetime prescription benzodiazepine use at 9.2% and 10.0% (Hibell et al., 2004, 2009, 2012; Kelleher et al., 2003). Variation in the figure can be attributed in part to the difference in participant age with one study carried out by Kelleher et al. ranging from 13 to 19 years (Kelleher et al., 2003) while the rest had a narrower age range. Another contributing factor to the difference was that the participants in the Kelleher et al. study were recruited from three counties in the west of Ireland only, while the latter studies selected participants nationwide. This suggests that the higher end of the range is closer to the actual prevalence of non-prescription benzodiazepine use.

Period 2 (2007–2009): There were two studies in this period (Hibell et al., 2009; Morgan et al., 2008). There was a wide discrepancy between the values gotten in these two studies.

Period 3 (2010–2012): There was only one study in the third period, and this reported a level of use 9.0% (Hibell et al., 2012).

3.4.2. Lifetime benzodiazepine use without prescription

Period 1 (2000–2006): The levels ranged 2.0% to 5.6%, with the Kelleher et al. study reporting a level of 5.6% and the Hibell et al., 2004 study reporting 2%y (Hibell et al., 2004, 2009; Kelleher et al., 2003).

Period 2 (2007–2009): There were 3 benzodiazepine studies that measured lifetime non-prescription benzodiazepine use. Two of the studies had reported differing levels of usage. One of the studies reported a level of 3.0% (Hibell et al., 2009), while the other reports between 0 and 1.4% usage (Morgan et al., 2008). One of the studies reported both prescription and non-prescription benzodiazepine use at 10.8% (Palmer & O' Reilly, 2008). This level appears to be in agreement with the rest of the studies; however the study cohort was not a national sample nor were the participants randomly selected. Both of these factors mean that generalisation of the results is not possible.

Period 3 (2010–2012): There was a single study in Period 3, and it reported a level of 3.0% (Hibell et al., 2012).

4. Discussion

4.1. Summary of evidence

This review examined available peer-reviewed research and other available reports on substance use in Irish young people since the year 2000. The review found a variety of studies that ranged from RCTs to online surveys and from small-scale rural studies to national studies. This allowed for a wide perspective on substance use. Some

overall trends were observed in the literature. The clearest pattern that was elucidated was a trend towards a decrease in all substance use over time between Period 1, Period 2 and Period 3. This decrease in use was consistent between the first period and the most recent period. An explanation for this trend is not suggested by the majority of authors, though something may be learnt from their observations. One author suggests that the fall in tobacco usage levels may be attributed in part to tighter government restrictions on the sale, display, and usage of tobacco products (McNeill et al., 2011). A likely significant factor to contribute to Ireland's decreasing substance use rates is the creation and publication of Ireland's first National Drug Strategy document in 2000 (Department of Tourism Sport & Recreation, 2000). It was the first time that a comprehensive and national approach to substance use was examined. There had been a report previous to this, Government Strategy to Prevent Drug Misuse 1991 (Department of Health, 1991), but this had separate strategies for Dublin and the rest of the country. The National Drug Strategy paper introduced for the first time in Ireland the four pillar system. These pillars are supply, prevention, treatment, and research. This allowed resources to be allocated to areas where they are needed. It allowed "the bringing together of key agencies, in a planned and co-ordinated manner, to develop a range of appropriate responses to tackle drug misuse…" (Department of Tourism Sport & Recreation, 2000). The report resulted in the creation of a National Awareness Campaign which used traditional media such as brochures and radio, and newer forms of promotion i.e. Facebook, Twitter and Drugs.ie website to increase awareness of the effects and consequences of substance use. The most recent National Drug Strategy document (Department of Community Rural & Gaeltacht Affairs, 2009) builds on the determination to lower substance use. The biggest change in this report is the inclusion of alcohol as a drug of abuse. The high level of alcohol use nationally amongst adults and young people, and the cost to the public health system warranted its inclusion. Another stated reason for its inclusion was "For many, alcohol is also seen as a gateway to illicit drug use, particularly for young people, while poly-drug use – which very often includes alcohol – is now the norm amongst illicit drug users". A recommendation in the report aimed at school students was the delivery of drug education to primary and post-primary students in schools through the Social, Physical, and Health Education (SPHE) curriculum.

It would appear that the combination of more harsh sale restrictions and increased education and awareness has had its intended effect on drug levels. The efforts of those involved should be applauded, and their support should be continued to maintain this positive trend. This work should be augmented by international good practice such as the WHO's guidelines on reducing harmful alcohol use (World Health Organisation, 2010). These recommend implement various strategies should as pricing changes, closely regulating the advertisement of alcoholic drinks, and modifying the system of selling alcohol, such as reducing the hours of retail sales, and regulating the number and location of businesses that can sell alcohol. Further reduction in illicit substance use may come from educational interventions as outlined by Faggiano et al. (2005, 2010). By continuing efforts such as these, the burden of substance use on young people can be reduced.

As stated above, tobacco and alcohol use followed the trend of decreasing use across all measures of use, experimental, occasional, or regular. The fall in the levels of use is a positive step in the reduction in the burden caused by "the single most preventable cause of death in the world today"; cigarettes (World Health Organisation, 2008), and reducing the level of total alcohol consumption amongst the Irish, who rank second highest in the EU and 15th highest in the world (World Health Organisation, 2011). Sustaining these trends could result in reduced burden on the healthcare system due to chronic treatment for preventable diseases, and on the justice system owing to reduced public order violations. The trend in decreasing tobacco use in Ireland mirrors that of Europe. The average lifetime use of tobacco for 15/16 year-olds across the 34 countries included in the ESPAD study fell from 67% to 60% between 2003 and 2007 (Hibell et al., 2009). The same report gave a similar description for tobacco use in the previous month, and daily smoking; the former falling from 32% to 28%, while the latter fell from 10% to 8%. An opposite trend was observed in relation to alcohol use. There was no change in the average lifetime use of alcohol from 2003 to 2007 (Hibell et al., 2009), and the percentage of 15/16 year-olds who consumed alcohol in the previous month fell from 65% to 62% over the same four-year period. When looking broadly, it is positive to see a reduction of the levels of both experimental and regular use of these widely-available substances when compared to our European counterparts (Hibell et al., 2009).

There was a trend, amongst Irish adolescents, of decreased lifetime cannabis use, use in the previous 12 months, and use in the previous month over the length of the study period (Hibell et al., 2004, 2009, 2012). The pan-European levels indicated by the latter report were similar to the levels of use in Ireland in 2007 (Hibell et al., 2009). Ireland differs from the European average however as the level of Irish use decreased while the European level increased from 12% in 2003 to 19% in 2007. Most of this increase can be attributed to countries in the east of Europe, as the United Kingdom, France, Italy, Germany, Norway, Sweden, and Austria also had decreased lifetime cannabis use between 2003 and 2007. A similar pattern was observed in the category of cannabis use in the previous month (Hibell et al., 2009).

Benzodiazepine usage was unchanged across the time periods studied. European levels appear to vary from Irish levels according to the most recent survey of benzodiazepine usage (Hibell et al., 2012). The estimated average level of illicit benzodiazepine use was 6%, compared to 3% in Ireland. The level of prescribed use of benzodiazepines in Ireland was 1% higher than the European average of 8%. The levels of prescription and non-prescription use in Ireland did not appear to have changed significantly throughout the years of reference of this review. An explanation that may account for the steady level of benzodiazepine use in Ireland is that no campaign on the dangers of inappropriate benzodiazepine usage has been active in the country in the last ten years, since the launch of the Benzodiazepine: Good Practice Guidelines for Clinicians document in, 2002. Such a campaign could encourage a young person or their parents to ensure that prescription usage is within safe limits, and deter its illicit use.

4.2. Limitations

A limitation to this systematic review is that the conclusions are only as accurate as the studies it returns. This is a limitation with every systematic review and literature review. To minimise the impact of low quality studies on the review, it was decided to quantify the quality of the studies using the Methodological Index for NOn-Randomised Studies (MINORS) tool (Slim et al., 2003).

An important limitation in the studies in this review was the lack of consistency in survey design. An example of this is evident in Table 2 under the column "Tobacco use in the previous month". It is a standard, internationally-used question used to estimate regular use of a substance. Some studies chose to survey regular use with questions such as "Are you currently smoking?" and "Do you smoke one or more cigarettes each week?" Each question is attempting to measure the same outcome but because of the differences in the actual questions, it makes cross-study comparisons inappropriate and difficult. This limitation affected the ability to make comparisons between studies surveying tobacco, alcohol, cannabis, and benzodiazepine use.

There were few papers found in the literature search that surveyed benzodiazepine usage. A comprehensive search of scientific databases and grey literature could only find five relevant papers. Each of these studies measured usage superficially; one or two questions were asked as part of a section dealing with illicit substance use. It is difficult to get a clear understanding of benzodiazepine usage from these papers. It is important at present to look closer for patterns in benzodiazepine use because it was the only substance in this review whose usage did

not appear to be decreasing. This could be the first stage in the development of a targeted educational campaign highlighting the dangers of inappropriate benzodiazepine usage.

There is a category of young person that is excluded from most of the studies in this review. As can be seen in the 'Notes' column in Table 1, twelve of the seventeen studies chose participants from pupils attending the schooling system in Ireland. This method of selection has many advantages; it is more efficient to randomly select young persons around the country, and it saves time because the students are all in the same place at the same time. However, this misses out on early school-leavers, who account for up to 14.1% of school-leavers in total (Byrne, McCoy, & Watson, 2008). This cohort of young persons is a significant absence from any study reporting on substance use. International studies have shown that early school-leavers are more likely to use both legal and illegal substances (Townsend, Flisher, Gilreath, & King, 2006). Excluding this group has the potential to underreport the true level of substance use in young persons.

4.3. Conclusions

This review has shown that substance use is still occurring in Ireland. Much of the research that is being undertaken on this topic in Ireland is of high quality and it indicates that the level of use is declining across many substances. However, there is still further work that can be done by policy-makers to ensure that this positive trend will continue. However, the fall in use is not evident with some substances and efforts must be increased to inform the public on their risks. Future work should redress the imbalance in substance use research that sees the majority of researchers looking at a few substances while little work is done on the others. Knowledge derived from these papers and reports, and from future work should guide the development of targeted drug prevention programmes that are directed at the sections of population that will benefit the most from them.

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Contributors

SB, LS, and SL conceived the original idea for, and designed the review criteria. KM carried out the database searches and wrote the introduction, methods, results, discussion and conclusion. SB, LS, and SL reviewed all drafts and suggested modifications. All authors contributed to and have approved the final manuscript.

Conflict of interest

All authors declare that they have no conflicts of interest.

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10.4 Appendix IV – MINORS rating of reviewed studies

MINORS rating of reviewed studies

Study	1. A clearly stated aim	2. Inclusion of consecutive patients	3. Prospective collection of data	4. Endpoints appropriate to the aim of the study	8. Prospective calculation of the study size	Total
Currie	2	2	2	2	2	10
Curtin	2	0	0	2	0	4
Flanagan	2	2	2	2	0	8
Hibell 2004	2	2	2	2	2	10
Hibell 2008	2	2	2	2	2	10
Hibell 2012	2	2	2	2	2	10
Kabir	2	2	2	2	0	8
Kelleher	0	2	2	2	0	6
Manning	2	2	2	2	0	8
McNeill	1	2	2	2	0	7
Moran	0	0	2	2	0	4
Morgan	2	2	2	2	0	8
O' Cathail	2	0	2	2	0	6
OTC	2	2	2	2	2	10
Palmer	1	0	2	2	0	5
Share	2	2	2	2	2	10
Smyth	2	2	2	2	0	8
UNICEF	2	0	2	2	0	6

A score of 0 is given if the item is not reported, 1 if reported but not adequate, and 2 if reported and adequate

10.5 Appendix V – Ethical approval for study in Chapter 3

Tel: + 353-21-490 1901
Fax: + 353-21-490 1919

Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

17th July 2013

Our ref: ECM 4 (o) 06/08/13

Dr Stephen Byrne
Senior Lecturer in Clinical Pharmacy
School of Pharmacy
University College Cork
College Road
Cork

Re: Prescribing of benzodiazepines to children and adolescents in Ireland.

Dear Dr Byrne

Expedited approval is granted to carry out the above study at:

- University College Cork.

The following document has been approved:

- Signed Application Form.

We note that the co-investigators involved in this study will be:

- Dr Laura Sahm, Dr Suzanne McCarthy, Dr Sharon Lambert and Kevin Murphy.

Yours sincerely

Professor Michael G Molloy
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

10.6 Appendix VI – Ethical approval for studies in Chapter 4 and 5

Tel: + 353-21-490 1901
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Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 4 (d) 02/10/12

11th September 2012

Dr Stephen Byrne
Senior Lecturer in Clinical Pharmacy
School of Pharmacy
Room 2.02
Cavanagh Pharmacy Building
University College Cork
College Road
Cork

Re: Prevalence and correlates of substance misuse amongst attendees of a treatment centre.

Dear Dr Byrne

Expedited approval is granted to carry out the above study at:

- School of Pharmacy, University College Cork
- Matt Talbot Services, Cork.

The following document has been approved:

- Application Form.

The co-investigators involved in this study will be:

- Dr Laura Sahm, Dr Sharon Lambert and Kevin Murphy.

Yours sincerely

Dr Michael Hyland
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

10.7 Appendix VII – Sample National Drug Treatment Reporting System form

NDTRS
National Drug Treatment Reporting System, Health Research Board

Please check information is visible on carbon copies.

PLEASE COMPLETE USING A BALL POINT PEN

please fold here

A. Administrative details

Name _____ Address _____

1. HSE Area (see Appendix 2) **2a. Centre** **2b. Type** **3. Client number**

B. Demographic details

4. Gender (circle) 1. Male 2. Female

5. Age (years)

6. Date of birth Day Month Year

7a. Living with whom (circle)
1. Alone 2. Parents/family
3. Friends 4. Partner (alone)
5. Partner & child(ren) 6. Alone with child(ren)
8. Foster care 7. Other
9. Not known

7b. Living where (circle)
1. Stable accommodation
2. Institution (prison/residential care/halfway house)
3. Homeless
4. Other unstable accommodation
9. Not known

8a. Area of residence
(DED, see pink book or Appendix 4)

8b. Community Care Area
(see Appendices 4/5)

9. City/county
Car registration code
(see Appendix 4)

10a. Nationality (circle, if other please specify)
1. Irish 3. Irish traveller 2. Other 9. Not known
Nationality _____

10b. Ethnic background (circle)
1. White Irish 2. White Irish Traveller
3. Any other white background 4. Black African background 5. Any other black background
6. Chinese background 7. Any other Asian background
8. Other 9. Do not wish to answer this question

11. Employment status (circle)
1. In paid employment 2. Unemployed
3. FAS/training course 4. Student
5. Housewife/husband 6. Retired/unable to work
8. Other (specify) _____
9. Not known

12a. Age left primary or secondary school (not third level)
(years, or circle code below) Years
01. Never went to school
88. Still at school
99. Not known

12b. Education: highest level completed (circle)
0. Primary level incomplete 1. Primary level
2. Junior cert 3. Leaving cert
4. Third level 5. Never went to school
6. Special needs education 8. Still in education
9. Not known

C. Referral/assessment details

13. Date of referral Day Month Year

14. Main reason for referral
(based on main problem, circle)
1. Alcohol 2. Illicit drug 3. Licit drug 4. Other problem
Specify main drug/problem _____

15a. Source of referral (circle)
1. Self 2. Family 3. Friends
4. Other drug treatment centre 5. General practitioner
6. Acute hospital service excluding A&E
7. Social services/Community services
9. Court/probation/police 10. Outreach worker
11. Mobile bus 12. School 13. Prison
14. Employer 15. Mental health liaison nurse at A&E
16. Accident & emergency other
17. Mental health facility (including psychiatrist)
99. Not known
If 4, 5, 6, 13, 15, 17, please complete Q15b

15b. If client was referred from another treatment centre, please give reason for referral (circle one)
1. Client moved address
2. Client management / security
3. Dual diagnosis (psychiatric/substance use co-morbidity)
4. Treatment for blood borne diseases
5. Client unstable requires substitution treatment
6. Other treatment required (excluding substitution)
7. Client stable, transferred to satellite clinic or GP
8. Other (specify) _____

16. Date of initial assessment Day Month Year

17a. Assessment outcome (circle one)
1. Suitable 2. Unsuitable
If 2, STOP and return form to HRB.

17b. Assessment criterion fulfilled (circle)
1. Yes 2. No 3. Pending 8. Not applicable
If 2, STOP and return form to HRB.

17c. Date assessment criterion fulfilled
Day Month Year

18a. Client's treatment status (circle one)
1. Offered treatment (proceed to Q19)
2. Placed on waiting list for opiate substitute
6. Placed on other drug treatment waiting list
4. Psychiatric assessment only
3. Transferred to another site
Specify site _____
If 3 or 4, STOP and return form to HRB.
If 2, 6, go to 18b, if 1 go to 19

18b. If client was on waiting list, please give reason client removed from waiting list (circle one)
1. Treatment offered with this centre
2. Client did not fulfil criteria to commence treatment
3. Client did not accept substitution/other drug treatment
4. Client transferred/commenced treatment with another centre. Specify centre _____
5. Service unable to contact / locate client
6. Client admitted to hospital
7. Client sent to prison
8. Client died
9. Other (specify) _____
If 1 continue form, otherwise STOP and return to HRB

19. Accepted place at this treatment agency (circle one)
1. Yes 2. No
If 2, STOP and return form to HRB.

D. Treatment details

20. Number of times started treatment in this centre this year (Jan-Dec)
(excluding continuous care and previous referrals or assessments)
(Enter 1, if first time this year) Times

21a. Date THIS treatment started Day Month Year

21b. If received an opiate substitute (methadone/suboxone) date THIS substitution started Day Month Year

22. Ever previously treated for problem drug or alcohol use
(If main problem is alcohol, circle appropriate answer in alcohol options or if main problem is a drug, circle appropriate answer in drug options)
Alcohol 1. Never treated 2. Previously treated 8. Not applicable 9. Not known
Drug 1. Never treated 2. Previously treated 8. Not applicable 9. Not known

23. Type of contact with this centre (circle)
1. First treatment 2. One or more treatment periods 9. Not known

please go to section E →

please fold here

E. Substance use

24a. Age first used any drug
(excluding alcohol and tobacco) years (if not applicable code 88)

24b. Specify first drug used
(excluding alcohol and tobacco) _____

a. Problem substance(s) including alcohol (write in words)	b. Route of administration	use codes	c. Frequency of use in last month	use codes	d. Age at first use (years, if unknown 99)
25. Main substance name		1. Inject 2. Smoke 3. Gastronic 4. Snift/snort 5. Sublingual 6. Rectal 7. Topical 9. Not known		1. Once a week, or less 2. 2-6 days per week 3. Daily 4. No use in past month 9. Not known	
26. Substance 2 name*					
27. Substance 3 name					
28. Substance 4 name					

*In addition to the main problem substance, record any secondary substances that are part of the client's CURRENT problem alcohol or drug use.

If alcohol is listed as a problem substance at Q25-Q28, please complete Q29a to Q29h; otherwise go to Q29a.

29e. Please specify the preferred types of alcohol consumed
(circle all that apply)
2. Beer 3. Spirits 4. Wine 5. Fortified wine 6. Cider 7. Alcopops
8. Other (e.g. methylated spirits)
Specify _____

29f. How many were consumed on a typical drinking day over the past month?
(if none write 0) Standard drinks

29g. Please specify the number of days alcohol was consumed within the past month (if none write 0) Days

29h. Please categorise the extent of the drinking problem (circle)
2. Hazardous drinker 3. Harmful drinker 4. Dependent drinker

F. Risk behaviour

29a. Injected in past month (circle) 1. Yes 2. No 9. Not known

29b. Ever injected (circle) 1. Yes 2. No 9. Not known

29c. If yes, age first injected years (if not applicable code 88)

30. Ever shared any injecting equipment (circle)
1. Yes 2. No 8. Not applicable 9. Not known

G. Activity details

33a. Treatment interventions provided (please tick all treatment interventions provided and circle the main treatment intervention)	33b. Date commenced each type of treatment intervention	33c. Date completed (or of last visit) for each intervention	33d. Number of sessions/ visits for each intervention
1. Brief intervention			
2. Alcohol detoxification			
3. Benzodiazepine detoxification			
4. Detoxification symptomatic medication			
5. Opiate detoxification (suboxone/subutex)			
6. Opiate detoxification (lofexidine)			
6b. Other detoxification Specify _____			
7. Methadone detoxification			
8. Methadone substitution			
9. Other substitution (excluding methadone) Specify _____			
12. Medication-free therapy (psychosocial therapy, therapeutic community, Minnesota Model etc)			
13. Psychiatric treatment			
14. Individual counselling			
15. Group counselling			
16. Social and/or occupational reintegration			
17. Family therapy			
18. Brief intervention: individual education /awareness programme			
19. Group education/ awareness programme			
20. Structured aftercare programme			
21. Complementary therapies			
22. Medication to maintain alcohol free status			
23. Strengthening family programme			
25. Key Worker appointed			
26. Case Manager appointed Specify service where appointed _____			
27. Care Plan			
28. Facilitated detox			
24. Sent to another site for an additional intervention not provided here	Specify site name _____		

H. Exit details

34. Outcome for main treatment intervention (circle)
1. Treatment completed
2. Transferred stable* (including release linking patient to other treatment site or other prison treatment)
3. Transferred unstable
4. Client did not wish to attend further treatment sessions because he/she considered him/herself to be stable
5. Client refused to have further sessions or did not return for subsequent appointments
6. Premature exit from treatment for non-compliance
7. Released from prison but not linked to other treatment site
8. Died 9. Sentenced to prison
11. General medical transfer or medical issue 12. No longer lives in the area
13. Mental health transfer 14. Prison to prison transfer
10. Other _____
*A client is stable when he/she has engaged with this service provider, is responding to treatment, and making an effort to reduce drug/alcohol use or to remain drug/alcohol free.

35. If outcome for main treatment intervention is premature exit from treatment site (Q34 code 6), main reason for non-compliance (circle)
1. Drug taking 2. Violent behaviour 3. Illegal activities
5. Alcohol taking 4. Not observing other rules

36. Client's condition at discharge or when last seen (circle)
1. Stable 2. Unstable 3. Died 4. Other _____

37. Date of final discharge or transfer Day Month Year

38a. Client referred to ongoing aftercare programme provided by this centre 1. Yes

38b. For clients transferred to another site for additional treatment upon discharge
Specify name of transfer site _____

39. Please specify the number of family members or significant others (who were not treated for a personal addiction) involved in this treatment (please write 0 if none)

42a. Urine screening during treatment (circle)
1. Yes 2. No

42b. If yes, screening ordered by
1. Treatment provider 2. Court

40. Vaccination (please circle any interventions provided at this centre during this treatment episode) Hepatitis A and B vaccination
1. First dose 2. Second dose 3. Third dose
4. Booster dose 1 5. Booster dose 2 6. Adequate titre protective

41. Viral screening uptake (please circle any interventions provided at this centre during this treatment episode)
1. HIV test 2. Hepatitis B test 3. Hepatitis C test

10.8 Appendix VIII – Sample Initial Assessment form

TRABEG LAWN
Matt Talbot Adolescent Services

ASSESSMENT CONSENT FORM
TO BE COMPLETED BY YOUNG PERSON

I _____, give my full and informed consent to Matt Talbot Adolescent Services to receive and give information and reports to and from the below ticked ☑ professional services and other organisations that have been involved with me while I am a client of Matt Talbot Adolescent Services.

Doctors	☐
Psychologists	☐
Psychiatrists	☐
Juvenile Liaison Officers	☐
Probation and Welfare Officers	☐
Social Workers	☐
Schools	☐
Other Treatment Centres	☐
Counsellors	☐
Care Placements	☐
Others, please list:	☐

_____

_____

_____

I consent to the use of formal assessment results (ensuring my name/identification has been removed firstly ensuring confidentiality) being used for audit/ research purposes including the accumulation of data for research purposes.

I give consent to the above:

Young Person: _____ Date: / /

Counsellor: _____ Date: / /

INITIAL ASSESSMENT FOR YOUNG PERSON.

NAME OF YOUNG PERSON: _____
ADDRESS:

_____

_____

PHONE NUMBER:

_____

DATE OF BIRTH:

_____

TIME AND DATE OF SESSION:

_____

FIRST SESSION.

LIST OF PROBLEMS:	**RATE EACH PROBLEM ON IT`S SEVERITY OF 1 - 5**

WANTS:

_____

_____

_____

_____

_____

_____

_____

_____

I agree to attend Matt Talbot Adolescent Services to have a look at the above problems (and any others that might emerge for me) over the next number of weeks. After this I will decide with my counsellor what help I need.

Signed _____ Date: _____

Young Person.

Signed _____ Date: _____

Counsellor.

TRABEG LAWN
Matt Talbot Adolescent Services

INITIAL ASSESSMENT
RED FLAG LIST

PART ONE. DETAILS
Date: _____

Young Person's Name: _____ Date of Birth: _____

Young Person's Address: _____

_____

Referring Agent: Name: _____ Organisation: _____

PART TWO. DRUG AND ALCOHOL HISTORY

		First used/Frequency
Tobacco	☐	_____
Alcohol	☐	_____
Cannabis	☐	_____
Amphetamines	☐	_____
Cocaine	☐	_____
Ecstasy	☐	_____
Opiates	☐	_____
LSD	☐	_____
Magic Mushrooms	☐	_____
Petrol/ Glue/ Paints	☐	_____
Benzodiazepines	☐	_____
MDMA	☐	_____

Favourite drug of choice _____

Drugs used on a daily basis: _____

1. _____ 2. _____

☐ Pre-contemplative	☐ Pre-contemplative
☐ Contemplative	☐ Contemplative
☐ Planning	☐ Planning
☐ Action	☐ Action

PART THREE GENERAL BEHAVIOUR CHANGES

☐ Temper Outbursts

☐ Dramatic Attention seeking behaviour

☐ Increased Irritability

☐ Hyperactivity

☐ Extreme apathy

☐ Impulsive behaviour

☐ Low moods

☐ Relationships with Peers, siblings, parent affected. Who? _____

☐ Suicidal ideation

☐ Suicidal attempts

☐ Money/objects missing from home that could easily be converted into cash

☐ Alcohol or prescription drugs going missing or dwindling in the house

☐ Increased time spent alone in room/withdrawn behaviour

☐ Paranoia

☐Changing friends and moving away from old ones

☐ Loss of interest in sports and hobbies

PART FOUR PHYSICAL WARNING SIGNS

Self-Report on Physical condition during first appointment _____

_____

☐ Intoxicated during first session

☐ Blackouts

☐ Short-term memory loss

☐ Loss of/increased appetite

☐ Weight loss/gain

☐ White or pale face

☐ Bloodshot eyes that appear glassy or vague

☐ Loss of fine motor co-ordination e.g. holding a glass

☐ Excessive sleeping

☐ Insomnia

☐ Vomiting or flushed complexion

☐ Young person's appearance has deteriorated

TRABEG LAWN
Matt Talbot Adolescent Services

PART FIVE LEGAL PROBLEMS

☐ Under JLO currently
JLO _____

☐ Under probation scheme currently
Probation officer _____

☐ Pending Court Case. For: _____

Other charges:

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____

TIER 2 COMMUNITY INTERVENTION

☐ LDTF Involvement _____

☐ Intervention tired _____

☐ Date of Intervention _____

☐Successful ☐ Unsuccessful

PART SIX WORK/SCHOOL RELATED PERFORMANCE

Currently in employment /education Where? _____
Age left education: _____
Loss of interest in school/work Comment _____
Consequences in work/school due to use/drinking _____

_____

PART SEVEN OTHER INTERVENTIONS ACCESSED

☐ Tier 1 e.g. GP= _____

☐ Tier 2 e.g. Youth projects _____

☐ Tier 3 e.g. Arbour House _____

☐ Tier 4 e.g. MTAS/Aislinn _____

☐ Detox _____

☐ Social worker _____

☐ In Care: _____

☐ Psychiatric Services _____

Other/comment _____

_____

Signed: Counsellor: _____ Date: _____

PART EIGHT. OUTCOME

Identified risks/red flags:

Drugs and alcohol

_____
_____

Risk Behaviours

_____
_____

Legal Involvement

_____
_____

Family

_____
_____

Health

_____
_____

Referral to: _____

Comment: _____

_____

Signed:_____ Date:_____

TRABEG LAWN
Matt Talbot Adolescent Services

Name: _____ Date: _____

Problem:

_____
_____
_____
_____
_____
_____

What was going on?

_____
_____
_____
_____
_____
_____

What popped into your head? 

_____
_____
_____
_____
_____
_____

What was that like for you (how are you feeling)?

_____
_____
_____
_____
_____

What did you do?  

_____
_____
_____
_____
_____

Signature: _____

10.9 Appendix IX – Ethics approval for Chapter 6 research

Tel: + 353-21-490 1901
Fax: + 353-21-490 1919

Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 4 (b) 12/06/12

2nd May 2012

Dr Stephen Byrne
Senior Lecturer
School of Pharmacy
Room 2.02
Cavanagh Pharmacy Building
University College Cork
College Road
Cork

Re: Substance use in adolescents in Cork.

Dear Dr Byrne

Expedited approval will be granted to carry out the above study in:

- Matt Talbot Services, Cork
- School of Pharmacy, UCC

subject to receipt of the following:

- Interview guide – Appendix 1, mentioned on page 3 of application form, was not included with the submission.

The following document was approved:

- Application Form.

We note that the co-investigators involved in this study will be:

- Dr Laura Sahm, Dr Sharon Lambert, Dr Suzanne McCarthy and Kevin Murphy.

Yours sincerely

Dr Michael Hyland
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

The Clinical Research Ethics Committee of the Cork Teaching Hospitals, UCC, is a recognised Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, and is authorised by the Department of Health and Children to carry out the ethical review of clinical trials of investigational medicinal products. The Committee is fully compliant with the Regulations as they relate to Ethics Committees and the conditions and principles of Good Clinical Practice.

Tel: + 353-21-490 1901
Fax: + 353-21-490 1919

Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 3 (bb) 03/07/12

21st June 2012

Dr Stephen Byrne
Senior Lecturer
School of Pharmacy
Room 2.02
Cavanagh Pharmacy Building
University College Cork
College Road
Cork

Re: Substance use in adolescents in Cork.

Dear Dr Byrne

The Chairman approved the following:

- Interview Guide.

Full approval is now granted to carry out the above study.

Yours sincerely

Dr Michael Hyland
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

Tel: + 353-21-490 1901
Fax: + 353-21-490 1919

Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 3 (oo) 05/02/13

25th January 2013

Dr Stephen Byrne
Senior Lecturer
School of Pharmacy
Room 2.02
Cavanagh Pharmacy Building
University College Cork
College Road
Cork

Re: Substance use in adolescents in Cork.

Dear Dr Byrne

The Chairman approved the following:

- Additional study sites at Ballyphenhane Action for Youth Project, Knocknaheeney Youth Project and Matt Talbot Services Cork.

Yours sincerely

Dr Michael Hyland
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

10.10 Appendix X – Information sheet and consent form for Chapter 6 research

Information Sheet (Briefing for Participants)

Purpose of the Study. As part of the requirements for my PhD at UCC, I have to carry out a research study. The study will look at why young people try benzodiazepines, and why they continue taking them after that.

What will the study involve? The study will involve a single interview which should last between 30 and 60 minutes, allowing a small amount of extra time for explaining the aims of the study, your questions about the study and how you feel after the interview.

Why have you been asked to take part? You have been asked because you have taken benzodiazepines in the past.

Do you have to take part? Participation is voluntary. If you agree to participate you'll sign a consent form, and you'll get to keep a copy of this information sheet and the consent form. You can withdraw at any time even if you have agreed at first to participate. You can withdraw your permission to use your interview within two weeks of the interview; if you withdraw permission, then the interview will be permanently deleted.

Will your participation in the study be kept confidential? Yes. I will ensure that no clues to your identity appear in the thesis. Any extracts from what you say that are quoted in the thesis will be entirely anonymous.

What will happen to the information which you give? The data will be kept confidential for the duration of the study. On completion of the thesis, the data will be retained for 5 years from the date of the interview.

What will happen to the results? The results will be presented in my thesis. They will be seen by my supervisors, a second marker and an external examiner. The thesis may be read by future students. The study may be presented at scientific conferences and/or published in an academic journal.

What are the possible disadvantages of taking part? It is unlikely for there to be negative consequences if you take part. Although unlikely, it is possible that talking about your experiences in this way may cause some form of distress.

What if there is a problem? At the end of the interview, I will discuss with you how you found the experience and how you are feeling. If you subsequently feel distressed, you should contact me, the researcher or the seek support from your local counsellor.

Who has reviewed this study? Approval has been granted to do this study by the Cork Research Ethics Committee of the Cork Teaching Hospitals.

Any further queries? If you need any further information, you can contact the researcher, Kevin Murphy, by telephone (0863993086) or email, kev.mur21@gmail.com

If you agree to take part in the study, please sign the consent form overleaf

Consent Form

I _____ agree to participate in Mr. Kevin Murphy's research study.

The purpose of the study has been explained to me and I understand it.

I am participating voluntarily.

I give permission for my interview with Mr. Murphy to be tape-recorded.

I understand that I can withdraw from the study, without repercussions, at any time whether before it starts or while I am participating.

I understand I can withdraw my permission to use the data within two weeks of the study, in which case the material I have provided will be deleted.

I understand that anonymity will be ensured in the write-up by disguising my identity.

I understand that disguised extracts from what I say may be quoted in the thesis and any subsequent publications if I give permission below:

(Please tick one box)

- I agree to quotation/ publication of extracts from my data □
- I do not agree to quotation/ publication of extracts from my data □

Signed_____ Date: _____

Parent (if necessary)_____ Date: _____

Parent (if necessary)_____ Date: _____

10.11 Appendix XI – Ethical approval for Chapter 7 research

UCC
Tel: + 353-21-490 1901
Fax: + 353-21-490 1919
Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 4 (h) 09/04/13

14th March 2013

Dr Stephen Byrne
Senior Lecturer in Clinical Pharmacy
School of Pharmacy
Room UG06
Cavanagh Pharmacy Building
University College Cork
College Road
Cork

Re: Young person benzodiazepine use from counsellors' perspectives.

Dear Dr Byrne

Expedited approval will be granted to carry out the above study subject to receipt of the following:

- Information Leaflets for Parents/Guardians and Participants
- Consent forms for Parents/Guardians
- Consent/Assent Forms for Participants.

The following documents have been approved:

- Signed Application Form
- Interview Topic Guide.

We note that the co-investigators involved in this study will be:

- Dr Sharon Lambert, Dr Ciara Staunton, Dr Suzanne McCarthy, Dr Laura Sahm and Kevin Murphy.

Yours sincerely

Professor Michael Molloy
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

UCC
Tel: + 353-21-490 1901
Fax: + 353-21-490 1919
Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee
Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 3 (m) 07/01/14

11th December 2014

Dr Suzanne McCarthy
Lecturer
School of Pharmacy
Room 2.02
Cavanagh Pharmacy Building
University College Cork
College Road
Cork

Re: GP views of benzodiazepine prescribing to young people.

Dear Dr McCarthy

Approval for amendment dated 29th November 2013 will be granted subject to receipt of the following:

- Revised Study Protocol
- Revised Information Leaflet
- Revised Consent Form
- Copy of Interview Guide.

The following document has been approved:

- Amendment Application Form.

Yours sincerely

Professor Michael G Molloy
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

The Clinical Research Ethics Committee of the Cork Teaching Hospitals, UCC, is a recognised Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, and is authorised by the Department of Health and Children to carry out the ethical review of clinical trials of investigational medicinal products. The Committee is fully compliant with the Regulations as they relate to Ethics Committees and the conditions and principles of Good Clinical Practice.

UCC

Tel: + 353-21-490 1901
Fax: + 353-21-490 1919

Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 3 (l) 04/03/14

4th February 2014

Dr Stephen Byrne
Senior Lecturer in Clinical Pharmacy
School of Pharmacy
Room UG06
Cavanagh Pharmacy Building
University College Cork
College Road
Cork

Re: Young person benzodiazepine use from counsellors' perspectives.

Dear Dr Byrne

The Chairman approved the following:

- Information Leaflets and Consent Form for Participants.

Full approval is now granted to carry out the above study.

We note that the co-investigators involved in this study will be:

- Dr Sharon Lambert, Dr Ciara Staunton, Dr Suzanne McCarthy, Dr Laura Sahm and Kevin Murphy.

Yours sincerely

Professor Michael G Molloy
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

10.12 Appendix XII – Information sheet and consent form for Chapter 7 research

Information Sheet (Briefing for Participants)

Purpose of the Study. As part of the requirements for my PhD at UCC, I have to carry out a research study. The study will look at why young people try benzodiazepines, and why they continue taking them after that.

What will the study involve? The study will involve a single interview which should last between 30 and 60 minutes, allowing a small amount of extra time for explaining the aims of the study, your questions about the study and how you feel after the interview.

Why have you been asked to take part? You have been asked because you are a drugs worker/counsellor that has treated/is treating a young person that has taken benzodiazepines in the past.

Do you have to take part? Participation is voluntary. If you agree to participate you'll sign a consent form, and you'll get to keep a copy of this information sheet and the consent form. You can withdraw at any time even if you have agreed at first to participate. You can withdraw your permission to use your interview within two weeks of the interview; if you withdraw permission, then the interview will be permanently deleted.

Will your participation in the study be kept confidential? Yes. I will ensure that no clues to your identity appear in the thesis. Any extracts from what you say that are quoted in the thesis will be entirely anonymous.

What will happen to the information which you give? The data will be kept confidential for the duration of the study. On completion of the thesis, the data will be retained for 5 years from the date of the interview.

What will happen to the results? The results will be presented in my thesis. They will be seen by my supervisors, a second marker and an external examiner. The thesis may be read by future students. The study may be presented at scientific conferences and/or published in an academic journal.

What are the possible disadvantages of taking part? It is unlikely for there to be negative consequences if you take part. Although unlikely, it is possible that talking about your experiences in this way may cause some form of distress.

What if there is a problem? At the end of the interview, I will discuss with you how you found the experience and how you are feeling. If you subsequently feel distressed, you should contact me, the researcher at the number below.

Who has reviewed this study? Approval has been granted to do this study by the Cork Research Ethics Committee of the Cork Teaching Hospitals.

Any further queries? If you need any further information, you can contact the researcher, Kevin Murphy, by telephone (0863993086) or email, kev.mur21@gmail.com

If you agree to take part in the study, please sign the consent form overleaf…

Consent Form

I _____ agree to participate in Mr. Kevin Murphy's research study.

The purpose of the study has been explained to me and I understand it.

I am participating voluntarily.

I give permission for my interview with Mr. Murphy to be tape-recorded.

I understand that I can withdraw from the study, without repercussions, at any time whether before it starts or while I am participating.

I understand I can withdraw my permission to use the data within two weeks of the study, in which case the material I have provided will be deleted.

I understand that anonymity will be ensured in the write-up by disguising my identity.

I understand that disguised extracts from what I say may be quoted in the thesis and any subsequent publications if I give permission below:

(Please tick one box)

- I agree to quotation/ publication of extracts from my data □
- I do not agree to quotation/ publication of extracts from my data □

Signed_____ Date: _____

Information Sheet (Briefing for Participants)

Purpose of the Study. As part of the requirements for my PhD at UCC, I have to carry out a research study. The study will look at the challenges faced by General Practitioners prescribing benzodiazepines/Z-type nonbenzodiazepines to people less than 18 years of age.

What will the study involve? The study will involve a single interview which should last between 30 and 60 minutes, allowing a small amount of extra time for explaining the aims of the study, your questions about the study and how you feel after the interview.

Why have you been asked to take part? You have been asked because you are a General Practitioner in the Cork/Kerry area.

Do you have to take part? Participation is voluntary. If you agree to participate you'll sign a consent form, and you'll get to keep a copy of this information sheet and the consent form. You can withdraw at any time even if you have agreed at first to participate. You can withdraw your permission to use your responses within two weeks of the focus group; if you withdraw permission, then your responses will be permanently deleted.

Will your participation in the study be kept confidential? Yes. I will ensure that no clues to your identity appear in the thesis. Any extracts from what you say that are quoted in the thesis will be entirely anonymous.

What will happen to the information which you give? The data will be kept confidential for the duration of the study. On completion of the thesis, the data will be retained for 5 years from the date of the interview.

What will happen to the results? The results will be presented in my thesis. They will be seen by my supervisors, a second marker and an external examiner. The thesis may be read by future students. The study may be presented at scientific conferences and/or published in an academic journal.

What are the possible disadvantages of taking part? It is unlikely for there to be negative consequences if you take part. Although unlikely, it is possible that talking about your experiences in this way may cause some form of distress.

What if there is a problem? At the end of the interview, I will discuss with you how you found the experience and how you are feeling.

Who has reviewed this study? Approval has been granted to do this study by the Cork Research Ethics Committee of the Cork Teaching Hospitals.

Any further queries? If you need any further information, you can contact the researcher, Kevin Murphy, by telephone (0863993086) or email, kev.mur21@gmail.com

If you agree to take part in the study, please sign the consent form

Consent Form

I _____ agree to participate in Mr. Kevin Murphy's research study.

The purpose of the study has been explained to me and I understand it.

I am participating voluntarily.

I give permission for my responses in the focus group to be tape-recorded.

I understand that I can withdraw from the study, without repercussions, at any time whether before it starts or while I am participating.

I understand I can withdraw my permission to use the data within two weeks of the study, in which case the material I have provided will be deleted.

I understand that anonymity will be ensured in the write-up by disguising my identity.

I understand that disguised extracts from what I say may be quoted in the thesis and any subsequent publications if I give permission below:

(Please tick one box)

I agree to quotation/ publication of extracts from my data □

I do not agree to quotation/ publication of extracts from my data □

Signed_____ Date: _____