THE LIVED EXPERIENCE OF ‘OPIOID USE DISORDER’ IN IRELAND IN THE 21ST CENTURY

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“Nobody will laugh long who deals much with opium: its pleasures even are of a grave and solemn complexion.”

(Thomas de Quincy, English essayist, “Confessions of an English Opium-Eater”, 1785-1859)
Abstract

The lived experience of ‘Opioid Use Disorder’ in Ireland in the 21st Century

Dr Lisa Moran MB BCh BAO MICGP, MSc.

Introduction

This thesis focuses on three critical phases in the life journey of a person with an opioid use disorder (OUD); Initial, random intermittent opioid use, termed ‘Recreational Sporadic Use’, transitioning to increased persistent opioid use, labelled ‘Intensified Sustained Use’, culminating in complete impulsivity and full opioid dependence, coined, ‘Loss of Control’. The crucial role of the neurobiology of dependence, explored in depth in this thesis, underpins these key phases in developing and sustaining an opioid dependence. Building on this framework the thesis unravels the effect of Adverse Childhood Experiences on the likelihood of experimenting with opioids and subsequently cultivating a dependence. It then recounts the effect of both dual diagnosis and concurrent benzodiazepine abuse on sustaining and intensifying one’s dependence until an individual eventually surrenders to the inevitable destructive effects of an opioid dependence and loses all voluntary control over their usage. The thesis then delves further into the lives of individuals with OUD by illuminating both positive and negative factors in their life journeys, which influence the remitting, relapsing nature of their illness. Invariably, given the neurobiological factors nourishing drug dependence the negative factors triumph, and relapse to drug use prevails. In unravelling the complexities of the neurobiology of dependence, this thesis, highlights that undoubtedly the best approach to help, support and where possible treat individuals with an OUD is under the umbrella term of harm reduction. A special focus is placed on the harm reductive properties of methadone as a therapeutic agent in combatting OUD, with a particular emphasis on the need to educate all members of society on its therapeutic benefits. Undoubtedly, the most harrowing outcome for all in this often-thwarted journey is fatal overdose (OD), unfortunately the outcome for which far too many individuals succumb. Therefore, the most pivotal of harm reduction strategies to ebb the flow of death in OUD, ‘Take Home Naloxone Programmes’ (THNPs) are examined in the latter half of this thesis, with particular scrutiny given to Ireland’s THNP. As this thesis highlights, in Ireland, we have made much progress in our approach to addressing the opioid crisis but, as always, there is much room for improvement and advances.

Aims

The predominant aim of this thesis echoes a key strategic purpose of Ireland’s latest drug strategy, ‘Reducing harm, supporting recovery: a health-led response to drug and alcohol use in Ireland 2017-2025’, which is to reduce the morbidity and mortality associated with OUD. Two studies are undertaken to achieve this purpose. Study 1 aims to give clients of the Mid-West of Ireland’s Programme for Methadone Maintenance Treatment (MMT) a voice, to document their lived experience of opioid dependence before, during and after their ‘three-phase journey’ through OUD. It aims to co-develop with clients a tailored care plan to enhance their chance of successfully engaging with the MMTP. Study 2 aims to
gain an overall appreciation of Ireland’s national THNP to optimise its functioning. A second objective of this study is to improve the likelihood of a patient attending hospital post administration of naloxone in the community, a step that is associated with overall better survival rates.

Methods

This thesis employs a mixed method research design. Study 1 is a qualitative study; Study 2 employs a quantitative method.

Results

Study 1 reveals an enriching insight into the personal experience of each individual client’s journey. Their journeys, though each unique, had common chronological sub-themes which are recounted in depth. Subsequent data analysis identifies common life experiences, which influence their journey both negatively and positively. Final data analysis identifies clients’ individual suggestions for improving their journey. The results of Study 2 reveal inadequacies in the current reporting mechanism currently in place on the use of naloxone in the community setting in Ireland. Descriptive analysis then looks at the characteristics pertaining to overdose patients themselves and subsequently the characteristics of the overdose scene are documented. Thereafter, using a logistical regression model, statistical results on the variables that influence a patient’s hospital attendance are presented.

Conclusion

The thesis concludes with recommendations for improvement in the management of OUD. It proposes how knowledge of ACEs should influence the MMTPs in Ireland and internationally, to adopt a more ‘trauma informed’ ethos. Subsequently, recommendations centre on dually diagnosed individuals, with a specific focus on addressing benzodiazepine misuse. Next, the theme of therapeutics is explored, listing specific proposals on how to both promote education and reduce stigma in relation to methadone, as a treatment option in OUD. Finally, the thesis focuses on recommendations with regard to THNPs. Initial suggestions focus on improving the Irish THNP and subsequently general recommendations applicable to THNPs internationally are addressed.
Declaration of originality

I declare that this thesis, which I submit to the University of Limerick for examination in consideration for the award of MD, is my own individual work, and was prepared with the guidance of my supervisors Dr Khalifa Elmusharaf and Dr Eamon Keenan.

I have not already acquired a degree in University of Limerick or elsewhere based on this work. Additionally, appropriate care was taken to ensure that the thesis is original, and, to the best of my knowledge, does not breach copyright law. Where any text was attained from others, it has been appropriately cited and acknowledged within the text.

Publications derived from this thesis


Signed:


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Date: 31.01.19
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I would like to offer a huge thank you to the participating clients of the Health Service Executive’s Mid-West Limerick Drug and Alcohol Services, as without their involvement key research in this thesis could not have been possible. I must also acknowledge all clients of the service in which I have worked over the years. Their personal, often harrowing stories of opioid use disorder, which they willingly shared with me, were truly the inspiration for this thesis.

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<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome</td>
</tr>
<tr>
<td>ACE</td>
<td>Adverse Childhood Experience</td>
</tr>
<tr>
<td>BLS</td>
<td>Basic Life Support</td>
</tr>
<tr>
<td>BMJ</td>
<td>British Medical Journal</td>
</tr>
<tr>
<td>BZD</td>
<td>Benzodiazepines</td>
</tr>
<tr>
<td>CHO</td>
<td>Community Healthcare Organisation</td>
</tr>
<tr>
<td>CPI</td>
<td>College Of Psychiatrists</td>
</tr>
<tr>
<td>CPR</td>
<td>Cardiopulmonary Resuscitation</td>
</tr>
<tr>
<td>CTL</td>
<td>Central Treatment List</td>
</tr>
<tr>
<td>EMA</td>
<td>Ecological Momentary Assessment</td>
</tr>
<tr>
<td>EMCDDA</td>
<td>European Monitoring Centre For Drugs And Drug Addiction</td>
</tr>
<tr>
<td>EU</td>
<td>European Union</td>
</tr>
<tr>
<td>GABA</td>
<td>Gamma Amino Butyric Acid</td>
</tr>
<tr>
<td>GP</td>
<td>General Practitioner</td>
</tr>
<tr>
<td>GR</td>
<td>Glucocorticoid Receptors</td>
</tr>
<tr>
<td>HBV</td>
<td>Hepatitis B Virus</td>
</tr>
<tr>
<td>HCV</td>
<td>Hepatitis C Virus</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>HSE</td>
<td>Health Service Executive</td>
</tr>
<tr>
<td>ICGP</td>
<td>Irish College Of General Practitioners</td>
</tr>
<tr>
<td>IIOP</td>
<td>Irish Institute Of Pharmacy</td>
</tr>
<tr>
<td>IsuE</td>
<td>Intensified Sustained Escalated Drug Use</td>
</tr>
<tr>
<td>LoC</td>
<td>Loss Of Control</td>
</tr>
<tr>
<td>LR</td>
<td>Logistical Regression</td>
</tr>
<tr>
<td>LTD</td>
<td>Long-Term Depression</td>
</tr>
<tr>
<td>LTP</td>
<td>Long-Term Potentiation</td>
</tr>
<tr>
<td>MLA</td>
<td>Methyllycaconitine</td>
</tr>
<tr>
<td>MDT</td>
<td>Multi-Disciplinary Team</td>
</tr>
<tr>
<td>MMTP</td>
<td>Methadone Maintenance Treatment Programme</td>
</tr>
<tr>
<td>MTP</td>
<td>Methadone Treatment Programme</td>
</tr>
<tr>
<td>MWRDTF</td>
<td>Mid-West Regional Drugs Task Force</td>
</tr>
<tr>
<td>NGO</td>
<td>Non-Government Organisation</td>
</tr>
<tr>
<td>NOC</td>
<td>National Oversight Committee</td>
</tr>
<tr>
<td>OAT</td>
<td>Opioid Agonist Treatment</td>
</tr>
<tr>
<td>OATM</td>
<td>Opioid Agonist Treatment Methadone</td>
</tr>
<tr>
<td>OD</td>
<td>Drug Overdose</td>
</tr>
<tr>
<td>OUD</td>
<td>Opioid Use Disorder</td>
</tr>
<tr>
<td>PFC</td>
<td>Pre-Frontal Cortex</td>
</tr>
<tr>
<td>PSI</td>
<td>Pharmaceutical Society Of Ireland</td>
</tr>
<tr>
<td>PWIDs</td>
<td>People Who Inject Drugs</td>
</tr>
<tr>
<td>ReS</td>
<td>Recreational Sporadic Drug Use</td>
</tr>
<tr>
<td>SIFs</td>
<td>Supervised Injecting Facilities</td>
</tr>
<tr>
<td>SmPC</td>
<td>Summary Of Product Characteristics</td>
</tr>
<tr>
<td>SUD</td>
<td>Substance Use Disorder</td>
</tr>
<tr>
<td>THNP</td>
<td>Take Home Naloxone Programme</td>
</tr>
<tr>
<td>TEDS</td>
<td>Treatment Episode Data Set</td>
</tr>
<tr>
<td>US FDA</td>
<td>US Food And Drug Administration</td>
</tr>
<tr>
<td>VTA</td>
<td>Ventral Tegmental Area</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation</td>
</tr>
</tbody>
</table>
Chapter 1 Introduction

1.1 Chapter Overview

This chapter first defines ‘Opioid Use Disorder’ (OUD). It then outlines the natural history of OUD, with a subsequent focus on the role of neurobiology, which underpins the evolution of OUD. Thereafter, the importance of ‘adverse childhood experiences’ (ACEs) in predisposing an individual to develop an OUD is summarised. The two main theories supporting drug dependency are then discussed. The latter half of the chapter delineates the global magnitude of OUD with a particular focus on both European and Irish landscapes. The mainstay of European management, ‘Opioid Agonist Treatment’ (OAT) is then explored. The harm reduction services available in the Irish service are then listed. Finally, overdose (OD) in the context of OUD is reviewed.

1.2 Defining Opioid Use Disorder

Abuse and misuse of opioids, termed an opioid use disorder (OUD), is a major health concern worldwide. (1) The opioid class of drugs comprises of natural opioids (e.g., morphine, codeine), semi-synthetic opioids (e.g., heroin, oxycodone) and synthetic opioids (e.g., methadone, buprenorphine, and fentanyl). (2) OUD is defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (3) as a “problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following, (Table 1 below) occurring within a 12-month period.”

Of note, in 1964 a World Health Organisation (WHO) Expert Committee suggested that the term ‘dependence’ should be used in lieu of ‘addiction’ and
‘habituation’ (4) when referencing drug reliance. For the purpose of this thesis, the term ‘dependence’ will have specific reference to both the physical and psychological elements of opioid dependence. In terms of an OUD, physical dependence refers to points 10 and 11 of the diagnostic criteria as listed below, while psychological or psychic dependence implies compromised or weakened ability to control opioid use.

Table 1: Diagnostic Criteria for an Opioid Use Disorder

<table>
<thead>
<tr>
<th>No</th>
<th>Diagnostic Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Use of an opioid in increased amounts or longer than intended.</td>
</tr>
<tr>
<td>2.</td>
<td>Persistent wish or unsuccessful effort to cut down or control opioid use.</td>
</tr>
<tr>
<td>3.</td>
<td>Excessive time spent to obtain, use, or recover from opioid use.</td>
</tr>
<tr>
<td>4.</td>
<td>Strong desire or urge to use an opioid.</td>
</tr>
<tr>
<td>5.</td>
<td>Interference of opioid use with important obligations.</td>
</tr>
<tr>
<td>6.</td>
<td>Continued opioid use despite resulting interpersonal problems, social problems (for example, interference with work), or both.</td>
</tr>
<tr>
<td>7.</td>
<td>Elimination or reduction of important activities because of opioid use.</td>
</tr>
<tr>
<td>8.</td>
<td>Use of an opioid in physically hazardous situations (for example, while driving).</td>
</tr>
<tr>
<td>9.</td>
<td>Continued opioid use despite resulting physical problems, psychological problems, or both.</td>
</tr>
<tr>
<td>10.</td>
<td>Need for increased doses of an opioid for effects, diminished effect per dose, or both†</td>
</tr>
<tr>
<td>11.</td>
<td>Withdrawal when dose of an opioid is decreased, use of drug to relieve withdrawal, or both†</td>
</tr>
</tbody>
</table>

Reference: Diagnostic and Statistical Manual of Mental Disorders, fifth edition (3)

* If two or three items cluster together in the same 12 months, the disorder is mild; if four or five items cluster, the disorder is moderate; and if six or more items cluster, the disorder is severe.
† If the opioid is taken only as prescribed, this item does not count toward a diagnosis of an opioid-use disorder.
1.3 Natural History of OUD

Evolution to drug dependence is composed of three successive and independent phases: successive, because admission to one phase is an essential stipulation to progress to the ensuing one; yet, independent, because entering one phase does not guarantee advancement to the next one. (5)

Phase 1 encompasses occasional, infrequent drug use, coined by Piazza as “Recreational Sporadic (ReS) drug use”. Drug use is random and accounts for only a small percentage of the individual’s day-to-day, even week-to-week activities. This behaviour can be judged as routine and “normal” and is commonplace in a certain percentage of the population. (5)

Phase 2, “Intensified Sustained Escalated (ISuE) drug use”, again coined by Piazza, commences with an escalation in occurrence, quantity, and incentive to acquire drugs. The ISuE phase is the first “moderate pathological state,” one in which the quantity of drug use is excessive but the individual’s conduct is still ordered. Everyday responsibilities are achieved and individuals still typically considered socially acceptable in society. (5)

The third phase heralds the start of the most severe pathological condition. Now, the individual has “Loss of Control (LoC)” of drug consumption and develops complete dependency. Drug acquisition becomes the individual’s chief goal, occupying most of their time and energy. Subsequently, social degradation and deprivation is unavoidable, and relapse to drug taking—even after sustained periods of self-restraint—is inevitable. (5)

It is important to highlight that during the evolution from “recreational” to “sustained” drug use, the first noticeable change in drug consumption is quantitative in nature. When transitioning from “sustained” use to “loss of
control” over use then the alteration is of a qualitative nature, the primary modification being not the quantity of the drug consumed but the individual’s now inability to restrict substance intake, a qualitative change.

1.4 The Neurobiology of Drug Dependency

The neurobiology of drug dependency underpinning the above ‘three phase process’ is expanded upon in the following section.

1.4.1 Phase 1

*Phase 1* on the path to developing a substance use disorder (SUD) is due to an increase in dopamine release in the brain’s nucleus accumbens, particularly the nuclear shell. Dopamine is a brain neurotransmitter that modulate amongst others, cognition, drive, and pleasurable emotions. The primary over-excitation of this system by opioids, which incentivises our natural behaviours, yields the euphoric effects of drugs, ensuring they are extremely likeable and pleasant and initially drives the recreational use of drugs.

1.4.2 Phase 2

Incorporating both a psychological and biological component, four core theories underpin *Phase 2* ‘the evolution from ReS to ISuE’.

1.4.2.1 Theory 1

*Increased sensitivity to dopamine*

Firstly, the motivational influences of drugs intensify, or *sensitize*, in the evolution of escalated and sustained drug use. For nearly 30 years research has proven that individuals who are susceptible for acceleration to drug use have a ‘*spontaneously sensitized dopaminergic system*’ (6) and an abnormally high response to their first experimentation with drugs. (7)
This *sensitized* reaction and the accompanying susceptibility to intensify one's drug use to a pattern of *sustained* use can be provoked by either repetitive stress or recurrent drug exposure. (8) When ‘stressed’, an upsurge in the transmission of dopamine is seen in the nucleus accumbens of vulnerable rats. (9) Advancing on this, later research showed that after *intensified* use, the motivational and fortifying aspects of drugs were amplified. (10)

These and associated research findings propose an overall increase in the susceptibility of an individual’s motivational drive—driving the individual to increasingly desire drugs—as a strong component in the development of drug dependence. (11)

**1.4.2.2. Theory 2**

*Impairment of the Pre-Frontal Cortex (PFC)*

A properly functioning PFC is necessary for healthy neuropsychological functioning as it exhibits control over emotion, reasoning and behaviour. This explains why PFC disturbance in drug dependence negatively affects a broad spectrum of behaviours.

Imaging studies and pre-clinical investigations (12, 13) show a disordered functioning of the PFC gives rise to a syndrome that is typified by assigning undue importance to the drug and drug-related prompts, a diminished respect for non-drug related positive reinforcers and a decreased capacity to prevent maladaptive or destructive actions. (14)

Because of these fundamental shortfalls, the search for and acquisition of drugs becomes the primary motivational force, sacrificing other undertakings (15) and climaxing in risky, often life-threatening actions in the quest for drugs. (16)
1.4.2.3 Theory 3

*Relationship between glucocorticoid hormones and the dopaminergic system*

One of the most critical controllers of dopaminergic activity in the accumbens is glucocorticoid tone. (17) Vulnerable rats produce a larger amount of glucocorticoids (18) and these hormones are an essential element in shaping their susceptibility to drug abuse (19). Glucocorticoid receptors (GRs) are expressed by neurons that distend back to the ventral tegmental area (VTA).

Explicitly subduing the glucocorticoid receptors (GRs) in these neurons radically diminishes the overall activity of dopamine in the accumbens and induces a behaviour indistinguishable from abuse-resistant rats (8). In stark contrast, dispensing glucocorticoids repetitively escalates vulnerability to the self-administration of drugs. (20) As such, because of this GR over-stimulation, some individuals progressively desire additional quantities of a drug and have a greater susceptibility to cultivate ISuE.

1.4.2.4 Theory 4

`'Allostasis: a patho-physiological means that anchors sustained drug use’`

Le Moal and Koob first suggested the foundation of an ‘allostatic state’ was a critical component in establishing drug dependency. (21) As such, following lengthy exposure to drugs, reward systems acclimatize to this everyday overexposure by altering the ‘homeostatic set point’ (allostasis) to adjust to this constant excessive stimulus. For this reason, the drug state gradually becomes the norm and the nondrug state is now sensed as a pathological, or at least, as highly undesirable and hostile. Drugs increasingly move from being intensely desired to also stalwartly required.
The chief first-hand evidence for this theory is the alteration of the ‘set point’ detected in rats that develop drug dependency. In such rats, the sensitivity of their incentive lessens and over time requires increased stimulation to attain the same level of reward. (22) With the evolution of a downregulated reward system, an individual’s progression to intensified, continued drug use is now complete.

1.4.3 Phase 3

The final step, phase 3, results from a compromised synaptic flexibility and with it the advancement to loss of control of drug use and full dependence.

It is generally understood that synaptic malleability, controlled by ‘long-term potentiation’ (LTP) and by ‘long-term depression’ (LTD) within the synapses, denotes the brain’s ability to reinforce or dampen neuronal pathways in order to uphold adaptive behavioural responses to alterations in one’s environment. (23) If a significant incident results in a current behavioural sequence not providing adequate or appropriate adjustment to the environment or situation, the brain can dampen the synaptic power in the affected circuit and concurrently increase synaptic strength in a new circuit, thus facilitating a novel and more responsive behavioural sequence to respond to the needs of the individual. The equilibrium between potentiation (LTP) and depression (LTD) can vary from behaviour to behaviour preserving a malleable and adaptive behavioural response.

In OUD, loss of this flexibility in regions such as the nucleus accumbens and the pre-frontal cortex, have devastating consequences. Behaviour remains crystallized around one behavioural goal, the acquisition and intake of opioids and cannot change to another. Pronounced doggedness to attain the ‘crystallized goal’ of opioid intake, no matter the losses or penalties is evident. Externally, this manifests as a substantial ‘loss of control’ over drug intake. However, this is not
a state of obsessive pathological impetus for the drug but instead a ‘prison’ from which the behaviour preserved around one exclusive goal, drug consumption, is not very likely to evade.

Pier Vincenzo Piazza and colleagues describe an excellent metaphor to explain this phenomenon. (5) It is to envisage that the brain is a chamber full of water and behavioural goals are containers of varying shapes. Under normal circumstances, one can simply remove a given container and immerse a different one, and alter behaviour. However, if the water freezes, i.e., crystallizes (loss of synaptic plasticity), it will trap the original contained behaviour (taking drugs), and one will be imprisoned in this behavioural goal. With some aid, much exertion, and grating (agonizing first stage of any detoxification treatment), you might succeed in extracting the original cylinder from the crystallized water. However, it will be unfeasible to plug the enduring cavity with any other behavioural container. One’s behaviour is now crystallized, you may adapt to living with the crater for a period (abstinence) but eventually the temptation will be too strong, given the occasion, (stress, exposure to drug paraphernalia) to re-fill it with the only container that fits: drug taking (rapid relapse to drug dependence even after lengthy abstinence). Of course, the water could melt and the individual could re-claim control or plasticity over its behaviours. However, this seems to occur in a very small subset of individuals; rather, drug dependence becomes a ‘frozen’ long-term relapsing disease in 90 % of instances. (5)

In the case of drug dependence, research indicates that the areas governing drug use advance from the VTA to the accumbens and lastly to the cortex. Thus, on initial exposure, the VTA is modified but the accumbens appears fully unaffected. Subsequently, alterations in the accumbens appear but before the emergence of full drug dependence-like behaviours. The final area of modification is the
synaptic plasticity of the prefrontal cortex. (24) This data strongly supports the idea that the process of drug dependence is facilitated by independent but consecutive phases.

1.5 Predisposition to OUD

Of importance to note, though research indicates that recreational drug use can be considered customary behaviour in a certain cohort of the population, certain individuals are more predisposed than others are to drug seeking and taking behaviours, namely those who have experienced adverse childhood experiences (ACEs). ACEs are defined as, “stressful experiences occurring during childhood that directly hurt a child (e.g. maltreatment) or affect them through the environment in which they live (e.g. growing up in a house with domestic violence)”. (25)

Felitti, Anda and colleagues in their groundbreaking study, “Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) Study” first described ACEs in 1998. (26) Through a prospective study on 17,421 insured, well-educated adults, these researchers identified ten childhood experiences (tabled below), that have a clear association with the development of chronic illness in later life. (27) Their original study remains one of the most thorough research studies ever done on ACEs. In their study, ACE scores ranged from zero to 10 and were measured through a clear, straightforward ten-stem questionnaire, with each stem signifying one specific area of adversity. A positive answer accounts as one ACE. Five of the ten ACEs represent personal adversities with the remaining five relating to familial circumstances.
Table 2: Adverse Childhood Experiences

<table>
<thead>
<tr>
<th>Experiences</th>
<th>Personal (abuse and neglect)</th>
<th>Familial (household dysfunction)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Emotional Abuse</td>
<td>Loss of parent though divorce, death or abandonment</td>
</tr>
<tr>
<td>2.</td>
<td>Physical Abuse</td>
<td>Mother treated violently</td>
</tr>
<tr>
<td>3.</td>
<td>Sexual Abuse</td>
<td>Substance abuse in family</td>
</tr>
<tr>
<td>4.</td>
<td>Emotional Neglect</td>
<td>Mental illness in family</td>
</tr>
<tr>
<td>5.</td>
<td>Physical Neglect</td>
<td>Incarcerated family member</td>
</tr>
</tbody>
</table>

In Summary, the Felitti’s study found:

- **ACEs occur frequently.** For instance, 28% of participants recounted physical abuse and 21% testified to experiencing sexual abuse. Many also described parental loss or parental mental health and/or having parents with a substance use disorder.

- **ACEs cluster.** Nearly 40% of the participants recounted 2 or more ACEs and 12.5% suffered four or more. Because of this finding, subsequent studies focused on the aggregate consequences of ACEs rather than their individual influence.

- **ACEs have an exposure-response affiliation with long-term well-being.** Over time, research has found that an individual’s aggregate ACE tally has a robust, ranked correlation to various health, social, and behavioral issues during their life course, including the misuse of substances. In addition, many difficulties related to ACEs tend to cluster and co-occur.
It showed a definite causal relationship between the depth of exposure to personal abuse or family dysfunction during childhood and many of the risk factors for the leading causes of adult mortality, inclusive of illicit drug abuse. Emotional control is the capability of a person to regulate their expressive state to adapt and deal with the stresses of their environment. Bowlby’s attachment theory is often referenced as a necessary step in acquiring the ability to successfully regulate one’s emotion. (28) If a child’s development is impaired, their aptitude to obtain competencies such as affect regulation may be compromised. This impairment often leads to dependence on avoidance coping mechanisms such as substance abuse, which in turn thwarts their development of self-regulation capabilities in a cyclical manner. (29)

ACEs can set individuals on a path of self-destructive behaviours; intensifying their probability of embracing health-harming activities such as misuse and abuse of opioids. (25) A mounting body of research validates the persuasive long-term influence of ACEs on substance use disorders in adulthood. (30, 31)

Multiple childhood adversities may also be an indicator of more protracted and chronic exposure to stressors that are liable to result in a more lasting and intense negative effect than once off, solitary encounters. (32) Evidence shows that anxiety or traumatization from ACEs may result in enduring neurobiological modifications in the brain circuitry, escalating one’s vulnerability to stress-related health disorders and mental health illnesses, including drug dependence. (33) ACEs’ robust relationship with both physical and mental health illnesses is often explained by a complex interplay between genetic factors, epigenetic processes, dysregulation of stress related hormonal mechanisms (e.g. dysfunction in the production of cortisol in the hypothalamus-pituitary-adrenal axis), and immune factors. (34, 35) Self-medication or stress-reduction theories associated with
substance abuse also propose that ACEs lead to early commencement of substance misuse as a survival strategy, which can further promote the recurring interplay of hazardous activities, increased stress, and additional substance abuse. (32) Enduring this chronic, relentless stress in childhood can lock individuals into a greater state of constant vigilance, permanently primed to deal with further trauma. The negative psychological impact of ACEs can result in individuals suffering low self-esteem and promote a vulnerability for activities proposing short-term reprieve and sacrificing health and well-being in the long-term. This toxic combination results in affected individuals being inclined to engage in risky behaviours such as substance misuse. (36) Research also confirms that the correlation between ACEs and the ensuing establishment of a substance use disorder may be partially facilitated by post-traumatic stress disorders, mood, and anxiety disorders from ACEs. (37)

Children of those affected by ACEs are at a heightened risk of exposing their own children to ACEs. (38) This perpetuation of ACEs is commonly known as the ‘cycle of violence’. (39)

This continuous cycle can lock generation into OUD. It follows that stopping ACEs in one generation or minimising their impact on children can help not only those individuals but also their offspring. Such a cycle of childhood adversity can lock successive generations of families into opioid dependence. Findings from this study were replicated in a recent systematic review and meta-analysis conducted in Wales (40) confirming the intergenerational effects of ACEs which can subject families to repetitive phases of misfortune, deprivation, and chronic illness.
Accordingly, inhibiting ACEs in a single generation or lessening their influence on children can help not only those individuals but also future generations. Public Health play a central role in breaking the cycle of violence but they require help and support from relevant community health care services such as Drug and Alcohol Services. (25)

Even though ACEs may not be wholly preventable, interventions aimed at their early detection and suitable interventions for their subsequent removal is likely to play an important role in preventing the scourge of substance use disorder. Taking all the above into account, a convincing case exists for increasing international attention on averting ACEs, progressing programmes to augment resilience, and implementing procedures and practices that support both.

### 1.6 Theories on drug dependency

Stemming from the above research findings are two independent groups of theories on drug dependency, drug centred theories and individual centred theories.

Drug focused theories are the ones most often cited in experimental research. This category of theories encompasses all viewpoints on drug dependence for which repetitive consumption of drugs is the chief foundation for drug dependence. These theories state that the psychopharmacological modifications that ensue due to chronic drug use result in dependency. The focus is on explicit drug-induced alterations, inclusive of tolerance (41), sensitization (42, 43), withdrawal and allostasis (44) or drug-provoked transformations in cognitive function such as impulsivity (45), decision making (46), and conditioning. (43) These theories were strengthened by long-established research on the very substantial neurobiological alterations at molecular, cellular (47), synaptic (48), and network
levels (49, 50) that result from long-term drug consumption. Research confirming that the longer the ‘within-or between-day exposure to a drug’, the greater the probability of intensified drug intake (51) and the subsequent emergence of symptoms of ‘loss of control’ (52) also support this collective opinion.

Individual focused theories agree that drugs are necessary for the development of drug dependence but are not in themselves wholly adequate in its cultivation. According to this theoretical agenda, a few susceptible individuals, with a vulnerable biological phenotype, succumb to a pathological response to the drug, and as a result, drug dependency ensues. Abundant research confirms that this phenotypic vulnerability results from a multifaceted interaction between genetic factors (53) environmental factors (54) developmental factors (55) and a specific inter-play between gene + environment interactions (56).

The reason why the differences in both theories are important to note is not merely academic, they significantly influence both the medical treatment and the societal attitudes to drug dependence. The two families of theories generate opposing scientific, medical, and social understandings of drug dependence and advise opposing strategies to deal with this health issue.

Drug-centred theories recommend resourcing strategies, which prevent exposure to drugs, by either preventative or repressive methods, such as criminalising drug use and/or punitive repercussions for its use. From a research perspective, a chief focus should be to isolate and reverse the brain alterations prompted by drug use. Individual-centred theories, classify drug dependence as a true psychiatric illness. Most psychiatric illnesses result from stimuli which though largely benign for the general population are extremely pathological for a cohort of susceptible individuals. Putting this in tangible parameters, from a psychiatric perspective,
anxiety disorders such as fear of spiders, arachnophobia, fear of germs, mysophobia, and fear of rats, musophobia which although are commonly experienced as disagreeable to many individuals do not prompt pathological responses in most people. Likewise, as defended by individual focused theories, drug consumption in the general population is not in itself, an adequate condition for drug dependence, as dependence occurs only in a subset of vulnerable individuals. Therefore, there is no reason to classify drug dependence differently from other psychiatric diseases.

Most developed countries have unreservedly validated drug centred theories of drug dependence: Repressive and preventive measures account for the majority of public expenditure in relation to drug dependence, and most publicly subsidised drug dependence research examines the consequences of chronic drug consumption on brain physiology. Lastly, in most countries, an ‘addict’ is classified not as a person living with a mental illness but as an individual who became ‘addicted’ to a substance due to deficiency of willpower—as someone with an inherent flaw. Disappointingly, the destiny we retain for ‘addicts’ differs significantly from that of individuals with well-accepted psychiatric diagnoses, such as depression. In the latter instances, even persons undertaking major felonies are treated in tertiary psychiatric services and not imprisoned, as most often occurs to ‘addicts’.

The individual centred theories do not refute the drug centred theories but believe they are a component of a more complex, individual disease process. In summary, the transition from the first to the second step of exaggerated, constant, intensified drug use occurs in a cohort of susceptible individuals who have an oversensitive response to dopamine and an impairment in the functioning of their prefrontal cortex. Persistent and protracted drug use fosters an ‘allostatic’ state
that ensures drugs are not only intensely desired but also fundamentally required. The evolution to the third and last step, ‘loss of control’ and full drug dependence, is due to a second susceptible phenotype, characterized by a long-term demise in synaptic flexibility in the brain’s reward circuitry in the brain inducing a form of ‘behavioural crystallization’ resulting in drugs now not only being craved and needed but also pathologically bemoaned when absent. This is the working theory of this thesis and as such, the best treatment options tailored to treat opioid dependence are those based on the philosophy of harm reduction.

1.7 The global magnitude of OUD

The worldwide encumbrance of ailments from illnesses due to OUD approaches close to 11 million lost life-years from health issues, morbidities, and early mortality. (57) Approximately 16 million people around the world suffer with a current or previous OUD, of which nearly 3 million reside in the United States. (58) The ‘US Department of Health and Human Services’ declared the catastrophic misuse and abuse of opioids “a public health emergency” in October 2017. (59) From a European perspective, statistics reveal that there are roughly 1.3 million hazardous users of opioids in the EU where opioids are implicated in 84% of fatal ODs. (60) In the EU, heroin is the most widespread opioid in the drug market. 2013 figures indicate it has an approximate minimum trade worth of EUR 6.8 billion (likely ranging from EUR 6.0 billion to EUR 7.8 billion). (60) Additional opioids obtainable on illegal European markets are inclusive but not limited to, opium and the medicines morphine, methadone, buprenorphine, tramadol and different fentanyl by-products. Several opioid compounds are re-routed from authentic medicinal suppliers, while others are illicitly synthesised.
1.7.1 Health and Social Outcomes relating to OUD

Literature reporting the medical problems linked with opioid misuse is plentiful and all outcomes signal that opioid-related harms are intensifying. (61) Numerous factors compound the acute and chronic health complications linked with OUD inclusive of the pharmacokinetics and pharmacology of the opioids, their route of consumption, individual susceptibilities and the social environment in which drugs are consumed. Acute physical harms include immunosuppression (62), endocrinopathies (63), opioid induced bowel dysfunction (64) and hypertension. (65) Psychological harms take account of sleep disturbance (66), anxiety (67), abusive and aberrant behaviour. (68) Evolution to intravenous drug use increases health risks such as cellulitis, phlebitis, abscesses (69) wound botulism and necrotizing fasciitis (70) and exposure to infectious diseases such as the human immunodeficiency virus, hepatitis C virus (71) syphilis and tuberculosis (72) are reported to be more prevalent in individuals with an OUD than in the general population.

The typical life course of those with an opioid-use disorder comprises phases of deterioration and subsequent periods of remission, but the core susceptibility to opioid misuse never abates. (73) Once an OUD is diagnosed, the damaging effects on quality of life and well-being are considerable. The individual, familial and societal repercussions are also substantial. Illnesses resulting from insobriety or unlawful pursuits, such as skull trauma or gunfire injuries are also more frequent. (74) The toll associated with a reduced quality of life from OUD spreads beyond the personal, affecting the physical and mental well-being of the individual’s household, too. (75) From a societal perspective, escalating state expenditures related to healthcare, work force, and the law have a huge negative impact. (76)
Individuals with an OUD use considerably more healthcare resources, inclusive of the emergency services, community outpatient facilities, out-of-hours services and inpatient hospital departments. (77)

There are a continuum of strategies available to positively impact on the encumbrance on OUD from diagnosis, treatment and rehabilitation to prevention (such as preventing ACEs or indeed creating supportive social environments for health) but the focus of this thesis will be on harm reduction strategies as advised by the Council of the Ministers of the EU.

1.8 OUD in Europe

In 2003, to tackle both the morbidity and mortality associated with OUD, the Council of the Ministers of the EU endorsed the need to prevent and lessen health-related ills resulting from drug misuse. Member States were counselled to implement a number of relevant harm reduction policies. In 2007, the Commission of the European Communities ratified that drug-related harm reduction should be a public health objective in all countries. Therefore, in general, there is an understanding within Europe on the importance of decreasing harms, specifically the proliferation of infectious diseases and of course, drug related morbidities and death. The EMCDDA’s 2025 strategy (78), is dedicated to contributing to a healthier Europe by appropriately responding to the adverse health and social penalties associated with SUD. It promises to keep abreast of harm-reduction approaches and to assist its stakeholders in identifying and implementing evidence-based practices.

Currently, medical treatment with opioid agonist treatment (OAT), supported by psychosocial expertise, is the chief intervention for individuals with an OUD, and
ensuring appropriate, timely admission to optimum treatment facilities is a fundamental aim of the European drug strategy.

1.8.1 Opioid Agonist Treatment (OAT)

OAT has certain characteristics, which optimises its effectiveness including an oral route of administration and a prolonged duration of action. An oral route of administration is more satisfactory to individuals improving Individual compliance. It removes the danger of contracting blood-borne diseases linked with intravenous drug use and the potential use of contaminated or shared drug paraphernalia. The symbolic association to an illegal lifestyle is broken and the need for individuals to congregate to share needles and syringes is eliminated. A 24-hour interval between appropriate doses accommodates a once daily dosing regimen. It removes the occurrence of opioid withdrawal symptoms. Key physiological functions unsettled by long-term misuse of opioids are stabilised.

On establishing the correct daily dosing regimen of methadone, tolerance is not established to the critical benefits of methadone, which are, inhibition of opioid withdrawal and deterrence of drug desire. As a result, regular, continuous doses may be used for years to treat OUD effectively. (79) As a result of these findings, OAT has proven to have hugely positive results in respect to retaining individuals in treatment, reducing opioid use, decreasing recounted hazardous behaviours, and minimising drug-related morbidity and mortality statistics.

Typically in Europe, specialist outpatient centres account for the single largest supplier of OAT in terms of registered individuals. The second leading provider of OAT is primary health care centres. General Practitioners are employed in both settings to prescribe OAT. The pharmacology of OAT is subdivided into full or partial agonist. Complete agonists, such as methadone, attach to the mu opioid
receptor producing a dose-reliant upsurge in physiological effects. Partial agonists, such as buprenorphine, bind to the receptor but even at full saturation exercise less influence than that achieved by full agonists. In both settings, methadone is the most frequently prescribed opioid agonist treatment, where almost two-thirds (63%) of OUD individuals in Europe receive it. (80) A further 35% of individuals receive buprenorphine, which is the principle drug treatment in the following eight countries: Croatia, Sweden, France, Norway, Finland, Czech Republic, Greece, and Cyprus. In Ireland, buprenorphine-naloxone (buprenorphine/naloxone) is presently only obtainable on a restricted named patient basis (81) although this is currently expanding.

1.9 OUD in Ireland

The most recent estimate of opioid misuse dates to 2014 when a “four-source capture-recapture method” accounted for 18,988 opioid users (6.18 per 1,000 population aged 15-64 years) in Ireland. (82) In 2006 less than one third of opioid users were 35 years or older. However, in this more recent 2014 study, greater than half were, suggesting a definite ageing effect in this cohort, which is in line with European findings. The data was collected over a four-year period (2011-2014), allowing opioid use prevalence estimates for 2014 to be compared with estimates from 2011, 2012, and 2013. There was an increase each year, rising from 17,387 in 2011 to 18,988 in 2014. (83) Data from the Irish drug treatment facilities suggest that opioids (mainly heroin) are the most common main drug of dependence amongst those commencing treatment. (82) The Health Service Executive (HSE), which governs Ireland’s public health division, oversees the provision of all publicly financed drug treatment. Its Primary Care Division oversees all drug treatment facilities, including OUD. It
also manages a number of national care groups. From a treatment perspective, Ireland mirrors the current European structure. Methadone is the most commonly prescribed opioid agonist drug, which has been available in Ireland since the 1980’s. The 1998 legislation, the Misuse of Drugs (Supervision of Prescription and Supply of Methadone) Regulations, implemented a specific administrative structure designed to monitor treatment delivery and patient trends, the confidential Central Treatment List (CTL). The legislation also enforced a protocol for the prescribing of methadone, the Methadone Treatment Protocol, which provides for the delivery of methadone treatment in the Irish context. As in Europe, in Ireland, under this legislation, methadone is provided for in both specialist outpatient centres and in Primary Care Centres, both chiefly staffed by General Practitioners (GPs). At year-end 2017, the total number of individuals in Ireland receiving Methadone was 10,316 of which 9,695 were in the community and 621 were in prison. Eighty HSE specialist outpatient centres providing OAT were in operation. Across both the clinics and the GP community setting, 362 GPs delivered the Irish service. (84)

1.9.1 The Irish Management of OUD

Launched in 2017, Ireland’s national drug strategy, ‘Reducing harm, supporting recovery: a health-led response to drug and alcohol use in Ireland 2017-2025’, is the third consecutive long-term drug policy and strategy document adopted in the country. (85) Its main aim is to curtail the ill effects resulting from the misuse of substances by empowering people with drug use disorders to access appropriate, tailored treatment. It also wishes to fulfil its aim by reducing overall mortality rates associated with drug misuse and abuse. (85) The strategy aims to promote ‘a healthier and safer Ireland, where public health and safety is protected and the
harm caused to individuals, families and communities by substance misuse are reduced and every person affected by substance use is empowered to improve their health and wellbeing and quality of life’. Harm reduction underpins its philosophy as it aims to specifically, ‘minimise the harms caused by the use and misuse of substances’.

(85)

The Department of Health, run by the Minister for Health, has overall accountability for implementing the strategy. A Minister of State supports the Health Minister and is responsible for the strategy. The National Oversight Committee in turn supports the minister for health. This committee meets quarterly and benefits from statutory, community and voluntary representatives. The committee also includes representatives from academic and the Professional bodies, the ICGP and the College of Psychiatrists (CPI). A key voice at the table is the service user and also from the National Family Support Network. The NOC itself is supported by a standing sub-committee, which is chaired by a senior official at the Department of Health. This sub-committee convenes monthly to reinforce the implementation of the strategy, as well as assisting in ensuring coordination between relevant national, regional and local bodies. The Drugs Policy Unit at the Department of Health is tasked with delivering impartial and informed analysis and guidance to the National Oversight Committee.

At a sub-national level, local and regional Drug and Alcohol Task Forces (comprising statutory, community and voluntary representation) are accountable for tactical implementation of the strategy. The National Drugs Strategy 2001 – 2008 endorsed the foundation of the Mid-West Regional Drugs Task Force (MWRDTF) to research, instigate, cultivate and oversee a co-ordinated response to illicit drug use in counties Clare, Limerick, North Tipperary and Limerick City.

The ‘Health Service Executive Mid-West Limerick Drug and Alcohol Services’,
in which study 1 of this thesis was undertaken, falls in the geographical area of the MWRDTF, and are responsible for the clinical element of the service in that area.

1.9.2 Harm Reduction Services in Ireland

From an Irish perspective the available harm reduction services available are

1. Opioid agonist therapies, (OATs), mainly methadone (OATM) but recently also buprenorphine/naloxone combination therapy
2. Take Home Naloxone Programmes, THN Programmes
3. Needle and Syringe Exchange Programmes
4. Outreach support
5. Supervised Injecting Facilities (in development phase)

1.10 Overdose

While individuals with an OUD are at risk of succumbing to an array of acute ills, drug overdose (OD) in this population is the most grave of these. New synthetic opioids are evolving as a detrimental hazard to individual and public health. Since 2009, 38 novel opioids have been identified on the European marketplace - 13 of which were recorded for the first time in 2017. Of the 38 novel opioids, 28 were by-products of fentanyl, of which 10 were identified for the first time in 2017. (60) Fentanyl is approximately 50 times more potent than heroin and 100 times stronger than morphine. (86) As such, these newly synthesised opioids can be intensely intoxicating, with miniscule amounts adept at causing life-threatening poisoning from rapid, severe respiratory compromise. This brands them particularly treacherous, especially for naïve consumers.
Furthermore, fentanyl derivatives appear to be highly addictive with grave
dependence-producing capabilities, which could exacerbate the public health and
social difficulties frequently linked with OUD.

Among European adults, OUD is a well-documented source of avoidable
mortality. Overall mortality rates of high-risk drug users typically range from 1–2
% per year. Most recent records show that in Europe, drug OD remains to be the
main cause of mortality among high-risk drug users, with the majority of ODs
being male (79 %). Heroin or its metabolites are implicated in the majority of
fatal ODs.

It is important to emphasise three distinct sub-populations are at risk of opioid
overdose; 1. Individuals with a chronic OUD; 2. Individuals experimenting with
other drugs who inadvertently ingest opioids; 3. Individuals intentionally
overdosing, intentional poisoning. This thesis focuses on the first sub-population,
individuals with a chronic OUD where accessibility to the opioid reversal agent
naloxone is of the upmost importance.

Statistically, relative to their peers of the same gender and age, Europeans with an
OUD are 5 to 10 times more likely to die. (60) Higher mortality rates among
individuals with an OUD are predominantly associated with OD, but other
grounds for mortality, circuitously related to drug use, such as incurable
infections, calamities, violent incidences and poisonings, are also notable. Again,
it is important to distinguish between accidental poisonings and intentional self-
poisoning in relation to opioid misuse. This thesis focuses on accidental
poisonings in the context of OUD. The treatment of intentional self-poisoning
would require psychiatric expertise.
In addition to the above ailments, chronic poor health, manifested by an accumulation of interlinked conditions is present. Longstanding respiratory, cardio-vascular and hepatic conditions are commonplace and explain some of the reasons for increased mortality among senior and seasoned misusers or opioids. (87)

Statistics pertaining to OD, particularly the European aggregate, should be interpreted with caution. The reason being that some countries systematically under-report their figures while lengthy record-keeping procedures result in recording delays in others. As a result, yearly estimates reflect a conditional minimum number. From an age perspective, in the European Union (EU) between 2012 and 2016, in all age groups above the age of 30, deaths due to OD increased. Fatalities in the over-50 age category enlarged by 55%. In comparison, life losses among those aged 30–49 increased by 25%.

The increasing trend in the recorded number of ODs in the elderly population highlights the ageing effect on individuals with an OUD in Europe, who are at maximum jeopardy of fatal OD. Most recent figures reveal that greater than 40 deaths per million population were recorded in eight northern European countries, with the highest rates reported in Estonia (132 per million). Ireland ranked fourth in the list with a death toll of 70 deaths per million. (60)

The magnitude of OUD and the burden of the disease on the individual, their families, and society as a whole are undeniable. Reducing morbidity and mortality associated with OUD is a major public health challenge in Europe and unquestionably in Ireland. We need to improve our management of the disease if we are ever to kerb its spread and ultimately gain control of its harrowing effects. Prevalence estimates of OUD in Europe range from less than 1 to more than 8
cases per 1 000-population aged 15–64. (60) Ireland has one of the highest at 6.18 per thousand-population aged 15—64 years (95% CI: 6.09—6.98). (88) Ireland’s drug-related deaths among adults (aged 15-64 years) are greater than three times the most recent European estimate. (82)

Where methadone is the chief OAT prescribed in both Europe and Ireland, the medicine most effective bar none at reversing opioid OD is naloxone. Naloxone can reverse the depressant effects of opioids on the respiratory system both safely and effectively. It has a powerful affinity for opioid receptors, most notably μ receptors, and it works by challenging the opioid and displacing it from the receptor, thereby deactivating the receptor and reversing OD induced respiratory compromise. (89) Manufactured for the first time in the early 1960s, the Japanese company Sankyo applied for its patent, with a second tender submitted by Fishman and Lewenstein in New York in March 1961. (90) Naloxone was considered a more reliable and effective opioid antagonist with a better side effect profile than previously used drugs which resulted in it gaining regulatory endorsement from the US Food and Drug Administration (US FDA) for intravenous, intramuscular, and subcutaneous use. (89) Over the following 40 years, subsequent research supplemented its safety profile by confirming that, even if inappropriately administered to opioid-naïve individuals, it does not cause harm (91) because in the absence of opioid antagonists, it exhibits essentially no pharmacological activity. Naloxone is most effective in reversing the effects of a heroin or a morphine OD, but of huge significance in the current opioid epidemic, it also works to reverse respiratory depression caused by other opioids, including fentanyl. (92) The World Health Organization endorses it and indeed methadone as an ‘essential medicine’. 
The majority of ODs occur in the presence of others, and most ‘people who inject drugs’, PWIDs, have observed or have first-hand experience of an OD. Therefore, PWIDs, or their friends and family, are likely to be first on the scene to manage an OD emergency. (93) These familial and cordial networks, with suitable training, can be employed for medical intervention at an OD scenario with the very likely outcome of preventing death. WHO guidelines on the management of opioid OD in the community setting recommend improving the availability of naloxone among those who are likely to be bystanders at an opioid OD. (94) In order to make naloxone available where ODs occur, opioid OD prevention programmes train potential bystanders on how to recognise and respond to opioid OD and provide them with the medication. These so-called ‘take-home’ naloxone programmes (THNP) exist in Australia, Canada, Europe and the United States. (90, 95-97)

From an Irish perspective, the Early Warning and Emerging Trends Committee of the Irish Health Research Board keeps up to date with European and national data sources of information to ensure Ireland is abreast of any significant developments. In Ireland, an exclusive register retained by the Health Research Board, records the number of drug-related deaths, or as they refer to it, ‘drug-induced deaths’. (98) This document, most recently published in 2017, tabulated the most up-to-date Irish figures which concern 2015, where the number of ‘all poisoning deaths’ were recorded as 348. Of these deaths, there were 252 ‘instances’ of opiates (includes heroin, methadone, morphine, codeine, unspecified opiate-type drug, other opiate analgesic) recorded as present in 209 individual deaths. The majority of the deceased were male in their late 30s. Of the 209 individual deaths, 84 were not alone at the time of death and the overwhelming majority, 185, did not occur in a public place. Both of these figures
support the need for THNPs. (99) Of the 209, 179 had two or more drugs implicated, most commonly benzodiazepines. Overall, the risk of early mortality from OUD, predominantly from an unintentional OD, trauma, suicide, or a communicable disease is increased by a factor of 20 from the average population. (100) Irish research supports the need to equip individuals with an OUD with the skills and education to prevent OD. (101) Ireland rolled out a national THN Programme in October 2015, following a short pilot programme. (102)
Chapter 2 Literature Review

2.1 Chapter Overview

This chapter focuses on the importance of harm reduction in combatting opioid dependence. A particular focus is shone on harm reduction programmes currently operating in Ireland. The chapter then reviews recent literature confirming the relapsing nature of opioid dependence and as such outlines the rationale for this thesis in optimising both MMTPs and THNPs. The chapter closes with the aims and objectives of the thesis itself.

2.2 Harm Reduction

The following section opens with a brief look at the increasing opioid epidemic and its toll on society. It will then define harm reduction. It will focus on one of the many grave illnesses associated with OUD, the spread of blood borne viruses, and the effective role harm reduction can play in kerbing their spread and as a result benefitting society hugely. Following a brief look at both the European and Irish current perspectives on harm reduction the chapter focuses on the four main harm reduction services currently available in Ireland with a final look at a potential fifth service, supervised injection sites, which should be up and running in Ireland shortly.

2.2.1 Background

Over the last 30 years, public opinion of opioid use has slowly begun to shift from the discussion of drug users as criminals with character flaws (103) to viewing drug dependence as a chronic brain disease. (104) Even with the positive initiatives and effective policy reform enacted thus far, the adverse toll OUD has on society endures. With the increasing accessibility to potent opioids—inclusive
of fentanyl and carfentanil— the opioid crisis is expanding. (105)

Notwithstanding the encumbrance of opioid misuse on society is challenging to estimate, it is well recognised that the expenditures associated with OUD are extensive. (106) Social costs due to unemployment, criminal activity and violence all of which are inextricably connected with OUD, can result in crippling the economic budget. (107) Moreover, OUD is often linked with deprivation and social isolation. This can lead to acute and chronic illnesses both of which are costly to treat. (108) Therefore, it is understandable that harm reduction interventions have historically had low public support (109) because these strategies aim to reduce the harms of drug use but do not focus on eliminating drug use itself. (110)

2.2.2 Defining Harm Reduction

Harm reduction embraces interventions, programmes and policies that primarily endeavour to decrease the impact of the adverse health, social and financial ramifications of drug misuse without necessarily decreasing drug consumption. (111) Harm reduction strategies respect the individuals’ right to consume such substances. A central principle of harm reduction is to address the immediate health and social requirements of individuals with substance use disorders, particularly the socially marginalised, by offering a suite of services inclusive of Opioid Agonist Treatments, Take-Home Naloxone Programmes, Needle and Syringe Exchange Programmes, Outreach Services and Supervised Injection Sites. Recently, new opportunities for bettering the scope and usefulness of harm reduction strategies have come to the fore, especially through advances in the arena of information technology. Novel methods include, for example, engaging with e-health applications to convey brief interventions. (60)
2.2.3 Curtailing the spread of blood borne viruses

Opioid harm reduction policies are hugely important as individuals with an OUD, particularly those who inject, are in danger of developing infectious diseases through the sharing of drug use paraphernalia. Intravenous drug use continues to play a dominant role in the spread of blood-borne infections such as the hepatitis C virus (HCV) and, in some countries, the human immunodeficiency virus (HIV). (112)

Most recent European statistics indicate that at > 8 cases per million population, Ireland remains to have one of the largest number of newly diagnosed HIV cases because of injecting drug use. (112) Ominously, in 2016, half of the new HIV diagnoses due to drug injecting in the European were not diagnosed until the virus had already begun to impair the immune system. This ‘late HIV diagnosis’ results in delays in commencing anti-retroviral treatment which in turn increases patients’ morbidity and mortality. Timely diagnosis and commencement of anti-retroviral treatment offers those affected a normal life expectancy but this prospect is squandered with late diagnosis. (112) Early treatment also reduces the likelihood of cross contamination and transmission of the infection, which is of paramount importance among clusters with higher risk behaviours, such as people who inject drugs (PWIDs).

In Europe, viral hepatitis, chiefly infection with the hepatitis C virus (HCV), is extremely prevalent among PWIDs. For every 100 people infected with HCV, untreated, 75 to 80 will develop chronic infection. (113) Worryingly, infected individuals often feel no obvious symptoms, and many are oblivious to their infection. As such it is often denoted the ‘hidden’ epidemic. (114) A devastating consequence is that chronic HCV infection, often exacerbated by heavy alcohol
consumption, will result in increased morbidity due to a greater number of cases of severe liver disease, including cirrhosis and cancer, among an ageing cohort of high-risk PWIDs which ultimately increases overall mortality rates. This places a major burden on healthcare systems. (114)

HCV is more common among older PWIDs than among the younger generation, emphasizing the amassing risk over time, and the great encumbrance of infection among the ageing cohort.

In Ireland, in 2016, PWIDs accounted for greater than one third of hepatitis C virus (HCV) cases. In line with Europe, old age (older than 34 years) was a noticeable characteristic of intravenous drug users among HCV notifications in Ireland. (82) As documented above, chronic HCV infection coupled with an ageing population implies that the number of cases of advanced liver disease will undoubtedly rise in the next decade placing an even greater toll on our already deplete health services. Yet HCV is both preventable and curable. (115)

Ireland’s first national hepatitis C strategy 2011-2014 published in 2012 but had no financial provision for its enactment. (116) As a result, it was not until 2014, that the Government sanctioned the rollout of the ‘National Hepatitis C Treatment Programme for 2016-2026’. (117) The programme is staffed with a Programme Manager, who oversees operations and a Clinical Lead, who oversees the clinical aspect of the programme. In July 2017, comprehensive National Clinical Guidelines on screening for Hepatitis C were circulated in Ireland. HCV treatment is currently delivered through specialist services based in the acute hospital setting. Once clinically prioritised and referred by their doctors, PWIDs can also avail of this service. In 2018, on a trial basis, the HSE commenced offering HCV treatment in the specialised Methadone outpatient clinics to affected individuals in
opioid agonist treatment in order to maximise treatment coverage as experience had indicated a number of PWIDs were reluctant attendees at hospital based services. (117)

Amongst PWIDs, hepatitis B virus (HBV) infection is less prevalent than HCV infection. In Ireland, from a HBV perspective, a descending trend in the number of notifications was noted between 2008 and 2014; however, recent data indicates that numbers of cases identified and reported upon are now stable. PWIDs are also at risk for contracting other infectious diseases, such as hepatitis A and wound botulism. (118)

2.2.4 Increasing Mortality Rates

However, immeasurable in monetary terms, the most expensive cost of the opioid epidemic is undoubtedly the associated loss of life. In 1993, the ‘European Monitoring Centre for Drugs and Drug Addiction’ (EMCDDA) was established. It provides the EU and its Member States with an accurate synopsis of European drug harms and a concrete evidence base to inform policymakers’ decisions on drug laws and strategies. It defines ‘drug-related death’ as a death unequivocally due to the consumption of illegal substances. Typically, these fatalities occur quickly post the ingestion of the drug and are therefore termed ‘directly caused by drugs’. In the United States and the increasingly in the EU the term applied is ‘drug-induced deaths’. ‘Poisonings’ is the word used in the International Classification of Diseases or in nonprofessional references the term overdose (OD) is cited. (119)

From a mortality perspective, latest statistics from the EMCDDA reflect that ‘drug-related deaths’ in Europe have increased for the fourth successive year. (120) Data from 30 countries, 28 EU and Turkey and Norway report an estimated
9,138 deaths have occurred in 2016 representing a 4% increase from 2015. As OUD is now a leading cause of death worldwide, it is the resultant loss of life that has helped gain more traction for harm reduction strategies in recent years (121) but society has still a long way to go before fully embracing them.

2.3 Opioid Agonist Therapy

OAT is currently the evidence based gold standard treatment option for individuals with an OUD, optimising their general well-being from a safety and overall physical health perspective. (122) For this reason, the World Health Organization lists the OAT, methadone on their register of essential medicinal products. (123) Evidence to defend the effectiveness of OAT is well documented in academic literature. Research shows it significantly reduces crime rates, increases employment and improves affected individuals’ social well-being. (124) OAT results in decreased rates of infectious diseases related to injection drug use. (125) A recent study in the BMJ showed retention in methadone treatment results in a considerable decline in the risk for all-cause mortality in individuals with an OUD. (126)

In Ireland OAT is initially prescribed by befittingly trained specialist General Practitioners (GPs) with level 2 training. (127) Typically, this occurs in specialist OAT clinics or less frequently in the general practice setting, where GPs (at level 2 training) with the appropriate expertise working in their own community practices initiate OAT. Once a patient’s dosing regimen is stabilised on OAT, and their overall care plan is optimised in the specialist setting their transfer to less experienced GPs (at level 1 training), working in community practices can occur. Here the patient can avail of ongoing maintenance management of their illness.
Training for GPs in relation to ‘opioid substitution prescribing’ is organised by the Irish College of General Practitioners in conjunction with the HSE.

Studies from 2013 and 2016 show a generally optimistic attitude of prescribing GPs toward OATM treatment in Ireland. (128, 129) Prescribing GPs work diligently with both statutory and non-statutory bodies to ensure optimal provision of OAT. (81)

As noted above, the pharmacology of OAT can be sub-divided into full agonist or partial agonist. Methadone, which is expanded upon below, is a synthetic full mu-receptor agonist that is usually administered daily to patients for oral consumption to treat their OUD. (130) Buprenorphine is a partial mu-agonist that is administered sublingually. In both Europe and Ireland, methadone is the most common preparation prescribed. (80) In Ireland, the combination OAT buprenorphine-naloxone is presently only obtainable on a limited named patient basis. (81) Although this is expanding since the passing of legislation to include buprenorphine containing products in the treatment of opioid dependence in Ireland. (131)

In the absence of a formal protocol, methadone was prescribed in Ireland from the early 1980s to certain vulnerable cohorts such as those diagnosed with HIV (132) and also pregnant women. (133) By the early 90’s, the availability of methadone on prescription was still limited to the capital, Dublin. To address the need for methadone to be available nationwide, in 1993, an ‘expert group’ undertook to publish a formal protocol for the prescribing of methadone nationally entitled, ‘Report of the Expert Group on the Establishment of a Protocol for the Prescribing of Methadone’. On foot of this report, in 1998, the ‘Misuse of Drugs (Supervision of Prescription and Supply of Methadone) Regulations’ were
published which clearly outlined specific regulatory requirements for the
prescribing of methadone. (134) Rolled out in 1998, the Methadone Treatment
Programme (MTP) protocol guided OAT treatment delivery in Ireland, ensuring
appropriate protocols for methadone prescribing, fitting standards for the
management and support of clients, specialist-training prerequisites for GPs, and
best practice procedures to undertake clinical audit. (134)

Since its inception in 1998, several appraisals of the MTP have been performed,
both internally in 2005 by the ‘Methadone Prescribing Implementation
Committee’ itself and by external bodies in 2010. (135) All clients in receipt of
methadone are registered on the confidential Central Treatment List (CTL). Each
client is assigned one specific prescriber and a single pharmacist. The Irish
College of General Practitioners (ICGP) delivers and oversees the specialist
training for GPs to upskill and prescribe OAT. Since 1998, year on year, the tally
of specially trained GPs has increased steadily. (84) The introduction of the
scheme encouraged General Practitioners and pharmacists in community settings
to become involved with the prescribing of OAT. (136)

Originally unveiled as an analgesic in 1939 (137) methadone was first launched as
a treatment option for opioid dependence by Dole, Nyswander, and Kreek in
1964. (137, 138) The extended half-life of methadone results in a “narcotic
blockade” which eradicates withdrawal symptoms for up to 36 hours. Given in
appropriate doses, it also moderates opioid craving (139) and in doing so frees the
client from the daily cycle of searching for, purchasing, and consuming illicit
opioids. (140)

In 2017, the regulation S.I. No. 522 replaced the 1998 Regulation S.I. No. 225.
(131) The new regulation adds buprenorphine-containing products to the schedule
of products authorised for OAT in Ireland. As a result, individuals with a specific medical diagnosis, which results in methadone, being contraindicated or not suitable can now be offered an alternative OAT, in the form of a sublingual tablet, buprenorphine/naloxone. (141) As a partial agonist, buprenorphine has less sedating and euphoric effects than full agonists, such as methadone, do. Though a partial agonist, it does exhibit a high affinity for the \( \mu \) receptor, binding more firmly to opioid receptors than other opioids or opioid antagonists. This allows it to block the effects of concurrently administered opioids, reducing the risk of relapse in buprenorphine maintained clients. (142) It has a bell-shaped dose-response curve, and hence a long duration of activity which allows for less than daily dosing. (143) Naloxone does not diminish the efficacy of sublingual buprenorphine but its inclusion deters intravenous misuse of the drug (144) and hence the formulation of both buprenorphine and naloxone, is used in Ireland. Previous research in Ireland had identified buprenorphine injecting as a problem hence the combination product is the preferred product here. (145) Each sublingual tablet contains 2 mg buprenorphine (as hydrochloride) and 0.5 mg naloxone (as hydrochloride dihydrate). Buprenorphine/Naloxone when administered sublingually reaches peak concentration after 90 – 150 minutes. However, as in Europe, in Ireland the majority of OAT is methadone based and as such is the focus of this thesis. Opioid agonist treatment with methadone (OATM) has been validated as an effective treatment for opioid dependency by more than 50 years of research (137) and today, Cochrane reviews show robust evidence to support its use. (146, 147)

Internationally, significant qualitative research with respect to individuals’ perspectives of a MMTP has been published. Much research has been done focusing on ‘out-of-treatment’ individuals (148) and on retaining individuals in
treatment (a significant predictor of outcome). (149) For those in treatment, qualitative studies focusing on individuals’ access to treatment (150), level of influence on their treatment plan (151), quality of life (152) and their overall satisfaction in methadone treatment (153) are well documented. Similarly, in Ireland, qualitative studies attempting to address issues with OATM from the perspective of the Individual have been undertaken. (154-156)

However, both internationally and nationally, very few, if any, of these studies focus on the most complex of individuals, those who remain entrenched in the specialist system, for whom the service appears to fail, as they never progress to the community setting for treatment. The Methadone protocol in Ireland advocates for OAT to be delivered ideally by the patient’s community GP but some patients never attain this goal. To date, no Irish study has specifically investigated this cohort. This thesis, in researching their individual journeys, hopes to establish patterns of similarity in their lives, which would flag their high-risk status on admission to OAT and allow all relevant services to collectively intervene appropriately and optimise their individual care plan sooner.

2.4 Take Home Naloxone Programmes

In 2015, the EMCDDA conducted a systematic review of 21 studies on ‘take-home naloxone’. This review confirmed that knowledge acquisition on the appropriate management and administration of naloxone by individuals with an OUD and their peers improved dramatically with appropriate education and participation in training courses, which had the resultant benefit of decreasing the ‘drug-related death’ rates. (157)

THNPs target three specific populations: individuals with OUD, their carers (inclusive of peers and familial relations) and employees in agencies likely to
interact with opioid users, such as staff of MMTPs. Therefore, in the event of an opioid OD, where medically indicated, naloxone may be administered to the OD victim in advance of the arrival of the emergency services. Following naloxone administration by laypersons, the reported effectiveness of naloxone in reversing respiratory depression is as high as 75–100%. (96) As such, evidence confirms THNPs should be considered effective in reducing the death toll associated with opioid OD. (158)

Initially introduced in pilot format, today, universally, a broad range of THNPs is today. The diversity in the individual programmes reflects the need to modify each programme to the available assets, local environment and most importantly, each individual country’s regulations on the supply and use of naloxone.

However, worldwide, practical and regulatory hurdles have hampered the adoption of take-home naloxone programmes, particularly because naloxone must be pre-prescribed by a doctor directly to the person for whom it was intended. In response to a strong increase in the number of opioid overdoses, worldwide, solutions have been found to facilitate increased access to naloxone inclusive of its legal recognition as an emergency medication (Ireland, United Kingdom, Italy), repeal of prescription restrictions (Australia, Canada, France and several US states), and local and temporary legal exemptions for THNPs (Denmark, Norway).

Another huge step forward in making naloxone more accessible was its recent approval as a nasal spray as up until the very recent past, available products were solely destined for parenteral use. However, extensive research on its pharmacokinetics proved that naloxone is sufficiently absorbed through the nasal mucosa to exert an antagonist effect upon opioids, which have caused the symptoms of overdose. (159) As a result, in November 2015, *Narcan Nasal Spray*
was launched by Adapt Pharma and became the first USFDA non-injectable naloxone product for the treatment of opioid OD to be sanctioned. This new intranasal route of administration was considered relevant for use by laypersons and non-medical responders in community-based programmes. In July 2017, following a 12-month trial, France became the first European country to authorise the marketing of a nasal naloxone spray. In November 2017, the European Commission granted authorisation for the marketing of an intranasal product across the European Economic Area, which in addition to the European Union includes Iceland, Lichtenstein and Norway. With increasing implementation of THNPs, the evidence base as to their effectiveness is growing. (160)

Ireland rolled out a national THN Programme in October 2015, following a short pilot exercise. In its current format, opioid users, their peers, familial members, carers and relevant agency employees agreeable to partake in the programme must attend a video-based teaching session and pass a post-training test questionnaire. Training, approved by the Pharmaceutical Society of Ireland and the Irish Institute of Pharmacy, respects and obeys the ‘instructions for naloxone administration’ as listed in its ‘Summary of Product Characteristics’ (SmPC). If opioid users can demonstrate sufficient understanding of opioid OD signs, emergency management (calling an ambulance, basic life support and recovery position), and naloxone administration they are issued a take-home naloxone kit by prescription (102) as in Ireland, naloxone still remains a prescription only medicine.

However, in a move to embrace laypersons’ trained skills in opioid reversal, Ireland now legally recognises naloxone as an emergency medicine. Therefore, legislation, passed in Ireland in 2015, allows for the emergency administration of naloxone by non-professionals who have completed an approved course of training in its use, without the need for a prescription. Entitled, ‘S.I No. 449/2015
- Medicinal Products (Prescription and Control of Supply) (Amendment) (No. 2) Regulations 2015’, this legislation allows for the procurement and administration of naloxone in an emergency. Since 2015, injectable naloxone has been available for community use in Ireland in a 2ml pre-filled graduated syringe. One dose is 0.4ml, thus, each syringe has a maximum of five individual doses. In line with current training, one may repeat the dose of 0.4ml every 2-3 minutes until the contents of the syringe are deplete. Its intended use is in the home or other non-medical settings. Post administration, each use should be reported to the ‘Chief Pharmacist, Addiction Services, Health Service Executive’, who leads and manages the THN Programme and has overall responsibility for procurement and replenishment of supply.

Intranasal naloxone was first launched in Ireland in August 2018 and is currently being rolled out nationally under the tradename nyxoid. The recommended dose is 1.8 mg administered into one nostril (one nasal spray). In some cases, further doses may be necessary. The appropriate maximum dose of nyxoid is situation specific. If the patient does not respond, a second dose should be administered after 2-3 minutes. If the patient responds to the first administration but then relapses into respiratory depression, a second dose should be administered immediately. Further doses (if available) should be administered in alternate nostrils and the patient should be monitored whilst awaiting arrival of the emergency services.

As noted above, no independent adverse effects are associated with naloxone. However, it can trigger an acute withdrawal syndrome if administered to a person whose µ receptors are pre-saturated with opioids. (89) Opioid withdrawal symptoms may consist of nausea, gastric spasms, muscle stiffness, muscle spasms/jerking, pains and discomforts, restlessness, retching, perspiring,
tachycardia, hyperventilation, hypertension, quivering and aggressive behaviour. (161) These symptoms occur in varying proportions and to varying degrees dependent on the dose of naloxone and the degree and type of opioid dependence.

Naloxone has a relatively short half-life and as such with emerging new synthetic opioids, repeated doses, often in the hospital setting, may be necessary for the effective reversal of opioid induced respiratory depression. (162) One-quarter (163) to almost one-third (164) of opioid ODs need repeat doses of naloxone to avoid ‘recurrent opioid toxicity’. As such, transfer to hospital, post naloxone administration in the community, is hugely advisable to monitor both the withdrawal symptoms and to treat potential recurrent opioid toxicity.

2.5 Needle and Syringe Exchange Programme

These programmes allow intravenous drug users to access sterile syringes and appropriately dispose of used syringes in the community setting safely. Evidence shows these programmes reduce infectious disease rates arising from the hazardous and risky sharing of needles. (165) In Ireland, the programmes play a pivotal role in the delivery of harm-reduction services. Three differing programme models exist: ‘fixed-site’ services, ‘outreach syringe’ facilities and ‘pharmacy-based’ programmes. All models typically provide a suite of sterile injecting paraphernalia, inclusive of varying sizes and brands of both needles and syringes, sterile swabs, and citric or acetic acid. Condoms, sterile disposable cookers, non-toxic foil (for smoking heroin) and tourniquets are also obtainable.

The ‘pharmacy-based’ programmes commenced in 2011. They have grown to expand substantially and today, apart from counties Dublin, Kildare and Wicklow, which are well serviced by both ‘fixed-site’ and ‘outreach syringe’ facilities, all remaining counties partake of their services. They dispense packages containing
the necessary injecting apparatus for either 3 or 10 sterile uses. By year-end 2017, 111 pharmacies nationwide provided needle exchange facilities, and on a monthly basis in 2018, approximately 1,760 individuals availed of the service. (80) In areas without 'outreach syringe' facilities, pharmacy employees aid the dissemination of injecting paraphernalia with 'backpacking', a system whereby injecting material is distributed by staff directly to known individuals with a SUD. Regular audit and review of existing programmes are essential to maintain standards and improve outcomes, such as a review of the Irish needle and syringe programme. Published in 2015, results confirmed that the ‘pharmacy-based’ programme was performing well overall but it identified the need to for standard setting in the censoring of services delivered, to augment the uptake of testing for blood-borne infections, perhaps by offering in-pharmacy testing. Vaccination rates also needed to be increased. (166) Further recommendations were to increase the competence of pharmacy staff in giving harm reduction advice and support, and most importantly to reduce stigma. (166)

2.6 Outreach Services

These services connect individuals with drug use disorders with relevant harm reduction facilities. The ethos underlying outreach work is that individuals are 'out there' abusing substances and not aware or in contact with facilities which could help them better manage their illness. Particularly vulnerable are society’s youth who often engage in 'chaotic drug use', those who are homeless and those participating in the sex trade. Outreach services prioritize 'hard to reach' and 'hidden' individuals. (167). In Ireland, the type of outreach work may be mobile or grounded in one location, domiciliary or community/street based, but always incorporates harm reduction approaches. The service also catalogues the number
of new clients registered each month, the number of clients who remain in contact with outreach services extending greater than three months and the number of clients who referred on a monthly basis to other services. This information is critical in gaining knowledge on the most marginalised of individuals in Irish society. (80)

2.7 Supervised Injecting Facilities

This service provides legal medical supervision to individuals wishing to inject previously purchased opioids or other drugs. Research shows that these facilities reduce the incidence of injecting rates in public, decrease the incidence of drug-related communicable infections and lessen the overall drug-induced mortality rate. (168, 169) Internationally, public support is better (170) than previously recorded. (171) Approximately 90 supervised injecting facilities (SIFs) operate worldwide. Seventy-eight of these facilities are up and running in six EU Countries (Denmark, Spain, Germany, France, Luxembourg, Netherlands) and Norway. (120) Their objective is to not only reduce the consumption of drugs publically but more importantly to access marginalised, chaotic individuals with a drug disorder to lessen their high risk of contracting blood borne illnesses and death. (172)

From a public use perspective, a reduction in the occurrence of public injecting with an associated decrease in drug related debris is evident. Most impressively, no escalation in drug abuse or in drug-related criminal activity has been seen. (173)

By providing a secure, sheltered environment, guidance on safer injecting techniques and medical supervision prepared for the treatment of drug OD SIFs significantly lessen drug related morbidity and mortality. In overseeing millions
of injections, not one fatality has occurred in the facilities. Evidence from robust studies documents that by connecting clients to a wider network of care their access to health and social services increases, further improving their overall quality of life. (120)

Currently, Irish law distinguishes between drug ‘possession for personal use’ and ‘possession for sale or supply’. Consequences for ‘possession for personal use’ are contingent upon the category of drug and on the harshness of the penal proceedings, that is, whether a summary conviction or a conviction on indictment is sought. Regardless of the severity, the Criminal Justice (Community Service) Act 2011 necessitates that courts contemplate imposing a ‘community service order’ instead of a custodial sentence in all scenarios where up to 12 months’ incarceration might have been sanctioned.

In May 2017 the Minister for Health Simon Harris and the Minister of State for Communities and the National Drugs Strategy, Catherine Byrne supervised the enactment of the ‘Misuse of Drugs’ (Supervised Injecting Facilities) Bill 2017’. The Bill allows the first supervised injecting facility in Ireland to be opened. It provides an exemption for licensed providers to allow clients to possess or prepare controlled substances for personal use in its premises. When in the facility, clients are exempt from legal proceedings in relation to personal drug possession or consumption, regardless of the drug category. Ownership of controlled drugs will remain to be an offence outside of the SIFs. Possession for sale or supply will remain to be illegal both inside and outside a SIF.

2.3 Thesis Rationale

Due consideration must be given to the fact that even the most advanced approaches in harm reduction techniques cannot fully tackle the unforgiving,
relapsing nature of drug use which is currently entrenched in the chronic lifecycle of drug dependency. (3) Since as far back as the early 90’s laboratory studies have shown that being in contact with particular ‘stressors’ escalates drug desire, as documented by subjective self-reporting. (174) Ecological momentary assessment (EMA) techniques are well established in assessing the association of both daily stressors and negative moods with drug use in the real world. A decade ago, the first study to employ EMA to assess the direct effects of stress and negative affect on day-to-day opioid use in the real world setting showed a positive correlation between them. (175) At the same time, the importance of neuroimaging in assessing relapse was making a break through. Imaging studies testing prefrontal executive functions, inclusive of restraining impulsivity and judgement showed significant deficits and decreased responses in the pre-frontal cortex of individuals with a SUD as compared with the control group. (176, 177). More recently, research has proven that cue-induced cravings for opioids stimulate specific areas of the prefrontal cortex, amygdala, hippocampus, insula, and ventral tegmental area. (178) A most recent 2018 publication showed that a ‘sensitised reward response’, ‘strong stress-reactivity’, fused with ‘impulsivity’ are all likely to increase the likelihood of relapse (179), as do other neuro-cognitive correlates of drug dependency such as poor insight (180), and reduced capacity for voluntary choice. (181, 182) A second 2018-publication shows relapse is linked to drug-related prompts such as locations of drug use, drug equipment, the drug itself, or anxiety/trauma, emphasizing the critical role memory plays in drug relapse. (183) Accordingly, OAT is the preferred option for many. It is imperative, therefore, in the treatment of OUD that MMTPs serve their clients optimally.
Secondly, the effectiveness of THNPs in reducing mortality rates in opioid overdose is well researched. Put simply, they work. Therefore, it is crucial to maximise their effectiveness.

2.4 Thesis Aims and Objectives

The first study in this thesis is an in-depth qualitative study, which undertakes to determine why the HSE’s methadone maintenance treatment programme (MMTP) situated in Limerick City, in the Mid-West of Ireland fails to work for a cohort of Irish OUD individuals. These individuals are likely the most complex of OUD individuals in treatment. This thesis aim to empower them to voice their personal experiences of their journey to and through the MMTP. Secondly, it would be a failing of this thesis not to address the most emotive and difficult of outcomes for persons with an OUD, opioid OD. In line with the aim of our drug strategy, ‘to reduce mortality rates associated with drug abuse’, this thesis aims to enhance our understanding of the newly established Irish Take Home Naloxone Programme (THNP), to ensure it is functioning optimally in its campaign against OD.

2.4.1 Aim Study 1

To establish the barriers to progressing through a Methadone Maintenance Treatment Programme (MMTP) by exploring the perspectives of the individuals in Ireland’s ‘Health Service Executive Mid-West Limerick Drug and Alcohol Services’

2.4.2 Objectives Study 1

1. To understand from the perspectives of persons with lived experience of OUD a) how they came to develop an OUD, b) why the current
programme is not working for them, and c) what they propose that would be more effective.

2. To co-develop with people with lived experience innovative approaches to addressing OUD in ways that are more acceptable to clients and therefore more likely to have greater uptake on effectiveness.

2.4.3 Aim Study 2

To optimise Ireland’s national Take Home Naloxone Programme

2.4.4 Objectives Study 2

1. To conduct an in-depth review of Ireland’s THNP

2. To analyse which variables most significantly impact on a person’s hospital attendance post naloxone administration, a factor known to improve overall survival rates in the management of opioid overdose

OUD individuals themselves narrate this thesis. Documenting their voice in addressing the complexities of OUD is ultimately, what will determine our success in combatting the adverse outcomes of OUD. Secondly, shining a focus on the Irish THNP gives us an appreciation of its effectiveness and highlights potential means to better its overall efficacy particularly in relation to hospital attendance, a key necessary factor in the management of OD and thus ensuring the voice of OUD individuals is not lost to a premature death.

2.5 Chapter Conclusion

The opioid crisis is a multifaceted, complex issue (184) and individuals with an OUD continue to be highly stigmatized in society. (154) Poverty, mental health illness, and resultant social exclusion are inextricably enmeshed in the opioid scourge. (185) Low socioeconomic status, homelessness, and incarceration also
play a pivotal role in perpetuating the opioid crisis. (186) As such, individuals with an OUD often find it impossible to achieve abstinence and escape their drug dependence. Treatments based on the philosophy of harm reduction, which minimise the risks associated with their illness, as opposed to treatment options based on abstinence, are often the most effective and suitable treatment. The association between opioid dependence and the above social determinants of health is essential to emphasise, as relevant policy makers must give appropriate recognition to the benefits of employing a harm reduction strategy. (185)
Chapter 3 Methodology

3.1 Chapter Overview

This chapter opens with a brief explanation as to why both the ontological and epistemological perspectives underlying the philosophy of this thesis are important and subsequently they are described in detail. Two studies underpin this thesis and the methodological approaches undertaken in both are then examined. Study 1 is a qualitative study, study 2 a quantitative one. As such, this thesis employs a mixed method study design. Qualitative data allows for the “voice” of the participants to be heard and interpretation of observations. On the other hand, the quantitative data in study 2 includes closed-end information that undergoes statistical analysis and results in a numerical representation. As study 1 is a qualitative study the phenomenological perspective underpinning its methodology is first defined and subsequently the studies overall design, setting, sample size, and the methods for both collecting and analysing its data is documented. The latter half of the chapter focuses on the quantitative study in this thesis. This study was a cross sectional study reviewing the ‘Irish National Naloxone Database’. Initially variables were extracted from the database for descriptive analytical purposes. Subsequently, statistical analysis was undertaken to determine which of these variables, if any, influence a patient’s hospital attendance post naloxone administration in the OD setting.

3.2 Theoretical Framework

Philosophy provides the field of social sciences with the broad ideologies underpinning theoretical thinking of which two main branches exist. The first branch is ontology, which in essence is the ‘study of being’, what actually exists in the world. The second branch is epistemology, which fundamentally is
the ‘study of knowledge’. Philosophy differentiates between ‘being’ and ‘thinking’. Ontology and epistemology are inextricably connected with one other and, according to some, are indivisible: ‘to talk of meaning is to talk of meaningful reality’. (189)

The philosophical perspective underpinning this thesis reveals the assumptions that were made about the research, leading to choices that ultimately informed the rationale, outline, methodology, and methods of the thesis, as well as analyzing, interpreting and summarizing its findings. As such, it is crucial to outline its philosophical basis.

3.2.1 Ontological Perspective

Ontological perspectives range from ‘realists’ to ‘idealists’. Realist ontology believes in the presence of one solitary ‘reality’, which can be examined, interpreted and experienced as a ‘truth’. A confidence that the ‘real’ world exists autonomous of human experience. Contrastingly, in idealist ontology it is supposed that ‘reality’ is fabricated within the human psyche, such that there is no one ‘true reality’. Reality is ‘relative’ depending on the individual experience at any given period and location. The external world has no independent existence from our thoughts, language and representations. (190) Constrained idealists, such as I, believe, the existence of an external world places both ‘constraints and opportunities on the reality constructing activities of social actors, but regard social constructions as having a high level of autonomy from it’. (190) In other words, social interactions influence our perception of reality but the external physical world influences our experience of this reality. It is this ontological philosophy, which frames this thesis.
3.2.2 Epistemological Perspective

Epistemology encompasses all features of the legitimacy, possibility and means of knowledge acquisition. It is notable because it shapes how academics structure their research in their attempts to uncover truths. Epistemological viewpoints range from ‘objectivists’ to ‘constructionists.’ Objectivist epistemology adopts the belief that reality lives outside, or ‘independently’, of the individual brain. Objectivist research is useful in providing consistent, external validity.

Constructionist epistemology refutes the concept that objective ‘truth’ exists and is lingering ‘out-there’, awaiting discovery. As an alternative, ‘truth’, or sense, unfolds from our interaction with the ‘realities’ in our biosphere. Constructionist research gives context specific meaning to a subject or issue. The term social constructionism, coined by Blaikie, merges both views. That is to say, ‘knowledge is neither discovered from an external reality nor produced by reason independently of such a reality. It is the outcome of people having to make sense of their encounters with the physical world and with other people.’ (190) This is my epistemological positioning and the one on which this thesis is constructed.

Originating from ontology and epistemology are philosophical viewpoints. These viewpoints shape our beliefs that then ultimately influence our actions. (191) At either end of the philosophical spectrum lie positivism and interpretivism.

Positivism takes an impartial, objective view, which relies on specifics and tangible data. It is a philosophy, which accepts only things that can be seen or proved. (192) Conversely, interpretivism, accounts for individual, personal human pursuits and emphasises meaningful interpretation rather than hard data.

Interpretivism aligns with the philosophical position of idealism, and refutes the positivist view that meaning resides within the world independently of
conscience. (192) According to the interpretivist approach, it is important for the researcher to appreciate differences between people (193) and as such underlies my philosophical perspective.

Two studies underpin the research of this thesis. This section will first review the methodological approach of study 1 and subsequently outline the methodological approach of study 2.

3.3 Study 1, Qualitative Study

‘Barriers to progressing through a Methadone Maintenance Treatment Programme: Perspectives of the Individuals in Ireland’s ‘Health Service Executive Mid-West Limerick Drug and Alcohol Services’

3.3.1 Study 1 Phenomenological Perspective

Within the perspective of interpretivism lies the methodological approach of phenomenology. The rationale of this approach is to pinpoint ‘phenomena’ through the lens of the research participants. This typically results in the researcher assembling ‘profound’ insights and observations through inductive, qualitative methods. The researcher then presents it from the viewpoint of the research participants. (194)

Epistemologically, phenomenological methods embrace the personal knowledge and subjectivity of each participant, and highlight the significance of their peculiar viewpoint and individual interpretation. The methods strategically gain insights into participants’ drives. (194)

Pure phenomenological enquiries aim fundamentally to define rather than explain, and to commence from a standpoint free from theories or prejudices. (195) Lately,
researchers have contested the ability of a researcher undertaking a study 'free from preconceptions or biases’.

Instead, they highlight the significance of the researcher stating clearly how the findings in their study have been interpreted and understood. The researcher is discernible in the ‘frame’ of the study as an attentive, independent player rather than an isolated and removed observer. (196) This approach is particularly effective at supplementing the research with an interpretative element allowing it to have practical applicability to inform, support or challenge policy and action. This is the phenomenological approach underpinning Study 1.

**3.3.2 Study 1 Design**

The goal of the research undertaken in study 1 is to understand better why the programme failed to work as expected in this patient population. It describes the ‘lived experience’ of chronic opioid users in receipt of long-term methadone treatment in Ireland’s HSE Mid-West Limerick Drug and Alcohol Services. It is a qualitative analysis of narrative data. In essence, the emphasis is on meaning, understanding the realities of developing and sustaining an OUD while in receipt of methadone.

**3.3.3 Study 1 Participants and Setting**

At year-end 2016, 134 individuals were receiving treatment with the opioid agonist, methadone, in the Specialist Drug and Alcohol Treatment Programme, Slainte, based in the HSE Mid-West Limerick Drug and Alcohol Services. Of these 134 individuals, only 20 (15%) transferred to the lower risk, GP setting in the community (197).

Slainte operates 10 methadone clinics weekly. Each clinic monitors approximately 14 clients. Clients are randomly assigned to their assigned clinic. I oversee three
of these clinics, resulting in an average exposure to 40 clients weekly, with a male to female ratio of 3:1. Therefore, this client exposure reflects a good representative sample of the overall population of the clinic.

Trust was integral to achieving an honest account of each individual’s lived experience. I had worked closely and built a good rapport with all individuals over the preceding two years. I compiled an information sheet, incorporating all-important details of the study. As many of the potential participants were illiterate or had only very basic literacy skills, I verbally explained the information leaflet to them and asked them to bring it home where they could further review it with their families. After this information giving session, each potential participant was given an opportunity to think about his or her possible involvement and discuss the research with me as necessary. A minimum period of one week was allowed before following up and asking them if they were willing to sign the consent form. All individuals who were approached agreed to participate in the study.

3.3.4 Study 1 Sample Size

Qualitative research often employs ‘purposeful sampling’ to identify and select the most appropriate and informative of cases (198) that are particularly well-informed or skillful in the subject matter. (199) In addition to knowledge and understanding, the importance of their readiness and disposition to partake, and their aptitude to communicate their experiences and attitudes in an eloquent, open, and reflective style is documented in the literature. (200) In contrast, random sampling is employed to minimise bias in recruitment and to allow for the potential influence of identified and unidentified variables (201), safeguarding the generalizability of findings.
There exist numerous purposeful sampling designs. The design employed in study 1 of this thesis is criterion-i. (198) The aim of this method is to pinpoint and select all instances that fulfil some predetermined condition. In this study, the inclusion criteria was that each individual had spent a minimum of two years on the MMTP, Slainte. As such, 24 of my clients were eligible for inclusion in the study, choosing those who had been longest on the programme first to participate. Qualitative methods chiefly emphasize saturation (i.e., procuring an in-depth appreciation by continuing to sample until no new essential information is attained). (202) Three main factors shaped this study’s optimum sample size, or ‘saturation’, the depth of the data conveyed by the interviewees, the emergence of common themes during data analysis and the pragmatic restrictions I was working under, mainly time constraints. Considering this, 17 of the eligible 24 individuals were interviewed of which 13 were male and 4 were female, reflecting a male to female ratio similar to the overall population of the clinic, 3:1. The 17 participants had each spent on average 7.5 years engaging with the MMTP.

3.3.5 Study 1 Data Collection

Phenomenological based research can employ an array of methods to fulfil its needs inclusive but not limited to interviews, individual surveillance, focus groups and scrutiny of transcripts. 1:1 semi-structured interviewing was the method employed to collect data for this study. This data collection method enables the researcher and the participant to engage in a real time discussion. It also provides a forum for novel and unforeseen issues to arise, allowing the researcher to subsequently investigate issues in more detail with further questions should the need arise. ‘Minimum structure and maximum depth’ underpins the ethos of this method (194), where the researcher aims to balance maintaining a focus on the
research issues whilst avoiding undue influence over the individuals’ contributions.

3.3.5.1 Interview guide

In writing the interview questions, the authors were cognizant to safeguard participants’ ability to provide in-depth, complete accounts of their journey to and through the MMTP, Slainte. Six key factors (see below) framed the broad structure of the guide but ensured it was malleable enough to permit the interviewer to follow-up and further explore interesting foci as they appeared. The interviewer met with participants at a time that was most convenient for them. A reminder phone call to each individual was made 24 hours before the scheduled time.

3.3.5.2 Interviews

I conducted individual comprehensive semi-structured interviews in a confidential office space situated in the HSE Mid-West Limerick Drug & Alcohol Services in Limerick City. At the outset, I explained the voluntary nature of the interview to each participant. Their choice to withdraw at any point and an explanation of how confidentiality was going to be upheld throughout was also clarified before both the participant and I signed the consent form.

I opened the interview with an icebreaker and then inquired as to the individuals’:
1) Childhood & Education, 2) Early Adulthood & Criminality, 3) Drug History prior to opioids, initiation of opioid use and current usage, 4) Current health, inclusive of mental health, 5) Current social circumstances (housing, employment, familial relationships), and 6) Engagement with MMTP (initial & current). The length of each interview varied, ranging from 10 to 47 minutes, with an average of 24 minutes across the 17 interviews. There were no follow-up interviews.
3.3.5.3 Audio Recordings

Individual names were purposely omitted from the recordings. The digital data was password protected before a professional transcribing company typed the recordings verbatim. An offer was extended to all participants to review their transcripts on their return but all declined this proposal.

3.3.6 Study 1 Data Analysis

Qualitative thematic analysis is a method for detecting, analysing, unifying and recounting themes found within a data set (203) and as such is a perfect fit for this study. The inductive thematic analysis of this study, presented below, was undertaken using the *Braun and Clarke Structure* of six levels of analysis. (203) Firstly, data familiarization and code generalization was completed. Then theme search, review and naming were carried out. An inductive analysis of the themes was subsequently undertaken. The overall process itself was both iterative and reflective and involved a continuous ebb and flow between the phases. Finally, a summary report was generated.
### Table 3: Inductive Thematic Analysis of Study 1

<table>
<thead>
<tr>
<th>Phases</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phase 1</strong></td>
<td><strong>Data Familiarisation</strong></td>
</tr>
<tr>
<td></td>
<td>This involved the main author, LM, reading the first transcript closely a number of times and checking the transcript back against the original audio recording for accuracy. Each review of the recordings provided some new understandings and LM began taking personal notes focusing on content, language use, context, and initial interpretative comments.</td>
</tr>
<tr>
<td><strong>Phase 2</strong></td>
<td><strong>Initial Code Generalisation</strong></td>
</tr>
<tr>
<td></td>
<td>LM coded interesting features of the data using the computer software NVivo for qualitative data administration. LM worked methodically through the full data set. She gave complete and uniform consideration to each item, tagging and naming selections of text with each data item.</td>
</tr>
<tr>
<td><strong>Phase 3</strong></td>
<td><strong>Theme search</strong></td>
</tr>
<tr>
<td></td>
<td>Merging and deviation of themes within the data were noted, leading to the development of the next phase, transforming codes into emergent themes. This involved LM working more with her notes rather than with the transcript and again inputting findings into the NVivo software package.</td>
</tr>
<tr>
<td><strong>Phase 4</strong></td>
<td><strong>Theme review</strong></td>
</tr>
<tr>
<td></td>
<td>LM firstly ensured all coded data extracts formed a coherent pattern and then progressed to considering the validity of each individual theme.</td>
</tr>
<tr>
<td><strong>Phase 5</strong></td>
<td><strong>Theme naming</strong></td>
</tr>
<tr>
<td></td>
<td>LM scanned for links between emergent themes, assembling them according to conceptual similarities. Each cluster was then allocated a descriptive label. Using NVivo allowed for short descriptions of themes and subthemes, using links to appropriate passages in the transcript.</td>
</tr>
<tr>
<td><strong>Phase 6</strong></td>
<td><strong>Final Report</strong></td>
</tr>
<tr>
<td></td>
<td>LM produced a report of the analysis undertaken.</td>
</tr>
</tbody>
</table>
Subsequent to this initial assessment, a further sixteen interviews were undertaken. A similar analysis of the data from these interviews was conducted. Themes were reconfigured and re-labelled. Analysis of the 16th and 17th interviews revealed no new data and as a result, no additional interviews were deemed necessary as ‘saturation’ had been achieved.

3.4 Study 2, Quantitative Study

‘An in-depth review of Ireland’s Take Home Naloxone Programme’

3.4.1 Study 2 Design

Study 2 was a secondary data analysis on the ‘Irish National Naloxone Database’ from October 2015 to March 2018.

3.4.2 Study 2 Setting

In Ireland, training in the use of naloxone in the community incorporates an explanation on the need to complete an ‘incident report form’ post naloxone administration in the OD setting. Established in 2015, the ‘Irish National Naloxone Database’ (INND) processes these forms. This allows for the HSE to record data on the use of naloxone in community OD scenarios. Typically, staff of the homeless hostels, General Practitioners, staff of Methadone Maintenance Clinics, government employed key workers or peers/family members of OD victims trained in the use of naloxone in the community submit these forms. The data is recorded for each ‘Community Healthcare Organization’ in Ireland, of which there are nine. Community Healthcare Organisations (CHOs) divide the country into nine geographical boundaries, (see below) within which a broad range of community health services, inclusive of the Irish Drug and Alcohol Services, are delivered through the HSE and its funded agencies.

3.4.3 Study Population

The database recorded the following information, as shown in table 4, from October 2015 to June 2017. From June 2017 onwards, due to poor compliance in completing all sections of the form, variables highlighted in bold were no longer recorded, in the hope that a shorter form would entice a better response rate.

Table 4: Study Population

<table>
<thead>
<tr>
<th>Details of person providing information</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Date of Birth</td>
<td></td>
</tr>
<tr>
<td>Area of residence</td>
<td></td>
</tr>
<tr>
<td>Date &amp; place of where OD took place</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Details of person who overdosed</th>
<th>Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>If receiving opioid agonist therapy</td>
<td></td>
</tr>
<tr>
<td>Relationship to person providing information</td>
<td></td>
</tr>
<tr>
<td>Substances involved (If known)</td>
<td></td>
</tr>
<tr>
<td>Had the person injected heroin?</td>
<td></td>
</tr>
<tr>
<td>Was the OD fatal?</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Details on ‘Sequence of Events’</th>
<th>Were you present when the person overdosed?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>If yes, how long did it take for them (from point of using) to overdose? If No, please provide reason</td>
</tr>
<tr>
<td></td>
<td>What were the signs/symptoms of the OD?</td>
</tr>
<tr>
<td></td>
<td>How many others were present?</td>
</tr>
<tr>
<td></td>
<td>How many doses of naloxone were administered?</td>
</tr>
<tr>
<td>Question</td>
<td>Answer</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>--------</td>
</tr>
<tr>
<td>Was the ambulance called? <strong>If so, what information did you give the handler?</strong></td>
<td></td>
</tr>
<tr>
<td>Was CPR performed? If no, please provide reason</td>
<td></td>
</tr>
<tr>
<td>Was the person who overdosed placed in the recovery position? If no, please provide reason</td>
<td></td>
</tr>
<tr>
<td>Did you wait with the person who overdosed until help arrived?</td>
<td></td>
</tr>
<tr>
<td>How long was it before the ambulance arrived?</td>
<td></td>
</tr>
<tr>
<td><strong>How long did you stay with the person who overdosed after the paramedics left?</strong></td>
<td></td>
</tr>
<tr>
<td>Did the person who overdosed attend hospital? If No, please provide reason</td>
<td></td>
</tr>
<tr>
<td>Did the Gardai attend? Details of any action taken by the Gardai</td>
<td></td>
</tr>
<tr>
<td><strong>Was the used Naloxone Pack given to the ambulance crew?</strong></td>
<td></td>
</tr>
<tr>
<td>Additional Details</td>
<td></td>
</tr>
<tr>
<td>Any additional information(including how person feels following incident)</td>
<td></td>
</tr>
<tr>
<td>Was refresher training provided?</td>
<td></td>
</tr>
<tr>
<td>Was a new naloxone kit re-issued?</td>
<td></td>
</tr>
</tbody>
</table>

### 3.4.4 Study 2 Data Recruitment

Initial review of the above data exposed that many variables were missing from the dataset. A more in-depth review of the reporting system in Ireland highlighted it to be quite onerous and not user friendly. From 2015-2017 the reporting process involved manually completing a lengthy form and then sending it by post or scanning it to the HSE. Often these forms were misplaced by the recipient or incompletely or inaccurately filed out by the sender. To address this issue, the reporting system did change mid-way through 2017 to an electronic excel spreadsheet format, which is what is currently being used. Unfortunately, the excel sheet is also quite tedious to fill as the headings are unclear and the overall
format lacks structure or clear explanatory notes. As a result, many blanks and mistakes were evident at the time of review.

3.4.4.1 Check Exercise

To explore if, due to the onerous reporting mechanism, under-reporting of naloxone was a potential issue, a check exercise was completed on the recorded uses of naloxone in 2017 in hostels located in CHO areas 7 and 9. The main author telephoned all hostels in this catchment area who had submitted forms to the HSE on naloxone use in an OD setting and cross-matched their in-house recorded uses of naloxone against the HSE’s recorded number. In 2017, 53 uses of naloxone were documented. Of these, 37 uses were recorded in CHO areas 7 and 9. Of the 37, 35 occurred in hostel accommodation across the city of Dublin, which provide supported accommodation for those who find themselves homeless. Results showed a measurable difference with hostel records recording 54 uses of naloxone in 2017, a difference of 19 or a factor of 1.54 in comparison to HSE records.

3.4.5 Study 2 Data Analysis

Data analysis was essentially undertaken in a 2-step process. Step 1 was to tabulate specific data drawn from the database and undertake a subsequent descriptive analysis of the selected data. Step 2 statistically analysed the data to ascertain what if any variables influenced a patient’s hospital attendance. Using an excel spreadsheet breakdown on the below listed variables was tabulated to get a broad sense of this secondary data.
### Table 5: Variables extracted from the National Naloxone Database

<table>
<thead>
<tr>
<th>Characteristics of Victim</th>
<th>Characteristics of OD Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Fatal or non-fatal.</td>
<td>Where the OD occurred.</td>
</tr>
<tr>
<td>2. Sex of the OD victim.</td>
<td>Number of others present at the OD.</td>
</tr>
<tr>
<td>3. Age of the OD victim.</td>
<td>If an ambulance was called.</td>
</tr>
<tr>
<td>4. If they were a registered Individual on a MMTP.</td>
<td>The number of others present at the OD.</td>
</tr>
<tr>
<td>5. If they had injected heroin at the time of the OD.</td>
<td>If an ambulance was called.</td>
</tr>
<tr>
<td>6.</td>
<td>Where relevant, how long it took the ambulance to arrive.</td>
</tr>
<tr>
<td>7.</td>
<td>Where relevant, was basic life support administered.</td>
</tr>
<tr>
<td>8.</td>
<td>The number of doses of naloxone administered.</td>
</tr>
<tr>
<td>9.</td>
<td>Who administered the naloxone.</td>
</tr>
<tr>
<td>10.</td>
<td>If the Gardai were present.</td>
</tr>
<tr>
<td>11. If the OD victim accompanied the ambulance team to the hospital setting.</td>
<td></td>
</tr>
</tbody>
</table>

International literature indicates that a better understanding of the factors that influence whether a patient attends hospital or not post naloxone administration is important in the management of opioid OD. Therefore, the statistical analysis undertaken in this study undertook to determine which factors, if any, influenced a patient’s hospital attendance. The fact that the response variable in this study is binary (yes or no to hospital attendance) means that models suitable to conduct
the analysis include ‘Decision Tree’, ‘Random Forest Classifier’, and ‘Logistic Regression’.

To generate a model comparison, the data was randomly split with 60% being used to train a decision tree, a logistic regression, and a random forest classifier. Twenty percent of the remaining data was then used to test the accuracy of each classifier, with the final 20% of data used as a validation set on the 'winning' model. This process was repeated 100 times. The results generated by the model comparisons are summarised in Table 6 below.

Table 6: Model Comparison - Model wins and average accuracy

<table>
<thead>
<tr>
<th>Decision Tree</th>
<th>Logistic Regression</th>
<th>Random Forest Classifier</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>42</td>
<td>39</td>
</tr>
<tr>
<td>57.69%</td>
<td>65.06%</td>
<td>68.19%</td>
</tr>
</tbody>
</table>

Although the random forest has a higher mean classification accuracy on the validation set (68%), the logistic regression model was most often chosen as the most accurate model (42 times). A logistic regression model also yields ‘interpretable’ results, as opposed to the ‘blackbox’ random forest model. This allows the model to be inspected and potential inference to be derived from it. A logistic regression model was chosen as the most appropriate to analyse the data.

The statistical analysis in this paper was done using R and R-studio. (204, 205) The classification trees and random forest classifier were done using the 'r-part' and 'random-Forest' packages, respectfully (206, 207). The logistic regression model was calculated using the 'MASS' package, the ROC curve and classification analysis was done using the 'ROCR' package. (208, 209)
A logistic regression (LR) model was used to determine independent factors affecting a person’s attendance at hospital post naloxone administration. LR models the probability that a certain instance should be classified into a category.

A LR model is of the form (1) where $\rho$ is the probability of the event occurring. In this study, $\rho$ is defined as the probability that a person will go to the hospital after an administration of naloxone.

$$\rho = \frac{\exp(\beta_0 + \beta_1x_1 + \beta_2x_2 + \cdots + \beta_ix_i)}{1 + \exp(\beta_0 + \beta_1x_1 + \beta_2x_2 + \cdots + \beta_ix_i)}$$

(1)

We can rearrange (1) to get:

$$\text{Logit}(\rho) = \log \left( \frac{\rho}{1-\rho} \right) = \beta_0 + \beta_1x_1 + \beta_2x_2 + \cdots + \beta_ix_i$$

(2)

This is the log-Odds or logit model.

In the results’ section of this study, section 5.4.3 the LR model coefficients are represented by $\beta_1, \beta_2 etc.$ in (2) above.

It is much easier, however, to consider the Odds of an event instead of the log Odds. This is simply:

$$\left( \frac{\rho}{1-\rho} \right) = \exp(\beta_0 + \beta_1x_1 + \beta_2x_2 + \cdots + \beta_ix_i)$$

(3)

This value can never be negative but may be larger than one.

Finally, we consider the Odds Ratio, OR, to allow us to compare how strong each factor is in affecting the outcome. It is given by:
\[ OR = \frac{\left(\frac{\rho_1}{1-\rho_1}\right)}{\left(\frac{\rho_2}{1-\rho_2}\right)} \]

(4)

In the results’ section of this study, section 5.4.3.1 the interpretation of the odds ratio was derived using (4) above.

### 3.5 Ethical Considerations

Research on interviewing marginalised groups, such as those with an OUD, reflects on ethical considerations, the employment of incentives and the capability of research participants to provide informed consent. (210-212). Distressing life events such as abuse and abandonment often permeate their lives, (213) are shared during the interview and as such, the principle investigator must be cognisant of this at all stages of the research process. On an encouraging note, many participants view their contribution to research positively as it allows their voices to be heard which in turn might benefit others. (214) Nevertheless, since qualitative research is dependent upon the disclosure of personal and sensitive information, clear and deliberate steps were taken to safeguard the self-worth and welfare of participating clients in Study 1 of this thesis.

Participating clients are dependent on me, their prescribing doctor, to receive their weekly methadone prescription and as such, there is an obvious unequal relationship between us, which warrants further explanation. To address this understandable bias, prior to conducting the research, I had spent 2 years consciously building a rapport with these clients, ensuring I gained their trust. Clients were fully aware of the ethical motivations underpinning this research, which ultimately aimed to better address their needs by improving the delivery of
their MMTP. In doing so, I ensured, to the best of my ability, that client participation was both optional and truthful.

The potential risks were minimal. However, as cited above, it had to be acknowledged that there was a risk of emotional distress for each participant during the interview given that they were discussing the personal challenges that are inherent in being a long-term client of a MMTP. To minimise this risk I worked with the multi-disciplinary team, MDT, to ensure any upset that occurred both immediately and in the longer-term was appropriately managed by offering both immediate and regular follow-up counselling services. Reassurance of confidentiality were given and participants were assured that they could cease the interviews at any point if they so wished.

No incentives were given to participate in the study. Prior to the interviews, clients were urged to chat openly and honesty but were also advised that they were under no obligation to reply to all questions asked. During the interviews, new themes or foci of interest were signposted with clients in advance, removing any element of surprise and ensuring clients were happy to discuss the new area under review. Of uppermost importance, an outlook of needing to learn from the clients was portrayed and sustained throughout the interview process, which bolstered clients’ self-esteem and worthiness. It was reiterated that, through their participation in the study, they would be the key contributors to affecting positive change in the administrative policies and procedures of the MMTP. Empathy permeated the interviews and flashes of both melancholy and comedy were responded to appropriately.

Following the University of Limerick Records Management and Retention Policy, E-transcripts were stored on a password-protected computer and hard copies were
locked in a cabinet in the main author’s office. University Hospital Limerick’s Research Ethics Committee granted full ethical approval for this study: REC Reference 131/16.

Study 2, ‘Review of Ireland’s Take Home Naloxone Programme’ was a quantitative study on secondary data extracted from Ireland’s National Naloxone Database. This study received full ethical approval from University Hospital Limerick’s Research Ethics Committee: REC Reference: 079/18.
Chapter 4 Results Study 1

4.1 Chapter Overview

This chapter focuses on the results of Study 1, ‘Barriers to progressing through a Methadone Maintenance Treatment Programme: Perspectives of the clients in Ireland’s ‘Health Service Executive Mid-West Limerick Drug and Alcohol Services’. Results are structured chronologically. Initially, as seen in Diagram 1, emergent themes in the chronological development of an OUD as depicted by the participating clients of the HSE Mid-West MMTP in Limerick City. Firstly, results pertaining to the theme of childhood adversity are documented. Thereafter, as the clients moved from frivolous, recreational use through to full dependency the common chronological factors sustaining and nurturing their three-step journey unfold. Once their OUD was established, subsequent data analysis, as seen in Diagram 2, identified common life experiences, which influenced their illness. The majority of these influences were negative but some positive factors emerged and are documented accordingly. Finally, as seen in Diagram 3, participating clients of the MMTP voiced their own suggestions for improving their journey through an OUD.
4.2 Individuals’ personal journeys to and through the MMT Programme in the HSE Mid-West Limerick Drug Services

The following section expands on the main themes which emerged from the study in the development of an OUD as depicted by the participating clients of the HSE Mid-West MMTP in Limerick City.

4.2.1 Adverse Childhood Experiences (ACEs) permeated their upbringing

Childhood adversity was an exceptionally common occurrence across the interviewees, with all ten ACEs permeating the transcripts.
4.2.1.1 Personal ACEs

In the category of ‘Personal ACEs’ all five adversities were documented.

Reports of both emotional (1) and physical abuse (2) were common, with particular emphasis on paternal physical abuse.

“I’d a traumatic experience in national school, I got bullied badly. I was suicidal even at about 11 or 12. And my father would have been a teacher then, and he never, he didn’t stick up for me…..” Interviewee 6

“I suffer from problems over my father and my father is very physical to me here he broke my collar bone he broke my ribs, he broke my finger, he broke a lot of my bones you know what I mean my father when I was a child. Like and he played me all of my life growing up you know what I mean” Interviewee 2

Sexual abuse (3) was also reported.

“When I was young like I used to be walking up and down it’s called the ‘Boirin Lane’ and there used to be a man with a black fluffy dog the whole time. I would always see him like, but he was just a bad man. Then he did bad things to me” Interviewee 17

Emotional (4) and physical neglect (5) permeated the transcripts.

“I’d an unhappy childhood. It was very difficult. My parents didn’t get on” Interviewee 8

“In 1975, I was only 11. I was in a, a what do you call it, you know them Christian Brother schools, locked away, eight years for taking nine apples, I got locked away in a school for nine apples. Life there was ‘Horrible,
horrible, horrible, horrible, some terrible things, Oh I don’t even want to talk about them…” Interviewee 9

4.2.1.2 ACEs relating to household dysfunction

All five ACEs pertaining to household dysfunction involving other family members were also documented.

Mother being treated violently (6) was evident.

‘‘I’d a father an alcoholic growing up. He was very abuse to all of us like, we all got it, my mother and all, you know. Interviewee 3

Most interviewees reported exposure to a culture of illicit alcohol and drug misuse from a very young age, accounting for the ACE, ‘substance abuse in family’. (7)

“I hate drink do you see because my brother and father years ago they used to drink and they used to kill each other so to drink I don’t like drink no I hate drink” Interviewee 11

“I first saw drugs at home, my father was smoking hash…then he moved to cocaine” Interviewee 16

“I ended up losing my mother when I was eight years of age; a drug went bad for her after she taking it…you know... Interviewee 17

Mental illness (8) permeated these households adding to the adversities experienced in childhood.

“My dad was very deep for reasons I know now like, but I didn’t know then. He was sick in the head” Interviewee 07

“My brother is a schizophrenic” Interviewee 11

“My brother hung himself” Interviewee 17
“I was in care for a bit & stuff. My mam died and my father couldn’t handle me” Interviewee 14

Familial members in incarceration (9) was common.

“My brother died after coming out, he done 9 years in prison and got out and died” Interviewee 11

Finally, loss of parent (10) though death or abandonment was documented.

“My father died when I was young enough…about 14 I’d say. Alcohol killed him” Interviewee 5

“My mother left me when I was 7. My dad has another family” Interviewee 10

“My dad started like going out and he was meeting other women and stuff like that. And he was always kind of like you know ‘shush don’t tell your mother’ kind of stuff like you know what I mean so” Interviewee 1

4.2.2 Continuous exposure to adversities into adulthood

perpetuated their ‘Recreational Sporadic Use’ of drugs

Misfortune and difficulties continue to infiltrate their lives from childhood onwards. Often, their inability to cope with these relentless stressors resulted in commencement of heroin abuse and indeed frequently perpetuated its continued use thereafter. The brief excerpts below summarises the struggles many individuals with OUD face on a daily basis.

“My sister got murdered, she got shot dead. The hit was meant for me. I was the last one with my sister when she got shot so I always get the blame for her dying... My other brother got stabbed to death.... My other brother, he done 9 years in prison and he got out and died in the shower of
a heart attack…. My little brother just died, meningitis in the brain got him. My other brother he is a schizophrenic he is and his friends should know not to give it [heroin] to him do you get me. My brother is the kind of one that will sit down and he will just talk to himself for the day do you know? If you give him a holy picture, he will talk to it for the day as well. It’s his friends that are doing it to him dragging him along now and making him rob this and rob that. He is a pure misfortune do you get me. He’s in and out of prison. He lives in a mental hospital now. My mam fell to the ground there oh about twelve weeks ago. She is still in hospital since with two strokes in each side of the brain. She is supposed to be getting fed through a tube now.” The most stable influence in my life was the presence of my father. Unfortunately, he passed away in 2016, when “I was in incarceration” Interviewee 11

4.2.3 Intensified Sustained Escalated Drug use

This was fuelled by both mental illness and benzodiazepine misuse.

4.2.3.1 Mental Illness, inclusive of Psychoses, Depression and Anxiety

More frequently than not, reports of personal mental illness were recorded in tandem with these individuals’ heroin dependence. Psychoses, depression and anxiety disorders were the most common mental illnesses documented. These illnesses may have been present from a young age.

“I suffered from psychosis since the age of fifteen. Schizophrenia psychosis I have” Interviewee 2

Alternatively, they may have emerged later in adulthood because of harrowing adversities.
“I lost two children in 9 days and I nearly lost one yesterday’. My son, he hung himself in prison, three days left in his sentence. His brother went out to the yard, they were in prison together. His brother was in the same cell as him but when he was out playing handball, the other was writing his suicide letter. My daughter committed suicide 9 days later. She went out, bought Xanax (alprazolam), and took the whole lot and just, she took about nine bags of heroin as well and just threw herself off the bridge. Afterwards, I tried to kill myself. But you can’t kill a bad thing….. He continues to suffer with depression and indeed was very low on the day of the interview itself, I’m on the verge of a breakdown and I know it myself, do you know, I feel like crying, I’m tormented, you know” Interviewee 12

Individuals often expertly captured their misdiagnosis by health care professionals due to suffering from both an OUD and a mental illness. They often felt that their psychiatric team solely focused on their drug dependence and not their concurrent mental illness.

“Yeah, I had depression there when I was out on bail for killing, for that incident, that really got me down, you know and I was the acute psychiatric unit for about two months, three months. They [the psychiatric team] were, they were mixing the two for me, they were trying to say that it was all got to do with the drugs and everything in my own heart and soul like it was because of what happened, you know”. Interviewee 3
4.2.3.2 Illicit BZD Usage

Not altogether surprisingly, an overwhelming proportion of interviewees were dually dependent on benzodiazepines (BZD). More often than not, individuals were buying these on the city’s black market. Due to the high demand for BZD outstripping local supply, the market was becoming more dependent on foreign suppliers, and purchasing them on the internet was commonplace. Individuals have no idea what they are purchasing, as these tablets are illegally manufactured and so do not resemble prescribed BZD in shape or size and indeed are often laced with other drugs.

“At the moment, Benzos are a big thing in Limerick. They’re Spanish supposed to be, now there’s two different types, there’s ones that say U94 on them. You can bust them in four, they’re supposed to be two milligrams and the shape of them is very funny, I’d say it would be very hard to copy them though. And then there’s other ones that says Xanax on the front of them, but they’re real thick and chunky and they have two on the back, they’re supposed to be two milligrams as well, but I took them and they made my urine dirty here”’ [A ‘dirty’ urine refers to a urine-testing positive for opioids] Interviewee 7

Often, their supply of BZD was from the same supplier as their heroin and as such, BZD usage perpetuating heroin usage was evident. The cost of feeding their dual dependence also surfaced as a stressor in their lives. The use of BZD to enhance the effect of heroin was also apparent. Chaotic, alarming use of BZD was evident, where the risk of accidental OD was undisputed.

“I mean if you are on benzos, you are half- asleep anyway so if you take heroin it’s going to push you over the edge like you know. You
can only go so far with benzos and once you reach that point if you took ten more benzos you still only get that far but if you took a bale of heroin you go that bit farther so I put them into the pot and inject then with the heroin with everything like so I inject them both together” Interviewee 12

“I am only after taking 6-7 sticks [Sticks are a potent form of street Xanax, approximate equivalent to 2 mg Xanax] now [before interview]. I could take 20-30 of them a day. I buy sticks over Xanax because they are stronger. They are sent back from Spain or somewhere, they are charging a fortune for them anyway. Two euro fifty for one stick. But I take Upjohn 90s [1mg Xanax] now as well, maybe 10-15 a day” Interviewee 15

4.2.4 Lack of Life Purpose, Boredom and Loneliness

This picture formed the backdrop to their final descent to ‘Loss of Control’ on their opioid dependence. Individuals expressed a significant lack of purpose in their lives. Boredom was a dominant reference and was described as a reason for their continued heroin use.

“Boredom is a big part I think, just sitting down at home with nothing to do thinking ‘I will smoke that now it might knock me out” Interviewee 16

Loneliness was a prevailing emotion linked to this subtheme. Lack of employment, a known contributor to the economic burden of this disease, had a significant negative impact on individuals’ self-worth. Many blamed having a criminal record for their unemployment. Inability to work due to disabilities related to their heroin abuse was also evident. Lack of motivation was also evident.
“It’s very hard, motivation is lacking big time, yeah. I’m on disability at the moment, it’s because I’ve had DVTs in both legs over injecting [into the groin]. I don’t think I am fit enough to work… and with a criminal record” Interviewee 3

4.3 Negative and Positive life experiences, which influence clients’ journeys

Subsequent data analysis identified common life experiences, which influenced their journey. The majority of these factors negatively influenced their life paths by sustaining and at times escalating their opioid dependence. However, recurrent positive themes also emerged from the data, which warrant focus and further exploration.

Diagram 2 Negative and Positive life experiences influencing clients’ journeys
4.3.1 Negative Factors

Six negative factors emerged from the data analysis as described below.

4.3.1.1 Turbulent Living Environment

On analysing the data, three specific unstable living conditions emerged which perpetuated the continued use of heroin, living with an individual who also had an OUD, living in hostel accommodation and finally being homeless. Living with an individual who also suffered an OUD resulted in individuals stating they often sought heroin on behalf of their partners as opposed to fuelling their own habit.

“If I had him sorted out there (referring to her current partner) I would be flying it’... If she did not source heroin on his behalf she felt he “would go out like do you know what I mean he would probably end up robbing something do you know I mean. It’s safer if I do it, do you know what I mean. I’m protecting, protecting him by getting it (money to fuel their habit) off my sister” Interviewee 1

The environment most associated with continued use or frequent relapse was for individuals living in hostel accommodation.

“I’m in a hostel now and there’s two people dealing fucking heroin. It’s full of addicts. I can’t open my eyes, I can’t go outside my room without bumping in to someone and they’re either talking about drugs or doing drugs or a way of getting them, you know. It’s not an excuse but it’s just a matter of fact like, the heroin is just, it’s just rampant in that hostel and it was just a matter of time before my brain... gives in. It’s just everyone
who’s on heroin goes there to, to live, to use there because they know it’s an easy option’’ Interviewee 3

Finally, homelessness was also reported as an environment that fuelled their need to use continuously. Motivation was hugely lacking in the homeless cohort, as being homeless secludes you from many basic needs.

"If you haven’t got your own address you can’t get any help, medically, doctors, on assistance on anything. No, you can’t even get the dole. That is one of the main reasons I continue to use’’ Interviewee 2

4.3.1.2 Ease of Access to Heroin

Data analysis highlighted that the heroin supply in Limerick was plentiful, easily accessible, cheap and spreading to other communities. Ease of access was also confirmed by confirming a reduction in the price of heroin and its spread to other communities.

“Oh yes oh yes in town yes. When asked if the regularly reported drug seizures were negatively affecting its supply, she replied, No it’s all over the place. ‘The other night whatever way I looked there was two fells that sells heroin sitting up on the next block of steps from my place’…. You would hear who has it do you know what I mean. They (the dealers) are waiting by pubs watching people coming out of the hostels and calling them asking telling them that they have gear…. You know now you can get three or four bags for fifty euro. About two year ago, it was twenty-five euro for a bag…. It’s getting bigger in the travelling community” Interviewee 1
4.3.1.3 Peer Influence

Data analysis confirmed that all individuals cited the term ‘friend’, ‘mate’ or ‘cellmate’ as the method by which all were first introduced to heroin. Though all 17 lives differed greatly on their individual journeys, peer influence on initiation of their dependence, was the one constant variable. Thereafter, continued friendships with other drug takers perpetuated their dependence.

A varying degree of insight with regard to these ‘friendships’ was noted. Nevertheless, even if they had this initial insight continued friendships with other drug takers perpetuate their continued use.

“He wasn’t no he was a friend of mine but he was a snaky friend yes”

Interviewee 15

“I don’t really have any friends who don’t take drugs. There is one or two but they have kind of stepped back away from me because they don’t like being around me when I am taking drugs” Interviewee 16

One potential solution, cited to address this issue, was to attempt complete isolation from their social scene. The only other escape from peer pressure was death.

“I’ve isolated myself from all other addicts like, do you know, I don’t talk to any of them, I don’t, I’ve blocked all the drug dealers’ numbers”

Interviewee 6

“A lot of my friends are dead, a good thirty of my friends are dead either murdered or because of heroin” Interviewee 2
4.3.1.4 Erroneous understanding of their illness and methadone as a treatment option

Uniformly, individuals had a poor understanding of the chronicity of their illness, the likelihood for long-term MMT or indeed of the rationale for using methadone as a medical intervention in their disease management. On initiation of treatment the average period, an individual felt they would need to be prescribed methadone was approximately 3-6 months.

"When I first joined I thought I would be on it three to six months and then I would be going yes grand I am fixed now. But no." Interviewee 12

The average time in MMT across the 17 individuals was 7.5 years. However, when asked re the likelihood for them needing ‘long-term’ methadone maintenance therapy, the vast majority of individuals were resolutely confident that they would not require long-term methadone therapy. Over the last 12 years, interviewee 4, had repetitively engaged and re-engaged with the programme, relapsing regularly during the time but when probed as to why he believed he would not need ‘long-term’ therapy answered confidently, “I think I’m passed that, you know, I think I am”

Individuals’ confidence in remaining opioid free was disproportionate to their actual achievement. At the time of interview, interviewee 11, had succeeded in not using heroin for just one week but was adamant she would remain opioid free forever more. Not only so, but as a result of her week’s sobriety she now wished to cease methadone completely. When probed if she knew of anyone that had successfully ceased methadone and remained opioid free thereafter she denied knowledge of it. At the same time she was confident in being successful without methadone.
‘Well I am clean now a full week. It’s my first time I am clean and I am
staying clean…. I don’t want it (the methadone) I am sick of it, it’s not for
me… To be honest with you. I can’t think of anyone there that came off
Methadone and stayed clean’’ Interviewee 11

When asked re their level of education with regard to methadone itself individuals
were uniformly poorly educated. Education levels of individuals’ families were
also poor, which in turn resulted in lack of familial support for the treatment.

‘‘I got given a leaflet, so I just read through that, you know.’ (I learned) a
little bit off YouTube’’ Interviewee 8

‘‘No, no one explained to me how methadone works’’ Interviewee 9

‘‘My mam, she hates the stuff, she hates it because she thinks it’s the
Devil’s drink’’ Interviewee 7

4.3.1.5 Poor Communication with allied health professionals

The majority of individuals reported a fragmented, poor and sometimes fractious
relationship with their General Practitioners. They reported the fear of being
stigmatised as the reason for hiding their heroin dependence and engagement with
the MMTP from their GP.

‘‘I didn’t tell my GP I had a heroin problem because I, I wasn’t telling
anybody that I had a heroin problem. I was so anxious and nervous that I
was going to get judged’’ Interviewee 8

However, on finding out the individual was on the MMTP their relationship
immediately disintegrated. The GP understandably felt there was no trust between
them as reported by the individual recalling the encounter. The GP stated,

‘‘there’s obviously no trust between you and me.’’ The GP recalled all the times
she prescribed opioid based medications for the individual because of his reported
pains and began to doubt the need or truth in his having needed them. As a result,
she felt she could no longer remain his GP. ‘‘I just can’t deal with you.’’ As a
result, the individual reported feeling abandoned by the health care system.

‘‘I felt like a complete, excuse me, piece of shit. When I walked outside
that door I never felt so lonely and so scared in my life’’. I’ve no GP
from then till now’’ Interviewee 8

As a result, many individuals refuse to engage with their assigned GP.

‘‘I don’t bother with him, being honest about it; I just go in for my
medication. I even went in the other day to get a 3-month script so I won’t
have to see him’’ Interviewee 9

Worse yet, some individuals reported having no access to primary care
whatever.

‘‘No, I’ve no GP at the moment. ‘I don’t know how to do it (get a new GP),
nobody is helping me with that’’ Interviewee 10

Reports of a similarly disjointed relationship with community mental health
services were documented. Poor communication between community day
hospitals and detoxification centres was evident and the client suffered as a result.

‘‘I was seeing a psychiatrist. I was on lyrica for general anxiety.... But I
haven’t gone to him in years. I got off the Lyrica when I went to treatment
you see’’ Interviewee 6

Unfortunately, the client’s anxiety remained untreated after in-house
detoxification failed to manage his drug dependence.

Individuals’ lack of understanding of their prescribed treatment also fueled the
mounting miscommunication between them and their psychiatric team.
“See they (referring to psychiatric day hospital) give out a load of drugs, like they, they put me on an antidepressant I know, but I don’t know why they put me on it when I’m coming down off Benzos… because I think it (concurrent anti-depressant medication) makes it harder to come off it (BZDs) in the long term. They didn’t explain nothing, (they just said) we’ll put you on this and it’ll help you like and now he’s after doubling my dose yesterday, I was on ten now I’m on twenty… Do you know I hope I’m not going to have a problem down the line with them” Interviewee 7

Furthermore, poor inter-communication between allied health professionals was also evident. Interviewee 12 reported suffering with panic attacks. His GP referred him to the local psychiatric hospital where benzodiazepines were prescribed as a treatment modality. However, he reports his GP not agreeing with this treatment plan.

‘‘When I came back to my GP he then took me off the benzos. I told him I still get panic attacks but he said, ‘‘it’s all in your mind’’ and to just exercise your way out of it like’’ Interviewee 12

4.3.1.6 Stigma

Individuals reported feeling stigmatised due to their engagement with the MMTP by not only their family, friends and neighbours but by society as a whole. Embarrassment was a common recurring phrase. As a result, they try to hide their methadone usage from everyone, often inclusive of their own family members. They are ashamed of their dependence and the negative connotations associated with needing treatment for it, as reflected in the following five short excerpts from the transcripts.
‘There is an awful stigma when people know what you are on. They will stop looking at you if you know what I mean’ Interviewee 2

‘I find it embarrassing in my own town. I just pull up in my van around the corner from the pharmacy and just kind of sneak in’ Interviewee 6

‘When I know someone that comes in to the pharmacy I just sit there like a zombie, embarrassed. It can be hard. People can look down their nose when you are on Methadone’ Interviewee 10

Interviewee 12 was embarrassed by the fact that the public was, ‘paying taxes for keeping people on methadone’. When challenged and asked if the public should not view opioid dependence as a chronic illness, much like diabetes, and requiring methadone was much like diabetics needing insulin he defended the public’s perception of heroin dependence

‘You are not born with the choice of diabetes but you are born with the choice of not taking heroin’ Interviewee 12

### 4.3.2 Positive Influences

Three positive factors emerged from the data as described below. These findings are of paramount importance as it is these factors which promote abstinence and improve the overall quality of life for the individual with a chronic dependency on opioids.

#### 4.3.2.1 Structured Living Environment

Often, the more regularised their living conditions were the greater their likelihood was of remaining opioid free. Three specific environments were tabulated, prison, hospital and when housed in a drug free environment. Interviewee 13 reported
finding the structure and governance that prison offered, ‘‘behind a steel door’’, a welcomed reprieve from their chaotic lives fueling their drug habit.

Reports of purposefully getting caught committing crimes to ensure imprisonment were documented, as individuals knew the strict regime of prison had the potential to help them succeed in their quest for sobriety.

‘‘I spent a lot of years in jail. It was down to drugs, theft to supply my habit. I was using gaol as a rehab, do you know, I was going out, committing crimes and getting caught on purpose just to go in to gaol to get off the gear. I couldn’t get off it you know on my own outside. Gaol saved me enough of times. I got clean in prison, yeah. I got a job as a cleaner and, do you know, kept my head down. It worked for me. It gave me structure that you don’t have on the outside’’ Interviewee 4

Interviewee 11 felt prison has saved her life. She was also so desperate to escape the clutches of her addiction that she voluntarily presented herself for incarceration.

”Oh, it done me the world of good I know. If I didn’t go to prison, I would have been found dead to be honest with you. I handed myself into the prison….Yes I had to, or else I would have fell to the ground and just died because I wasn’t eating, all I was doing was smoking smoking, smoking’’ Interviewee 11

In addition, when given the opportunity to move from hostel accommodation, as documented above, to a drug-free apartment successful cessation was noted.

‘‘I was in the hostel. Everyone was on heroin; nearly the whole building I’d say was on it. But, they got me and my partner an apartment, it’s beautiful. And ever since we got in to that apartment,
we had no one around us that was on heroin, so I think that’s what kind of helped us’’ Interviewee 5

Other ‘controlled’ environments where successful reprieve from their addiction occurred was when hospitalised for prolonged periods or indeed when housed in a specific drug-detoxification centre. Unfortunately, on termination of their ‘confinement’ in prison, hospital or a detoxification centre all individuals relapsed once they re-entered their own community setting. Even, those that were re-housed eventually re-engage with old ‘friends’ and habits and relapses were unanimously documented.

4.3.2.2 Familial Incentive

At various points in their journeys, these individuals had periods of sobriety driven by certain incentives, mainly family members, particularly children or younger siblings. Their dependence result in their journeys being chaotic and quite often unmanageable but their overall ultimate wish in life is for simplicity. Their aspirations are basic, a normal familial home with full access to their children, where the can function as a stable parent and ultimately gain the respect of their children, siblings and other family members.

‘‘My ultimate goal is to, just to have my family back around me and get the house back to normal’’ Interviewee 4

Interviewee 12, was motivated by his daughter’s acknowledgement that her classmates were referring to him derogatively as a ‘‘junkie’’.

‘‘That was kind of like one of the nails in the coffin for me, it was like going, Jesus Christ I had better get off this stuff…. But it’s an uphill struggle’’ Interviewee 12
Interviewee 11 did manage to remain opioid free when in prison and is aware of the benefits of a structured routine, as a result feels a detoxification centre may be her best option to rid herself of her addiction.

“I would go into treatment at some point. To get my kids back, to live normally, just being a normal mother for my kids, that’s all I want”

Interviewee 11

4.3.2.3 Belief in the medicinal properties of Methadone

An extremely favourable relationship with regard to the pharmacological properties of methadone was reported, particularly in the early phases of treatment. The reports ranged from the very basic to the more complex. Individuals were exceptionally grateful for methadone’s ability to prevent the symptoms of withdrawal, often giving a very honest description of the positive effects with regard to this. Beyond this basic function, other individuals viewed methadone as a step closer to a more ‘normal life’ as it releases them from the grip of their disease and allows them to choose their path in life. Others viewed it as giving ‘a glimpse of some kind of future’. Some viewed methadone as quite simply, “lifesaving”.

“I’m not waking up sick, I don’t have to think about who I am going to rob or where I am I getting the money you know” interviewee 14

“It just gives you time, it gives you a choice, methadone actually gives you the choice to take or leave heroin” Interviewee 3

“I went on Methadone because if I didn’t go on it I would’ve ended up dead. I was gone too far. My body couldn’t handle it no more” Interviewee 7
4.4 Clients’ personal proposals for improving their journey

Final data analysis identified individuals’ personal suggestions for enriching their journey. At the end of each interview, each individual was given the opportunity to suggest changes they would implement to the programme to optimise the effectiveness of the MMT Programme. The most common derived suggestion was contentious as it involved limiting individual time on the programme, which belies the harm reduction philosophy in treatment.

Diagram 3 Clients' personal proposals for improving their journey

Enforce Time Limits on phases of their journey

Employ a Multi-Sectorial Approach

Provide Education

4.4.1 Enforce Time Limits on phases of their journey within the MMT Programme

Interviewees suggested a very strict induction phase of treatment with a well thought out plan to enforce it. All new individuals would be limited on the programme to a 5-week treatment plan, increasing their dose incrementally by 5mls to a maximum of 50mls.

‘If you don’t bring back a clean sample after this, that is it for you, we will talk to you next month. We have someone else in line who

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needs to try this. Try it that way and see if it works or if it doesn't’’

interviewee 2

Other individuals not only supported the above measures but also took it one-step further by suggesting additionally increasing the weekly urine testing to twice weekly, admitting that individuals can orchestrate their opioid use during a once-weekly sampling regimen, to give false negative samples. When questioned as to the effect such sanctions would have on their own engagement with the programme some felt they would respond positively and that it might be the ‘wake-up call’ they needed.

‘‘Because I could leave here now today and use Friday, Saturday, Sunday and Monday and then come back on next Friday and give a clean urine’’ .... People are abusing the system’’ Interviewee 12

However, other individuals felt such sanctions would be inappropriate for their particular journey, citing long-term engagement in the programme as a justifiable reason not to adhere to it. Others could not rationalize why they were above sanctioning. Implying a harm reduction philosophy should be in place for them but not others.

‘‘But when you get to fifteen to twenty years like I am using methadone you have an understanding of it.... You need it’’

Interviewee 14

‘‘Throw them all out I would’… ’I would, but then when it comes to yourself and a doctor is telling you, ‘‘Oh I am going to throw you off the methadone’’ it’s a different story, do you know what I mean?’’ Interviewee 1
4.4.2 Employ a Multi-Sectorial Approach

Individuals strongly advocated for the integration of their methadone treatment with other relevant services, such as psychiatric services, GP and medical care and housing services. One of the most notable benefit to an integrated approach is that individuals would access these services more conveniently, thereby improving utilization of these resources.

“I just think ye yourselves doctors, and psychiatrists, and housing (representatives) if you could roll all that into this clinic it would be fucking dynamite. Can you image the amount of people in Ireland you would be helping? The organisation you create would be phenomenal it would be phenomenal supported by government and things like that because it would have to be supported by the government’’ Interviewee 2

“If we had people here to help with the house and maybe help with getting me a GP that’d be brilliant’’ Interviewee 10

4.4.3 Provide Education

This subtheme imbued many of the transcripts. References were made to educating the public and a specific suggestion was to revise our wording of methadone as a ‘substitute’ as this terminology had exceptionally negative connotations and participants believed as a result, fueled the publics’ misunderstanding of the treatment.

“Educate people, because when people hear you’re on methadone they just assume you’re on heroin and they don’t see it as a treatment, they see it as a substitute’’ Interviewee 8
Participants also felt their immediate family and friends ‘My mother still thinks it’s, you know... a substitute’ Interviewee 3, as well as society’s youth needed to be properly educated re methadone.

‘Oh Jesus the kids definitely need to be educated. A lot of these kids wound up taking drugs they didn’t know’ (what they were taking). Me, I hadn’t a fxxking clue. I thought if you smoke this stuff I thought grand you could drop it and that would be it. Little did I know four days later I walked out of that man’s house that I would wind up an addict’ Interviewee 12

4.5 Chapter Conclusion

Findings in this chapter are of upmost importance. It answers two exceptionally important questions. Firstly, section 4.3.2 highlights which factors improve the quality of life in a person with a chronic opioid dependency who has already suffered adverse childhood experiences and toxic stress. Of equal importance, in section 4.4 their suggested amendments to the current MMTPs in Ireland are key factors to be addressed if ever we are going to optimise the management of their OUD.

In conclusion, an enriching insight into the personal experience of each individual client’s journey to and through the Mid-West of Ireland’s Programme for Methadone Maintenance Treatment (MMT) emerged from the data analysis. Their journeys, though each unique, had common chronological sub-themes. Subsequent data analysis identified common life experiences, which influenced their journey both negatively and positively. Final data analysis identified clients’ individual suggestions for improving their journey.
Chapter 5 Results Study 2

5.1 Chapter Overview

This chapter documents the results of Study 2, ‘An in-depth review of Ireland’s Take Home Naloxone Programme’.

The results of Study 2 can be subdivided into descriptive analysis and statistical analysis. The descriptive analysis first looks at the characteristics pertaining to the OD patient themselves and subsequently the characteristics of the OD scene are shown. Thereafter, using a logistical regression model, statistical results on the variables that influence a patient’s hospital attendance, are presented. Results of the accuracy of the LR model in predicting the likelihood of hospital attendance shows an accuracy of 77%, which is highly reassuring in interpreting these results. As results indicated that the variable, which most significantly influenced hospital attendance, was, ‘if the patient received 3 or more doses of naloxone’, (P value of 0.01), subsequent testing using Welch t-tests were undertaken to analyse which variables, if any, influenced the number of doses administered. Results showed the only significant variable was age.

5.2 Descriptive Analysis

The descriptive analysis for this study can be subdivided into characteristics of the OD victim and characteristics pertaining to the OD setting itself.

5.2.1 Characteristics of Overdose Patients

There were no deaths recorded. As tabulated in Table 7, slightly more women than men received naloxone. Just over half of the dataset were aged between 30 and 40, with the average age being just over 33. The majority of ODs involved
people registered on an MMTP, with about the same number of people also having injected drugs at time of OD.

Table 7: Characteristics of Overdose Patients

<table>
<thead>
<tr>
<th>Characteristics of Overdose Patients</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>44</td>
<td>44%</td>
</tr>
<tr>
<td>Female</td>
<td>56</td>
<td>56%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 30 years</td>
<td>24</td>
<td>24%</td>
</tr>
<tr>
<td>30 – 40 years</td>
<td>55</td>
<td>55%</td>
</tr>
<tr>
<td>&gt; 40 years</td>
<td>15</td>
<td>15%</td>
</tr>
<tr>
<td>Unknown</td>
<td>6</td>
<td>6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Registration on MMTP</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>62</td>
<td>62%</td>
</tr>
<tr>
<td>No</td>
<td>23</td>
<td>23%</td>
</tr>
<tr>
<td>Unknown</td>
<td>15</td>
<td>15%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Had injected drugs at time of OD</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>60</td>
<td>60%</td>
</tr>
<tr>
<td>No</td>
<td>3</td>
<td>3%</td>
</tr>
<tr>
<td>Unknown</td>
<td>37</td>
<td>37%</td>
</tr>
</tbody>
</table>

5.2.2 Characteristics of Overdose Scene

As tabulated in Table 8, breakdown of naloxone use by CHO area in Ireland showed the majority of uses were in Dublin (CHO areas 7 & most predominantly, CHO area 9) with the south-west region (CHO 3), containing Limerick City, the next largest. Rarely a person was alone when they overdosed, with 1 or 2 people being the most common grouping. Hostel workers were in charge of the OD scene approximately 80% of the time, with peers overseeing the remaining 20% of OD...
scenarios. The hostel worker/peer factor was broken down further, looking at their individual response to an OD i.e. did they call an ambulance and did they administer Basic Life Support (BLS), as shown above. When called, the majority of ambulances arrived in 10 minutes or less. We can see that the distribution of doses administered is almost uniform for 1 or 2 administrations, with 3 or more doses having slightly less recorded instances. In the overwhelming majority of reported ODs, the Gardai were not present. Most notably, in over 40% of cases the victims did not avail of ambulance transfer to the hospital setting.
<table>
<thead>
<tr>
<th>Characteristics of Overdose Scene</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CHO area</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>3%</td>
</tr>
<tr>
<td>3</td>
<td>11</td>
<td>11%</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>5</td>
<td>9</td>
<td>9%</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
<td>4%</td>
</tr>
<tr>
<td>7</td>
<td>16</td>
<td>16%</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>9</td>
<td>54</td>
<td>54%</td>
</tr>
<tr>
<td>Unrecorded</td>
<td>2</td>
<td>2%</td>
</tr>
<tr>
<td><strong>Number of others present</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>11</td>
<td>11%</td>
</tr>
<tr>
<td>1</td>
<td>37</td>
<td>37%</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>30%</td>
</tr>
<tr>
<td>3 or more</td>
<td>22</td>
<td>22%</td>
</tr>
<tr>
<td><strong>Who was in charge of od scene?</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peer</td>
<td>17</td>
<td>17%</td>
</tr>
<tr>
<td>Worker</td>
<td>83</td>
<td>83%</td>
</tr>
<tr>
<td><strong>Ambulance called</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (n=91)</td>
<td>Peer</td>
<td>8/17 47%</td>
</tr>
<tr>
<td>Worker</td>
<td>83/83 100%</td>
<td></td>
</tr>
<tr>
<td>No (n=91)</td>
<td>Peer</td>
<td>9/17 53%</td>
</tr>
<tr>
<td>Worker</td>
<td>0/83 0%</td>
<td></td>
</tr>
<tr>
<td><strong>Length of time for ambulance arrival</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(for the 91 occasions for which it was called)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 10 min</td>
<td>60/91 66%</td>
<td></td>
</tr>
<tr>
<td>&gt; 10 min</td>
<td>28/91 31%</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>3/91 3%</td>
<td></td>
</tr>
<tr>
<td><strong>Specifics of the Basic Life Support (BLS) administered</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPR &amp; Recovery position</td>
<td>Peer</td>
<td>4/17 23%</td>
</tr>
<tr>
<td>Worker</td>
<td>53/83 64%</td>
<td></td>
</tr>
<tr>
<td>Recovery position only</td>
<td>Peer</td>
<td>10/17</td>
</tr>
<tr>
<td>------------------------</td>
<td>------</td>
<td>-------</td>
</tr>
<tr>
<td></td>
<td>Worker</td>
<td>18/83</td>
</tr>
<tr>
<td>Not given BLS</td>
<td>Peer</td>
<td>3/17</td>
</tr>
<tr>
<td></td>
<td>Worker</td>
<td>12/83</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of doses of naloxone administered in total</th>
<th>1</th>
<th>34</th>
<th>34%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>38</td>
<td>38%</td>
</tr>
<tr>
<td></td>
<td>3 or more</td>
<td>26</td>
<td>26%</td>
</tr>
<tr>
<td></td>
<td>Unrecorded</td>
<td>2</td>
<td>2%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Who administered naloxone</th>
<th>Peer</th>
<th>17</th>
<th>17%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Worker</td>
<td>83</td>
<td>83%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Were the Gardai present?</th>
<th>Yes</th>
<th>4</th>
<th>4%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>96</td>
<td>96%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Did patient go to the hospital with the ambulance (for the 91 occasions for which it was called)</th>
<th>Yes</th>
<th>53</th>
<th>58%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>38</td>
<td>42%</td>
</tr>
</tbody>
</table>

### 5.3 Statistical Results

Due to the small sample size in this study, results were deemed valid if they were significant at the 10% level i.e. had p-values < 0.1. This does increase the chance of making a type 1 error. The probability of this happening is the p-value of your test. Increasing the cut-off from 5% to 10% is not without its drawbacks, however given the context of the data, supported by literature, (215) it was deemed appropriate.
5.3.1 Logistical Regression (LR) Results

To assess the predictive ability of the LR model, the data was split, with 75% used to train the logistic regression model. The model was tested on the remaining 25% of the data. 17 were predicted correctly (the diagonal entries 9 & 8) and 5 (the off-diagonal entries 4 & 1) were incorrectly predicted, resulting in a classification accuracy of 77.27% (17/22), as summarised in Table 9.

<table>
<thead>
<tr>
<th>Yes/No</th>
<th>Predicted No</th>
<th>Predicted Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>4</td>
<td>8</td>
</tr>
</tbody>
</table>

The ROC curve (Diagram 4 below) confirms the accuracy of the LR model.
5.3.1.1 Interpretation of the LR Model Coefficients

Table 10 summarises the LR model coefficients, showing which factors impact the likelihood of the OD patient attending hospital. For statistical significance at the 5% level, the 95% confidence interval should ideally not cross zero. However, due to the relatively small population, data quality and data confidence issues we included variables that were more marginal. As is evident from the analysis the number of doses received is statistically significant if the patient receives 3 or more doses (P value of 0.01) and indeed receiving 2 doses has borderline significance with a P value of 0.12. Likewise being male has a negative borderline significance with a P value of 0.08 and the next variable of most significance thereafter is being on a methadone maintenance treatment programme which has a P value 0.14.

5.3.1.2 Interpretation of the Odds Ratios

A male is approximately 4 times less likely (0.258 times) to go with the ambulance than a female according to the model, all other things being equal. Registration on a methadone maintenance methadone programme equates with being almost 3.9 times more likely to go to the hospital than not. The more doses a person receives, the more likely they are to go with the ambulance. A person who receives two doses is 4.3 times more likely to go to the hospital than a person who only receives one, all other things being equal. If they receive three or more doses, they are over 13 times more likely to go to the hospital than if they just received one.
Table 10: Summary of the Model Coefficients to predict patients’ hospital attendance

<table>
<thead>
<tr>
<th>Variable Name</th>
<th>Coefficients</th>
<th>Standard Deviation</th>
<th>95% Confidence Interval</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>1.57646</td>
<td>2.119</td>
<td>-2.701 - +6.037</td>
<td>0.4569</td>
</tr>
<tr>
<td>Worker Administration of naloxone</td>
<td>-1.42377</td>
<td>1.167</td>
<td>-3.862 - +0.838</td>
<td>0.2224</td>
</tr>
<tr>
<td>Male Sex</td>
<td>-1.35459</td>
<td>0.78</td>
<td>-3.007 - +0.101</td>
<td>0.0824</td>
</tr>
<tr>
<td>Individual of MMTP* (Yes)</td>
<td>1.34900</td>
<td>0.927</td>
<td>-0.391 - +3.317</td>
<td>0.1455</td>
</tr>
<tr>
<td>Individual of MMTP (Unknown)</td>
<td>0.52819</td>
<td>1.308</td>
<td>-1.992 - +3.274</td>
<td>0.6863</td>
</tr>
<tr>
<td>Injected opioid at time of OD (Yes)</td>
<td>-1.14808</td>
<td>1.78</td>
<td>-5.081 - +2.551</td>
<td>0.5190</td>
</tr>
<tr>
<td>Injected opioid at time of OD (Unknown)</td>
<td>-0.02478</td>
<td>1.848</td>
<td>-4.101 - +3.754</td>
<td>0.9893</td>
</tr>
<tr>
<td>Number of others present at OD</td>
<td>0.04220</td>
<td>0.25</td>
<td>-0.484 - +0.526</td>
<td>0.8662</td>
</tr>
<tr>
<td>Not put in recovery &amp; No CPR administered</td>
<td>-0.814</td>
<td>1.184</td>
<td>-3.221 - +1.505</td>
<td>0.4916</td>
</tr>
<tr>
<td>Recovery position only applied (No CPR given)</td>
<td>-0.944</td>
<td>0.963</td>
<td>-2.959 - +0.911</td>
<td>0.3267</td>
</tr>
<tr>
<td>Age 30-40</td>
<td>-0.456</td>
<td>0.813</td>
<td>-2.129 - +1.111</td>
<td>0.5749</td>
</tr>
<tr>
<td>Age 40+</td>
<td>0.389</td>
<td>1.163</td>
<td>-1.878 - +2.771</td>
<td>0.7380</td>
</tr>
<tr>
<td>Two doses of naloxone administered</td>
<td>1.459</td>
<td>0.936</td>
<td>-0.282 - +3.453</td>
<td>0.1190</td>
</tr>
<tr>
<td>Three + doses of naloxone administered</td>
<td>2.589</td>
<td>1.059</td>
<td>+0.674 - +4.912</td>
<td>0.0145</td>
</tr>
<tr>
<td>Time for ambulance to arrive over 10mins</td>
<td>-0.615</td>
<td>0.852</td>
<td>-2.305 - +1.141</td>
<td>0.4697</td>
</tr>
</tbody>
</table>
5.4. Welch’s Test

Subsequent analysis employing Welch’s t-test was done to ascertain if any of the following variables influenced the number of naloxone doses administered: gender, registration on a MMTP at the time of OD, injecting heroin at the time of OD and a victim’s age. As preliminary analysis of the data set showed an imbalance in sample size allocations, student's t-tests were unsuitable to undertake this analysis and as a result, Welch's t-tests were performed instead. These tests are often referenced as "unpaired" or "independent sample" t-tests, as they are typically applied when the statistical units underlying the two samples being compared are imbalanced, such as in this case.

Gender was not found to have a significant effect (p-value 0.8). Likewise, whether a person was registered on a MMTP or not was not found to have an effect (p-value 0.85). If the person had or had not injected heroin at time of administration was also found not to have an effect (p-value 0.73).

5.4.1 Result of testing ‘Age’ in Welch’s Test

The only factor, which did influence the number of doses administered, was the person’s age. A person with an above average age received more doses (2.49) than those with a below average age (1.91) (p-value = 0.065), where average age was deemed to be 33 years.

![Welch Two Sample t-test](image)

- Welch Two Sample t-test
- data: mydata$Doses.Administered by mydata$AgeCat
- t = -1.8821, df = 62.024, p-value = 0.06451
- alternative hypothesis: true difference in means is not equal to 0
- 95 percent confidence interval:
  - [1.1884121, 2.03577568]
- sample estimates:
  - mean in group < 33: 1.913043
  - mean in group > 33: 2.489362
Chapter 6 Discussion

6.1 Chapter Overview

Three consecutive, independent phases in developing an OUD underpin the framework of this thesis: Initial sporadic, drug experimentation transitioning for some to a more intense, sustained pattern of opioid abuse to a final descent for a select cohort to complete loss of power over opioid consumption. With sustained, escalated use and full immersion into opioid dependence, a lack of life purpose was evident in all transcripts from Study 1, where boredom and loneliness imbued the participants’ lives. This is in line with other researchers findings. (216, 217). All too often, as Study 2 highlights, the desperate outcome for many of these individuals’ journey through OUD is death from OD.

The aim of Study 1 was to give clients of the ‘Drug and Alcohol Services in the HSE Mid-West Limerick MMTP’ a voice, to document their lived experience of opioid dependence before, during and after their ‘three-phase journey’ through OUD. The goal was to improve the service in a two-prong approach. Firstly by establishing patterns of similarity in clients’ journeys, which would flag the clients’ and their children’s high-risk status on admission to the MMTP. This in turn would allow an early tailored care plan to be put in place to optimise their chance of successfully engaging with the MMTP and other relevant, available services to gain the most from what they had to offer. Secondly, hearing from the voice of the service users themselves on how to improve the service would allow potential changes to be made to improve their overall experience and engagement with the service. Unfortunately, ‘opioid-induced deaths’ are all too commonly the outcome of an OUD. To combat these fatalities, Ireland initially piloted, and then rolled-out a THNP nationally in 2015. Study 2 aimed to gain an insight into the
programme in terms of number of reported uses of naloxone and the accompanying patient and setting characteristics since its inception in late 2015 until March 2018. This study had two primary objectives, descriptive and statistical analyses of the selected secondary data. Post naloxone administration, statistical analysis aimed to predict the likelihood of a patient attending hospital.

Many interesting, recurrent themes were disclosed to me the interviewer in Study 1. This chapter will initially focus on the power dynamic in the relationship between the participants in this study and me as their prescribing doctor. It will then further exploring ACEs, with an explicit focus on their relationship with stress in later adulthood. Subsequently, the discussion will centre on dually diagnosed individuals, with a specific focus on benzodiazepine misuse. The final theme explored will be that of therapeutics, with a specific focus on the fallacies surrounding methadone as a therapeutic agent, the stigma inherently experienced by those registered on a MMTP and finally, clients’ own insights on methadone as a therapeutic modality is explored.

The discussion will then move on to Study 2 of this thesis. In this study, initial analysis of the secondary data from Ireland’s THNP revealed the reporting mechanism in use to be quite onerous and as a result a potential barrier to the recruitment of data nationally. Descriptive data analysis in this study gave an overall picture of both patient and scene characteristics, which are important to note on Ireland’s THNP. This was the first analysis ever done on these variables. Finally, post naloxone administration in the community, statistical analysis aimed to create a LR Model from the data set, which could predict the likelihood of a patient attending hospital. The latter half of this chapter will discuss these three separate issues in detail, the reporting mechanism, the characteristics of the data set and the LR Model.
Diagram 5 Summary of the lived experience of ‘Opioid Use Disorder’ in Ireland
6.2 Power dynamic in the patient-doctor relationship

It would be a failing of this thesis not to further explore the ethical challenges that my being both the researcher and the participants’ prescribing doctor had on the study. Undoubtedly, an unequal balance of power exists in this relationship. Qualitative health researchers agree that researchers must be mindful of this imbalance as often boundaries are blurred in the relationship. (218) Also the effect of the sensitive and emotive issues under discussion on the researcher must be acknowledged. (219, 220) The ethical dilemmas which arise due to the changeable, interpersonal nature of qualitative research must also be addressed. Building rapport and ‘camaraderie’- developing techniques can cause misconstructions (221) and result in ‘shifting boundaries’ within the therapeutic relationship (222) These techniques aim to create a relaxed, friendly and ‘non-hierarchical atmosphere’ favorable to the disclosing of personal information (223, 224) but concurrently can distort the doctor patient relationship. Supported by current research (225), reflexivity or continuous ‘critical reflection’ on these issues throughout the research process was essential. (226) Reflexivity, as documented by Phelan et al, can be ‘used as a tool to enact ethical practice’. (227) Supervisory meetings always ensured to allow time for critical reflection on sentiments, principles and attitudes in relation to the research. They re-centred and refocused my approach to ensure I was engaging appropriately with participants during each interview, as appropriate practices in qualitative research are ‘fluid’ and not prescriptive. (226)
6.3 Adverse Childhood Experiences

The theoretical concept of ‘Adverse Childhood Experiences’ and their impact on acting as a catalyst for recreational sporadic drug use and subsequently perpetuating an opioid dependence was explored in the literature review chapter of this thesis. It was noted that Felitti, Anda and colleagues first described ACEs in 1998. (26) Over the intervening 20 years since Felitti at al’s seminal study, ACEs continue to be of increasing international concern and consequently there is a mounting wealth of research, which validates that chronic stressful experience in childhood, can lead individuals on a health-harming life course inclusive of illicit drug use. (30) More recently, research tells us that ACEs occur frequently - 67% of the population have experienced a minimum of one ACE. (228) However, high ACE scores (scores of four or more) are robustly linked with an increased risk to a person’s overall health status. (40)

In 2015, Public Health Wales surveyed 2,028 Welsh adults (25) using Felitti’s internationally indorsed questionnaire. (26) In total, 4.4% of respondents admitted to experimenting with crack cocaine or heroin. However, the frequency of heroin or crack cocaine use increased with each ACE count, increasing from less than 2% in those with no ACEs to greater than 20% for those reporting four or more ACEs. This correlation remained constant after adjusting for age, gender, ethnicity and social class. The probability of respondents who had endured four or more ACEs partaking in heroin or crack cocaine use were greater than 15 times than those who had undergone none. After amending the data to match the demographic of the national population, findings indicated that if no persons were subjected to ACEs, then the incidence of participants who had ever experimented with heroin or crack cocaine could be lessened by 66%. A take-home stark
statistic of this Welsh study on ACEs showed that compared with no ACEs, those with exposure to 4 or more ACEs were found to be 16 times more likely to have used crack cocaine or heroin.

Studies specific to illicit drug use show that the risk of early experimentation with substance abuse increases 2-4 times for each ACE and nearly two thirds of injection drug use can be linked to ACEs. (229) From a gender perspective, research indicates that ACEs are more prevalent in females than males and that there are noteworthy gender variances in the correlation between separate classifications of ACEs and ‘mental and substance use disorders’ (MSUDs). (230) For instance, physical abuse was associated with female mental health disorders but with male substance use disorders (231), which may also explain increased reports of female mental health = and greater rates of male substance use disorders. (232)

A most recent study conducted in 2017, examined the association of ACEs with lifetime mental and substance use disorders among men and women aged over 50. Given the aging cohort of opioid use disorder, this study is particularly relevant. Increasing rates of substance misuse in mature adults is often credited to a more liberal culture of substance use amongst the ‘baby boomers’ who are now entering adulthood. (233) Set in the US, the study tested links between ten types of childhood adversities and MSUDS in the growing older-adult population. Results confirmed that just over half of participants stated suffering one or more ACE, and ‘parental/other adult’s substance abuse’ was the most frequently reported ACE, which supports the theory of the ‘cycle of violence’, as explored in the literature review of this thesis. From the perspective of acquiring a substance use disorder, results showed physical, sexual, psychological abuse and/or exposure to parental/other adult’s substance abuse significantly increased one’s risk. For men
only parental divorce was a significant factor for drug use disorder. The link between sexual abuse and drug use disorder also appears to be greater for males than females.

From an Irish perspective, a recent survey undertaken by Dr. Sharon Lambert and Graham Gill-Emerson, surveyed the level of trauma among Cork Simon service users ‘Cork Simon Community: Moving Towards Trauma Informed Care. A Model of Research and Practice.’ (234) The Simon Communities in Ireland are comprised of eight self-regulating communities based in Cork, Dublin, Dundalk, Galway, the Midlands, the Mid West, the North West and the South East.

Supported by a national office, they have served to tackle all forms of homelessness throughout Ireland for over 45 years.

In this survey, from a drug dependency perspective, the second highest ACE experienced by this homeless cohort was ‘substance misuse by a family member’, experienced by over 70% - more than twice what the public in Felitti’s original ACE study reported. (26) From an age perspective, substance abuse in the family was reported by 100% of the youngest age category, 18-26 year olds, which was 1.3 times higher among this age group compared to the next highest scoring age group. Those with ACE scores of 4 or more initially engages with alcohol and drugs at an earlier age and reported double the rate of drug od compared to those with ACE scores less than 4. (234) These findings highlight the importance of psychosocial interventions that aim to meet the health care needs of victims of childhood maltreatment which will ultimately reduce the number of people with drug dependency in Ireland.

Trauma in early childhood impacts how we respond to stress throughout our lives and as stress plays an integral role in developing and sustaining an OUD (235), it
merits a brief look here. Exposure to early stressors in life, such as, poor parenting, family dysfunction, and adverse neighbourhood characteristics establishes a lower “set point” for a child’s internal stress system. It has been found that early life trauma can alter the brain’s stress regulatory systems, which influences an individual’s ability to regulate emotion and respond to fear. (236) Consequently, individuals may be more vulnerable to health harming behaviours in later life. (237) If an individual has a heightened stress response, they are likely to attribute a high worth to substances that offer temporary relief such as opioid misuse. In contrast, activities, which typically offer satisfaction, such as, meaningful, familial relationships, are undervalued because in the Individual’s life they have never been fulfilling. (238) It is well established that as dopamine levels decrease, the craving for drug use increases. Stress reduces the function of dopaminergic receptors in the emotional circuits of the forebrain (239) and consequently increases the long term craving for opioids. The reward value in drug use is enhanced by stress and even after periods of abstinence, stress can provoke relapse. (240)

6.3 Dual Diagnosis

Unsurprisingly, adversities in childhood more often than not were the steppingstone for continued adversarial challenges into adulthood. As a result, mental illness and illicit use of non-prescribed benzodiazepines (BZDs) permeated the lives of the individuals in Study 1. Dual diagnosis is, as defined by the Royal College of Psychiatrists, 2002, ‘the co-existence of both mental health and substance misuse problems including both drugs and alcohol’. (241) Each disorder in itself is chronic and relapsing, travels an independent course and is
capable of influencing the other disorder. Dual diagnoses increase the risk of individuals who recreationally engage in opioid use developing an opioid use disorder (242). Similarly, in comparison with the general public, the frequency of psychiatric disorders, including other SUDs, increase in individuals with an established opioid use disorder. (243) The analysis of the transcripts from study 1 showed a complex relationship between the two as diagnoses vary as listed below:

1. A primary psychiatric disorder with secondary substance misuse
2. A primary substance misuse disorder with secondary psychiatric illness
3. An underlying traumatic experience resulting in both substance misuse and mood disorders

Implications of a dual diagnosis are far reaching. Dual diagnoses present with substantial clinical challenges and negatively influence an individual’s ability to initiate and respond appropriately to treatment. They result in a greater use or misuse of services and increased morbidities and death rates. (244) For individuals with a dual diagnosis, optimizing treatment of their psychiatric disorders is essential to improving the outcome of their opioid use disorder.

Furthermore, the earlier an individual initiates opioid use the more likely they are of developing a co-morbid psychiatric illness. (245) Knowledge of this should inform our clinical practice in identifying individuals at an increased risk of dual-diagnosis.

Two main barriers in addressing the needs of dually diagnosed individuals lie in firstly diagnosing the problem and secondly collaborating with relevant stakeholders to ensure their treatment plan is optimal. A frenzied lifestyle is often synonymous with undiagnosed co-existing requirements. This negatively affects individuals’ ability to attend scheduled appointments and engage with mainstream
facilities. The resultant outcome being dually diagnosed patients are the most vulnerable and marginalised in society.

In the current Irish health and social care system, services are poorly equipped and resourced to address concurrent illnesses. The system serves to meet the primary need of an individual, substance or mental health. Often treatment is provided from separate divisions within the HSE, not working collaboratively but in isolation. In addition, many support services are delivered by the NGO sector who may be working independently of statutory providers. The input of the Mental Health Service is clearly of paramount importance in meeting the needs of individuals with an OUD. In the Mid-West MMTP, counselling and out-reach support is available but the coordinated input of a mental health multidisciplinary team is lacking.

### 6.3.1 Benzodiazepines

30 years of research has shown that worldwide benzodiazepines are among the most frequently prescribed psychotropic drug. (246) According to the admissions’ count of the ‘Treatment Episode Data Set’ (TEDS) in the US, the figure representing the amount of clients requesting treatment for their BZD dependence virtually tripled between 1998 and 2008. (247) This data also indicates that BZDs are often concurrently misused in tandem with other drugs, most notably opioids. (247) Study 1 of this thesis confirmed this by revealing a particularly chaotic use of benzodiazepines (BZDs) amongst its individuals. Few studies show marginal clinical significance in the pharmacokinetic interactions between BZDs and opioids (248) and therefore, it is likely that, it is their pharmacodynamic interactions, which underlie their co-abuse. To that end, preclinical research
indicates that the fulfilling and fortifying effects of opioids are increased by BZDs and this is likely the reason why they are used concurrently. (249) Synergistic use amplifies the μ agonist effects of opioids often resulting in opioid intoxication. (250) In 2011, Chen reported that among methadone individuals reporting a history of BZD use, greater than 45% responded that they did so to “get high,” “have a good time,” or “produce an intense, exciting experience.” (251) Research confounds the reports in Study 1 that injecting BZDs increases the euphoric effect of opioids. (252) Research also indicates that comorbid sedative use disorder is associated with increased rates of continuing opioid use. (253) Complications of BZD and opioid co-abuse are numerous, the most worrying being an increase is OD fatalities. (248) One’s respiratory drive is inhibited via the mu opioid receptor. BZDs augment the effect of GABA. GABA receptors are also highly concentrated in these respiratory centres and hence both opioids and BZDs, used separately or concurrently, are capable of altering respiration frequency. (248) Approximately half of all individuals with a heroin use disorder recount at least one non-fatal od (254), with BZDs being present in 50–80% of heroin-induced deaths. (255) Concurrent BZDs abuse with OATs also increase the risk of death, more so with complete agonists, for example, methadone. (256) Supporting these findings, internationally BZDs have been found in 40–80% of methadone-induced mortalities. (257) Irish figures also reflect this trend. As noted above, of the 209 individuals who died as a result of opioid drug over-dose, 179 had two or more drugs implicated in their death, of which benzodiazepines were the most commonly found. (98) Most worryingly, the synergistic abuse of both opioids and BZD negatively affects naloxone’s ability to reverse respiratory depression in an OD. (248) Research indicates that in comparison to individuals with a sole OUD, concurrent
dependence on both BZDs and opioids results in individuals using opioid considerably longer, (258) in much higher quantities and are at an increased risk of abusing supplementary drugs (excluding BZDs). (259) Research also indicates that clients of MMTPs who had a co-morbid BZD disorder were prescribed larger methadone doses and more often abused alcohol. (258) Individuals in receipt of OAT worldwide appear to be particularly susceptible to a co-morbid BZD and Opioid use disorder as used concurrently it appears an individual can attain a more powerful opioid effect often described as “heroin-like.” Additional research is needed to elucidate the increased abuse potential of this drug combination.

(248)

6.4 Therapeutics

This section expands on the myths surrounding methadone as a therapeutic agent, the clinical language used in relation to methadone and methadone programmes, the stigma associated with registration on a MMTP and finally clients’ own understanding of methadone as a therapeutic modality is explored.

6.4.1 Myths encircling Methadone

Methadone is a complex treatment modality and its complexity serves to fuel this myth. For over 50 years, we have known that individuals with OUDs require methadone to combat withdrawal symptoms and suppress cravings thereby freeing the patient from the daily cycle of searching for, purchasing, and consuming heroin. (137) As such, there is no denying they are hugely reliant on their medication and are very much likely to relapse to opioid abuse if treatment is suspended, much like a person diagnosed with schizophrenia would likely relapse if they missed their anti-psychotic medication. So in essence, yes, the individual
with an OUD is ‘dependent’ on their methadone but its place in their treatment plan allows them to attain abstinence from illicit opioid misuse and abuse. (260) The benefits on their mental and physical health and subsequently their overall better social integration are superbly well documented (261), but unfortunately not reaching society’s wider audience.

From a therapeutic perspective, likely the largest myth surrounding the use of methadone is the belief that it is a ‘substitute’ for heroin and that ‘addicts’ are simply replacing one drug of ‘addiction’ with another.

A second myth is based on the side effect profile of methadone as it is often cited to damage teeth and destroy bone health. Methadone does not directly affect teeth or bones. Intake of methadone may result in xerostomia, and the ensuing lack of saliva may increase one’s susceptibility to dental issues. Moreover, clients often commence methadone treatment after a long period of neglecting their dental hygiene. Individuals sometimes feel “bone ache” during treatment — likely reflecting the symptoms of their opioid withdrawal, which they incorrectly attribute to methadone. (262) However, as the following example a show, understanding of this, even in health advocacy circles, published in reputable journals is shockingly poor. Cleo Silvers, is a well-known, remarkable Bronx health activist and a much respected figure in health advocacy circles in the US with more than five decades of health advocacy experience—an activism notable for its insistence on the inextricable links between health and socioeconomic well-being. In a 2016 interview she gave to Alondra Nelson, published in the American journal of Public Health, (263) she gave the following account of methadone.

“We know the horrors of the use of methadone and all the horrible things that happen to people. Their bones become brittle; it eats the bone
marrow. It was the worst possible chemical to use to help people with drug rehabilitation.” Cleo Silvers, health activist.

A letter refuting Silvers’ claims written by Lawrence Brown and Stephen Kritz (262) was submitted and subsequently published by the journal. Silvers declined to respond.

6.4.2 Clinical language in relation to drug dependence

The clinical language of ‘addiction’ only further shrouds methadone and methadone clinics in rumour, myth and misconception. Words like ‘abuse’ and ‘abuser’ evoke perceptions of a willful, self-regulated action and that the individual is more of a ‘criminal’ engaging in deliberate misbehaviour. In reference to urine toxicology showing positive for opioids, the term ‘dirty’ carries obvious negative connotations. Labelling an individual by their illness with words like ‘addict’ or ‘junkie’ also increases stigma. To reduce prejudice and improve care we must use person-centred language, describing those with an ‘addiction’ as people with a substance, or in this case, opioid use disorder. Integral to this change is also the need to alter the language of treatment. The much cited medical term ‘substitution’ or ‘replacement’ therapy enforces the most widely held and stigmatizing belief that methadone is a ‘replacement addiction.’ The notion that opioid agonist treatment is not an effective stand-alone treatment is widely supported, even by some ‘addiction’ professionals (264) even though research repeatedly refutes this claim. (265) Since 2009, the WHO recommends to not withhold medication if someone refuses counselling (266) supporting the overriding efficacy of opioid agonist therapies such as methadone in treating OUD. It most certainly is not ‘substitution’ for an illicit drug. (267)
6.4.3 Stigma, specifically in relation to the therapeutic agent, methadone

Notwithstanding its effectiveness and extensive use, treatment of OUD with the therapeutic agent methadone, remains shrouded in stigma. (268) Indeed, of all treatment modalities MMT evokes particularly potent shame. (269)

From a clinical perspective, in study 1, individuals’ often-acrimonious relationship with their GP and the poor communication cited between allied-health professionals in their lives often served to fuel their habit further. Abundant research supports the claim that individuals with SUDs encounter stigma from healthcare professionals. (270) Most worryingly, research on this phenomenon validates that stigma from healthcare professionals acts as a commanding negative influence on drop-out rates among people living with an array of stigmas. (271) This in turn may impede treatment retention in MMTPs. (269) This stigma often cited in the literate as ‘institutional’ stigma is well researched. (154)

In study 1, the stigma participants experienced from not only the public, but also their own family and friends, served to heighten their embarrassment in relation to all aspects of their illness but most obviously methadone as a therapeutic modality. This is in keeping with other studies where very high percentages of individuals reported experiencing discrimination from family, friends and their neighbourhood. (269, 272, 273) Stigma from one’s familial and social network may hamper their interpersonal relationships and jeopardise their social support, both of which are fundamental for psychological wellbeing and attainment in treatment. (274)

Finally, analysis of the transcripts in Study 1 revealed participants’ own self-stigma (275) in relation to availing of methadone to treat their OUD, which is
another facet of stigma needing to be addressed. Self-stigma arises when individuals allow public attitudes and behaviours to become part of their own nature by unconscious assimilation. This more often than not leads to damaging ramifications for the individual, inclusive of lessening their self-worth and self-regard. (276)

6.4.4 Patients’ understanding of Methadone as a long-term, maintenance agent.

Examining the transcripts from study 1 highlighted that a definite negative influence on individuals’ journeys was their own erroneous understanding of their illness and methadone’s place in its treatment. Research indicates that treatment-seeking individuals are typically driven by acutely pressing conditions such as the symptoms of withdrawal and have limited insight. They understand that craving is the leading contributory factor for relapse but lack long-term disease awareness, which means they deny the chronic nature of their dependence. Affected individuals live in the ‘here and now’ and solely focus on their immediate circumstances. They equate spontaneous short-term abstinence with full remission and any subsequent relapse is viewed as an isolated episode. (277) Moreover, as was evident in the above study, it is just when individuals achieve relief from acute withdrawal that their insight often regresses, in the sense that on cessation of acute withdrawal they immediately believe they have full ‘control’ over their substance use. It is difficult for them to accept any relapse-prevention perspective, as they are often blind to the concept of OUD as a chronic relapsing disorder. The most unfortunate outcome associated with this misconception is the increased incidence of ‘drug-induced death’ rates as relapse, after a period of abstinence, is often a likely prequel to opioid overdose.
6.5 Drug-induced deaths

‘Drug-induced deaths’, as seen in the next section of this thesis, are increasing annually. The number of ‘drug-induced deaths’ in Europe peaked at the start of the millennium as a result of the heroin epidemic which broke in the 1980s. (278) Most worryingly, a new record number for the countries reporting to the EMCDDA (28 EU Member States, Turkey and Norway) was registered in 2016, with a staggering figure of 9,138 OD deaths, the highest number ever recorded. (120) At an individual country level, the most recent data from a number of the countries with relatively robust reporting systems, including Ireland, shows an increase. (120)

As most ‘drug-induced deaths’ result from the misuse and abuse of opioids, predominantly the injection of heroin, (89) the importance of THNPs cannot be over-emphasised. It is imperative that Ireland’s THNP functions optimally if ever we are going to effectively curtail this rising death toll. Through descriptive analysis, study 2 aimed to gain an overall appreciation of Ireland’s THNP. By analysing its reporting mechanisms, it aimed to uncover any areas of redress to optimise its register. Finally, as discussed in the literature review in this thesis, and as expanded upon below, the importance of transfer to hospital for on-going monitoring has never been more necessary as extremely intoxicating new synthetic opioids are emerging as a significant player in the increasing number of ‘opioid-induced deaths’ in Europe. The new fentanyl derivatives, which account for the majority of the new opioids identified by the EMCDDA’s Early Warning system, are wreaking particular havoc. (279) Because of their high potency, minute quantities can be life threatening, due their ability to cause rapid and severe respiratory depression.
In an opioid OD, respiratory depression decreases the levels of circulating oxygen and if sustained can lead to loss of consciousness, multi-system failure and death. (280) Several risk factors influence the probability of OD, including, but not limited to, the category of opioid, its potency and the quantity of opioid that crosses the blood brain barrier. Personal factors inclusive of tolerance, current medical history, length of use and genetics add to its complexity. (89) Research confirms that the dearth of response or incompetent interventions by those present at the scene of an OD heightens the risk of the event having a fatal outcome. Reported contributing factors are limited experience in the skills of basic life support, inadequate access to naloxone or the dread or panic of legal ramifications for peers witnessing an OD. (281) These three specific factors all too often result in overdoses occurring in the domiciliary setting. A Norwegian study also confirmed that in the context of OD, emergency response times were more likely to be lengthier for private, home settings; additionally, these patients were less likely to attend hospital, post naloxone administration. (282) Therefore, it is imperative to train potential bystanders on how to recognise and appropriately respond to opioid OD, particularly peers in the home setting, through the rollout of THNPs.

6.6 Ireland’s Take Home Naloxone Programme

Currently, in Ireland, the person who takes the lead at an OD scenario must complete an electronic report on the course of events which transpired at the OD scene using excel software and subsequently email it to a nominee of the HSE. However, training in excel or indeed in the completion of this form is not part of the THNP training course. As such, not all trained users of naloxone particularly
hostel workers, outreach workers and the most important cohort to capture, peers, in the community, have the capacity to report their use of naloxone in the setting of an OD.

6.6.1 Check Exercise Outcomes

The initial check exercise on the reported use of naloxone nationally in 2017 provided a strong argument for both revising this current reporting mechanism and simplifying the form’s existing content and structure.

Firstly, the use of excel adds a layer of complexity to the reporting which, most likely, exacerbates its poor uptake.

Secondly, there is no flow or sequential logic to the layout of the excel sheet. The information collected is also unnecessarily excessive. In 2017, in an attempt to rectify this issue, the form was shortened but it remains tedious to fill and the use of confusing terminology confounds its ambiguity. An example being, the stand-alone statement, ‘relationship to person providing information’. On data analysis, this response was often left blank or reported as ‘none’ as the information giver either did not understand the statement or was not directly related to the victim and as such, felt the appropriate answer was ‘none’. In addition, the person providing the information was not necessarily the person who administered the naloxone, which again confused the issue.

Thirdly, it is imperative at an OD scenario that BLS is administered correctly. However, the current reporting mechanism does not lend itself to assessing this critical information. The line of questioning on the form does not establish from the outset if the victim was breathing or not. This is essential information. It influences the correct next steps to be taken in order to manage the OD appropriately.
Fourthly, a full section on whether the person was there or not at the exact time of the OD is also slightly redundant as information on ‘the length of time from point of using to OD’ and the ‘signs/symptoms of OD’ though interesting are very individual and likely beyond the scope of the current database’s remit.

Listed in Chapter 7, section 7.5.1, are key recommendations on how to address the above concerns.

6.6.2 Selected Dataset Analysis

Subsequent to the check exercise, analysis of the selected dataset, showed the majority of naloxone uses were in Dublin (CHO areas 7 & 9) with the south-west region (CHO 3), containing Limerick City, the next largest. In this study, workers in homeless hostel shelters administered the vast majority of naloxone, 83%. The likely reason for this being the process involved in reporting an OD requires the time, presence of mind, interest in contributing to data collection nationally and a working understanding of excel. The only way a ‘peer’ can report the use of naloxone is by presenting to a recognised, institution or person equipped to complete and submit the on-line form on their behalf. As it stands, the majority of peers do not report use of naloxone. Literature indicates that fear surrounding involving law enforcement and subsequent repercussions, such as arrests, for the individual and the peers with whom they were using drugs at the time of OD still prevails. (283) In the US and Canada ‘Overdose Good Samaritan laws’ protect individuals who call for emergency support in the event of an OD from being detained or prosecuted for drug possession. These laws aim to embolden peers to call for the emergency services if they experience or witness a drug OD. As of July 2017, 40 states across the US had instituted Good Samaritan laws. (284) In Ireland, typically, as reflected in this study, the Gardai do not attend ODs,
however, no specific such laws are in place and though the general understanding is that the Gardai will not interfere with or make arrests at the time of an OD, there is no definite law in place stating same. The role of the Gardai is shrouded in obscurity, and as such, it is very likely a deterrent to ‘peers’ to call for help, as this cohort of individuals already have a fractious relationship with authoritative bodies. This was reflected in the analysis of Study 2 where 100% of hostel workers appropriately called for 911 assistance in stark conflict to ‘peers’ who called for emergency assistance less than half of the time.

As well as fear of arrest, (285-287), having misplaced confidence in their ability to manage the situation and resuscitate the individual themselves is cited in the literature for reasons as to why peers do not call for help. (286, 288) To address this issue, the importance of medical expertise at all OD scenarios must be reinforced at the time of training, and, thereafter, reiterated regularly at refresher update courses.

Witnesses of overdoses, particularly peers, also worry they will be branded a drug user or ‘druggie’ if they bring attention to their affiliation with the OD victim, suggesting stigma can also make people less willing to call for help. (289) Chronic unemployment and subsequent reliance on social welfare benefits coupled with homelessness have played a role in the negative perception society as a whole has of individuals with an OUD. Augmenting this negativity, during the course of their dependency, individuals often develop stigmatizing illnesses such as AIDS and hepatitis C. Finally, co-morbidities with mental illness, particularly within the judicial system, intensify this damaging opinion and serve to stigmatise individuals with OUDs even more within society. (290)
From a gender perspective, the most recent Irish statistics show that under one third of the estimated opioid users in Ireland are female (88) and as such one would not predict that they would account for greater than half of the dispensed naloxone uses in Ireland. However, analysis of data recorded on Ireland’s national THN database showed females received naloxone slightly more often than males, 56% versus 44%. A finding which surprisingly is in keeping with some literature elsewhere (291) but the majority of research to date indicates that females typically receive naloxone less frequently than males in the OD setting. (292, 293)

From the perspective of age, over half of the dataset were aged between 30 and 40, with the average age being just over 33. This is in keeping with current findings, reflecting that 60% of Ireland’s opioid users fall in the 35—64 age category, in comparison to less than one-third in 2006, signifying a certain ageing cohort effect. (88)

In this study, the majority of OD victims were registered on a MMTP. This may be reflective of the fact that the majority of recorded uses of naloxone were in homeless shelters. Often those affiliated with community services such as housing also engage with community services such as drug treatment as they are au fait with being in the system engaging with service providers across a spectrum of their needs. Ireland is also recognised as being among the countries with a higher percentage of opioid users receiving OAT in Europe as identified by the EMCDDA in their 2018 Drug report.(82)

It was only known in 3 instances of the recorded instances of OD that drugs had not been injected, with definite signs or reports of injecting in greater than 60% of cases. This is in keeping with international findings where individuals lacking
obvious signs of intravenous drug abuse such as drug equipment or ‘track marks’, were three times less likely to receive naloxone. (292)

Only 11% of cases in this study were alone at the time of initial OD, with 1 or 2 people being the most common occurring grouping in attendance. This is in keeping with other Irish (294) and international findings (295) and supports the use of naloxone by laypersons in the community setting.

Distribution of doses administered was almost uniform, with 1, 2 and ‘3 or more’ doses having almost the same number of instances of use. Naloxone administration is like balancing on a tightrope, offsetting reversing opioid toxicity with avoiding opioid-withdrawal syndrome, as frequent incidence of the latter may lessen the readiness of peers to administer naloxone in the setting of an OD. (296) As the following excerpt from Lewis Brown, who has experienced recurrent opioid overdoses, indicates withdrawal symptoms are often why patients refuse hospital attendance. (297)

“Diarrhea, throwing up, nose snotting, cold shakes, you know, you don’t want to feel that. So, instead of going to the hospital and getting more treatment, I went and got more heroin. The same thing that just almost took my life, I ran right back and got again.”

However, the risk of under-medicating with naloxone, far outweighs the possible menaces of advancing opioid withdrawal, as the latter is disagreeable but rarely fatal, while not adequately reversing the respiratory depression associated with opioid overdose is frequently fatal, especially as the rates of OD due to powerful synthetic opioids increases. (280)
6.6.3 Hospital Attendance Post Naloxone Administration

For the instances where the ambulance attended, less than half of the recipients of naloxone attended hospital. This is in keeping with current literature. (298) The absolute necessity for hospital attendance in today’s opioid problem is outlined in the following section. Most worryingly, in today’s opioid crisis, proliferating and unrelenting contamination of heroin with synthetic opioids that have volatile or unidentified pharmaco- and toxico-kinetics is on the rise. These novel fentanyl ‘spinoffs’ are highly intoxicating substances that pose a somber danger to both individual and public wellbeing. Evidence of the devastating consequences of their use is evident in the US where deaths due to illicit opioid overdose have reached historic proportions (299). Opioid overdose is that widespread that the American Heart Association include naloxone in its ‘emergency response algorithms.’ (300) Worldwide, OD rates due to heroin- and fentanyl are increasing. Overdose rates have increased by 327% in Canada, 64% in the United Kingdom and 61% in Australia. (301) In Ireland, prior to 2011 no deaths were recorded because of fentanyl abuse. However, by 2015, fentanyl was implicated in 7 deaths. (302)

In this era of protean heroin adulterants, the most experienced of toxicologists are obliged to admit that the only thing we do know about the current heroin epidemic is that heroin is no longer just heroin. (303) Hospital monitoring is not just necessary for those who have injected opioids as orally consuming counterfeit pills containing fentanyl may lead to a delayed OD necessitating repetitive intramuscular dosing or indeed an infusion of naloxone in the secondary care setting. (304)
With the increased incidence of heroin adulterated with synthetic opioids such as fentanyl, counterfeit products, and the advent of novel opioids with unknown pharmaco- and toxicokinetics, we can no longer safely predict a patient’s naloxone requirement or the safest duration of observation. Until more data exist regarding pharmacokinetics, toxicokinetics, and expected clinical effects following exposure to synthetic opioids, it is prudent to ensure both hospital transport after naloxone administration in the community and a period of observation in the Emergency Department of at least 4 hours. (303)

After reversal of respiratory depression, it can occur that a patient’s breathing centre is re-suppressed, a phenomenon known as ‘recurrence of toxicity’.

Naloxone’s ability to block opioid receptors may wear off, as its half-life may be less than some of the newer synthetic opioids. This in turn may lead to relief from withdrawal symptoms but with re-emergence of respiratory depression. To quote Clarke et al. (305), ‘clinicians are clearly walking a tightrope between precipitating acute withdrawal symptoms and avoiding recurrence of toxicity’.

Moreover, the duration of time for which further monitoring is required is dependent upon the class of opioid used which is often not known by the paramedics assessing the case and with today’s market rife with new emerging synthetic compounds it is even more difficult to judge. (306)

This potential for ‘recurrence of toxicity’ following a preliminary reversal with naloxone is well recognised in peer-reviewed literature for over 20 years. (307, 308) This phenomenon can be fatal, particularly if an OD victim declines hospital transfer or self-discharges against medical advice on arrival at the hospital. (279)

Another valid reason for hospital attendance is that reports of recent non-fatal OD are independently associated with subsequent OD mortality. (309) Individuals
who suffer non-fatal OD should engage with intensive OD prevention interventions in order to reduce subsequent OD mortality among opioid users. The most appropriate place to initiate this intervention is in a secondary setting such as a hospital as soon after the OD event as possible.

For the above reasons, attendance at hospital is essential. However, as is evident from study 2, in which 40% of victims refused to attend hospital, and many others internationally (298) attendance at hospital is sub optimal.

The LR Model generated in this study allows us to predict the likelihood of patients attending hospital. However, it must be recognised that the Irish THN Programme is not yet 3 years established and as a result, our sample of 100 uses of naloxone, is small. With such a limited sample size, we had to include variables with borderline significance. Ideally, the LR Model should be tested on a larger cohort of clients to ensure validity.

Results showed that a patient receiving 3 or more doses of naloxone was a highly significant factor in determining hospital attendance, (P value of 0.01).

Subsequent analysis using Welch’s t-test assessed what factors, if any, influenced the number of doses received. The age of the person who overdosed (p-value 0.06) was shown to be the only significant factor, which is in keeping with international findings. (310)

Thereafter, the two most significant factors influencing hospital attendance was gender and registration on a MMTP. Male patients had a negative borderline significance with a P value of 0.08 and enrolment on a MMTP had a P value 0.14.
Chapter 7 Summary and Recommendations

7.1 Chapter Summary

This chapter concludes the thesis and provides key recommendations. Its structure mirrors the chosen themes of the discussion chapter. Initially recommendations will focus on how knowledge of ACEs should influence the MMTPs in Ireland and internationally, to adopt a more ‘trauma informed’ ethos. Subsequently, recommendations will centre on dually diagnosed individuals, with a specific focus on addressing benzodiazepine misuse. Next, the theme of therapeutics will be explored, listing specific proposals on how to both promote education and reduce stigma in relation to methadone, as a treatment option in OUD. Finally, the thesis will focus on recommendations with regard to THNPs. Initial suggestions will focus on improving the Irish THNP and subsequently general recommendations applicable to THNPs internationally will be addressed.

7.2 The role of ACEs in influencing a ‘Trauma Informed’ MMTP

In giving appropriate recognition to the influential role ACEs have on both developing and sustaining an OUD, MMTPs in Ireland and internationally should ensure their programmes are ‘trauma informed’. Specific stages necessary to create a high quality, functioning ‘trauma informed service’ should include an evaluation of the incidence and magnitude of the ‘trauma loaded environment’ experienced by each client through an assessment of their level of childhood adversity.
In both acknowledging and understanding the prevalence and impact of ACEs in their clients’ lives all employees of a Drug and Alcohol service will have a better appreciation of the multifaceted and diverse journeys clients travel in search of healing and recovery. Trauma informed training delivered to all staff would also be essential in ensuring they respond appropriately to clients’ revelations.

As is evident in the above thesis, ACEs play a central role in the potential development of an opioid use disorder. From a European perspective, the 2015 Welsh study on ACEs (25) contributed most significantly to our understanding of the importance of identifying ACEs and intervening to halt their progression as soon as possible. Wales is currently pioneering a broad scope of procedures and processes from which Ireland and others internationally could learn.

One such programme is, ‘The Building a Brighter Future: Early Years and Childcare Plan 2013-2023’ (311) which aim to address the following:

1. Ensure that knock-on adversities from substance misuse and abuse are uncovered, tackled and their influence on children reduced

2. Detect and intervene where children may already be experiencing adversities

3. Equip families with the appropriate competencies to prevent ACEs occurring within the home setting

MMTP are the ideal setting for these improvements to be addressed.

7.2.1 ACEs and Resilience

In physics, resilience is the capability of a substance to absorb energy (such as from a knock) and discharge that energy as it ‘springs back’ to its initial profile. This physical phenomenon is comparable to a person’s aptitude to ‘spring back’ after an unsettling life event. Within the context of ACEs, resilience can be
viewed as a person’s capability to sidestep damaging behavioural and physiological alterations because of chronic stress. Some individuals are born with an innate resilience, most others have received external supports and guidance to attain the resilience necessary to adjust effectively to stress, trauma and long-term adversity. (312) To complement the ACE questionnaire, ‘resilience questionnaires’ are employed (313-315) to establish if children have the necessary support structures available to them to help minimise the short and long-term effects of ACEs on their current and future well-being. Once more, MMTPs are ideally placed to identify these at-risk children and work with public health bodies to ensure those at risk have the necessary armour to protect against ACEs and the skill set required to develop and sustain resilience.

7.2.2 Stress Management

Study 1 of this thesis highlighted the critical role clients’ stress played in both developing and sustaining an OUD. In the treatment of OUD, incorporating a focus on stress and its management improves treatment outcomes. (235) Evidently, there is a considerable public health cost associated with drug use and such improvements in the treatment of clients’ stress would pay a sizable dividend to all. Tailored interventions for the treatment of stress in individuals’ with an OUD from psychologists, counsellors, nurses, psychiatrists and General Practitioners (GPs), all working collaboratively, would have far-reaching benefits.

7.3 Dual Diagnosis

Goals for effective change for dually diagnosed clients should focus on collaboration between and education of all stakeholders (both statutory and non-statutory). It is vital that mental health staff receive drug and alcohol awareness training. Similarly, staff of the drug and alcohol services should receive mental
health training. This would enable staff to better refer and work collaboratively. Information sessions delivered by counsellors and psychologists to relevant stakeholders would be beneficial. Multi-disciplinary forums would allow staff to tease out challenges and capitalise on opportunities with clients. The advantages of well-trained staff are obvious as inevitably this will improve results and make for a more efficient MMTP.

To address the need for better services in relation to Dual Diagnosis, the HSE Mental Health division in conjunction with the College of Psychiatrists has set up a Clinical Programme (CP), entitled, ‘Co-morbid Mental Illness and Substance Misuse’. The overall aim of this CP is to design and progress an evidence-based model of care for the treatment of co-occurring mental and substance use disorders nationally. Integral to the overall plan will be the development of ‘Community Dual Diagnosis Teams’ with access to inpatient drug treatment and rehabilitation units. Recent research would suggest on-site and combined mental health and substance use disorder services in a MMTP might improve mental health outcomes compared with off-site, non-combined care. (316) The HSE has set a tight timeframe of 2 years from the establishment of this CP to mainstream operation in Mental Health Services. As such, this group is expected to finalise the Model of Care in 2019 with a subsequent roll out of the programme nationally. Our study highlights the need for this strategy and identifies the need to ensure funding remains in place for its completion and maintenance thereafter.

7.3.1 Benzodiazepines

A significant proportion of deaths result from poly-substance use, chiefly the mixing of heroin with other depressors of the central nervous system, such as BZDs. (317) To address this issue locally, the HSE Addiction service, the ICGP
and Novas, an NGO service, support the ‘Mid-West community detox programme’. The primary aim of this programme is to help individuals wishing to access secure, structured detoxification from BZDs, in an outpatient setting. Clients’ family practitioners, key workers and community-based partner organisations all work together to offer a personal, tailored care plan to each client.

Established in 2012, the programme operates from the HSE Mid-West Limerick MMTP’s offices, Slainte, 2 days a week. The programme is an excellent example of how two services, run out of the same establishment could work synergistically, for the benefit of the individual with a dual dependency. Clients of the MMTP with a concurrent BZD dependence can avail of their timely on-site support at the time of their assigned weekly methadone clinic. Potentially, it allows the methadone team to work in conjunction with the BZD team to optimise a tailored care plan for each respective client. However, the actual workings of this programme need addressing.

Firstly, a current key requirement of the ‘Mid-West community detox programme’ is that opioid dependent clients must be ‘opioid-free’ for a minimum period of 1 month prior to being able to approach a GP in the community to request BZD detoxification. Unfortunately, given their opioid dependence, this period of abstinence is not always feasible and often restricts those in most need of detoxification, in being able to avail of the service. Often clients, in their understandable quest to detoxify from BZDs, give false negative samples for testing, in attempt to attain the required number of opioid free urinalyses. Thereafter, even if a client does meet the requirement of remaining free from opioids for the specified duration, GPs in the community are not always readily
available and willing to engage with clients to address their needs. The quantities of prescribed BZDs necessary to initially stabilise and then commence detoxification are typically well in excess of recommended daily guidelines for the general population, and day-to-day GPs in the community feel inexperienced to prescribe same.

A recommendation to address the above would be to have experts, both nationally and internationally, in this area create a specific policy on prescribing larger than typical doses of BZDs to concurrently dependent opioid users which would give GPs the knowledge, confidence and legal backing to adequately address this cohorts’ needs.

Of note, Novas functions primarily as a housing organisation helping the homeless or those who are at risk of being homeless. Operating on a voluntary basis, it recognises the multifaceted reasons, which result in homelessness, most notably, SUDs, and endeavours to contribute to all-inclusive, longstanding resolutions, such as the programme above. A subsequent recommendation is to ensure to continue to have their expertise and resources in addressing homelessness available to the clinic and for this clinic and all clinics to expand and engage with other homeless organisations, as many of the clients grapple with remaining in secure accommodation. This approach is supported in our National Drug and Alcohol strategy via action 2.1.12: ‘Strengthen the implementation of our National rehabilitation framework via key working, care planning and case management promoting interagency cooperation’.
7.4 Therapeutics

Recommendations on this issue were borne from the clients of the HSE Mid-West Limerick MMTP, when in Study 1 of this thesis they impressed upon the need to educate not only themselves but also their doctors, friends, family and the public as a whole on the therapeutic rationale and associated benefits underpinning methadone as a treatment option for OUD. This is insightful and warrants further exploration. Thereafter, the pivotal role stigma in relation to methadone treatment plays in perpetuating OUD is explored.

7.4.1 Education

Advances in our understanding of the neurobiological processes that arise following acute and chronic opioid consumption have helped enhance our scientific understanding of how dependence develops. However, the concept of ‘neurobiology of dependence’ is exceptionally complex and as a result often poorly understood, even amongst professionals in the medical community. However, developing an understanding of the neurobiology of drug dependence can be extremely valuable to the clinician. It can offer an insight into individuals’ behaviours and difficulties, which in turn can help establish patient centred attainable objectives and define the overall goal of their treatment plan. (318)

Clinicians need to first educate themselves and subsequently impart evidence-based truths with regard to the habit-forming processes which underlie opioid use disorder, to not only their clients but also their clients’ families and the general public to optimise the functioning and overall success of any MMTP.

From a client perspective, health care professionals collectively must work with OAT clients at their level, to educate them on the neurobiological origins of their opioid dependence. Clients in turn will benefit from understanding that the
biological basis of their illness is in need of long-term, often life-long therapy. On a positive note, individuals in study 1 and for over 40 years internationally (319), acknowledge methadone’s ability to curb dependence and this unwavering belief should be integral to build on their psychoeducation.

The term ‘psychoeducation’ in opioid dependence refers to a form of communication between the clinician and their client that acknowledges the client’s role in understanding and dealing with the realities of their illness.

One such stark reality is the need for clients to act appropriately to ensure their methadone is stored appropriately. A study conducted in Ireland in 2016 revealed that though study 97% of patients were aware of the dangers of methadone use 86% did not place their take-home methadone in a locked place. (320)

The overall purpose being to get the client to believe in the efficacy of their treatment to improve their adherence, which in turn should reduce the occurrence of relapse and most importantly, ‘drug-induced death’ rates.

Familial members must also be educated on the over-riding benefits of methadone as a therapeutic agent. Acceptance and support from a client’s family is pivotal in their ability to adhere to their treatment plan. Insightful appreciation of the complexities of OUD by the client’s familial network is key influences on their rehabilitative journey. (321) Research proves that individuals with an OUD profiting from family assistance fared better from a treatment outcome perspective. (322)

Broadening on the theme of education, the public needs to be educated not only on the benefits of methadone but also on the over-riding benefits of harm reduction policies in the fight against OUD. Ireland can learn from internationally initiatives. For example, the provision of drug paraphernalia to aid the injecting of
drugs, which understandably could be viewed by many as ‘ludicrous’ (323) was successfully reframed by Switzerland as a policy to reduce the spread of HIV. (324) In doing so, Swiss society could immediately see the tangible benefit of the initiative and supported it wholly. In addition, OUD spans all classes of society. Vancouver, Canada used this evidence to gain national support to fund harm reduction initiatives (325) and in doing so brought all classes of society together to collectively tackle its opioid crisis. Vancouver and Switzerland are examples of how ‘positive spin’ can sway societal attitude and entice people to work collectively, which has the possibility to affect positive change.

If we do not take this, three prong approach to educate clients, their families and the public on the overriding benefits of methadone as a treatment modality in the fight against OUD the negative effects of stigma will not only prevail but also ultimately triumph.

7.4.2 Stigma

Paradoxically, stigma serves to amplify drug use in individuals with a SUD as they use it as a coping strategy to combat the stress and negative sentiments inextricably linked with discrimination. (326) For clients of a MMTP, using drugs in this way may have remarkably negative significances on clients’ mental health and recovery endeavours. Given its prevalence, it is critical for society as a whole to address this stigma. In Ireland, policies and ideological points of view are shifting into more preventative, holistic, patient centred models. However, stigma, blame, and competing ideologies continue to exist in relation to the optimal means to treat drug dependence. (81, 327, 328)

Ireland must learn from successful international initiatives. Vancouver, Canada successfully brought a broad range of stakeholders together, with expertise
straddling many fields (political, academic, legal and community based) to concentrate on finding a united resolution to the opioid crisis. (329)

The current approach of our National Drugs and Alcohol Strategy, ‘Reducing the Harm and Supporting Recovery’ does bring together many of the key players from the Community and Statutory arenas to address the issue more comprehensively.

7.5 Take-Home Naloxone Programmes

This section will first review specific recommendations with regard to Ireland’s current reporting mechanism on the uses of naloxone nationally. It will then broaden its scope to incorporate general recommendations with regard to improving the effectiveness of THNPs.

7.5.1 Specific recommendations regarding the reporting of naloxone uses in Ireland

The check exercise on the recorded uses of naloxone in Ireland in 2017 afforded a clear rationale for both amending the current reporting mechanism and streamlining the form’s current layout and line of questioning.

7.5.1.1 Mechanism to report naloxone use in the Irish Community setting

A better, more user-friendly system would be to revert to the manual report, which could be in the packaging of each naloxone kit. The HSE should restrict the information recorded to the absolute minimum, perhaps just the simple 15 questions drawn from the data set for this study. Importantly, this would also be in
line with the EU General Data Protection Regulation, which took effect on May 25th 2018 as the current format requests potential identifiers not in line with these regulations. On receipt of the paperwork a nominated individual within each CHO area could submit an excel sheet once monthly to the HSE on its recorded uses of naloxone.

### 7.5.1.2 Clarifying the details required on the form

It is beyond the scope of this thesis to address all the potential amendments that could be made to the current THNP reporting form in use in Ireland. Here, we will just address two issues raised in the discussion section of this thesis.

Firstly, in respect to the line of questioning on the ‘relationship between the person filling the form and the patient’ a clearer line of questioning would be:

1. Did you administer the naloxone? If not, who did?

2. Are you a relative or personal friend or working at the site of the overdose? - Please circle as appropriate. If none of these describes your relationship with the victim can, you explain how you happened to be present at the scene of the overdose.

Secondly, and most importantly, from a BLS perspective, the effectiveness of BLS training in the context of THNPs is not assessable from the current reporting mechanism. Current training teaches that if a patient is not breathing, the appropriate next step is to contact the emergency services and then administer CPR, 30 cycles of chest compressions followed by 2 rescue breaths. After one round of CPR, naloxone should then be administered. However, if a patient is unarousable but breathing normally, the correct next step is to place them in the recovery position and administer naloxone. Therefore, a better way of assessing witnesses’ appropriate use of BLS would be to segregate the two pathways of
BLS administration after clarifying if their patient was or was not breathing on their arrival at the OD setting.

### 7.5.2 General Recommendations regarding THNPs

A clear deterrent to both the calling for assistance and reporting of naloxone use by peers is the fear of legal prosecution. Ireland and other countries internationally could benefit from adopting a similar approach to the US and Canada in combatting this fear by introducing ‘Overdose Good Samaritan laws’ which safeguard peers from being incarcerated or impeached for drug possession in the setting of an OD.

Stigma also plays a critical role in hampering appropriate peer management of an OD as it negatively influences peers to call for help or report the events retrospectively. A resolution to the detrimental repercussions of stigma will not be found until the misinterpretations about all aspects of OUD and its treatment are addressed, challenged, and explained. This may be achieved with affected individuals and relevant authorities collaborating in an extensive, coordinated media-based national effort. (330)

The LR Model generated in Study 2 permits first responders and paramedics to pre-empt the likelihood of a patient refusing hospital attendance. This allows both parties to be pre-warned as to the potential volatility of the patient in question and allow them to prepare accordingly, perhaps in the case of paramedics for a more experienced team to be deployed to certain overdose situations. Secondly, it highlights those who may specifically benefit from education on the necessity of hospital attendance. Accounting for the small dataset in Study 2, a specific recommendation of this thesis is to test the validity of the LR model on a bigger international dataset. Thereafter, its findings should be employed to inform first
responders and emergency personnel on the likelihood of their patient attending hospital. Secondly, the overwhelming benefits of hospital attendance should be impressed upon the specific cohort who the model predicts to be likely not to attend hospital in a targeted educational campaign.
7.6 Chapter Conclusion

One of the largest obstacles restraining our combined capacity to tackle the opioid problem not only in Ireland but worldwide, is the un-coordinated, mismatched concepts of suitable resolutions.

Relevant stakeholders in the medical, pharmacological, public health and legal fields as well as all community-based programmes differ significantly in their beliefs regarding the best, most appropriate solutions to tackle the opioid crisis. (107) It is critical to align philosophical beliefs and public attitude with evidence based research, if we are ever to develop and implement effective policies and programmes to address this epidemic.

Recommendations from the evidence-based research conducted in study 1 of this thesis aimed to do just this. MMTPs are integral to addressing the opioid dilemma. Ensuring these programmes function optimally is a critical step in tackling the problem. Incorporating the voice of the clients themselves on how best to optimise these programmes’ objectives shone new light on the issues. In summary, having a ‘trauma informed’ MMTP, which places appropriate importance on both clients’ ACEs and client resilience, is essential. A key step, identified in this study, in achieving this is addressing clients’ stress management. Another outcome of this study was the importance of appropriately servicing dual diagnoses in clients with OUD, particularly their dependence on BZDs, which is starkly evident throughout this research. The importance of imparting applicable knowledge to all relevant stakeholders in OUD was a recurrent important theme. Professionals need to be educated on the neurobiology of dependence and clients need intensive psychoeducation. Familial members need to be informed of the pharmacological benefits of methadone as a treatment not a substitute for opioid
dependence. Finally, the public need to be instructed on the harm reductive benefits associated with appropriate OUD treatment, which dramatically improve the societal burden of the disease. This in turn should lessen the overriding stigma associated with OUD.

Secondly, optimising THNPs worldwide will improve the death rates associated with OUD. Understandably, each THNP works within its country’s legal and economic framework but all programmes can learn from the research conducted in study 2 of this thesis. Ensuring an appropriate, accurate, succinct reporting mechanism is in place on the use of community naloxone would be beneficial to all. Safeguarding that peers who report naloxone use are protected by well established, publically advertised good Samaritan laws would increase the reporting of naloxone use in the most vulnerable and chaotic of cohorts, those with OUDs themselves. Gaining a better understanding of this cohort would be most beneficial to appropriately addressing their needs.

Finally, the logistic regression model generated in study 2 of this thesis, which predicts the likelihood of patients attending hospital post naloxone, has the prospect to better equip first responders on the potential volatility of their patient and secondly allow relevant services to identify and target those least likely to avail of secondary care.

Researchers play an integral, pivotal role in forming future policy regarding OUD through the dissemination of evidence-based knowledge. In doing so they contribute significantly to the quality of public discourse and debate which ultimately should unify society’s approach to tackle OUD. It is hoped that the findings of this thesis, in line with other research (107), will inform policy
makers’ decisions regarding how best to tackle OUD and will motivate them to continuously strive to make evidence-based informed decisions.
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