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Identifying Profiles of 'Probable Suicide' and Drug-Related Death: the Merits of Routine Healthcare Databases

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Identifying Profiles of ‘Probable Suicide’ and Drug-Related Death: the Merits of Routine Healthcare Databases

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Table of Contents

List of Tables

List of Figures

i. Acknowledgements

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Finally, from first to last, *Deo Gratias*.

ii. Signed Declaration

I declare that I, Catherine Maria-Inmaculada Arkwright, am the author of this thesis, that I have consulted all references cited herein, that I have conducted all the work recorded in this thesis, and that it has not been previously accepted for a higher degree.

Signature of Candidate: Catherine M Arkwright Date: 07/01/2023

Signature of Supervisor: Keith Matthews Date: 07/01/2023

iii. Abstract

Globally and historically, deaths from ‘probable suicide’ or drug-related causes have carried compelling and varied emotive and societal weights. Recently, both ‘probable suicide’ and drug-related deaths (DRD) have been combined with chronic alcohol-related deaths into a mortality category of “deaths of despair”. For several decades, governments and international bodies have attempted to systemically prevent, and therefore reduce, the number of deaths. Prevention strategies for ‘probable suicide’ advocate for the expansion of psychiatric healthcare, predominantly talking therapies and (more controversially) antidepressant prescriptions, while DRD intervention strategies typically focus on prescribed opioid substitution therapy (OST). Both therapeutic approaches are associated with some improvements in patient health and small reductions in mortality, yet none of these approaches have significantly ameliorated the rising death rates. There are, not infrequently, suggestions that ineffective and inefficient healthcare services are to blame for the continuing high death rates, however, little conclusive data has been presented supporting, or indeed challenging, these claims due to a widespread reliance upon simple analyses of observational data. A large bank of previously collected healthcare data was available from a study undertaken before this doctorate began. Thus, the aim of this thesis was to investigate the healthcare usage at a variety of services of those who died from ‘probable suicide’ or DRD, contrasted with matched community controls, using this pre-existing database. Specific aims were to examine the rates of salient interventions, and provide data with which to question assumptions of poor healthcare.

Using linked, administrative healthcare records for the Tayside region, held within a certified data Safe-Haven, 677 individuals classified by the National Records of Scotland as a ‘probable suicide’, DRD or both, were identified during the period 01.01.2009-31.12.2014. Each of the deceased were matched with 4 non-deceased ‘controls’ (using sex, age and estimated socio-economic status). Healthcare data, including key prescriptions, were extracted for the twelve-month prior to death. After healthcare usage comparisons, based on the total cohorts, sub-sections within these, and pivotal treatment-related measures (e.g., OST dosage per day), a clustering analysis was performed. This analysis used a partitioning around medoids (PAM) algorithm, which accounts for mixed-type data by standardising each variable into a numerical value of dissimilarity, averaging the dissimilarity value across all

variables, and applying that average as a measure of distance, from which similar individuals can be grouped into clusters. The variables read into the PAM algorithm included categorical demographic variables and binary or frequency healthcare attendance measures. A goodness-of-fit measure, known as a silhouette width, was calculated for values from 2 to 10 clusters. Independent analyses were run for the 'probable suicide' and DRD groups, with a final iteration including both cohorts, attempting to isolate patterns of antecedent healthcare usage that were unique or shared across study samples.

Initially, 605 individuals were extracted from the National Records of Scotland (NRS) for the 'probable suicide' cohort, however only 586 were validated with official cause of death criteria. Correspondingly, 311 DRD individuals were extracted from the NRS, however only 288 were validated. Those who died a 'probable suicide' or DRD attended all healthcare services and received a higher rate of psychotropic prescriptions than matched community controls. Of those receiving salient prescriptions (antidepressant or OST, respectively), those who died attended services at higher rates than the controls, likewise considered "in treatment". Comparisons confined to Accident and Emergency presentations showed that after possible self-harm events, those who went on to die received more psychiatric follow-up in the 21 days after, than the controls with identical presentations. Finally, within the cohorts of 'probable suicide' and DRD, those "in treatment" were evidently attending healthcare services and receiving prescriptions at higher rates than those not "in treatment". The clustering analysis, performed on the 'probable suicide' only, DRD only and a combined cohort identified three basic patterns across all cohorts; low attendance (associated with a large group of men), attendance at specific services (antidepressant prescriptions or methadone prescriptions, generally associated with women and men respectively) and high attendance at all services (including an unforeseen group of women with antidepressant, methadone and benzodiazepine prescriptions, in all 3 analyses).

Each comparison showed both the 'probable suicide' and DRD cohorts to have higher historic rates of healthcare utilisation, consistent with the poorer health often associated with "deaths of despair" and their association with poverty, psychological distress and illicit drug use. Furthermore, specifically "in treatment" comparisons demonstrated similar patterns to the total cohort comparison, in that those who went on to die had higher rates of healthcare usage. Specific comparisons indicated the ‘probable suicide’ group redeemed more antidepressant prescriptions, while no difference in methadone dosage between DRD and controls in OST were found; these results seriously challenge the idea that gaps in the healthcare system are largely responsible for these types of death. Multiple clustering analyses demonstrated the difficulties of differentiating meaningfully between ‘probable suicide’ or DRD deaths, and in 10-cluster analyses, found three attendance patterns, associated with particular demographic groups, though significant heterogeneity in cluster compactness was noted. This thesis demonstrates various sub-groups can be identified in both ‘probable suicide’ and DRD cohorts, which could potentially improve the efficacy of interventions, if targeted appropriately.

iv. Abbreviations

DRD	Drug-Related Death
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
HIC	Health Informatics Centre
ICD-10	International Classification of Diseases Version 10
ISD	Information Services Division
NDRDD	National Drug-Related Death Database
NRS	National Records of Scotland
NSSI	Non-Suicidal Self-Injury
ONS	Office of National Statistics
OST	Opioid Substitution Therapy
PWUD	People Who Use Drugs
SCOTSID	Scottish Suicide Information Database
SIFT	Suicide Information Framework Tayside
SIMD	Scottish Index of Multiple Deprivation
TDRDD	Tayside Drug-Related Death Database
WHO	World Health Organisation

1. Introduction

Anthropological research into ancient human history contributes significantly to furthering our understanding of human development, as well as the psychological and sociological similarities and differences between our ancestors and ourselves. This is particularly relevant considering ancient views on death, and the types of death that were understood differently to our modern-day conceptualisations. Ancient Greek, Roman, Chinese and Indian cultures each had well-known examples of ‘probable suicide’ (Barbagli, 2009), and each with their own specific understanding of the causes of, and appropriate social responses to, these kinds of death. Some of these deaths would have overlapped with those contemporary deaths that are now considered drug-related deaths (DRD), due to being ‘probable suicides’ mediated by drug overdose. DRD, outside of ‘probable suicide’, is less well chronicled through history, however there is growing evidence for early cultivation of certain drugs, and regular usage therein (e.g., cannabis as summarised in Crocq, 2020 or opiates in Stefano et al., 2017). These records are coupled with accounts demonstrating ancient understanding of the threats and dangers of over-reliance on these substances (Africa, 1961, Nathan, Conrad and Skinstad, 2016, Stefano et al., 2017). These would now be recognised as detailing forms of addiction, but the over-reliance was often seen, in earlier times, as a moral failing on the part of the individual, unless usage was in closely specified religious or shamanic circumstances (Crocq, 2020).

Current conceptualisations of these types of deaths, particularly in the West, focus on their ‘pathological’ nature, their undesirability, their stigma and their assumed preventability. ‘Probable suicide’ has been overwhelmingly associated with mental illness in the literature (e.g., Barraclough et al., 1974., Cavanagh et al., 2003), while ‘probable suicide’, DRD and deaths related to alcohol use are commonly combined to form a “deaths of despair” category and are linked to socio-economic deprivation and social marginalisation (Sterling and Platt, 2022). Indubitably, both ‘probable suicide’ and DRD are emotive and complex types of death. The presumed psychological distress underpinning both has resulted in their widespread adoption as salient indicators of wider cultural and sociological health (Sterling and Platt, 2022, WHO Suicide, 2021, WHO, 2022).

Recent international reports suggest that at least 700,000 deaths per year worldwide are attributable to ‘probable suicide’ (WHO Suicide, 2021), with 494,000 deaths attributed to drug-related causes in 2019 (UNODC, 2022). As an important caveat to the figure for DRD, this includes so-called indirect deaths from drug use; the majority of these being deaths from HIV/AIDS contracted from drug use. These are generally excluded from more specific measures of DRD, yet the wider definition highlights the elevated mortality broadly associated with drug use. International reports emphasise the premature and preventable nature of these deaths; however, both the historical prevalence of 'probable suicide' and DRD, and the absence of complete models explaining the causes and mechanisms that result in these types of deaths, demonstrate the difficulty of implementing effective preventative interventions.

1.1. International Definitions and Statistics

Many of the World Health Organisation's (WHO) Sustainable Development Goals aim to reduce certain kinds of mortality, as well as to measure and then to lessen the impact of chronic health conditions on healthcare systems globally (WHO, 2022). The key targets are so-called premature and preventable deaths, meaning deaths that occur in those under 70 years of age, and that could theoretically be avoided if appropriate public health, societal and healthcare interventions were in place. Recent shifts, however, in the global burden of mortality and disease have demonstrated that the mortality rates of communicable diseases are decreasing, while the burden of non-communicable diseases is increasing (GBD Collaborators et al., 2015). As such, a complementary shift in our view of global medicine and the intervention therein will be needed to appropriately address the future healthcare requirements of the world.

Measuring the developments of mortality, morbidity and healthcare across time and across the globe is complex. The practice of classifying causes of death has a long history, from rudimental approaches based on the ancient Greek belief in disease causation relating to humours within the body, leading slowly to the first widely accepted international statistical publication dating from 1893 (Alharbi, Isouard and Tolchard, 2021). Valid international comparisons hinge on standardised criteria for definitions, comparable data collection protocols, and a recognition of the differences across countries, especially relative to cultural taboos and the legality of suicide or relevant substances, which could affect data completeness. To facilitate these international mortality comparisons, the WHO (since its inception in 1948) develops and publishes its International Classification of Diseases (ICD) on a regular basis, with the eleventh revision in use from this year (Harrison, Weber, Jakob and Chute, 2021). The ICD codes are alphanumeric, which allows for a very large number of categories and facilitates fine-grained analyses of trends within categories. For example, using these codes, it is possible to investigate the number of deaths categorised as intentional, undetermined or accidental poisoning events, as well as examine the number of deaths attributed to opioid versus cocaine misuse (through the use of substance specific T-codes, in conjunction with the poisoning codes).

These standardised codes are used by healthcare and national death registries worldwide; however, the protocols within each country for investigating, categorising and validating causes of death exert significant impact on the data quality and comparability of the data feeds sent to the WHO for their databases. Countries have different methods for their medico-legal investigations and different timeframes established for their completion. The first code on a medical certificate of the cause of death, known as the underlying cause of death code, is the basis for statistical classifications. The only guidance available states that the underlying cause of death should follow a logical sequence; for example, an elderly person who presented to hospital after a fall, yet died of an infection contracted in hospital, would be ruled as a death due to a fall, as the prevention of the fall would have prevented the infection (Scottish Government, 2018). Many countries use an automated coding system to code deaths (known as Iris and detailed on the German Federal Institute for Drugs and Medical Devices website https://www.bfarm.de/EN/Code-systems/Collaboration-and-projects/Iris-Institute/Iris-and-ICD-11/_node.html;jsessionid=9906227AB1F5351883CD132D348AC63F.intranet2421), though generally complex deaths involve further investigation and are coded manually (NRS, 2021 (a and b), ONS, 2020). As such, while the international coding system is an impressive achievement and does facilitate the production of comparable figures, there are multiple steps in the procedure that could result in significant differences between the figures collected by each country, which would clearly affect the reliability of the international reports more than is commonly acknowledged.

1.1.1. Defining 'Probable Suicide'

A common definition of 'probable suicide' is "the act of deliberately taking of one's life", given by the WHO (WHO Suicide, 2021). A recent review found as many as 26 definitions published in the literature from 1964-2016 (Goodfellows, Kõlves and De Leo, 2019). They identified 4 key components of a definition of 'probable suicide': agency, knowledge of the potentially fatal outcome, intent and outcome. These criteria are not included in all definitions, with some even allowing for other-inflicted 'probable suicide', despite the review excluding publications defining assisted death or euthanasia. Philosophically, there are many complications with defining 'probable suicide' consistently; some have used the example of Socrates being commanded to drink poison as a challenge to the self-inflicted clause (Goodfellows, Kõlves and De Leo, 2019). Others have questioned to what extent neglecting to eat or neglecting to take life-saving medication represents intent to die (Hill, 2011). The lack of clarity in precisely what constitutes a 'probable suicide' is a significant challenge for the field, and a significant challenge for standardised research. It does, however, highlight that there is a great deal of variety within the types of deaths that might be labelled 'probable suicide' and points towards the need for greater flexibility in our conceptualisations of both the phenomena itself and possible interventions for it.

Setting aside this wider philosophical concern, the simple definition given by the WHO appears intuitive. Standardising this concept into a set of ICD-10 codes is, however, problematic. There are codes referencing intentional self-harm, which logically form the basis of most statistical definitions of 'probable suicide' reports. There are however, categories of accidental and undetermined deaths that are pertinent to the statistical definition of 'probable suicide'. These primarily concern deaths related to poisoning, though falls and injuries can also be ruled as events of undetermined intent. Neither the United States (CDC, https://www.cdc.gov/nchs/hus/sources-definitions/cause-of-death.htm) nor the WHO include events of undetermined intent in their records of 'probable suicide' (WHO Department of Data and Analytics, https://cdn.who.int/media/docs/default-source/gho-documents/global-health-estimates/ghe2019_cod_methods.pdf?sfvrsn=37bcfacc_5). Reports published in the UK do include events of undetermined intent in their 'probable suicide' statistics (ONS, 2020, NRS, 2021 (b)). The WHO do filter the data feeds they receive, however, countries with different investigation methods may have distinct percentages ruled as intentional or undetermined events of self-harm. As such, countries could appear to have rates of ‘probable suicide’ that varied greatly between the WHO records and their own national reporting.

Many deaths of undetermined intent are poisoning-based, with the other classifications available being intentional or accidental self-poisoning. These distinctions hinge on the confidence that post-mortem medico-legal investigations can reliably and accurately differentiate between these three categories. Certain contexts facilitate these rulings; poisonings accompanied by a note explaining the motivation of the deceased would be ruled as intentional self-poisoning and included in ‘probable suicide’ statistics. An intentional self-poisoning could likewise be present in DRD statistics, if the toxicologist identified illicit drugs within the timeframe for additional codes to be added to the cause of death records. Deaths without this external context would be ruled as undetermined (included in both DRD and ‘probable suicide’ reports in the UK, but not in ‘probable suicide’ reports in the States) or accidental (included in DRD reports if illicit drugs were present). A re-evaluation study of Danish, Swedish and Norwegian mortality registers found that as much as 26% of accidental deaths were changed to the category of undetermined intent, following discussion by a panel of 8 experts (Tøllefsen et al., 2016). From a theoretical perspective, Rockett et al. (2014) questioned the validity and utility of the classification of accidental deaths. After listing the names of a number of celebrities who died of an overdose, they state: “*Although their deaths may have been unintended, there was nothing unintentional about their use of intoxicating substances. Therefore, the resulting fatal drug overdoses or interactions were not true accidents*.”

This aspect of intentionality is further complicated by qualitative reports into the intentions and thoughts of individuals who survived overdoses of illicit drugs. Several studies have highlighted that self-reported measures examining the most recent overdose indicated some desire to die in over half of the sample (e.g., Connery et al., 2019, Gicquelais et al., 2020). Admittedly, these samples were both relatively small (e.g., only 120 individuals were recruited by Connery et al. and only 274 individuals were included by Gicquelais et al.), however, these studies reveal that it is likely that many individuals who die by poisoning overdoses have some degree of “passive” suicidal intent. As noted by Pergolizzi et al. (2021), this group of overlapping ‘probable suicide’ and DRD, combining passive intent and illicit drug use, are rarely specifically addressed in literature discussing prevention of either cause of death. That deaths by poisoning are relatively common means that this oversight needs to be addressed urgently, and some studies are beginning to call for greater integration of ‘probable suicide’ prevention with overdose prevention (Oquendo and Volkow, 2018).

Throughout this thesis, the phrase ‘probable suicide’ will be used. This is an attempt to acknowledge the variation in intent (that is, both intentional and unintentional injuries or poisonings, with either passive or active suicidal desire) behind the action that resulted in death. Furthermore, it reflects the terminology and ICD-10 codes used by the National Records of Scotland in the yearly updates on ‘probable suicide’, which include events of undetermined intent.

1.1.2. Defining Drug-Related Death

Defining a DRD has similar theoretical complications. As mentioned, there are direct and indirect deaths from drug use. Direct deaths are generally overdoses, while indirect deaths constitute deaths from secondary causes, for example those from HIV/AIDS as contracted from drug use. The UNODC includes both direct and indirect deaths, however, the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA, 2022) includes data only on directly attributable deaths (https://www.emcdda.europa.eu/publications/topic-overviews/content/faq-drug-overdose-deaths-in-europe). Evidently, both statistics would be valuable contributions to understanding the true burden and mortality of drug use. More direct measures would be key for emergency and addiction healthcare service metrics, and indirect mortality rates would be important for understanding the chronic conditions associated with drug use (Beynon et al., 2007).

The subsequent complication is deciding which types of drugs should actually be included; relatively recent political history has focused on the “War against Drugs” and, therefore, the statistics published aim to quantify the effect of illicit drug use. As such, the most widely available drug, alcohol, is not included, despite bearing a significant healthcare and societal burden, as well as commonly being accepted in a deaths of despair categorisation (Sterling and Platt, 2022). Similarly, deaths related to overdoses using only over-the-counter medications are not included (NRS, 2021 (a)). Furthermore, countries are beginning to diverge politically relative to drug decriminalisation, legalisation or continuation with the current, combative policies. Each country collects mortality data according to their own definitions; therefore, differences in the legal status of a drug could rapidly and seriously affect the comparability of international statistics. Countries with fewer illicit drugs would likely report notably lower values than countries regularly updating lists of controlled substances. These concerns demonstrate that international consensus is required to reframe the debate, as the focus on examining primarily illicit drug overdoses is likely to be ideologically driven rather than empirical.

There is also an important debate about the differences between: recreational users, those who seem to have died from an accidental overdose, those whose overdose is considerably more ambiguous in intent, and those who die after chronic drug misuse (prescription or illicit), potentially even from secondary complications rather than an actual overdose (Hickman et al., 2006, Pergolizzi et al., 2021, Rockett et al., 2014). Can all these individuals be referred to simply as DRD? Should they be? Does it not conflate very different groups of individuals, with varied pathways into drug use and, therefore, groups likely to require uniquely targeted interventions?

1.2. What do we think we know?

National and international reports recording mortality rates aim to demonstrate the number of different types of death and track how these proportions may change each year. These longitudinal archives allow for research into whether preventative policy initiatives have been effective, and may highlight concerning trends for further investigation or modifications to current policy (e.g., the increase of gabapentinoid drugs in post-mortem toxicology over several years led to them becoming controlled substances in the UK in 2019; NRS, 2021 (a)). Accurate data is crucial for analysis, reflection and adaptation to changing contexts, and this is largely available, definitional issues notwithstanding. National reports include demographic data on the individuals who died, usually their sex, age and deprivation score (NRS, 2021 (a and b), ONS, 2020, and further discussed in section 1.5, page 59). These are well-established "risk factors", though their utility for prevention is challenging to determine.

As well described by Franklin et al. (2017), there are important distinctions between a correlate, a risk factor and a causal risk factor. A correlate is simply a factor with some association to the outcome, and for which further study is required to elucidate the relationship more clearly. A risk factor, determined through longitudinal studies, is a correlate that precedes the outcome and the presence of which could be used to divide the population in low and high-risk categories. Risk factors may have indirect effects on the outcome of interest, hence the concept of a causal risk factor; when this risk factor is modified, the probability of the outcome, systemically and consistently, is likewise affected. Evidently, a causal risk factor would represent the best candidate for an effective intervention target, while risk factors with undefined mechanisms of action would constitute less effective levers.

A useful illustration of this distinction, and its practical value, is the common statement that being male constitutes a risk factor for both 'probable suicide' and DRD (Chan et al., 2016, Sterling and Platt, 2022, Santo et al., 2021). Indeed, up to 70% of 'probable suicide' and DRD are men (Large, 2018, NRS, 2021 (a and b)). Using the schema outlined in Franklin et al. (2017), being male could be classified as a risk factor, but can it be reasonably classified as modifiable, as psychometric measures like hopelessness might be? Would it be reasonable to apply an intervention to all men, on the basis that they have a higher average rate of 'probable suicide' and

DRD than women? Evidently, it is entirely unfeasible to target 50% of the world's population, therefore what value does the focus on this unmodifiable "risk factor" truly have? Various campaigns have used it to raise awareness of the unequal distribution of death, and there are qualitative studies examining men's perspective on mental health and help-seeking (Chandler, 2021). It highlights that the injunction to "talk more" neglects overarching concerns around economic stability that cannot be solved with talk therapies, even if distress may be partially ameliorated. Furthermore, a recent review examined the efficacy of interventions targeted towards men (Struszczyk, Galdas and Tiffin, 2019) and reported that some awareness campaigns demonstrated only small, short-term reductions in the rates of male 'probable suicide'. It is key to note that the interventions analysed did not modify "maleness" itself, but rather attempted to reduce psycho-social barriers to psychiatric healthcare usage for men. For example, help-seeking was reframed as "brave", therefore was seen as a more acceptable act (Struszczyk, Galdas and Tiffin, 2019). Men are not a homogenous group, so while identifying their gendered challenges is important, it cannot be the main avenue for research and intervention. Expressed another way, maleness constitutes a correlational, and not causal, risk factor, therefore it can only be one of many indirect pathways of intervention.

The distinction between these types of risk factors is key for using them appropriately in designing and targeting preventative interventions, as well as in creating predictive models that may facilitate these aims. Predictive models, especially those using routinely collected, administrative data, are being touted as the best tools for improving the efficiency of healthcare provision (Belsher et al., 2019, Bharat et al., 2021). There is, however, some debate concerning whether their predictions would ever be accurate enough to be clinically useful (Large, 2018). A key area of this debate is the "signal to noise" ratio; the outcomes of both 'probable suicide' and DRD are rare, even in groups thought to represent high-risk (e.g., those with diagnosed depression and those with substance use disorders). Comparatively, some risk factors are very prevalent, especially large demographic groups like men or the socio-economically deprived. It is plausible that accurate prediction, in the whole population, is numerically almost impossible. This has led to suggestions that universal, rather than targeted interventions, ought to be prioritised (Large, 2018, Sterling and Platt, 2022). To further investigate this numerical imbalance, the prevalence of both types of death, and theoretically closely related phenomena were extracted from the literature and summarised.

1.2.1. Prevalence of 'Probable Suicide'

The most recent report from the WHO estimated at least 700,000 deaths were attributable to 'probable suicide' in one year worldwide (Suicide, 2021). This WHO factsheet also notes that the vast majority of these deaths are in low- or middle-income countries, which already highlights a substantial problem: the majority of current research is undertaken in high-income countries and is likely to be unrepresentative of the rest of the population. Furthermore, calculating the true prevalence of 'probable suicide' within even one country is complex. This is compounded in regions which may lack the infrastructure to collect and record accurate mortality data or countries where 'probable suicide' is illegal, from which the reports are likely to underestimate the number of 'probable suicide' deaths.

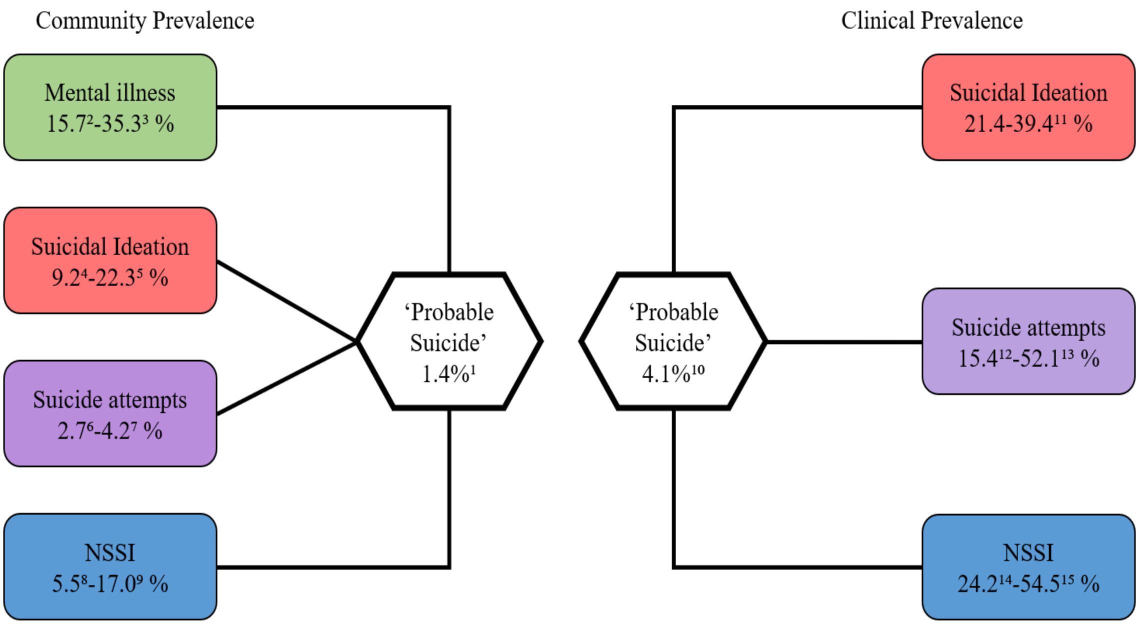
Current theories of 'probable suicide' centre on the pathway from suicidal ideation to action, hinging on the concept of "acquired capability"; that both the physical and psychological means to enact self-directed violence are necessary for 'probable suicide' attempts and 'probable suicide'. Two examples would be the Interpersonal Theory of Suicide, described in Van Orden et al. (2010) and the larger Integrated Model by Hamza, Stewart and Willoughby (2012). Both of these theories posit that self-harm, military service or other kinds of exposure to violence lead to fearlessness about death and a greater tolerance for physical pain, allowing the individual to move from suicidal ideation to potentially fatal acts. This has been somewhat corroborated by the literature (e.g., Bryan et al., 2015, discussed in the non-suicidal self-injury (NSSI) section, page 35), however there are a variety of other theories with more sociological (Durkheim, 1951, Martin et al., 2020) or psychological foci (e.g., unbearable pain, termed "psyche-ache" by Shneidman, 1968). As yet, there is no overarching paradigm to understand the risk factors for 'probable suicide', nor how these factors interact to increase risk (Franklin et al., 2017).

Further complicating the construction of a single model is that a wide variety of loosely defined risk factors have been identified; psychiatric illness, suicidal ideation, 'probable suicide' attempts and self-harm are all emphasised in studies constructing predictive models of subsequent ‘probable suicide’ (Chan et al., 2016, Carroll, Metcalfe and Gunnell, 2014, Bostwick et al., 2016). Other risk factors that are well-established, but considerably less emphasised in preventative campaigns, include poverty (especially unemployment, homelessness and significant socio-economic inequality in a country), as well as chronic pain, disability and other situational stressors, like bereavement or relationship breakdown (Sterling and Platt, 2022, Clapperton et al., 2018, Chandler, 2021).

Constructing a relevant model including all of these factors would be beyond the scope of this thesis. To add context for the discussion around the best prevention methods, and the validity of predictive models, the prevalence of theoretically more specific risk factors was investigated. General population surveys have been undertaken which attempt to define the prevalence rates of suicidal ideation, self-harm and ‘probable suicide’ attempts (e.g., Nock et al., 2008, De Leo, Cerin, Spathonis and Burgis, 2005). These rates have not been clearly contrasted with the prevalence rates in clinical environments, despite these two populations representing very different groups, each with distinct needs and more suited to universal or targeted interventions respectively. Therefore, as a key piece of context for attempting to understand and potentially predict ‘probable suicide’, the relative percentages of these phenomena, over the lifetime, were extracted in both populations and displayed in Figure 1-1.

The first prevalence identified was the rate of ‘probable suicide’ in the general population. A value of 1.4% of all premature deaths worldwide was attributed to ‘probable suicide’ and was extracted from Bachmann (2018), based on WHO data. Evidently, calculating a lifetime prevalence of ‘probable suicide’ would be impossible, and even the best estimates would be affected by the debate surrounding how to best prove intentionality in a globally standardised manner. The breadth of the data collected by the WHO means that it is the most reliable source for providing an illustrative estimate on the prevalence of ‘probable suicide’. Furthermore, using the data visualisation tool from Institute for Health Metrics and Evaluation (IHME https://ghdx.healthdata.org/gbd-2019), which contains all the Global Burden of Disease study data over time (GBD 2019 Mental Disorders Collaborators, 2022), demonstrates that the rate in 1990 was similar, at 1.6%, thus corroborating the value in Bachmann (2018). One limitation is that relying on WHO data means that events of undetermined intent are excluded, thus this percentage is an underestimate, and possibly a relatively significant one.

Figure 1-1. Prevalence and Risk Factors for 'Probable Suicide'



The left-hand side of the diagram illustrates the lifetime prevalence as calculated by a variety of longitudinal and survey studies in the general community setting. For example, 1.4% of deaths worldwide are reported to be 'probable suicide', while between 9-22% of individuals report some suicidal ideation over the course of their lives. The right-hand side of the diagram includes measures on the same suicidal and parasuicidal behaviour, but includes studies and percentages from 'clinical' samples identified from psychiatric clinics or other populations where psychiatric disorders have been diagnosed.

The superscript numbers refer to the articles providing the percentages, which were:

[1] Bachmann, 2018. [2] Stansfeld et al., 2016. [3] Auerbach et al., 2018.[4] Nock et al., 2008.
[5] Mortier et al., 2018. [6] Nock et al., 2008. [7] De Leo, Cerin, Spathonis and Burgis, 2005.
[8] Swannell, et al., 2014. [9] Whitlock, Eckenrode and Silverman, 2006.

[10] Holmstrand et al., 2015. [11] Baldessarini and Tondo, 2020. [12] Anestis and Joiner, 2011.
[13] O'Hare, Shen and Sherrer, 2014. [14] García-Nieto et al., 2014. [15] Yang et al., 2022

1.2.2. Risk Factors for ‘Probable Suicide’ in the General Population

1.2.2.1. Psychiatric Illness

Overwhelmingly, in the literature and public health prevention campaigns, ‘probable suicide’ is closely linked to mental illness. It is implicitly assumed that treating mental illnesses will prevent many deaths attributed to ‘probable suicide’; the evidence for this comes primarily from psychological autopsy studies. These studies require trained clinical interviewers, usually psychiatrists, to interview family and friends of the deceased, and compare the answers received against a modified handbook to diagnose psychiatric illness by proxy. Initial studies established that approximately 90% of individuals categorised as ‘probable suicide’ decedents could be diagnosed with a psychiatric illness with this method (Barraclough et al., 1974., Cavanagh et al., 2003).

The first limitation of this association is that these foundational studies included no more than at most 120 individuals in the review by Cavanagh et al. (2003) and 100 individuals in Barraclough et al. (1974). These are, evidently, very small sample sizes with which to build a foundation for an outcome as prevalent as ‘probable suicide’. Furthermore, considering the method of psychological autopsy itself, it is a significant flaw that there is no standardised guide or list of questions. Nor is there a common rule establishing the extent to which family histories of mental illnesses are recorded (Hjelmeland et al., 2012). Even more concerningly, there is no recognised standard for the number of people interviewed, the nature of their relationships to the deceased, nor how to resolve differences between the data collected from the interviewees (Fang and Zhang, 2010, Pouliot and De Leo, 2006). Moreover, a confirmation bias may be at work whereby the motivation for ‘probable suicide’ is primarily associated with psychiatric illness, despite medical records and witnesses in medico-legal investigations indicating a presence of other potential motivations like physical illness, or adverse life events (Fegg et al., 2016).

It is plausible that there are a significant number of deaths categorised as ‘probable suicide’ which are not eligible for a psychiatric diagnosis. The highest number of individuals *ineligible* for mood disorders, anxiety disorders and psychotic disorders, using this same psychological autopsy method, was 66.7% in Italy (Milner, Sveticic and De Leo, 2012). As such, a problematic oversimplification begins to emerge, which suggests that the vast majority of deaths deemed ‘probable suicide’ are primarily related to psychiatric illness, and therefore that simply improving psychiatric healthcare will be a viable and effective intervention design. This ignores that the vast majority of people with a psychiatric diagnosis do not go on to die of 'probable suicide', indeed with long-term rates of at most 16% in men suffering from co-morbid depression and alcohol misuse, but only 6% in patients with diagnosed depression over approximately 50 years (Holmstrand et al., 2015). There has been an accusation that the field of suicidology is being ideologically constrained by refusing to consider alternative, compelling explanations that do not label all instances of 'probable suicide' as necessarily signs of mental illness (Hjelmeland and Knizek, 2017). It is undoubtedly true that there is an association between psychiatric illness and increased risk of 'probable suicide', however, there is likewise strong evidence that considering psychiatric illness as the primary causal factor for 'probable suicide' is an oversimplification.

Within the prevalence diagram, the lower bound of 15.7% for a mental illness was extracted from a national study, which used a probability sampling technique to identify 7,546 individuals for interview, with the intention to accurately represent the adult population of private households in England (Stansfeld et al., 2016). The diagnostic criteria used primarily focused on common mental disorders, and of these, predominantly mood and anxiety disorders were reported. Evidently, there are limitations in that individuals who are homeless report higher rates of mental illness and were excluded from this study, as were those in shared accommodation (e.g., like university students) who likewise report higher rates of mental illness (e.g., Mortier et al., 2018). This study was chosen, however, because many other surveys and studies include substance abuse in this value, and as a DRD cohort was separately available for analysis, the aim was to keep the diagrams exclusive. Even this lower bound demonstrates that mental illness is considerably more prevalent than 'probable suicide', and that further risk factors, which more closely align with 'probable suicide', must be discovered for a deeper understanding of the mechanisms leading to this type of death.

The upper bound on the diagram, showing a prevalence of 35.3% for psychiatric illness within the general population, came from web-based self-reports completed by incoming university students in 8 high-income countries (Australia, Belgium, Germany, Mexico, Northern Ireland, South Africa, Spain, and the United States;

Auerbach et al., 2018). The total sample was 13,984 individuals, however as this was a feasibility study for later WHO surveys, there was no attempt at randomisation, with colleges simply chosen by convenience. This study did include substance abuse, and the study did not state whether diagnostic criteria were exclusive, therefore the base rate concluded by the authors was used without modification. There has been some discussion surrounding the higher prevalence reported in college samples than in the general population (e.g., in Bruffaerts et al., 2019), which note that it is a time of transition and uncertainty, as well as significant academic and social stress. As such, it is reasonable that disorders exacerbated by stress would express at higher levels in this sub-population. The diagram included lifetime prevalence rates; therefore, this does not lessen the validity of including an age group with a notably higher rate. It corroborates the conclusion above, that mental illness itself is non-specific as a risk factor for ‘probable suicide’.

1.2.2.2. Suicidal Ideation

Suicidal ideation, as a risk factor, makes logical sense in that before an action is undertaken, it is first considered. Research into this field very rapidly encounters the same challenge as in ‘probable suicide’, which is that intent varies significantly. A distinction exists in the literature between passive and active ideation; passive denotes a general wish to no longer exist, while active is taken to mean that a plan has been decided or that there is particularly strong desire to injure oneself. This reasoning suggests, implicitly and occasionally explicitly, that active ideation is higher risk than passive, as future steps have been mapped out and are thought to be more likely to be enacted. Yet, a recent meta-analysis highlighted that passive and active ideation shared similar association rates with ‘probable suicide’ attempts, which suggests there may be less of a difference in risk profile than would be hypothesised (Liu, Bettis and Burke, 2020). Similarly, a comparison of emergency department presentations likewise found no significant difference between those with active or passive ideation, when examining subsequent ‘probable suicide’ attempts in the next 6 months (Naherkiak et al., 2019). Both of these articles examined ‘probable suicide’ attempts, which is a common limitation of research into suicidal ideation, as it may be distinct between those who attempt and those who die by ‘probable suicide’.

The lower bound, in the general population, for suicidal ideation was 9.2% according to the WHO World Mental Health Study; this involved trained interviewers across 17 countries who were given a standardised interview protocol and trained in its use (Nock et al., 2009). Those who were interviewed in each country were chosen using household probability sampling with the aim to match national socio-demographic distributions. A total of 84,850 individuals were interviewed and countries showed significant variation in response rate (e.g., 3.0% in Italy, to 15.9% in New Zealand). The majority of 'probable suicide' globally occurs in India and rural China, two areas that were not included in this WHO survey, which may have slightly decreased the rate of suicidal ideation. Other limitations were that certain disorders were omitted from research in some countries and not others (e.g., substance abuse was omitted in European research, while schizophrenia and similar psychosis-based disorders were universally excluded), which means that the average is not calculated across all criteria in all countries.

The higher bound of the prevalence of suicidal ideation, 22.3%, came from a meta-analysis of college student samples, though inclusion in the analysis was restricted to studies using probability sampling, in an attempt to prevent an over-representation of psychology and sociology students (Mortier et al., 2018). The average age-of-onset for suicidal ideation is thought to be late adolescence or young adulthood, essentially college age (Glenn et al., 2017). As such, while reports with college students do generally report higher rates than community samples, it is also true that individuals are not consistent in their reports of lifetime ideation, which could be the cause of some of the discrepancy (Eikelenboom et al., 2014). For these reasons, it seemed appropriate to use a large college meta-analysis as a ceiling prevalence for ideation.

1.2.2.3. 'Probable Suicide' Attempts

While discussed more in the context of non-suicidal self-injury (NSSI) below, a factor of great importance for greater 'probable suicide' risk is evidently self-directed violence, especially when coupled with serious intent to harm. This self-directed violence is thought to habituate the individual to physical pain and increase fearlessness around death, thus predisposing them to acting out more severe, and subsequently fatal injuries (Gratz, Spitzen and Tull, 2020). Furthermore, previous 'probable suicide' attempts are often included as factors in models attempting to predict ‘probable suicide’ and are thought to be one of the better predictors (Bostwick et al., 2016, Nock et al., 2018). As such, the general prevalence, relative to other known risk factors, was key to illuminating the prevalence of ‘probable suicide’, its risk factors, and whether the current records of prevalence rates point towards prediction being numerically possible.

The lower bound of the ‘probable suicide’ attempts in the general community, at 2.7%, comes from the same WHO World Mental Health Study as the value for suicidal ideation (Nock et al., 2009). The same caveats apply around a potential underestimation of the prevalence, as areas around the globe with the highest incidence of ‘probable suicide’ were not included.

The upper bound for ‘probable suicide’ attempts was 4.2% and came from a feasibility study for the World Health Organisation SUicide PREvention-Multisite Intervention Study on Suicide (WHO/SUPRE-MISS), which was piloted in Queensland, Australia (De Leo et al., 2005). The sample was randomly chosen from telephone numbers in a local directory, which was sex-stratified, and a total of 11,572 subjects responded. Those who endorsed ‘probable suicide’ attempts were sent a postal survey, which investigated suicidal behaviour in more detail. Brisbane and the Gold Coast were the cities chosen for the survey, therefore this research did not include any rural communities; this, then, may under-represent prevalence of ‘probable suicide’ attempts in the general population, as the rural population is associated with more loneliness and possibly more suicidal behaviour as a result (Fitzpatrick et al., 2021).

1.2.2.4. Non-Suicidal Self-Injury

While difficult to distinguish between self-harm and ‘probable suicide’ attempts, it is a necessary challenge; there is an intuitive progression from minor injury, that may or may not be related to suicidal ideation, to an acquired capability for more intense and damaging injuries that could be fatal (Glenn et al., 2017, Gratz, Spitzen and Tull, 2020). This features in some theories attempting to explain the progression from suicidal ideation to action (e.g., the Interpersonal Theory of Suicide; Van Orden et al., 2010 and the larger Integrated Model by Hamza, Stewart and Willoughby, 2012). Both of these theories posit that repeated, self-directed acts of violence could increase the acquired capability for further, more painful acts – this is corroborated by studies that demonstrate more severe NSSI is a stronger predictor of later ‘probable suicide’ attempts than moderate NSSI (Hamza, Stewart and Willoughby, 2012).

Furthermore, there is an important debate relative to the chronology of NSSI and suicidal ideation or desire. A study in American military veterans found that, for the majority of individuals with both NSSI and suicidal ideation, the ideation emerged first (67%; Bryan et al., 2015). This would suggest that the practice of NSSI can be a sign of more significant distress than the non-suicidal terminology may imply; these individuals were, to some degree, already experiencing suicidal ideation and then acted in self-injurious ways to navigate that desire. While the study could be influenced by the fact that it was a military personnel sample, the direction of impact would be hypothesised to reduce the need for prior NSSI. These individuals have likely been exposed to substantially greater levels of violence than the average citizen and may, therefore, have acquired capability for self-directed violence from other pathways. This debate over the chronology of NSSI, while salient for the whole field of ‘probable suicide’ research, is somewhat beyond the scope of this thesis, though it forms a key piece of context for the diagram, and the later investigation of possible self-harm events within my data.

In the general community, the lower bound reported for NSSI over the lifetime was 5.5%, according to a review and meta-analysis (Swannell, et al., 2014). The samples of the included studies could not be clinical, incarcerated, detained or intellectually unable to give informed consent and cumulatively came to 231,553 individuals, from studies between 1993-2012. This review constructively highlights a common problem with defining and researching NSSI, which was that the significant variation noted could be partially accounted for by differences in study design. Studies in which a binary measure for self-harm (yes/no) was used resulted in lower rates of self-harm, than studies in which a checklist of possible methods of NSSI were listed and participants were asked to select items relevant to their histories.

The higher bound, again in the general community, was 17% and again came from a college sample that was representative of the demographic profile of the student population of the university (Whitlock, Eckenrode and Silverman, 2006). It was conducted in the United States, however it was chosen as it had a relatively large sample size, with 2,875 individuals. As in the explanation given for the suicidal ideation prevalence, also based on college age participants, this value was chosen as it would likely represent the ceiling value, as the majority of self-harm is reported in adolescent samples and then decreases over time; this could suggest a change in the perspective of the individual or cohort effects (Vega et al., 2018). One more concerning explanation for why the prevalence of NSSI decreases over the age range, is a lack of consistency in individual's own self-reported histories. Studies have indicated that suicidal ideation or 'probable suicide' attempts were more likely to be reported at subsequent interviews, if the individual still displayed psychopathological symptoms, compared to those who had remitted (Eikelenboom et al., 2014). This aspect of continued or discontinued relevance is a key area for future research into meaning-making and memory.

1.2.3. Risk Factors for 'Probable Suicide' in a Clinical Setting

Following on from the general lifetime prevalence in the community of these risk factors, the right-hand side of the diagram was to represent the lifetime prevalence in individuals seen in psychiatric illness samples. The aim was to understand the rate of each of the risk factors, which would evidence the feasibility of creating strong predictive models that are primarily reliant upon these specific factors. The values reported all came from studies which focused either on individuals with a mental health diagnosis or were identified from psychiatric healthcare clinics; as these studies were found in a broad search across the literature, the diagnostic criteria and diagnoses examined in the papers does differ. As such, these rates do not precisely reflect the same populations and do not compare like-for-like, however an illustration of the clinical prevalence was valuable enough to be constructed despite this limitation.

The prevalence for death by 'probable suicide' within the population of people with a mental illness was calculated from the Lundby study, which was a long-term research project in Sweden; field interviews were undertaken in 1947, with subsequent waves of data collection in 1957, 1972 and 1997 (Holmstrand et al., 2015). Data was collected either from the original individual interviewed, key informants (e.g., family, clerics or doctors) or hospital or autopsy records. Over the study, 1,528 of the 3,563 individuals received a psychiatric diagnosis of some kind, and 62 of these diagnosed individuals died by 'probable suicide'. The prevalence, therefore, of 'probable suicide' in the sub-section of individuals with any diagnosis was 4.1% over 50 years. There are limitations to this study. Arguably most importantly, the diagnostic criteria used was unique and designed for the study, as there was no established diagnostic system in 1947. The 1997 data collection wave used the Lundby criteria, as well as the DSM-IV and ICD-10 for assessing psychiatric diagnoses; an investigation of inter-rater reliability on psychiatric diagnoses found a kappa score of 0.6 in a random sample of 200 individuals from the study (Nettelbladt et al., 2005) and an investigation into 'probable suicide' risk that also re-coded diagnoses with DSM-IV criteria found very similar risk levels across diagnostic criteria used, which suggests good agreement (Brådvik et al., 2008). Another limitation is that the study was conducted in a rural area of Sweden, and so may not accurately represent a present-day, urban population, though the risk levels identified in specific diagnoses (e.g., 6% 'probable suicide' risk in depression that was noticeably impairing the individual) is corroborated by other studies (Inskip, Harris and Barraclough, 1998).

1.2.3.1. Suicidal ideation

A recent study constructively noted that previous publications attempting to illustrate the prevalence of suicidal ideation, in a cohort of individuals diagnosed with a psychiatric illness, were often limited to specific subsets of disorders or used small sample sizes (Baldessarini and Tondo, 2020). As such, 6,050 patients from Sardinia were identified from a treatment centre for psychiatric disorders, with medical histories reported by patients at intake and summarised data extracted from medical records since 2000. The lower and upper bounds on the diagram were 21.4-39.4%, which was the 95% confidence interval for suicidal ideation across all psychiatric disorders considered by the study authors. These included anxiety, mood and substance misuse categories, as well as schizophrenia and psychotic-type conditions. The treatment centre specialised in supporting those with mood disorders, with diagnoses of major depression contributing 42% (2,560/6,050) of the patients. Therefore, the values for suicidal ideation will be affected by the considerably larger proportion of mood disorder patients, compared to those with other diagnoses, like substance use patients (86/6,050 or 1.4%). As depression and mood disorders are the most common psychiatric illnesses, the relatively wide margin given seemed appropriate as a likely range for the true prevalence of suicidal ideation within a clinical population.

1.2.3.2. 'Probable Suicide' Attempts

For the lower bound of a lifetime history of 'probable suicide' attempts, a study examining the interpersonal-psychological theory, specifically the acquired capability dimension, identified 492 patients from an outpatient clinic (Anestis and Joiner, 2011). These individuals filled out a variety of questionnaires detailing symptoms and measures around negative urgency (impulsivity related to a desire to distance oneself from negative emotion), as well as general history of suicide-related behaviours. Of these patients, 15.4% indicated at least one 'probable suicide' attempt on the Beck Suicidal Intent Scale, in which this is addressed in only one question and leads to similar concerns of under-reporting through the use of different criteria eliciting different responses from participants (Eikelenboom et al., 2014).

The upper bound for 'probable suicide' attempts was 52.1% (O'Hare, Shen and Sherrer, 2014). This value came from a study examining 4 community mental health centres in Rhode Island, but focused only on 371 individuals with serious mental illnesses (schizophrenia, major depression or bipolar disorder). This study was particularly interested in the effect of trauma in determining suicidality in cases of serious mental illness, therefore the interviews focused on those aspects, with only one question each for lifetime 'probable suicide' attempt and self-harm history. Medical records were investigated, though recall bias is likely to have affected the answers given by the participants. Including this study in the diagram is likely an over-estimation of the average prevalence in a clinic, as only serious mental illnesses were considered, however other papers often report lifetime 'probable suicide' attempts in the context of a study examining only one psychiatric disorder or report per 100 person-exposure years (Baldessarini and Tondo, 2020). Neither of these would be consistent with the rest of the diagram, thus this value was included.

1.2.3.3. Non-Suicidal Self-Injury

Finally, NSSI in the clinical population was hypothesised to be significantly greater than in the general population. In spite of this, finding studies considering NSSI directly, across the lifetime of the patient and including a wide age range was challenging. Many considered deliberate self-harm, with criteria that included suicidal intent (the importance of intent of self-harm is briefly discussed in Zetterqvist, 2015 and Goodfellows, Kõlves and De Leo, 2019), and many studies included primarily an adolescent or young adult population (Shahwan et al., 2018, Glenn et al., 2017). The focus was on NSSI specifically, and this limited the choice of paper for this aspect. As such, the lower bound in the diagram, which was 24.2%, came from a study of 239 adolescent outpatients recruited from a psychiatric service in Madrid from November 2011 to October 2012 (Garcia-Nieto et al., 2015). The patients were administered the Spanish version of the Self-Injurious Thoughts and Behaviors Interview, over the course of a semi-structured interview, yet corroboration with medical records seems to be missing and is one of the limitations of this paper. Other limitations are that the diagnostic criteria used seemed primarily focused on depression, rather than any other psychiatric illness, and that as an adolescent sample, the result cannot be a true lifetime prevalence. As noted, studies that examined a wider population investigated deliberate self-harm of all kinds, and therefore, would also introduce serious flaws into the diagram by conflating actions with suicidal intent and self-harm (Zetterqvist, 2015).

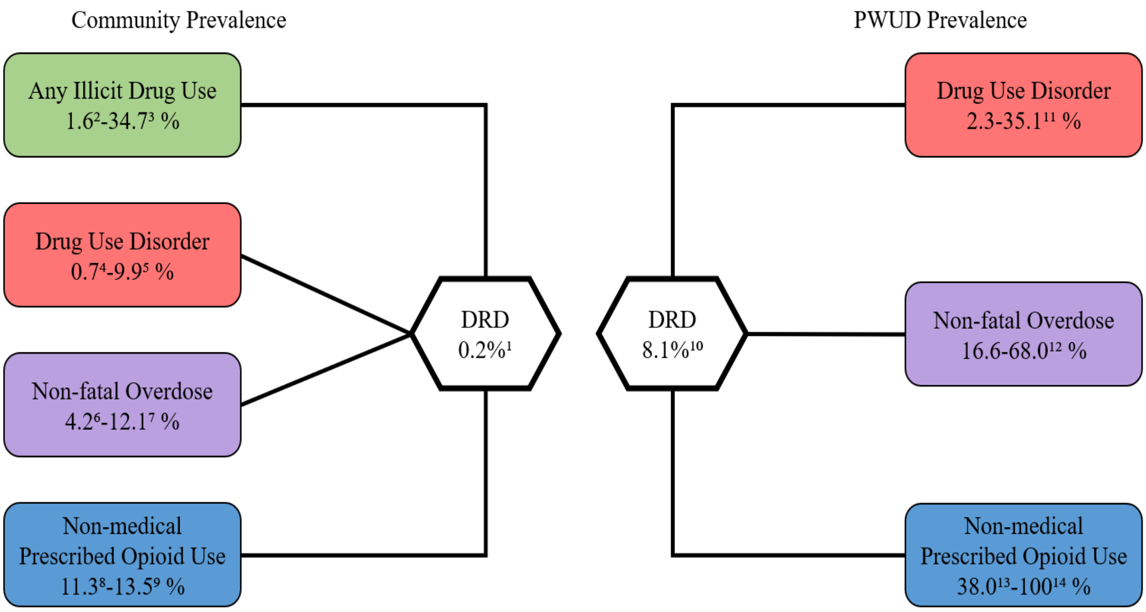
The upper bound for the prevalence of NSSI was 54.5% in a psychiatric outpatient sample from South Korea, with 191 participants aged between 18-60 years old (Yang et al., 2022). Patients were recruited from January 2019 to November 2020, with diagnoses of bipolar disorder (type I and II) or recurrent major depression and lifetime histories of self-harm were recorded on self-report questionnaires. This study was one of few that examined lifetime NSSI in adults rather than only young adults or adolescents; Shahwan et al. (2018) reported 58.8% NSSI across 400 outpatients between 14-35 years old, while Glenn et al. (2017) reported 79.2% of 106 outpatients between 12-19 years old endorsed NSSI in a structured interview. While there are certain limitations in Yang et al.'s paper, especially that patients were only included with one of two types of severe psychiatric illness, it was chosen because it was a recent example, with a wider age range than commonly reported. The limitations reveal an unanticipated gap in the literature, for which accurate data would be highly valuable.

1.2.4. Prevalence of Drug-Related Death

The construction of this diagram was more challenging than that of the complementary diagram for ‘probable suicide’, primarily due to the variety of substances that could possibly be included. As such, the ranges are significantly larger than in those reported in the ‘probable suicide’ risk factors diagram, because some values come from studies examining rare and severe profiles of substance use (e.g., those who inject heroin), versus drug use considered to be lower threshold and more prevalent (e.g., cannabis use). As a note, the majority of the research used in this diagram comes from studies set in the United States, due to the longer-term and considerably larger epidemic of DRD.

As with the prevalence for ‘probable suicide’, the data for the prevalence of DRD was sourced from the Global Burden of Disease study, as available in the IHME portal (https://ghdx.healthdata.org/gbd-2019). For 2019, the worldwide percentage for deaths from drug use disorder was 0.2%. The data seems relatively consistent, in that the value for 1990 was 0.1% worldwide. This is a considerably smaller definition than most DRD definitions, as certain relevant categories of ICD-10 codes were not included. Due to the coding format of the IHME portal, intentional and unintentional poisonings could not be extracted from a wider poisoning measure that includes accidental deaths, thus this was considered to be too non-specific. For reference, the poisoning value was 0.1% of deaths worldwide in 2019. On the other hand, the value for deaths from substance abuse could have been used. This category includes deaths from alcohol, and indeed, the majority of the ICD-10 codes that form the definition relate to alcohol use disorders. The percentage of global mortality for that category, in 2019, was 0.5%. As such, the value in the diagram is a notable underestimate, but in an attempt to follow convention and consider primarily illicit drugs, it seemed the most fitting to include.

Figure 1-2. Prevalence and Risk Factors for DRD



The left-hand side of the diagram illustrates the lifetime prevalence as calculated by a variety of longitudinal and survey studies in the average community setting. For example, 0.2% of deaths worldwide are reported to be DRD, while between 1.6-34.7% of individuals report some illicit substance use over the course of their lives. The right-hand side of the diagram includes measures on the same behaviour related to drug use and misuse, but includes studies and percentages from samples identified from for example, OST or needle syringe programs, ensuring that the individuals had at least a history of lifetime illicit drug use.

The superscript numbers refer to the articles providing the percentages, which were:

[1] GBD Collaborators, 2019. [2] Martins et al., 2017. [3] Home Office, 2015.[4] Martins et al., 2017. [5] Grant et al., 2016. [6] John et al., 2016. [7] Bohnert et al., 2018. [8] Grant et al., 2016. [9] Novak et al., 2016.

[10] Degenhardt et al., 2009. [11] Degenhardt et al., 2019 (a). [12] Martins et al., 2015. [13] Gittins, Missen and Maidment, 2022. [14] Havens et al., 2020.

1.2.5. Risk Factors for DRD in the General Population

1.2.5.1. Any Illicit Drug Use

Evidently, an important risk factor for DRD is prior drug use. The few estimates of DRD without prior drug use are limited to small-scale national mortality reports; one conducted by the ONS (2018) reported that 80% of the individuals had evidence of prior use, though only 115 individuals were investigated. The National Drug-Related Death Database (NDRDD) in Scotland likewise reports that 87% of those who died in 2018 were known to have used drugs prior to death. The sources for these percentages are somewhat unclear; the ONS used only coronial records and the NDRDD noted that the evidence came from "health, social care or other partner agencies" (NDRDD, 2022). No peer-reviewed published literature could be found that specifically produced reliable estimates of the number of individuals dying from drug-related causes who had no prior history of drug use. This is an area which requires further research, as understanding the profiles of first-time users versus regular or chronic users of substances, and the different associations with mortality, is key for designing targeted interventions.

As previously discussed, there is a compelling debate surrounding which substances ought to be classified within common DRD statistics, especially with the awareness of the changing political climate on drug legality. This key question is also relevant when attempting to identify the rate of past drug use, however to maintain coherence with the general literature, "drug use" in this diagram refers to use of illicit substances or those acquired illicitly.

The lower bound value in the diagram shows 1.6% of individuals reported heroin injection at some point in their lives, in an American population survey study conducted between 2012-2013 (Martins et al., 2017). This face-to-face interview study, the National Epidemiologic Survey on Alcohol and Related Conditions, is undertaken by the National Institute of Health, funded by the United States government to periodically measure population health. As the authors note, this was a notable increase since the 0.3% value reported in the 2001-2002 population study, and of serious concern for the general health of the population. One caveat is that this population study is based on households, and therefore does not include any data on rates of illicit drug use in the homeless or military veterans. Both of these groups are linked with high rates of illicit drug use, and, therefore, inclusion of them would likely have elevated this percentage further. Additionally, face-to-face interviews may result in fewer people endorsing lifetime drug use than is true. On the other hand, heroin and other-opioid misuse is significantly more common in the States than in other continents. As such, it was included as a proxy for a general low-bound of illicit drug use in the lifetime, specifically to highlight the variation in prevalence, and the very low rate of prevalence of the riskiest use profile (injection). A likely influence, unacknowledged by the authors and generally disregarded in the discussion of heroin usage, is that a significant volume of opium is produced in Afghanistan. Outside of literature specifically examining the history of opioid production, the rapid increase in opium cultivation after the overthrow of the Taliban regime in 2003 is unheeded (Farrell and Thorne, 2005, Todd, Safi and Strathdee 2005). These historical and geo-political influences exert an impact of the production and accessibility of drugs, and ought to be recognised in scientific debate.

The upper bound in the diagram reports that 34.7% of individuals, this time from a nationwide UK study, had ever use an illicit drug in their lifetime (Home Office, 2015). Chosen intentionally to contrast with the previous study, this relatively high percentage was overwhelmingly associated with lifetime cannabis use, rather than substances thought to be more severely detrimental to health. As with the American population study, data from particularly vulnerable and high-use groups like the homeless, were missing, therefore the rate across the general population could be slightly higher than this would suggest. Admittedly, the proportion of individuals who are homeless is relatively low, therefore any contribution to a national average of illicit drug use would be minor and should not reduce the utility of this study in providing an illustrative prevalence rate.

1.2.5.2. Drug Use Disorder

The rate of any drug use disorder is likewise challenging to identify; including only individuals undergoing medical treatment would exclude potentially as much as half of the relevant population (following estimates that around 40% of individuals indicated for OST actually receive these therapeutic prescriptions as described by Larney et al., (2017) and van Amsterdam, van den Brink and Pierce, (2021)). As such, epidemiological surveys were again searched for illustrative percentages for the prevalence of drug use disorders.

The lower bound reported came from the National Epidemiologic Survey on Alcohol and Related Conditions in the United States, as previously described, though this value came specifically from an analysis that characterised the rates of heroin use and investigated trends in the data from the wave in 2001-2002 and the 2012-2013 wave. It found a prevalence of heroin use disorder in the general population at 0.7% in the most recent data collection wave (Martins et al., 2017). The same limitations as before are relevant here; as a household survey, sub-sections of the population (especially homeless individuals) would not be included and the face-to-face interview protocol may have reduced the willingness of participants to admit to illicit drug use. Likewise, the rationale explained above, for using heroin injecting as the lowest bound for any illicit drug use (again from Martins et al., 2017), is congruent with the inclusion of heroin use disorder representing the lowest bound for lifetime drug use disorder prevalence.

The value of 9.9% was reported in the same National Epidemiologic Survey on Alcohol and Related Conditions, an interview-based survey administered to households on a periodic basis (Grant et al., 2016). This value specifically includes “amphetamine, cannabis, club drug, cocaine, hallucinogen, heroin, nonheroin opioid, sedative/tranquilizer, and/or solvent/inhalant use disorders”, and as such, reflected the key substances of interest. The limitations noted above are also applicable here. Other values were found for this box, primarily from the appendices of a summary of four systematic reviews investigating global drug dependence prevalence, published by Degenhardt et al. (2011). While data for lifetime prevalence was overwhelmingly missing, a small number of studies had been identified; one reported a value of 3.1% for methamphetamine dependence in New Zealand, however the study included individuals only up to the age of 25, which is evidently a very limited lifetime prevalence survey (Boden, Fergusson and Horwood, 2006). Other studies in these appendices used similarly limited age ranges. Therefore, the lack of other convincing options meant that the more recent data from the epidemiological study in the US was chosen. Reporting an illustrative value for the rate of drug use disorders, outside of the States, was challenging, which was unanticipated, and reveals a need for up-to-date data on the prevalence of these conditions for healthcare metrics.

1.2.5.3. Past Non-Fatal Overdose

Previous studies have highlighted that DRD mortality is associated with prior overdose, therefore the rate of non-fatal overdoses in populations of OST users has been investigated repeatedly (Sordo et al., 2017, Lyons et al., 2019, Martins et al., 2015). The rate of non-fatal overdose, without being limited to opioids and without the population being likewise restricted to individuals who use drugs has been little discussed. A study listing the lifetime prevalence of any kind of overdose could not be found, therefore the lower bound value included in the diagram (4.2%) was identified from a short-term study investigating non-accidental non-fatal poisoning, as documented in the electronic records of calls made to the ambulance service, across the entirety of Wales (John et al., 2016). Indisputably, it is undesirable to include this study. It covers a scant three months (December 2007 to February 2008) in a diagram attempting to summarise the lifetime prevalence of a variety of phenomena related to drug use. As other papers identify the rate only in populations who use drugs (Lyons et al., 2019, Martins et al., 2015), this study was chosen as an illustration of the lack of available, accurate data, despite electronic health systems that could be used to complement epidemiological surveys.

The upper bound for lifetime non-fatal overdoses in the general population was 12.1% from a study in Michigan (Bohnert et al., 2018). Recruitment occurred between 2011-2013, with days of the week covered on a rotating schedule and with 4,573 patients randomly chosen to be approached later for the survey, which included a lifetime self-report history on overdose experience. Males were more likely to refuse to participate, which is one of the limitations of the study, as men use and misuse substances at greater rates than women. The aim of this study was to investigate prior experience of overdose, relative to intent and medical symptoms, to inform brief interventions that could be administered in emergency services; therefore, it was not designed to collect the prevalence of the general population, however no study could be found that fulfilled the brief exactly. Therefore, while the study likely over-estimates the prevalence of non-fatal overdose in the wider community by relying on individuals presenting to emergency services, it did include a measure of lifetime overdose. In the absence of publications fulfilling the criteria more closely, this paper with a large sample size was included to counter-act the short-term survey acting as a lower bound prevalence.

1.2.5.4. Prescribed Opioid Misuse

One particularly challenging aspect of drug use and misuse concerns prescribed opioids. Defining the true prevalence of non-medical prescription opioid use in the general population is complex, due in part to ambiguous criteria and because much of the recently published literature focuses on determining abuse and dependence within populations of chronic pain patients. A commonly accepted paradigm is that non-medical use extends from taking medication in a way that does not conform to prescriber guidelines, to using drugs diverted from family and friends, or acquiring drugs illicitly. Chronic pain is thought to be present in anywhere between 19-51% of the population (Breivik et al., 2006, Fayaz et al., 2016), with sizable variance due to differences in rating scales for the intensity of pain and its interference with daily life and functioning. There is a debate about how best to manage chronic pain, especially due to the risk of addiction and dependence with prolonged opioid use. The origin of the recent opioid-related epidemic has been regularly linked to the serious under-representation of the risk of addiction after opioid prescriptions for pain management. As a result, there were exponential increases in opioid prescriptions, especially in the States and subsequent increases in misuse and addiction to opioid drugs (Salmond and Allread, 2019).

Few references could be found that gave a lifetime value for non-medical prescribed opioid use in the general population. Data from the same American survey described above (the National Epidemiologic Survey on Alcohol and Related Conditions) reported a prevalence of 11.3% from the 2012-2013 data collection (Grant et al., 2016). Previous limitations are pertinent here; as a household survey, sub-sections of the population (especially homeless individuals) would not be included and the face-to-face interview protocol may have resulted in fewer participants acknowledging illicit drug use.

A slightly higher value of 13.5% was reported, averaged across five European countries: Denmark, Germany, Great Britain, Spain and Sweden (Novak et al., 2016). Using a quota sampling technique, which attempted to determine nationally representative cohorts in each of the countries, individuals were identified on the basis of age, sex and marital status, as well as tobacco and marijuana use, as these were all expected to affect exposure to and use of illicit drugs. The sample size was 22,070 and of those, 20,038 were 18-49 years old, on the basis that this age range is when substance misuse commonly begins. An interesting result was that 44% of the individuals sourced their opioids through family or friends. There are some limitations, which is that some individuals for the study were recruited from open-air drug markets, needle exchanges and homeless shelters, as well as from advertisements in local newspapers and outreach at libraries. As such, it is plausible that the supposedly general population contained a much larger proportion of individuals who used drugs, which may have artificially increased the rate of non-medical prescribed opioid use reported. The rate of cannabis use reported by this study was very similar to that reported by other studies, which would suggest that the sample included represented the general population relatively well.

1.2.6. Risk Factors for DRD in PWUD

DRD risk is very dynamic and, therefore, is highly influenced by a variety of factors, like being in or out of treatment, the substances used and the route of administration, as well as being affected by demographic and socio-economic status (Degenhardt et al., 2019 (b), Sterling and Platt, 2022, Santo et al., 2021). For the right-hand side of the diagram, the value of 8.1% represents an approximation of the prevalence of mortality from direct drug-related causes in the population of people who use drugs, as identified from National Health Service records of OST prescription in Australia. This value was extracted from a study on mortality in those on OST over 20 years, in which 3,803/42,676 individuals died (Degenhardt et al., 2009). Appendix 5, available online, lists the causes of death, and shows that 3,340 of these deaths were due to specifically: accidental drug-related, accidental opioid-related and other drug-related causes. The inclusion of 'probable suicide' would have increased the total by 449 deaths, however there was no breakdown available for whether these deaths were self-poisoning or primarily other methods, and so these were omitted from the prevalence calculation. Based on the total number of individuals included in Appendix 5, the prevalence of DRD in a sample of people receiving OST was 8.1% over 20 years (3,340/41,390). It is probable that the true prevalence of DRD in PWUD is higher, as OST is well-known to decrease the risk of mortality (Santo et al., 2021). Studies researching illicit drug use regularly use samples from individuals on OST, as these are a more accessible group than those who use illicit substances without healthcare service engagement (Degenhardt et al., 2009). As such, this method was chosen.

1.2.6.1. Drug Use Disorder

Determining the rate of dependence or addiction in the population of people who use drugs appeared to be notable gap in literature, though this is likely affected by the previously acknowledged difficulty in contacting and researching cohorts of people who use drugs. Only one recent study could be found, which was based on the WHO Mental Health Survey (WMH), and specifically analysed the responses considering transition from use of drugs to physiological and behavioural problems that would indicate dependence or addiction, depending on the severity of the symptoms (Degenhardt et al., 2019 (a)). This global survey was administered in two parts, with the detailed questions about drug use asked only of the respondents who indicated prior drug use, however criteria between countries varied; some countries asked these questions following any slight indication of drug use, others only if the individual indicated use for five or more days, with 20 days of prescription misuse required by the Spanish survey to qualify for follow-up drug use transition questions. Potentially affected by the differences in criteria, the range for transition to dependence, or abuse, from initial use was quite large. Results from Bulgaria indicated only 2.3% progressed to fulfilling disorder criteria, while Australia reported 35.1% of drug users met criteria for lifetime drug use disorder. One key flaw with the WMH surveys is that they are household-based, with stratified sampling; this would, by nature, exclude individuals who are likely to report higher rates of drug addiction and dependence (e.g., people who are homeless or in prison).

1.2.6.2. Past Non-Fatal Overdose

Past non-fatal overdose is described as a common risk factor for DRD, and often represents a treatment outcome that research groups investigate to demonstrate that an intervention improves health and quality of life (Santo et al., 2021). This is corroborated by small-scale studies that have indicated that non-fatal overdose is indicative of some desire to die in the majority of individuals (Gicquelais et al., 2020, Connery et al., 2019). A global review reported between 16.6-68% of individuals who use drugs had ever experienced an overdose, and this wide range was included in the diagram (Martins et al., 2015). A significant number of the studies considered only heroin or drugs that were injected, which would reflect more severe profiles of drug use, and as such it is logical that this sub-population would have a greater rate of overdoses than people who have a less risky drug use profile. The lower bound actually came from a study which questioned overdose rates in the last 6 months, though the sample included was 772 individuals who had been injecting heroin for at least one year (Coffin et al., 2007), thus it is likely that the lowest bound for lifetime overdose is actually higher than 16.6%. The upper bound was 68.0% in two studies: Galea et al. (2006) and Darke, Ross and Hall (1996). Both studies were small, especially Galea et al.'s (2006) which was a pilot study of 25 individuals who injected drugs. These individuals were trained to recognise an overdose and administer naloxone, then followed up for three months to record their knowledge and willingness to intervene. Darke et al. (1996) interviewed 329 heroin users, with a detailed investigation of the substances used in their overdoses; however, the full-length version of this paper could not be accessed. A recent study gave a value of 62.5% of 469 participants experiencing a non-fatal overdose in their lifetime (Shrestha et al., 2021), which corroborates this high percentage in the sub-population of individuals who use drugs.

1.2.6.3. Prescribed Opioid Misuse

On the right-hand side of the diagram, considering the prevalence of prescription opioid misuse in the population of individuals who use illicit drugs, one review paper could be found which the authors noted was "thought to be the first review of the published literature pertaining to OTC/POM misuse in SMS (substance misuse services)" (Gittins, Missen and Maidment, 2022). No summary prevalence was calculated in their narrative review, and only papers analysing samples from the UK were included. Nonetheless, it constructively highlights the paucity of prevalence data in the UK, and demonstrates that the little data there is comes from studies with small sample sizes (the largest sample being 297 individuals). As such, the value in the diagram, was extracted from an older paper specifically interviewing 53 people who injected substances and were new attenders at NHS drug treatment facilities (Armstrong, 1992). This letter to the editor reported that 66% of the sample had abused over-the-counter medication at some point in their substance use history; a substantial percentage had abused a stimulant and 38% abused an opiate-containing preparation. Up-to-date data is urgently required.

A larger American study followed individuals in Appalachia, from 2008 to 2017, after an initial survey which identified networks of rural drug users through respondent-driven sampling (Social Networks among Appalachian People) (Havens et al., 2020). Initially, 503 individuals were identified as having used “prescription opioids, methamphetamine, cocaine or heroin for the purposes of getting high” in the past month and the follow-up rate over the decade was between 84-92%. All 503 individuals reported some non-medical prescription opioid use, which on the basis of the “getting high” caveat, represents misuse in their analysis and in my diagram. As misuse of prescription opioids was part of the criteria for study inclusion, it is likely that 100% of individuals misusing prescription opioids is a significant over-representation of the true prevalence. Studies investigating prescription opioid misuse in urban samples report a much lower prevalence of approximately 40%, which has been linked to the easier access to heroin in cities, and therefore less of a need for alternative opioids (Lake et al., 2015). Furthermore, prescribed opioids are a much greater concern in the United States, than in Europe, which prescribes a considerably smaller volume of opioids and does not seem to be undergoing an opioid crisis similar to that in the States (Pierce et al., 2021). This difference further demonstrates the need for current, geographically specific data, which takes into account the history and context of prescription and illicit drug use in each country.

1.3. Current intervention Strategies

Successful intervention strategies follow the simple principle of ameliorating the impact of causal risk factors. Franklin et al. (2017) described this principle well in their article, and emphasised that identifying these causal risk factors and understanding how to moderate them would be the most efficient and efficacious path to ‘probable suicide’ prevention. This can reasonably be extrapolated to DRD prevention. These principles are reliant on the knowledge of causal risk factors and how best to counter-act them. As ‘probable suicide’ is heavily associated, in published literature, with diagnoses of mental illness, the common and intuitive assumption is that greater provision of psychiatric healthcare would successfully prevent ‘probable suicide’. For DRD, post-mortem toxicology generally reports multiple drugs in the body, and that the majority of individuals had at least one opioid drug (NRS, 2021 (a), UNODC, 2022). As such, the predominantly recommended intervention is OST (Larney et al., 2017). While these strategies have been associated with some reductions in mortality (Fox et al., 2020, Santo et al., 2021), it is key to note that these are only small reductions. This section will give an overview of the benefits and limitations of these treatments, which are regarded as the best options available.

1.3.1. Preventative Interventions for ‘Probable Suicide’

As demonstrated by Fox et al. (2020) in their meta-analysis, there is a wide variety of available interventions that aim to reduce the rate of self-injurious thoughts and behaviours. Many of these are variants of cognitive and behavioural approaches (e.g., talking therapies), gate-keeper training in institutions and pharmacotherapy. Rather disconcertingly, the meta-analysis also reports that these interventions are associated with small reductions in mortality, and that the past 50 years of research have not measurably increased these effect sizes. Indeed, one of the most effective interventions to reduce ‘probable suicide’ has been the restriction of access to means, rather than any targeted intervention. This includes a range of actions, for example: changes to sizes of paracetamol packages, placing railings or preventing access to rooftops and changes from coal gas to natural gas in UK homes (Fox et al., 2020, Bachmann, 2018, Lim et al., 2021). These are important caveats to be aware of, during the discussion of how best to intervene and reduce ‘probable suicide’. As the data available for this project was NHS data, which included prescription records but had no record of talking therapies, only the context for antidepressant prescription and 'probable suicide' will be discussed subsequently.

It is evident that antidepressant prescriptions are efficacious medications and do reduce the severity of the symptoms of depression (Cipriani et al., 2018). Both the results of the previous meta-analysis and a large clinical trial (Gaynes et al., 2009) found very little difference between antidepressants in their efficacy of inducing remission, though certain prescriptions (e.g., escitalopram and mirtazapine) had higher response rates and lower drop-out rates. This indicates that certain drugs are more tolerable to adult patients, however available clinical guidelines are non-specific in terms of allocating certain prescriptions to one sub-group or other (NICE, 2022 (b), Fox et al. 2020). Indeed, the main recommendation is to ensure a minimum length of 6 months prescription after remission to prevent a relapse (NICE, 2022 (b)). Studies report that early discontinuation of antidepressant prescribing is very common, especially when prescriptions are filled by GPs (Solmi et al., 2021). This has not always been linked with an increased risk of 'probable suicide', though this may be due to a similarly high rate of discontinuation in the control sample (Castelpietra et al., 2018). In this study, treatment modifications were associated with slightly increased risks of 'probable suicide', which would logically imply that treatment-resistant depression is more concerning than symptoms that are ameliorated by the initial prescription. Between discontinuation not leading to a significant increase in 'probable suicide;' risk, and that prescriptions have been associated with only small reductions in mortality (Fox et al., 2020), it is likely that extending psychiatric healthcare will not deliver the significant reductions in mortality that national and international organisations aim for.

Additionally, there are reports of an increased risk of 'probable suicide' or suicidal behaviours in children and adolescents who are prescribed antidepressants, particularly selective serotonin re-uptake inhibitors (SSRIs) (Gupta et al., 2016). An umbrella review concluded that this finding, though statistically significant, was likely affected by confounding by indication (Dragioti et al., 2019). Due to the ambiguous nature of the available observational data, only fluoxetine is currently recommended for young patients (Cipriani et al., 2018). Further research is necessary to clarify the impact of antidepressant prescription in this age group.

The final piece of context for understanding the relationship between ‘probable suicide’ and antidepressant prescription, would be accurate data describing the prevalence of past-year and past-month antidepressant prescription in a cohort of ‘probable suicide’ decedents. In an Italian study, during the period 2005-2014, there were 1,260 ‘probable suicide’ decedents in the region (Castelpietra et al., 2017). Of these, 876 or 69.5% received an antidepressant prescription within two years of death, though only a quarter of these were reported to be adherent to their medication at the time of death. Unfortunately, the data reported could not be used to narrow down this ante-mortem period further. A more recent Swedish study focused on ‘probable suicide’ rate and antidepressant prescription only in young women; it found that 52% of young women had received an antidepressant prescription in the year before death, between 2009-2013 (Larsson, 2017). This study also reported that while the rate of antidepressant prescription in this demographic group had increased since 1999, so had the number of ‘probable suicide’ per year. As such, the author challenged the suggestions that increasing the rate of antidepressant prescribing would be a simple and effective avenue for ‘probable suicide’ prevention. Within Scotland, the latest ScotSID report considering the whole cohort of ‘probable suicide’ decedents in one year (2021 (b)) reported that 52.1% of the entire ScotSID cohort had received at least one antidepressant prescription within the year before death. As mental illnesses other than depression are also associated with an increased risk of ‘probable suicide’ (Baldessarini and Tondo, 2020), it would be incorrect to assume that the individuals without an antidepressant *ought* to likewise receive one.

Taken together, these results all suggest that the relationship between antidepressant prescribing, episodes of diagnosed depression and ‘probable suicide’ is quite complex. That antidepressants are effective treatments for depression is clear. Likewise, it is evident that a relationship exists between depression, particularly severe symptoms or treatment-resistant phenotypes, and an increased risk of ‘probable suicide’. That greater rates of antidepressant prescriptions will lead to a reduction in ‘probable suicide’ is considerably less supported by available data, with some reporting that increased prescriptions may be associated with higher numbers of ‘probable suicide’, due to confounding by indication (Larsson, 2017, Castelpietra et al., 2017). Further research, both at population and individual levels are required to clarify these interactions, and identify patient needs more accurately.

1.3.2. Preventative Interventions for Drug-Related Death

That so many DRD include an opioid of some kind has been of increasing international concern (NRS, 2021 (a), UNODC, 2022, Pierce et al., 2021). The majority of these deaths involve multiple substances, however especially with the contribution of opioid pain-killers to the epidemic (Salmond and Allread, 2019), treatment for opioid misuse has been the key focus. At the core of most opioid drug misuse treatment services, both globally and in Scotland, are the opioid substitution therapies (OST). Methadone represents the most widely prescribed substitution / maintenance treatment, although buprenorphine (a partial μ receptor agonist) is also prescribed and presents a lower risk in the event of overdose (Santo et al., 2021). Global reviews have highlighted that not all countries offer OST, and that even in countries that do offer it, considerably less than 40% of individuals estimated to require OST are in treatment (Jin et al., 2020, Larney et al., 2017). OST is somewhat controversial, due to differing perspectives on the value of harm reduction versus deterrence and abstinence, as enforced by criminal justice proceedings. There is, however, sufficient evidence that OST leads to reductions in criminality and blood-borne diseases, with an improved quality of life and limited reductions in all-cause and DRD mortality (Sordo et al., 2017, Santo et al., 2021).

There are several moderating factors on the protective impact of OST; first, the clinical dosage range for methadone is recommended to be between 60-120mg per day; however, many countries routinely prescribe it at lower doses than this range (Jin et al., 2020). Second, is that there are significant effects of time, with the first 4 weeks of OST and the first 4 weeks after treatment cessation associated with greatly elevated mortality risk (Sordo et al., 2017). Third, is that sedative co-prescriptions (e.g., benzodiazepines which may be prescribed to ameliorate the impact of withdrawal symptoms) are associated with an increased mortality risk, in a dose-dependent manner (Macleod et al., 2019, McCowan, Kidd and Fahey, 2009). Additionally, many studies note that the provision of OST for incarcerated populations is very low, despite significant indicated need (Larney et al., 2017, Degenhardt et al., 2019 (b)). Evidently, the rate of OST and its delivery in a country is fundamentally important for ameliorating the poor health associated with opioid misuse and reducing the impact of the social harms of drug use. With the relatively small levels of mortality reduction seen, a similar concern occurs as with antidepressant prescription; in that OST is likely to be insufficient to greatly reduce deaths and further acknowledgments of the wider social factors are not forthcoming in preventative campaigns (Sterling and Platt, 2022).

Clarifying the prevalence of OST, within those who die from opioid-related causes, is important for understanding the accessibility of treatment for those that could be classified as in need of this intervention. The global review, mentioned above, found that only 19 countries worldwide had a high coverage (over 40%) of OST in those estimated to be misusing opioids (Larney et al., 2017). According to this review, Scotland had only moderate to high coverage (20% to ≥40%), while England had high coverage. Another research group has suggested that the difference in DRD between England and Wales (as one unit) and Scotland may be due to lower accessibility and efficacy of OST in Scotland, leading to higher mortality (van Amsterdam, van den Brink and Pierce, 2021). They calculated that 45% of opioid users in Scotland were 'in treatment', compared to 54% of users in England and Wales. This was based on an estimated number of individuals misusing drugs, however the definitions used differed between countries, making this comparison questionable. The most recent NDRDD report found that, in 2018, 41% of the DRD cohort were receiving OST at the time of death (2022). This has increased significantly since 2009, when the comparative percentage of those "in treatment" was 21%. It is evidently promising that the number of individuals "in treatment" is increasing, however it is important to note that this is in the context of rapidly increasing DRD, which suggests other preventative interventions may be required.

In summary, the reductions in mortality that are attributed to OST are small (Santo et al., 2021, Sordo et al., 2017), however it is important to understand what the prevalence is and whether is it delivered according to best clinical guidance. Again, further research will be required, at population and individual levels, to understand the protective impact of OST, how to optimise it, and where other interventions may be required to more effectively prevent DRD. It is worth noting that there are recent calls to acknowledge the overlap between 'probable suicide' and DRD by integrating prevention strategies for 'probable suicide' with interventions designed for people who use drugs (Oquendo and Volkow, 2018), though these are not yet included in government publications.

1.4. Routinely Collected Data

The growth of electronic record keeping has meant that in recent years, incredibly large banks of data are being stored, at significant cost. Research studies are beginning to use these rich resources, and there are certain government initiatives to encourage the use of these records. There has, however, been significant controversy in the use of healthcare data for research, due to its sensitive nature and the history of breaches in data security (Oxford, 2022). These breaches have undermined patient trust in data confidentiality and led to reasonable concerns about how data is gathered, stored and utilised.

The benefits of using routinely collected administrative data are clear: the cost (to the researcher) is generally low, the sample sizes can be much larger than would be feasible for traditional study designs, a large pool of data can be linked and there is very little loss to follow-up (unlike in progressive surveys and questionnaires).

The challenges of using administrative data are also well-established: not all relevant data would be collected for any research study, the data can be several years old and there is the challenge of missing, or even inaccurately linked data records (Harron et al., 2017). Large-scale studies will also encounter the same issues as previously described; countries have different systems of archiving data and may require different burdens of proof or level of detail to allocate the same "standardised" ICD-10 codes. Additionally, some countries have mixtures of private and public healthcare, which may exacerbate these coding inconsistencies. Within Scotland, linking healthcare data is considerably more feasible because of the centralised nature of healthcare provision using the National Health Service (NHS). This counteracts some of the limitations of routinely collected healthcare data from other countries, like the US, which have healthcare systems that cover the population unequally. In that context, relying on one system of data collection could seriously misrepresent the frequency of healthcare usage in any sample, especially as there are demographic and socio-economic associations that influence access to private healthcare. Other more universal limitations relate to the simplicity of administrative data. For example, a patient redeeming their prescription does not necessarily mean that the patient is taking the medication at all, or indeed, if they are, that it is taken according to recommended dosages. Invariably, there are limitations of this nature included in the data, which the researcher has to acknowledge but can do little to correct.

Once the collected data has been linked, there tends to be a significant amount of time devoted to data preparation. This stage involves extracting and re-coding information so that it can be read into analyses and statistical tests, however this stage can create a significant risk of bias; for example, if an individual made an appointment with a service, yet did not attend, should it be coded in the same way as a patient who made no appointments and never presented to that service either? It would depend on what the research question was; research investigating the willingness of patients to make appointments, compared to research investigating basic attendance rates and quality of care could code that in opposing manners. Inevitably, the approach that researchers use must be specialised to their own research aims, however these potentialities highlight that even with a standardised recording system, like ICD-10 codes, data transformation would be non-uniform. Researchers are beginning to develop frameworks for reporting data coding and definitions, with the aim of improving transparency in research that relies on electronic records (Kotecha et al., 2022). This checklist includes 5 sections: dataset construction and linkage, data fit for purpose, disease and outcome definitions, analysis and ethics and governance. Each of these have minimum and preferred requirements on the level of detail. For example, the analysis section notes that the minimum expectation would be a description of the statistical methods and algorithms applied. The preferred option would be that a link to open-source machine code and the algorithms used would be provided to improve external validation of the results. This framework has not been adopted yet, and the authors note their expectation that iterative versions of it will be published after further discussion with researchers and key stakeholders in data management, however as a checklist for publication, it is a promising beginning.

1.5. Circumstances in Scotland

Using similar principles to those outlined above concerning routine data collection and its utility for research, the Scottish government publish their own brief reports on ‘probable suicide’ and DRD in the country. The organisations involved and their general style of reporting will be described here, with their methods of data collection and definitions of ‘probable suicide’ and DRD evaluated in the methods section as guidelines for the methods I used.

1.5.1. ‘Probable Suicide’ Statistics in Scotland

In Scotland, the aptly named National Records of Scotland (NRS) collects and stores all data on births, deaths, marriages and other socio-historical aspects of the country. The NRS publish relatively simple reports on the number of ‘probable suicide’ decedents registered each year, with some data on the demographic distribution of the individuals who died (NRS, 2021 (b)). As well as that, there is another organisation, ScotSID (Scottish Suicide Information Database), created in 2009 by the Scottish Government. It aims to publish more in-depth analysis of the antecedent conditions of those who died of ‘probable suicide’ in Scotland, with a view to informing policy and aiding prevention strategies.

Older ScotSID reports have been relatively simple long-term analyses of trends in demographics and mental health prescription rates in the year before death, since its inauguration in 2009 (ScotSID, 2018). Recent publications have examined a range of topics: ‘probable suicide’ in those 25 years old and younger (ScotSID, 2022), one examining the rate of unscheduled care in the year before death (ScotSID, 2020) and one comparing the demographic histories of those who died by ‘probable suicide’ before and during the COVID-19 pandemic (ScotSID, 2021 (a)). This particular report, investigating possible differences during the COVID-19 pandemic, showed 792 ‘probable suicide’ deaths occurred in Scotland in 2020, which was a minor decrease from the 816 deaths reported in 2019. While unrelated to the data presented in the rest of this thesis (as the data is from 2009-2014), it is of interest that there was no measurable increase in the rate of ‘probable suicide’ during the pandemic, nor were there many significant differences in the profiles of the individuals who died other than, for example, during the pandemic, a greater proportion of individuals who died were single and a smaller proportion of deaths were due to poisoning events (ScotSID, 2021 (a)). This result highlights that variation in the number of 'probable suicide' deaths may be less intuitive and more complex than is often acknowledged.

These ScotSID reports contain comparisons between the rates of healthcare contact within the cohort of 'probable suicide' and contact by the general population of Scotland. Healthcare attendance varies significantly with gender, age and socio-economic level (Stene-Larsen and Reneflot, 2017, Luoma, Martin and Pearson, 2002), due to differing healthcare needs (e.g., reproductive and maternity services account for a significant proportion of women's healthcare attendance (Wang et al., 2013). Furthermore, 'probable suicide' is specifically distributed across gender, age and socio-economic level (Sterling and Platt, 2022, Pirkis, Nicholas and Gunnell, 2020). As such, using the average population rate as a control comparison is flawed, because differences between the cohorts would be affected by the different distributions of factors known to influence healthcare usage. Studies are required that use a variety of specific control groups, thus ensuring that the differences found are truly present within the data.

1.5.2. Drug-Related Death Statistics in Scotland

Similarly, the NRS publish brief reports on the number of DRD each year (NRS, 2021 (a)). The additional publications on drug deaths in Scotland come from the National Drugs Related Deaths Database (NDRDD); likewise inaugurated in 2009, yet publications are more infrequent and generally every 2 years. The values reported by the NRS and the NDRDD are not precisely equal; the most recent year with data from both organisations was 2018, with the NRS reporting 1,187 drug-related deaths (2021 (a)), and the NDRDD reporting 1,209 deaths (2022). The NDRDD reports list a variety of reasons for this possible discrepancy within the appendices of their publication (specifically, in Appendix 2 of the 2022 publication). These differences all essentially relate to their distinct data collection protocols; the NRS collects data on all deaths in Scotland, and then identifies relevant deaths for their publications, while the NDRDD relies on Critical Incident Monitoring Groups in each health board region to identify cases and submit a report to Public Health Scotland. As such, the NRS may receive direct information from pathology and toxicology reports that include data not available to the Critical Incident Monitoring Groups (e.g., in the case of an on-going criminal investigation), resulting in deaths classified as drug-related by NRS and not by the NDRDD. Many of their possible explanations are similar, however they all implicitly suggest that the NRS would have a higher total than the NDRDD, which is not the case, and requires further explanation.

Within these NDRDD reports, there are no comparisons with the general population rates, however there are some internal comparisons between those ruled as self-poisoning deaths and those that were thought to be unintentional. These comparisons have demonstrated certain differences; for example, those who were ruled as intentional deaths were older on average, had a higher percentage of past ‘probable suicide’ attempts and had different distributions of drug types implicated in the deaths (primarily antidepressants and pain-killer opioids for intentional deaths NDRDD, 2022). These are certainly salient distinctions; however, this analytical sub-section is a relatively recent addition; early NDRDD reports excluded any deaths that were ruled as intentional self-poisonings, and, therefore, ‘probable suicide’ deaths. Until the report examining deaths in 2012, these were entirely omitted from the publications (NDRDD, 2014) and since then, have been analysed separately in a sub-section of the report (NDRDD, 2022). While a relatively small part of the cohort, it seems illogical to exclude only intentional self-poisoning codes on the basis of their being ‘probable suicide’ deaths, when poisonings of undetermined intent are likewise included in both ‘probable suicide’ and DRD definitions. That this has been corrected in recent reports is promising, however external comparisons with matched controls are required for similar reasons as those noted above; namely that DRD are strongly associated with certain demographic groups and so the external control group must be carefully matched to minimise the effect of these demographic distributions (Sterling and Platt, 2022).

1.6. Chapter Summary

This opening chapter has briefly noted that while ‘probable suicide’ and DRD are referenced in historical sources, our interpretation and understanding of them has shifted. These types of death are now understood in a framework that emphasises both their pathological nature, and the assumed preventability of them through healthcare interventions. ‘Probable suicide’ is overwhelmingly attributed to mental illness, while DRD is associated primarily with opioid misuse.

Increasing globalisation, and international health organisations like the WHO, has created a need for accurate, standardised records of morbidity and mortality. To facilitate reports comparing the prevalence of distinct types of death, these international organisations have developed standardised alphanumeric codes for recording illnesses and causes of death. In spite of these codes, this chapter has also highlighted the global variation in medico-legal investigation and the codes used to define ‘probable suicide’ or DRD statistically.

From a theoretical perspective, the difficulty of defining the intent of an action has been discussed. This features primarily in the discussion surrounding deaths due to overdose; those with legal substances are generally ruled as ‘probable suicide’, while deaths due to illicit substances are ruled DRD. Certain publications exist that challenge this framework, however current national and international statistical reports have not engaged extensively with this literature.

As noted, the general views of ‘probable suicide’ and DRD focus on their pathological nature, resulting in a large variety of risk factors being identified. Demographic factors tend to overlap, with men and the socio-economically deprived being high-risk categories for both types of death. The utility of these highly prevalent risk factors has been questioned, with previous literature noting that no intervention could reasonably target all men. More specific risk factors were identified from the literature (e.g., suicidal ideation or past non-fatal overdose). A diagram was constructed for each type of death, contrasting the prevalence rate of death with these theoretically more characteristic risk factors. Prevalence rates were extracted for the general community, and for an indicated sample of the population. The indicated samples were those with psychiatric diagnoses or those who were known to use illicit drugs. As hypothesised, the prevalence rates were significantly higher in the indicated population than the general community, though were generally present for about half of the “at-risk” samples. Thus, the limited predictive ability of these risk factors, based on current knowledge, was illustrated.

Subsequently, the main prevention strategies for ‘probable suicide’ and DRD were described; antidepressant prescribing and OST, respectively. There has been a suggestion that antidepressant prescriptions increase the risk of ‘probable suicide’, though this seems primarily to be reported in adolescent patients. As such, there is a recommendation not to prescribe antidepressants for this age group, but otherwise guidance is limited to prescriptions of at least 6 months duration to prevent relapses. Where OST is concerned, the improvement in quality of life and reduction in criminality are key benefits. Despite their value in ameliorating aspects of psychological distress, neither of these prescriptions have been linked to large reductions in mortality; thus, further preventative strategies or alternative intervention frameworks will be required.

A summary of the challenges and limitations of routinely collected data was then provided. The benefits are clear, in that large samples can be rapidly collated, depending on data sharing agreements. Furthermore, records from a wide variety of services can be linked together for more complete profiles. Being previously collected data, the researcher is limited to what was collected in administrative settings, which may not contain key variables of interest. A framework for reporting electronic records studies is in development, yet further stakeholder engagement is anticipated for greater refinement.

Finally, Scottish Government organisations, which publish reports on the rates of ‘probable suicide’ and DRD in the country, were described. These include brief reports into the demographic profiles of the deceased individuals, with secondary Scottish Government-funded organisations providing more in-depth analyses. None of these reports compare the deceased with an appropriate control group, which would be one that minimises the impact of the association of demographic characteristics with early death.

1.7. Aims

There is significant debate over the access to and efficacy of current interventions, however accurate data covering the use of several services in the same population is lacking (Vasiliadis, Ngamini-Ngui and Lesage, 2015, Lewer et al., 2020, van Amsterdam, van den Brink and Pierce, 2021). A previously existing databank, containing healthcare usage data from individuals in one Scottish region, was available, as it had been collected by my supervisor, prior to this doctorate. Thus, the primary aim of this thesis, using this existing databank, was to track the healthcare usage of individuals who died by 'probable suicide' and/or drug misuse, then to compare these with relevant control samples. Specifically, the key objectives were:

1. To interrogate the coding definitions used in relevant cause of death data for governmental publications in Scotland
2. To quantify healthcare attendance and prescription rates in a 'probable suicide' cohort and to compare with age, sex and socio-economically matched controls
    a. To attempt to identify sub-groups within the patterns of attendance by splitting the cohorts in various ways, primarily into those "in treatment", therefore those receiving antidepressant drug prescriptions.
3. To quantify healthcare attendance and prescription rates in a DRD cohort and to compare with age, sex and socio-economically matched controls
    a. To attempt to identify sub-groups within the patterns of attendance by splitting the cohorts in various ways, primarily into those "in treatment", therefore those receiving OST
4. To consolidate and contrast any healthcare usage sub-groups identified with established profiles of 'probable suicide' or DRD, as extracted from clustering or taxonomical publications

2. Methods

This chapter gives an overview of the processes by which large, sensitive datasets were collated within a secure, cloud-based storage system following the negotiation of data sharing agreements with key organisations and data holders. The initial aim of this data collection was to conduct a feasibility study of the linkage of administrative public sector datasets for the Scottish Government, particularly to investigate two key drivers of premature and preventable death in Scotland: ‘probable suicide’ and DRD. This data collection process was undertaken before the initiation of this studentship, hence only a brief explanation of the relevant processes will be provided. Instead, the focus of this chapter will be on specific elements relevant to this thesis, notably the cohort verification, cleaning and re-coding. Healthcare datasets will be described and the variables extracted from them defined. The description of the statistical clustering algorithm has been included in the relevant chapter (Cluster Analysis Methods, page 229), with the respective R code in Appendix 3.

2.1. Data Collection

Data were collected for a Scottish Government-commissioned study of the feasibility of linking routine, electronic, administrative datasets across public healthcare, social care and criminal justice systems, to better understand the antecedents of premature and preventable deaths (Higgins and Matthews 2020). Known as the Suicide Information Framework Tayside project (SIFT), it proposed to compare individuals who died a ‘probable suicide’ or DRD, between 01/01/2009 – 31/12/2014, with ‘live’ community control individuals on the same measures of healthcare usage for the year prior to death/index. Study methods and datasets were described in detail in Higgins and Matthews (2020), who reported the feasibility of the large-scale data linkage, but also highlighted the issues involved in negotiating data sharing agreements with a variety of organisations and the unexpected length of time between agreements being completed and data eventually being transferred. As noted, the SIFT project gathered the data before the doctorate began, thus the cohort definitions given to HIC and the healthcare services extracted were selected by other researchers.

2.1.1. Safe Havens for Data Storage

The SIFT feasibility study commissioned the Health Informatics Centre (HIC) at the University of Dundee to host all the sensitive data extracts requested for the SIFT project. HIC is one of four regional Safe Havens certified by the Scottish Government (the other Safe Havens exist in Aberdeen, Edinburgh and Glasgow), which are all bound by the same charter and form a federated network with a fifth National Safe Haven (https://www.gov.scot/publications/charter-safe-havens-scotland-handling-unconsented-data-national-health-service-patient-records-support-research-statistics/pages/4/). This National Safe Haven is contained within the Information Services Division (ISD) of NHS Scotland. Within ISD, there is a specific administrative and governance sub-group known as the electronic Data Research and Innovation Services (eDRIS) who advise on research project design and grant access to national datasets, which are required in large-scale data linkage studies.

These Safe Havens are designed to facilitate health informatics research across Scotland, and in their respective regional areas. As such, the HIC charter emphasises the importance of robust data governance and security procedures. This is primarily achieved by the infrastructure of HIC itself; the Safe Haven environment is a cloud-based, secure storage system that can only be accessed via remote virtual desktop (Citrix XenDesktop, Santa Clara, CA) with individual login characteristics. Within the Safe Haven environment, there is no internet access; therefore, neither can unapproved applications be installed, nor can research data be copied, or exported. Furthermore, prior to any individual accessing the HIC environment, an Information Security Awareness Course must be completed, which ensures that any user of the Safe Haven understands core principles of data security and the legal requirements of working with sensitive data. These primarily include the Data Protection Act of 1998 and the European Union's General Data Protection Regulation Act of 2016. These Acts establish that data must be processed fairly and legally, not retained for longer than necessary and stored with appropriate security. Evidence of satisfactory completion of the training module must be provided to HIC, who then generate a personal log-in for the remote desktop, for each individually approved researcher, and permission is granted to access the relevant project data only. Finally, any data to be exported must be aggregated into anonymised graphs or cumulative tables to ensure that no sensitive data may be extracted and result in patient identification.

Members of HIC staff analyse each output request placed into the relevant folder, to ensure compliance with these regulations, before sending it to the data user.

As a result of these rigorous operating standards, HIC has acquired a vast collection of electronic health records of individuals in Tayside who are registered with a local General Practitioner (over 400k residents and >99% of the population). Each individual in the NHS Scotland system has a Community Health Index (CHI) number—a unique 10-digit patient identifier—that permits linkage of healthcare data across time and services. Using these CHI numbers, building a comprehensive healthcare usage pattern is both feasible and reliable as matching individuals across datasets is relatively simple. These routinely collected healthcare datasets, all containing CHI numbers, include: Accident and Emergency Department attendances, general medical and psychiatric service outpatient appointments, general medical and psychiatric service inpatient admissions and community prescription histories. For further data protection, within HIC and after the linkage process, the CHI numbers were pseudo-anonymised to generate non-identifiable proxy CHI (proCHI) numbers. These pseudo-anonymised datasets were then made available to the approved researchers.

2.1.2. Data sources

The SIFT project was both a feasibility and a pilot study, therefore several mortality registers were requested as data sources to confirm that all relevant 'probable suicide' or DRD cases had been identified and included in the HIC healthcare extracts (process summarised in Figure 2-1). Specifically, these were:

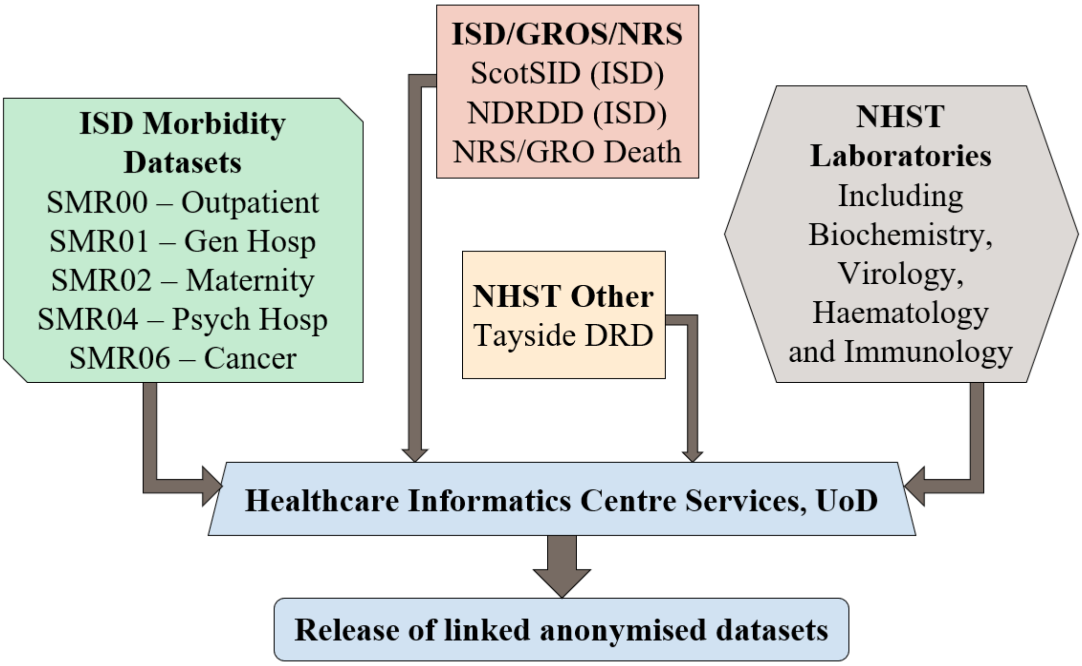
- National Records of Scotland (NRS) – the national mortality register in which all deaths in Scotland must be recorded. It was previously known as the General Register Office for Scotland (GROS), which was amalgamated with the National Archives of Scotland to become the NRS on the 1st April 2011. Causes of death are recorded using internationally standardised ICD-10 codes.
- Scottish Suicide Information Database (ScotSID) – this is a specialised database, held by ISD and initiated in 2009, which contains a register of all 'probable suicide' deaths in Scotland. It collects data on cause and date of

death, as well as demographic information and healthcare usage and publishes an annual report.

- National Drug-Related Death Database (NDRDD) – this is a specialised database, held by ISD and also initiated in 2009, which contains a register of all drug-related deaths in Scotland. The initial system of case identification was that data would be sent to ISD, though after 2014 this process was decentralised and since then, data has been entered into a secure database directly from each health board. It collects data on cause and date of death, as well as demographic data, known substance misuse, previous overdose and healthcare attendance records. It publishes a biennial report.
- Tayside Drug-Related Death Database (TDRDD) – this is a localised database, established in 2008, which collects very similar demographic, healthcare and criminal justice data as the NDRDD. The key source of information used to identify relevant deaths comes from Police Scotland reports and not the medical ICD-10 cause of death codes.

The following section details the definitions given by SIFT to HIC, who liaised with ISD to extract individuals from all these databases. These definitions were then examined and operationalised in a slightly modified manner in the current study. Then follows a detailed explanation of the types of data available within the healthcare datasets and the specific outcomes re-coded for use in the analysis later in the thesis.

Figure 2-1. Flow of data through the study



Adapted from Higgins and Matthews (2020). Figure illustrates the source of some of the key databases included in the project. Specifically, these included cause of death data from the National Records of Scotland (NRS, previously known as the General Register Office for Scotland (GROS)) and specialist mortality databases (e.g., Scottish Suicide Information Database (ScotSID) and National Drugs-Related Death Database (NDRDD)). Other sources of data included NHS Tayside Laboratories and attendance records at relevant healthcare services. Much of the data was extracted from the Information Services Division (ISD) of the NHS.

2.2. Data Transformation

2.2.1. Cohort Identification

As described above, the individuals SIFT requested from the national mortality databases, via HIC, were those who died either a 'probable suicide', or DRD, with an address registered in Tayside and a death that occurred between 01/01/2009 and 31/12/2014. The two cohorts were primarily identified using those individuals who fulfilled the criteria from the specialised databases (i.e., ScotSID and both the NDRDD and TDRDD). However, to further validate these cohorts, a set of ICD-10 codes were also used by HIC for separate and independent extraction from the NRS. The codes chosen for each cohort reflected general international classifications used in statistical publications, including those used by Scottish Government, however these definitions (especially relating to DRD) are subject to noticeable variation.

2.2.2. 'Probable Suicide' Cohort Definition

The 'probable suicide' definition, as used by SIFT, was exactly the same as the ICD-10 codes used for the annual NRS reports into 'probable suicide' deaths in Scotland (NRS, 2021 (b)). ScotSID note that they use these same codes, however their database *excludes* the death of any children under 5 years old on the basis that these deaths are highly unlikely to be "true suicides" (ScotSID, 2021 (b)). Specifically, these ICD-10 codes include both causes listing intentional self-harm as the medical cause of death, as well as codes where the intent could not be determined by medico-legal investigation, and therefore, are ruled as injuries or poisonings of undetermined intent (see Table 2-1).

2.2.3. Drug-Related Death Cohort Definition

Defining a DRD is considerably more challenging. The codes used in international statistics are less standardised than those used for 'probable suicide'. Simply within Scottish Government publications, there are two definitions: a wide and a narrow definition. In recent NRS publications, the wide definition resulted in a total of 1,461 deaths for 2020, with 1,339 deaths fulfilling the narrow drug-related death definition (NRS, 2021 (a)). The narrow definition requires that a death be related directly to a substance use disorder, based on a medico-legal investigation, or that an illicit drug be present in the body, and contributed to the death, from the perspective of the toxicologist. For poisoning events, these illicit drugs are identified with the use of additional T-codes that are specific to opioids, cocaine or amphetamine drugs, for example. These codes are listed in Table 2-2.

Table 2-1. ICD-10 Codes Defining 'Probable Suicide'

ICD-10	Definition
X60-X84	Intentional self-harm
Y87.0	Sequelae of intentional self-harm
Y10-Y34	Events of undetermined intent
Y87.2	Sequelae of events of undetermined intent

NRS, ScotSID and SIFT medical cause of death ICD-10 codes for ‘probable suicide’.

Table 2-2. ICD-10 Codes Defining Drug-Related Death, narrow criteria

ICD-10	Definition
F11	Disorders related or resulting from abuse or misuse of opioids
F12	Disorders related or resulting from abuse or misuse of cannabis
F13	Disorders related or resulting from abuse or misuse of cannabis of sedative, hypnotic or anxiolytic drugs
F14	Disorders related or resulting from abuse or misuse of cocaine
F15	Disorders related or resulting from abuse or misuse of other stimulants
F16	Disorders related or resulting from abuse or misuse of hallucinogens
F19	Disorders related or resulting from abuse or misuse of other psychoactive substances
	If a drug is present in the body that is listed in the Misuse of Drugs Act 1971, these are also included:
X40-X44	Accidental poisoning
X60-X64	Intentional self-poisoning by drugs, medicaments and biological substances
X85	Assault by drugs, medicaments and biological substances
Y10-Y14	Poisonings of undetermined intent

NRS narrow drug-related death ICD-10 code definition, as used in national statistics publications. Drugs in the body, for the second half of the table, are identified with the use of additional T-codes that are specific to distinct substances.

The wide definition additionally includes code F18 (disorders related to or resulting from abuse or misuse of volatile solvents) and removes the requirement for an illicit drug to be present (at post-mortem examination) for the second part of the table. As the narrow definition specifically *requires* illicit drugs to be present in the body for the second set of codes, the deaths included can change year on year due to changes in the legal classification of substances. One relevant example is the change that occurred in 2014 when tramadol and zopiclone both became controlled drugs. Previously, deaths resulting from tramadol or zopiclone, alone or in combination with other legal drugs (alcohol and over-the-counter pain-killers, for example) would only have been recorded in the wide definition, therefore not in the headline measure. From mid-2014 onwards, these were included in the narrow definition and could impact upon the consistency of the yearly comparisons. The possible magnitude of this change (as 27 deaths in 2013 were tramadol-only or tramadol and other legal substances, therefore not included in the narrow NRS total DRD for that year) lead to the NRS developing a "consistent series". This is published in the annexes of their reports and retrospectively re-codes the number of DRD, based on any new legal classifications in effect since then. For example, the 2021 report contains a longitudinal consistent series in which deaths involving tramadol, gabapentin or pregabalin are in the "standard" definition, while the consistent series total for the year 2013 includes deaths involving these substances as "extra" DRD (Annex F in NRS, 2021 (a) or table CS1 in the "Data" Excel spreadsheet https://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/vital-events/deaths/drug-related-deaths-in-scotland/2021). However, these consistent series values are not the headline data presented. Due to discrepancies of this nature, both media and NRS reports actually present larger increases in the number of DRD each year than there would be if both years had used exactly the same list of illicit drugs to refine their total. Thus far, the number of controlled substances has only increased, leading to a natural growth in the headline measures of year-on-year deaths. This highlights with a single example the difficulty with consistently defining a DRD, while ensuring that the statistics reflect the current legal and social contexts, and also why international comparisons are less clear and reliable than are commonly emphasised in the bodies of their reports.

The caveats above are particularly relevant because of the method of cohort identification used in this study. Several mortality databases were used to triangulate individuals who fulfilled the SIFT DRD criteria: individuals either had to be recorded with a specialised drug-related death database (NDRDD or TDRDD) or identifiable from the NRS extract with a slightly reduced list of ICD-10 codes. Both NDRDD and TDRDD use the filing of a Sudden Death Report by the Police to identify potential cases, as this process triggers a post-mortem (NDRDD, 2022, TDRDD, 2016). The toxicology results are available to a Local Critical Incident Monitoring Group and local Data Collection Co-ordinator who confirm whether the death fulfils their criteria. The NDRDD state that their criteria are the same as the NRS narrow definition given above. However, before 2012, the NDRDD *excluded* any deaths by intentional self-poisoning and have begun to analyse them in a separate sub-section of their reports. TDRDD give no further detail as to their criteria for ruling a death to be drug-related, however they do collaborate with national databases and share toxicology reports, therefore the databases are likely to include mostly the same individuals.

Within the SIFT project report, the DRD definition was any individual in the NDRDD or TDRDD, and any individual that could be identified from NRS records with cause of death codes similar to the narrow criteria (see Tables 2-3 and 2-2, respectively).

Table 2-3. ICD-10 Codes Defining a Drug-Related Death, SIFT criteria

ICD-10	Definition
F11	Disorders related or resulting from abuse or misuse of opioids
F12	Disorders related or resulting from abuse or misuse of cannabis
F14	Disorders related or resulting from abuse or misuse of cocaine
F15	Disorders related or resulting from abuse or misuse of other stimulants
F16	Disorders related or resulting from abuse or misuse of hallucinogens
F19	Disorders related or resulting from abuse or misuse of other psychoactive substances
X41[1]	Accidental poisoning by and exposure to antiepileptic, sedative-hypnotic, antiparkinsonism and psychotropic drugs, not elsewhere classified
X42[2]	Accidental poisoning by and exposure to narcotics and psychodysleptics, not elsewhere classified
X61[1]	Intentional self-poisoning by and exposure to antiepileptic, sedative-hypnotic, antiparkinsonism and psychotropic drugs, not elsewhere classified
X62[2]	Intentional self-poisoning by and exposure to narcotics and psychodysleptics, not elsewhere classified
Y11[1]	Poisoning by and exposure to antiepileptic, sedative-hypnotic, antiparkinsonism and psychotropic drugs, not elsewhere classified, undetermined intent
Y12[2]	Poisoning by and exposure to narcotics and psychodysleptics, not elsewhere classified, undetermined intent

SIFT ICD-10 codes to isolate additional drug-related deaths in the NRS data feed. [1]Codes X41, X61 and Y11 require an additional T-code T43.6 (poisoning by, adverse effect of and underdosing of psychostimulants). [2]Codes X42, X62 and Y12 require an additional T-code T40.0 – T40.9 (opium, heroin, other opioids, methadone, other synthetic narcotics, cocaine, other unspecified narcotics, cannabis, LSD and other unspecified psychodysleptics).

Before any analysis was undertaken, the cause of death codes for all individuals were investigated to ensure that they fulfilled relevant criteria. The dataset containing the information from the NRS includes the date of death, underlying cause of death and up to nine other columns for additional causes of death, all of which are taken from the Medical Certificate of the Cause of Death (MCCD; Scottish Government, 2018). Generally, statistical publications rely only on the underlying cause of death to select individuals for analysis, however SIFT added no caveats as to the primacy of the relevant codes. Each cohort had, therefore, a small number of individuals who were not present in the specialised databases. They were retained within this study on the basis that the relevant cause of death code was believed to have contributed significantly enough to be on the MCCD. Furthermore, as this study was interested in the variability of definitions used for each type of death and the heterogeneity of the samples, these extraneous individuals were retained to examine whether more inclusive definitions would reveal as yet unacknowledged sub-types of deaths.

2.2.4. Common Cause of Death Codes

Where individuals are categorised as overlapping 'probable suicide' and DRD, there was a decision to be made about whether to rely only on the underlying cause of death, or up to all 10 columns containing additional cause of death information. There were 190 individuals who overlapped based on *only* the underlying cause of death ICD-10 codes and 197 individuals using all possible information. Based on the same rationale as outlined above, to investigate a broader definition for this thesis, 197 individuals were categorised as having overlapping cause of death codes.

2.2.5. Demographic Data Definitions

Patient demographic data was provided by HIC, who receive a monthly CHI snapshot table from NHS Tayside health board. This file includes gender, date of birth (anonymised to within three months of the original date), a calculated age and an estimation of socio-economic deprivation status, based on postcode (SIMD).

Measures of socio-economic deprivation within HIC, and across national statistical publications, use a Scottish Government system: a SIMD score (Scottish Index of Multiple Deprivation (Scottish Index of Multiple Deprivation 2020 - gov.scot (www.gov.scot). SIMD was calculated by dividing Scotland up into data zones and measuring a variety of indicators of deprivation, which were split into seven domains: income, employment, health, education, geographic access, crime and housing. All data zones were ranked and then split into quintiles; 1 represents the most deprived zones, with 5 representing the least deprived.

Age, as calculated by HIC, was split into three groups: 25 and under, 26-50 years old and 51 and older, to allow comparisons between youth, middle-aged and older individuals, but without so many levels that group sizes were insufficient for analyses.

2.2.6. Control Matching Process

HIC Services extracted equivalent data for 'live' comparator cases using their comprehensive population level data to identify Tayside residents who matched the deceased with respect to gender, age, and SIMD. All possible controls, according to project specific guidelines, were identified (for this project, that the individuals were alive on the date of death of the matched "case"), and were matched based on demographic data. Every individual was matched with the first control, then each with the second, and so on. This method is chosen so that the first control, for each deceased individual, has a strong probability of being well-matched, with possible reductions in accuracy for the later controls as the bank available decreases. In this dataset, four comparator 'cases' were generated for each 'probable suicide', or DRD, and their healthcare utilisation data was identified within the Safe Haven.

As demonstrated in the cohort validation sections of each results chapter, a number of both the deceased and live individuals supplied by HIC lacked either all demographic data (age, sex and SIMD) or only their SIMD score. Very little meta-data was available explaining the data capture process or the matching process, however HIC were contacted and explanatory files within the Safe Haven were investigated. The supplementary document for the demography file notes that there are monthly transfers from each health board to the national CHI database, however there seems to be no explanation for how an individual could have a personalised pseudo-anonymised pro-CHI number (generated from the CHI number by HIC as a further data security step) and yet lack demographic data supposedly contained within these snapshot CHI records. The only possible explanation given for PROCHIs not present in the demography file was that the individual may have never lived in Tayside, according to the CHI records; as residence in Tayside at time of death was one of the inclusion criteria, this should not have been the cause. Further queries to the HIC team were unanswered on this point.

2.3. Healthcare Databases and Definitions

2.3.1. Healthcare Datasets

All of the databases, other than demography and cause of death data, were available only in a long format, in which each row of data corresponds to an event. Therefore, every variable of interest required re-coding into wide format, where each row corresponds to one individual and additional columns contain variables of interest. Each database contained data for the year before the date of death, or matched index date for the controls.

2.3.1.1. Inpatient Attendances

Healthcare datasets were all episode-based in the original databases, therefore each attendance was recorded on a separate row with the relevant diagnostic codes for that event. These general hospital inpatient attendances included both day patients and those with longer-term stays. Transfers between specialities or wards would be represented as a new record, with one column denoting linked stays. A code denoted whether the attendance was emergency or routine for each episode. To investigate the percentage of individuals with routine attendance, this was operationalised in a binary value covering the year before death. When individuals had multiple attendances, if any of these were routine, then the outcome for elective healthcare usage was coded as positive, even if the other attendances had been emergency.

2.3.1.2. Outpatient clinics

Outpatient appointments were split by clinical specialty into either psychiatric, including those specific to child or geriatric (‘old age’) psychiatry, or non-psychiatric visits. The database included information on whether the patient attended, attended but could not wait, or did not attend. Very few of the appointments were marked as could not wait. The few appointments with this code were included as though the patient attended, because a binary measure was used to dichotomise engagement with the healthcare service, and not the appropriateness, or efficacy, of treatment contacts.

It is important to note that the recording arrangements did not permit the identification and separation of ‘substance misuse service’ appointments from the larger category of psychiatric outpatient appointments. An exploration of the data showed that the location code within the Safe Haven could be matched to services that were registered as offering substance abuse services among other mental health services. As such, there were no guarantees that attendance at these locations would have been for substance misuse treatment. Furthermore, over 60% of outpatient clinics were at these locations in the DRD cohort. Therefore, the decision was taken to simply code psychiatric services as a unitary type of 'event' and to not create uncertain and unverifiable sub-groups. For data interpretation purposes, the one major implication (and study limitation) was that the supervised prescription of opioid substitution therapy (OST) would always be associated with increased rates of 'psychiatric outpatient' attendance.

2.3.1.3. Accident and Emergency

Initially, the primary purpose for the Accident and Emergency database was to collect information on waiting times to measure service performance against quality-of-care criteria. In July 2010, data collection was expanded to include information on diagnosis codes and whether or not alcohol was involved in the presentation to services. The majority of the columns designed to collect information on diagnosis were empty, therefore to define possible 'self-harm' attendances, a variety of sources were used. These included any reference to discharge to psychiatric hospital, referral to mental health services, a code referring to poisoning, or a 'psychiatry reason' for the attendance and lastly, any episode with a code denoting deliberate self-harm (further elaborated on in page 96).

Additionally, any presentations, possible self-harm or otherwise, in which the patient died were excluded from the analysis as the comparisons of interest were to do with the antecedents, not the occasion, of death.

2.3.2. Prescribing data

Prescription data were coded in a yes/no format over the whole year. Further details were extracted concerning antidepressant and methadone OST prescription, following initial exploration. The Prescribing Information System (PIS) includes all prescriptions dispensed in the community, whether written by GPs, nurses or hospital staff, and as such, covers the overwhelming majority of prescription scripts. For some individuals, there were prescription records that were dated after the date of death or index. This could have been caused by the length of time involved in data transfer and the defaults of the administrative system; data is received by PIS from pharmacies on a presumably regular basis, though no detail could be found in HIC that stated the regularity of the data transfer for this step. These pharmacy records are tagged with the year and month in which they were received by PIS. HIC then receive a monthly download from PIS that are approximately three months behind real time; for example, the data for December 2011 would be received in February 2012. The prescribed date available to me, within the Safe Haven, defaults to the first of the month that the data were received by PIS. As such, it is possible that prescriptions dated after the date of death were issued before the individual died. As there was no further information to facilitate the successful integration of prescriptions with the default dates, versus those with the actual prescription date, any prescriptions issued after the date of death (or index) were excluded for all individuals.

2.3.2.1. Psychotropic Prescriptions

Both British National Formulary (BNF) categorisation and key word searches were used to identify relevant records; antidepressants were solely within BNF category 4.3 and methadone prescriptions were only included from BNF category 4.10.3 to ensure the prescription was OST. Originally, all OST prescriptions were coded. However, as there were only 3 individuals with buprenorphine prescriptions, all within the DRD group, the decision was made to focus solely on those prescribed methadone. These were the two key prescriptions of interest, with antidepressant prescriptions operationalised to represent “in treatment” for the ‘probable suicide’ cohort, with methadone OST prescriptions representing the same for the DRD cohort. As demonstrated in the introduction, the key prevention strategies are thought to be these prescriptions, thus these definitions were used to consider possible differences and similarities between those theoretically receiving the best care and those not in specifically promoted treatment.

Benzodiazepines were identified using key words: diazepam, temazepam, chlordiazepoxide, lorazepam, nitrazepam, lormetazepam and clonazepam. The identification of ‘z-drugs’ used the key words zolpidem, zopiclone and zaleplon. Gabapentinoids refers to gabapentin and pregabalin, found in the same key word search method. Anticonvulsants were identified using BNF category 4.8.1, however, as another noted limitation, many of these were the previously identified gabapentinoids.

2.3.2.2. Preventative Prescriptions

The rate of prescriptions that could arguably be labelled anticipatory or preventative, was a proxy measure for the type of healthcare engagement that the cohorts had relative to their control groups. These preventative prescriptions indicate early recognition and treatment of long-term conditions like cardiovascular concerns and could indicate a greater rate of routine and planned healthcare; as such, it contrasts with the targeted psychotropic prescriptions identified above. The preventative prescriptions isolated from the prescription records were antihypertensive and statin drugs, based on BNF 2.5 and 2.12, respectively.

2.4. Statistical Analysis

Group differences were tested using Chi-square analysis and summarised in the results chapters, though comparisons with cells containing 5 or fewer individuals were analysed with Fishers Exact Test. Healthcare attendance variables that were key outcomes of interest (e.g., rates of antidepressant and OST prescription) were further investigated in logistic regressions, where the healthcare attendance would be defined as the outcome variable and group status and demographic categories as the factors. All explanatory variables in the regressions were entered as categorical, resulting in the creation of dummy variables, with the largest group set as the reference. Where the variable of outcome was binary, a binary logistic regression was employed, while count data was analysed using a Poisson regression. In one circumstance, a multinomial regression was used to investigate belonging to 1 of 4 categories.

The dose-time relationship for methadone was analysed by ANOVA that included case status and tested for an interaction with time. Mann-Whitney U tests were employed primarily in the DRD cohort, as these were independent samples that were small and not normally distributed (e.g., the mean positivity rate of urine drug screens was bounded at 0 and individuals with only one test resulted in a bimodal distribution towards 0% or 100%). All analyses were performed using IBM SPSS Statistics version 25.

2.5. Summary of Methods

The data used throughout this project had been previously collected for a Scottish Government study, which aimed to examine the feasibility of linking multiple routine, administrative databases. The project was known as the Suicide Information Framework Tayside (SIFT). SIFT commissioned the Health Informatics Centre (HIC), a trusted third-party service providing secure data linkage and storage, to maintain the databases collected and match the individuals across the feeds from various services. These feeds identified individuals who died in Tayside, between 01/01/2009 to 31/12/2014 and were officially recorded as either ‘probable suicide’ or DRD. HIC matched 4 individuals from the general live population of Tayside to each “case” to provide a “control” cohort. During the active timeframe, healthcare datasets for the year before death were successfully collated, however Local Authority data and criminal justice records were not accessible to the research team, despite the development of data sharing protocols.

Official cause of death records for each individual were stored by the NRS, who publish yearly reports on the number of ‘probable suicide’ and DRD deaths in Scotland. Additional reports are published by ScotSID (examining ‘probable suicide’ nationally) and the NDRDD and TDRDD (examining DRD nationally and only in Tayside, respectively). Despite all these organisations being linked to the Scottish Government and producing reports of Official Statistics standards, the protocol for data collection varies and there are minor differences in the statistical definitions used. All four databases were used by SIFT to triangulate “cases”.

Databases were in a long format; therefore, significant re-coding was required to summarise the data into a wide format that could be read into statistical software. Healthcare attendance rates were extracted, with initial measures recorded in a binary mode, and frequencies of attendance tallied for key services (e.g., psychiatric outpatient and accident and emergency presentations). Key prescriptions throughout the year were likewise recorded, with antidepressants serving as the definition for “in treatment” for the ‘probable suicide’ cohort and methadone OST prescriptions representing “in treatment” for the DRD cohort. Differences in rates of healthcare usage between groups were examined primarily with chi-square tests. Logistic regression models, predominantly binary or Poisson, were used to investigate the association between healthcare usage rates and demographic factors.

3. Results of the ‘Probable Suicide’ Cohort Analysis

This chapter details the results of the cohort validation procedures undertaken within the ‘probable suicide’ cohort, as well as the results of a variety of healthcare usage analyses. The chapter will be split into the following analytical sections, after a description of cohort validation: first, a comparison of the total cohort with all matched controls; second, a comparison of those who were deceased with the control individuals who had received antidepressant prescriptions; third, a series of analyses looking only at the deceased, partitioned on the basis of antidepressant prescription (as a proxy for being “in treatment”). Finally, I present an analysis of healthcare usage within the ‘probable suicide’ group, split on the basis of estimated level of socio-economic deprivation. Each comparison draws upon bespoke control, or comparison, groups to test different hypotheses, each with the aim of better understanding the context of healthcare usage before ‘probable suicide’, with the possibility of identifying potential sub-groups of interest.

3.1. Cohort Validation

3.1.1. Identifying the Database of Origin

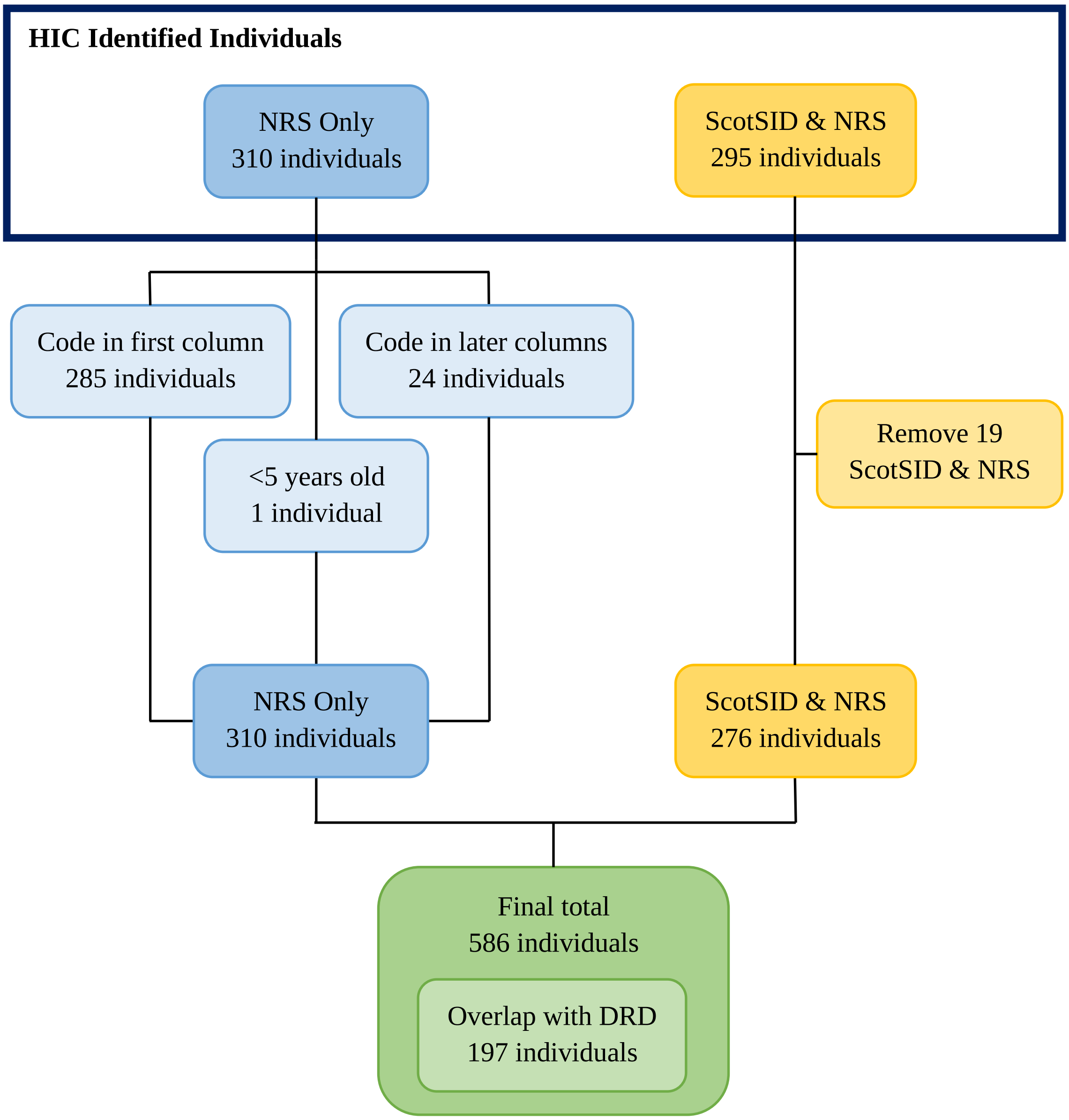
A comparison of the definitions from official statistical reporting systems revealed some minor differences that could affect how many individuals were recorded as ‘probable suicide’ in Scotland. Both the NRS and ScotSID indicate that they use the same ICD-10 classification codes. The main stated difference is that ScotSID remove any individuals under the age of five years old, on the basis that the death was more likely to be unintentional. Despite this apparently otherwise identical approach, out of the 605 individuals flagged by NRS as ‘probable suicides’ according to ICD-10 codes during the observation period, only 295 were present in the ScotSID data feed for the same period. Such a large difference in the number of potentially relevant individuals was unexpected, therefore the codes of death for each individual were manually cross-checked against the definitions used by each reporting body.

Of the original 295 individuals isolated from ScotSID, 19 did not appear to fulfil the required ICD-10 code definitions, even within the ten supplementary columns containing codes describing secondary medical causes of death (n.b. a table listing the underlying cause of death codes of these individuals is included in Appendix 1).

These cases were, therefore, excluded from study within this thesis, leaving a total of 276 individuals who were recorded within the ScotSID national statistics output.

There were 310 individuals identified, using the relevant ICD-10 codes, directly from the NRS database. These codes were examined to attempt to understand the discrepancies between the NRS and ScotSID totals; this process is summarised in figure 3-1. Twenty-four of these individuals had ‘probable suicide’ cause of death codes included within their records, but NOT as the primary cause of death and, therefore, should not be included in national statistical reporting, nor should they be present in ScotSID reports. These individuals were retained in the study because of my aim to investigate different types of ‘probable suicide’, especially those under-explored by current statistical reports, despite medical ICD-10 criteria indicating their relevance to the field. The remaining 286 NRS-only individuals fulfilled all criteria; they had cause of death codes that both NRS and ScotSID recognised as ‘probable suicide’ in the first cause of death column within the consolidated dataset and only 1 individual was under 5 years old and, therefore, eligible to be excluded from ScotSID reporting. The majority of these individuals had causes of death found within the poisonings category, therefore, many of these were also included within the DRD cohort. Following consideration of these issues, all 310 ‘probable suicide’ individuals with correct codes were retained within the present study, largely on the basis that there appeared to be no legitimate reason to exclude any of them, despite many being absent from the ScotSID reporting for this period. The reasons for their non-inclusion in ScotSID remain unclear. Furthermore, the volume of individuals missing from ScotSID seriously undermines the reliability of their reports and value in directing policy.

Figure 3-1. Flowchart of the 'Probable Suicide' Cohort Validation



SIFT requested that HIC extracted all individuals from the National Records of Scotland (NRS) who fulfilled the standardised cause of death code criteria, as well as all individuals captured by Scottish Suicide Information Database (ScotSID). Cause of death codes were then manually validated for each individual. Of the individuals recorded in the ScotSID feed, 19 did not meet criteria for study inclusion. All the individuals identified only from NRS fulfilled study criteria for cause of death codes, however the breakdown presented shows why at least 25 of the individuals would be excluded from the ScotSID database (those with codes in later data columns and the individual under 5 years of age). The final sample size was 586 ‘probable suicide’ individuals, of which 197 were also present within the DRD cohort.

3.1.2. Comparing the NRS and ScotSID cohorts

To explore the discrepancies between the two datasets (that otherwise indicated that they were using the same definitions), I sought to investigate whether there were systematic demographic differences between the individuals captured by ScotSID versus those present only in the NRS data feed. I investigated this with a binary logistic regression model, using presence in the ScotSID feed as the outcome measure. The model included the demographic measures of gender, age and socio-economic deprivation (SIMD) as the explanatory variables. The model was significant, X^2 (7, N=540) = 49.274, $p<0.001$, confirming that there were demographic associations with inclusion in the ScotSID data feed (see Table 3-1). Compared to the reference group of those aged 26-50, both those 25 years old or younger, and those 51 years old or older, were **more** likely to be included in ScotSID. Compared to the reference group of the most deprived socio-economic quintile (SIMD 1), those in the second-least deprived quintile (SIMD 4) were more likely to be included in ScotSID's data. These results suggest that, at least between 2009 to 2014, the data included in ScotSID reports relating to the NHS Tayside region did not accurately depict the scale, or the demographic backgrounds, of the individuals who died of 'probable suicide' in the area.

There were no clear reasons to exclude these NRS-identified individuals not in ScotSID, and indeed, retaining them could possibly highlight features less obvious in smaller cohorts. Therefore, all 586 individuals were maintained for analysis. Following this, the matching of the 'probable suicide' cohort and the respective controls was verified (summarised in Table 3-2). While the totals were 586 cases and 2344 controls, it was found that 20 of the 'probable suicide' individuals lacked complete demographic data, and a further 26 lacked a SIMD score. Additionally, 25 control individuals lacked a SIMD score. As mentioned in the methods section (page 78), further enquiries to the HIC team around the process of data collection and matching, and particularly missing demographic data therein, were unanswered.

Table 3-1. Regression predicting ScotSID inclusion

Variable	Exp(B)	95% CI for Exp(B)
Men	Reference	
Women	0.816	0.542-1.230
≤25 years old	**1.910**	**1.140-3.198**
26-50 years old	Reference	
≥51 years old	**2.458**	**1.595-3.787**
SIMD 1	Reference	
SIMD 2	1.472	0.921-2.354
SIMD 3	1.411	0.781-2.549
SIMD 4	**3.138**	**1.848-5.328**
SIMD 5	1.869	0.990-3.527

Odds ratios from a binary logistic regression model predicting presence in the ScotSID database as the outcome. Demographic measures were used as explanatory variables and the largest sub-group was set as the reference group. Bold rows indicate statistical significance. Both those 25 years old or younger, and those 51 years old or older were more likely to be included in ScotSID's data, as well as those in the second-least deprived quintile (SIMD 4).

Table 3-2. Demographic Data for 'Probable Suicide' and Control Groups

	'Probable Suicide' (n)	%	Control (n)	%
Men	418	73.9	1740	74.2
Women	148	26.1	604	25.8
≤25 years old	82	14.5	132	5.6
26-50 years old	335	59.2	1372	58.5
≥51 years old	149	26.3	840	35.8
SIMD 1	172	31.9	771	33.2
SIMD 2	136	25.2	475	20.5
SIMD 3	69	12.8	339	14.6
SIMD 4	106	19.6	510	22.0
SIMD 5	57	10.6	224	9.7
Total	566		2344	

Outcome of matching of 'probable suicide' cohort with community controls. SIMD - Scottish Index of Multiple Deprivation (reference) with 1 = most deprived quintile and 5 least deprived quintile. NB. Twenty 'probable suicide' individuals were missing all demographic data and a further 26 had gender and age information, but no SIMD score. 25 controls had no SIMD.

3.2. Analysis of ‘Probable Suicide’ and Matched Control Cohorts

3.2.1. Introduction

After cohort validation, the rate of healthcare utilisation and key prescriptions were extracted for each individual and analysed by group status. The aim was to contrast the rates of healthcare utilisation, in the twelve months before death, between the ‘probable suicide’ cohort and the matched control cohort (586 individuals compared to 2344 individuals, respectively). It was important to identify and describe any differences in healthcare usage across the full cohort for both groups, both to simply test whether there were group differences, but also to have greater context for attempting to isolate sub-groups in later stages of the analysis.

3.2.2. Healthcare Usage across ‘Probable Suicide’ and Matched Control Cohorts

At a group level, the ‘probable suicide’ cohort attended all healthcare services at significantly higher rates than their matched controls, during the 12m sampling frame (summarised in Table 3-3).

This was particularly striking where psychiatric healthcare was concerned. In total, 38.6% of the ‘probable suicide’ group compared to 3.6% of the controls had attended psychiatric outpatient services, with psychiatric inpatient attendances recorded at 9.7% to 0.3%, respectively.

Accident and Emergency attendances were also significantly elevated in the ‘probable suicide’ group compared to the controls (41.5% to 13.6%). Furthermore, when general hospital attendance was broken down into routine or emergency appointments, the ‘probable suicide’ group had a lower rate of routine appointment attendances. Overall, these data, combined, suggest notably higher rates of emergency/unplanned healthcare utilisation in the ‘probable suicide’ group.

Finally, while non-psychiatric outpatient attendances were also significantly higher in the ‘probable suicide’ group than the controls (26.1% to 20.0%). This difference was, however, much smaller than in the other comparisons.

Table 3-3. Healthcare Utilisation rates across 'Probable Suicide' and Control Cohorts

Variable	**'Probable Suicide' (N=586)**		**Control (N=2344)**		**X²**	**p value**
	%	(n)	%	(n)		
General inpatient	**30.2**	**177**	**8.2**	**193**	**205.107**	**<0.05**
Routine Attendance	**45.8**	**81**	**61.7**	**119**	**9.393**	**<0.05**
Psychiatric outpatient	**38.6**	**226**	**3.6**	**85**	**603.225**	**<0.05**
Non-psychiatric outpatient	**26.1**	**153**	**20.0**	**468**	**10.593**	**<0.05**
Mental Health Inpatient	**9.7**	**57**	**0.3**	**6**	**199.869**	**<0.05**
Accident and Emergency	**41.5**	**243**	**13.6**	**318**	**235.741**	**<0.05**

Comparison of those deemed 'probable suicide' with matched controls with respect to healthcare usage across a variety of services within preceding 12m. General hospital presentations included both day-patient and elective inpatient events, therefore 'routine attendance' was calculated for those with at least one of these general hospital codes. Outpatient clinics were split by clinical specialty, with psychiatric codes not distinguishing between mental health or substance misuse attendances. Chi-square tests were calculated, with rows in bold indicating statistical significance. The 'probable suicide' group attended all healthcare services at significantly higher rates than the matched control group, however, the 'probable suicide' group had fewer attendances coded as routine.

Table 3-4. Prescription rates across 'Probable Suicide' and Control Cohorts

Variable	**'Probable Suicide' (N=586)**		**Control (N=2344)**		**X²**	**p value**
	%	(n)	%	(n)		
Methadone	**16.6**	**97**	**1.3**	**31**	**260.295**	**<0.05**
Antidepressants	**43.3**	**254**	**12.5**	**293**	**293.747**	**<0.05**
Benzodiazepines	**22.2**	**130**	**4.1**	**97**	**213.607**	**<0.05**
Z-drugs	**17.6**	**103**	**3.2**	**74**	**171.736**	**<0.05**
Gabapentinoids	**10.8**	**63**	**2.3**	**55**	**85.673**	**<0.05**
Anticonvulsants	**15.4**	**90**	**3.6**	**85**	**114.898**	**<0.05**
Statins	7.8	46	9.6	224	1.632	>0.05
Antihypertensives	**6.1**	**36**	**8.8**	**207**	**4.453**	**<0.05**

Percentage and count data comparing prescription records for those deemed 'probable suicide' and controls. Chi-square tests were calculated, with rows in bold indicating statistical significance. The 'probable suicide' group were prescribed significantly higher rates of psychotropic treatment prescriptions compared to the controls; however, the controls received more preventative prescriptions (antihypertensives).

3.2.3. Prescription rates across ‘Probable Suicide’ and Matched Control Cohorts

There were higher rates of psychotropic drug prescribing across all categories within the ‘probable suicide’ cohort (Table 3-4). The increased rates of antidepressant and other sedative drug prescriptions (e.g., benzodiazepines, z-drugs and gabapentinoids) could, perhaps, have been predicted; given the reported association between ‘probable suicide’ and mental illness. Therefore, there is a logical association between ‘probable suicide’ and a history of receiving the drugs most commonly prescribed in managing the symptoms of common psychiatric disorders.

Additionally, within the ‘probable suicide’ cohort, 16.6% were receiving methadone for OST, compared to only 1.3% of the matched controls. As 197 of the ‘probable suicide’ cohort overlapped with the DRD cohort, a higher rate of OST prescribing might be predicted, based on the principle that those dying of drug-related causes are likely to be using specialised drug-related healthcare services. Of these 97 individuals receiving methadone within this ‘probable suicide’ cohort, only 74 were also present in the DRD cohort, indicating that 23 individuals receiving an OST prescription of methadone were ruled ‘probable suicide’ deaths only.

Lastly, although numbers of prescriptions were low, the opposite pattern was observed for drugs that might be considered proxy indicators of anticipatory / preventative health care – statins and antihypertensive drugs. Antihypertensive medication was higher in the control group, while the difference in the rate of statin prescription did not reach significance.

3.2.4. Evaluation of ‘Quality’ of Psychiatric Outpatient Healthcare

To further investigate the differences in psychiatric healthcare between groups, the number of psychiatric outpatient attendances were tallied. Based on the principle that antidepressant prescribing guidelines recommend follow-up appointments for the management of medication side-effects, and the fact that patients receiving only talking therapies would also require more than one appointment for a course of treatment to be completed, the frequency of psychiatric outpatient attendances was investigated as a proxy for healthcare engagement and treatment quality.

Individuals with at least one psychiatric outpatient attendance were isolated and their records over the year were examined. The ‘probable suicide’ group had a median of 3, with a range of 1-86 attendances while the control group had a median of 2, with a range of 1-94 attendances. A Poisson logistic regression was calculated, with the number of outpatient attendances as the outcome. The model, including demographic factors and whether the individual was part of the ‘probable suicide’ cohort or the control group, was significant X^2 (8, N=300) = 106.547, $p<0.0001$. With each additional psychiatric outpatient attendance, it was more likely that the patient belonged to the ‘probable suicide’ group than the control group (odds summarised in table 3-5). By comparison, as the number of psychiatric outpatient attendances increased, it was less likely that the individuals belonged to the categories of those 25 years old or younger, or those 51 years old or older. Finally, each additional attendance lessened the odds that the individual was in SIMD 2, 3 and 4, compared to SIMD 1 (the most deprived quintile).

To further investigate healthcare engagement, the number of missed psychiatric outpatient attendances was also examined. The ‘probable suicide’ group had a median of 2, with a range of 1-20 missed appointments, and the control group had a median of 2, with a range of 1-23. Another Poisson logistic regression model was computed, using the frequency of missed appointments as the outcome variable. The model was significant X^2 (8, N=194) = 39.900, $p<0.0001$. As the number of missed psychiatric outpatient appointments increased, the individual was more likely to belong to the ‘probable suicide’ group than the control group (odds summarised in table 3-6). Individuals in the less deprived quintiles were all significantly less likely to miss multiple appointments.

Table 3-5. Regression predicting Psychiatric Outpatient Appointment Frequency

Variable	Exp(B)	95% CI for Exp(B)
Control Group	Reference	
‘Probable Suicide’ Group	**1.315**	**1.186-1.458**
Men	Reference	
Women	1.048	0.954-1.151
≤25 years old	**0.702**	**0.590-0.837**
26-50 years old	Reference	
≥51 years old	**0.791**	**0.700-0.893**
SIMD 1	Reference	
SIMD 2	**0.726**	**0.652-0.809**
SIMD 3	**0.715**	**0.600-0.852**
SIMD 4	**0.830**	**0.715-0.964**
SIMD 5	0.882	0.737-1.057

Odds ratios from a Poisson logistic regression model predicting the frequency of psychiatric outpatient attendances, across both groups, as the outcome. Demographic measures were used as explanatory variables and the largest sub-group was set as the reference group. Bold rows indicate statistical significance. The ‘probable suicide’ group were associated with higher frequencies of psychiatric outpatient attendance, while those 25 years old or under, 51 years old or older or in less socio-economically deprived quintiles were associated with lower frequencies of attendance.

Table 3-6. Regression predicting Missed Psychiatric Outpatient Appointment Frequency

Variable	Exp(B)	95% CI for Exp(B)
Control Group	Reference	
'Probable Suicide' Group	**1.291**	**1.080-1.543**
Men	Reference	
Women	1.018	0.870-1.191
≤25 years old	0.775	0.582-1.032
26-50 years old	Reference	
≥51 years old	1.220	0.970-1.535
SIMD 1	Reference	
SIMD 2	**0.724**	**0.608-0.863**
SIMD 3	**0.515**	**0.362-0.733**
SIMD 4	**0.640**	**0.466-0.879**
SIMD 5	**0.658**	**0.454-0.955**

Odds ratios from a Poisson logistic regression model predicting the frequency of missed psychiatric outpatient appointments. Demographic measures were used as explanatory variables and the largest sub-group was set as the reference group. Bold rows indicate statistical significance. The 'probable suicide' group were associated with higher frequencies of missed psychiatric outpatient appointments, while those in less socioeconomically deprived quintiles were associated with lower frequencies of missed appointments.

3.3. Possible Self-Harm Attendance at Accident and Emergency Services

3.3.1. Introduction

As previously described, self-harm is associated with a significantly higher risk of 'probable suicide', as well as premature mortality from other causes, including accidents or natural causes (Chan et al., 2016, Bergen et al., 2012). These studies also concluded that self-harm was non-specific as a predictive risk factor, due to the relatively high clinical rate of self-harm and the rarity of 'probable suicide'. Some studies have identified patients with these presentations and then investigated follow-up by the healthcare service, and have highlighted the difficulty with confounding by indication, in that the most intensive follow-up (mental health services inpatient admission) was associated with the highest risk of death (Kapur et al., 2015). Rarely do these studies go beyond simple observation and correlational analysis. However, the data available through HIC allowed a closer examination of healthcare usage and gave me access to data that could be used to test specific hypotheses. These were:

1. To test whether a definition of possible self-harm presentations could be constructed, using the Accident and Emergency dataset
2. To examine whether the rate of possible self-harm presentations differed between the 'probable suicide' group, with an Accident and Emergency presentation, and the control group, with the same service usage
3. To identify possible follow-up in the short-term period after the presentation, again compared between groups
4. To compare whether psychotropic prescriptions were modified after the possible self-harm presentation, and whether this rate differed between groups, to compare treatment received after a "crisis point"

3.3.2. Method

Once all Accident and Emergency presentations were identified, the meta-data files were further examined to identify which variables could be operationalised to represent a possible self-harm presentation. As the only data available was administrative, a wide definition of possible self-harm presentations had to be employed. While there was a data column designed to record the intent of the injury, which therefore could have been a good indicator for episodes of possible self-harm, it was empty for the vast majority of records (80.3% or 512/638 contained no data for the 'probable suicide', while the control dataset had no data in 65.5% or 277/423 of the presentations). The final definition identified relevant Accident and Emergency presentations by looking at reasons for attendance, discharge codes and data indicating subsequent healthcare referrals; specifically, the categories were: a code referring to "injury/trauma/poisoning", or a 'psychiatry reason' for the attendance, any episode with a code denoting deliberate self-harm, any reference to discharge to psychiatric hospital, and lastly, referral to mental health services. A small number of individuals fulfilled two of the criteria, while the diagnosis code for injury/trauma/poisoning was the modal cause for identification as a possible self-harm event (95% or 138/145 of the 'probable suicide' group, and 100% or 140/140 of the control group).

Afterwards, the discharge date of the possible self-harm presentations at Accident and Emergency services were cross-checked against the databases that would indicate potential psychiatric follow-up. For patients with multiple attendances, only the first possible self-harm event was considered. The databases of interest were prescription records, psychiatric outpatient attendances and psychiatric inpatient attendances. Since part of the definition used to identify a possible self-harm event within A&E was a referral to mental health services, it could have created a bias within the data. The follow-up rate could have been artificially increased by selecting individuals who were specifically referred for follow-up, compared to individuals who may have had a self-harm presentation without it being recognised or recorded in a way that fulfilled the study definition. As noted above, the vast majority of possible self-harm presentations were identified using the diagnosis code criteria, therefore this should have had minimal impact.

In all three databases, potential follow-up was limited to 21 days after the discharge date recorded in the Accident and Emergency database. This right-censor was chosen in an attempt to strengthen the link between the self-harm attendance and the potential follow-up, as there were no additional notes available that might have recorded the reasons for the psychiatric inpatient or outpatient attendance. Likewise, any prescription (or indeed prescription modification) could be unrelated to the possible self-harm event, even within the time limit of 21 days. The most fitting adjustment to minimise these risks was to limit the time-frame considered.

The criteria for identifying a modified prescription within 21 days was a change in the dosage (including the number of tablets dispensed), a new prescription, a prescription renewed after an interruption, or a prescription not reissued compared to the previous month. In some cases, the patient had an irregular schedule of prescription dispensation, thus making final classifications difficult. Additionally, as the interest was in follow-up changes, any prescriptions of interest (antidepressants, sedatives, antipsychotics or anticonvulsants) or psychiatric outpatient attendances on the same day as the possible self-harm event were discounted, as there were no additional sources of data to identify which healthcare service was attended first on the day in question.

3.3.3. Rate of Attendance compared across ‘Probable Suicide’ and Control Groups

Rates of Accident and Emergency presentation were significantly elevated in the ‘probable suicide’ cohort compared to the controls, as established above. Of those with an Accident and Emergency presentation, 60% of the ‘probable suicide’ sub-group had a possible self-harm attendance, compared to 44% of the controls. A chi-square test showed this to be a statistically significant difference between groups X^2 (1, N=561) = 13.491, $p<0.05$.

It is worth noting that the number of individuals with possible self-harm presentations to A&E in both groups was very similar: 145 ‘probable suicide’ individuals fulfilled criteria, along with 140 control group individuals. Of the total cohort, this would represent 25% and 6% respectively, which suggests that within the ‘probable suicide’ cohort as a whole, self-harm resulting in a healthcare presentation was less prevalent than might have been hypothesised.

3.3.4. Psychiatric Follow-up After Possible Self-harm

The first possible self-harm event in the year was identified for each individual, as the initial goal had been to examine healthcare over the course of the year, following possible self-harm. This was refined to a follow-up period covering only 21 days, as explained above. When any psychiatric healthcare follow-up was considered (inpatient or outpatient attendances, or psychotropic prescriptions), there was a very significant difference, with 48% of the ‘probable suicide’ group receiving any type of follow-up compared with only 12% of controls. The results are summarised in table 3-7. The magnitude of the difference was unanticipated, but corroborates the previous results associating a higher rate of psychiatric healthcare with those in the ‘probable suicide’ group, in contrast to the theory present in the literature that gaps within treatment provision are to blame for high ‘probable suicide’ rates (Vasiliadis, Ngamini-Ngui and Lesage, 2015).

These results were then filtered by the category of follow-up treatment received. Across both groups, the most common follow-up received after a possible self-harm event was a psychotropic drug prescription (i.e., an antidepressant, antipsychotic, anticonvulsant or sedative drug) at 32% of the ‘probable suicide’ group compared to 11% of the control group. Furthermore, several of these individuals attended a psychiatric outpatient clinic within this time period (20 of the ‘probable suicide’ individuals received both of these follow-up modalities, compared to 4 of the control individuals). None of the control individuals were admitted to a psychiatric inpatient ward in the 21 days after a possible self-harm event, while a small number of ‘probable suicide’ individuals were (13/145 or 9%). Again, this would suggest differences in distress levels were recognised, especially as 4 of these ‘probable suicide’ individuals were discharged to the psychiatric hospital directly from Accident and Emergency services.

3.3.5. Psychotropic Prescription Modification

As noted above, the proposition that there is a lack of appropriate treatment after possible self-harm events suggested that examining the responsiveness of healthcare modalities after an event would be a valuable analysis. Changes to any of the psychotropic prescriptions (antidepressant, antipsychotic, anticonvulsant or sedative drugs), compared to the previous month were identified. Modifications were noted in 27 (57.4% of those with a psychotropic prescription in 21 days) of the ‘probable suicide’ sub-group and 11 (68.8%) of the controls. Mindful of the small sample size, Fisher’s Exact test was not significant, when contrasting the percentage of individuals who had their prescriptions modified, within 21 days after a possible self-harm presentation. In both groups, over half of the individuals had their prescriptions modified, which does not support the argument that ‘probable suicide’ is linked to poor treatment responsiveness after possible self-harm.

3.3.6. High Frequency Possible Self-Harm Attendance Group Analysis

Finally, a “high risk” sub-cohort, containing those with 3 or more possible self-harm attendances, was identified. These were 21 ‘probable suicide’ individuals (median of 3 presentations, with a range of 3-13 attendances) and 7 controls (median of 3, with a range of 3-6 attendances). Of the 21 ‘probable suicide’ individuals, 13 (62%) had at least one type of follow-up in the 21 days after the first possible self-harm presentation. Out of the 7 controls, only 2 out of 7 (29%) fulfilled criteria for receiving follow-up, however the absolute numbers in both groups were very small. Fisher’s Exact test was non-significant, when comparing the rate of follow-up in this sub-group. Therefore, while the range of presentations was higher in the ‘probable suicide’ group, the medians and rate of follow-up did not reveal significant differences between those who died and the control cohorts, in this high frequency sub-group.

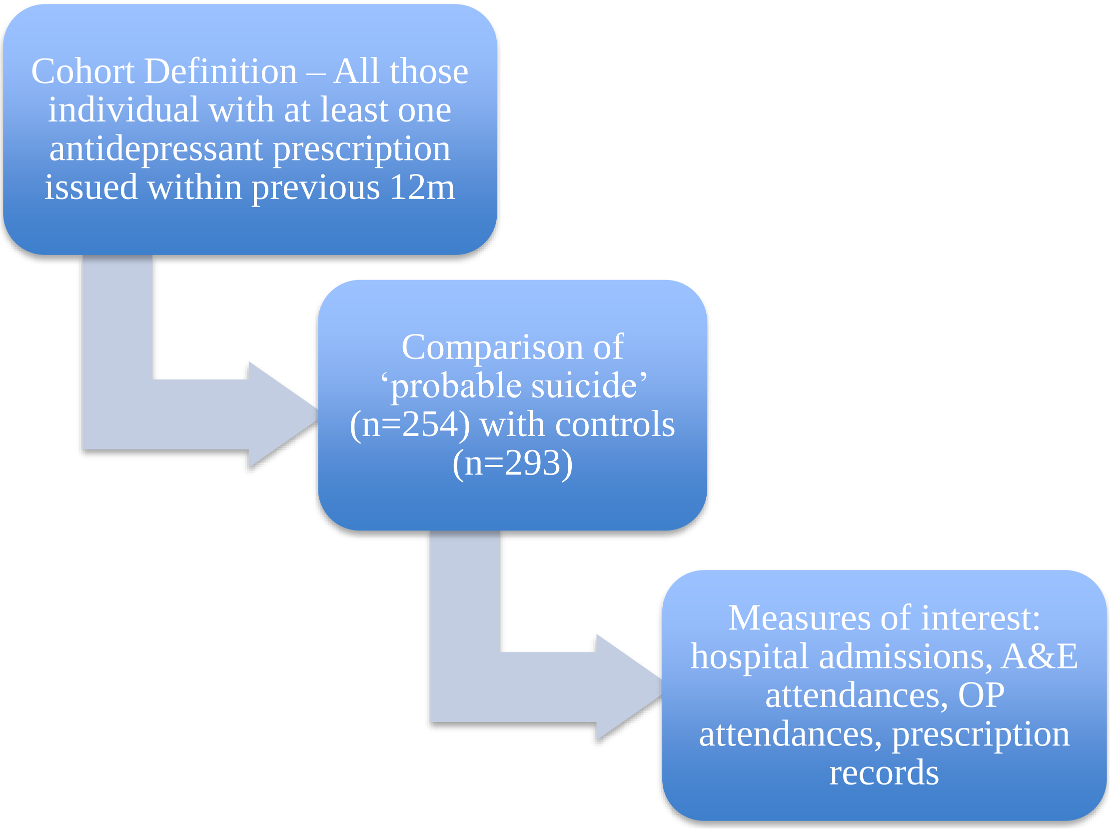
Table 3-7. Follow-up rates after Possible Self-harm Presentations

Variable	'Probable Suicide' (N=145)		Controls (N=140)		X^2	p value
	%	(n)	%	(n)		
Any follow-up ≤21 days after SH:	**47.6**	**69**	**12.1**	**17**	**42.468**	**<0.05**
Psychotropic Prescription	**32.4**	**47**	**11.4**	**16**	**18.217**	**<0.05**
Psychiatric Outpatient Clinic	**24.8**	**36**	**3.6**	**5**		**<0.05***
Mental Health Inpatient	**9.0**	**13**	**0.0**	**0**		**<0.05***

Comparison of possible self-harm attendances at Accident and Emergency Services, across 'probable suicide' and control groups, including psychiatric follow-up in the 21 days after the presentation. Possible self-harm was defined using a variety of codes (those recording a poisoning, intentional self-harm or a psychiatric complaint, those discharged to psychiatric hospitals or those discharged with a psychiatric referral. These statistics were based solely on the first possible self-harm presentation within the year. Chi-square tests were calculated, with rows in bold indicating statistical significance. * represents a low cell count, requiring Fisher's exact test rather than a Chi-square test. The 'probable suicide' group received more follow-up after a possible self-harm presentation than the control group.

3.4. Analysis of those with Antidepressant Prescriptions

Figure 3-2. Flowchart Identifying the Cohort with an Antidepressant Prescription



The first sub-section of the data analysis was focused on interrogating those arguably "in treatment", therefore, receiving an antidepressant prescription over the twelve months before death, or index date for the control group. Once the healthcare measures for the previous analysis had been coded, the individuals from the full cohort were filtered by antidepressant prescription and group status, which resulted in relatively similar-sized cohorts, as shown in box two. Finally, similar healthcare utilisations comparisons were undertaken, using the databases previously described.

3.4.1. Introduction

After comparing the healthcare utilisation of the entire cohorts of ‘probable suicide’ and control individuals, relevant sub-sections of the cohorts were extracted from the full cohort for further analysis. The first sub-section of interest was all individuals with an antidepressant prescription in the twelve months before death. As noted in the introduction, there is a strong association, in the literature and in public health campaigns, between depression and death by ‘probable suicide’. Retrospectively investigating all the individuals arguably belonging to this “high-risk” category of being in treatment for depression could reveal significant differences in healthcare usage. Specifically, the hypotheses of this section all relate to whether there were notable differences in healthcare utilisation between those who went on to die a ‘probable suicide’, versus those in the ‘live’ control group, while all individuals received an antidepressant prescription, within the study timeframe.

The analyses below, investigating both healthcare utilisation and prescription records, all apply to the antidepressant prescribed sub-section of the full cohort, amounting to 254 ‘probable suicide’ individuals, and 293 of the control individuals.

3.4.2. Healthcare Usage within the Antidepressant Prescribed Groups

Despite all these individuals being arguably recognised as requiring psychiatric support, the individuals in the ‘probable suicide’ group still had considerably higher rates of attendance at psychiatric healthcare services (see Table 3-8). This was especially noticeable concerning psychiatric outpatient attendances, which 63% of those who died had attended, versus 17% of the controls. Relative to psychiatric inpatient attendances, 19% of the ‘probable suicide’ cohort had at least one attendance, with only 0.7% of the control groups; however, rates of psychiatric inpatient admission were generally low. These differences suggest that the healthcare system had distinguished between groups with higher and lower risk profiles, which resulted in distinct intensities of intervention.

General inpatient admission was significantly different between groups, with 42% of the ‘probable suicide’ group attending compared with 17% of the controls. When these attendances were broken down into whether individuals had routine or emergency presentations, the chi-square revealed no differences in the rate of routine attendance. Interestingly, the rates of Accident and Emergency presentation were increased for both groups relative to the total cohort comparison, and still showed a much higher attendance in the ‘probable suicide’ group who had received an antidepressant prescription, than the controls who had received an antidepressant prescription (54% to 20%, respectively). This would still suggest that those who went on to die were associated with greater use of acute healthcare services than those who did not die, even though all were associated with psychological distress that was recognised by the healthcare service. Furthermore, both groups had a slightly over 60% of individuals in quintiles of severe deprivation (SIMD 1 and 2).

Furthermore, non-psychiatric outpatient clinic attendances were at a slightly higher rate than the previous comparisons using the full cohort (previous rates were between 20-25% of the cohort, here between 30-35% of individuals of both groups attended), however, the groups were not statistically distinguishable from each other.

Table 3-8. Healthcare Utilisation rates across all those with Antidepressant Prescriptions

Variable	'Probable Suicide' (N=254)		Control (N=293)		X²	p value
	%	(n)	%	(n)		
General inpatient	**42.1**	**107**	**17.4**	**51**	**40.474**	**<0.05**
Routine Attendance	45.8	49	52.9	27	0.707	>0.05
Psychiatric outpatient	**63.4**	**161**	**16.7**	**49**	**125.248**	**<0.05**
Non-psychiatric outpatient	35.8	91	32.4	95	0.702	>0.05
Mental Health Inpatient	**18.5**	**47**	**0.7**	**2**		**<0.05***
Accident and Emergency	**53.5**	**136**	**20.1**	**59**	**66.188**	**<0.05**

Including only individuals receiving an antidepressant prescription, a comparison of those deemed 'probable suicide' with controls with respect to healthcare usage across a variety of services within preceding 12m. General hospital presentations included both day-patient and elective inpatient events, therefore 'routine attendance' was calculated for those with at least one of these general hospital codes. Outpatient clinics were split by clinical specialty, with psychiatric codes not distinguishing between mental health or substance misuse. Chi-square tests were calculated, with rows in bold indicating statistical significance. * represents a low cell count, requiring Fisher's exact test rather than a Chi-square test. The 'probable suicide' group attended all but non-psychiatric outpatient clinics at higher rates than the controls, despite all receiving an antidepressant prescription.

Table 3-9. Prescription rates across all those with Antidepressant Prescriptions

Variable	'Probable Suicide' (N=254)		Control (N=293)		X²	p value
	%	(n)	%	(n)		
Methadone	**25.6**	**65**	**4.8**	**14**	**47.694**	**<0.05**
Benzodiazepines	**42.9**	**109**	**15.0**	**44**	**52.553**	**<0.05**
Z-drugs	**31.9**	**81**	**16.0**	**47**	**19.066**	**<0.05**
Gabapentinoids	**20.1**	**51**	**13.7**	**40**	**4.052**	**<0.05**
Anticonvulsants	**26.4**	**67**	**17.1**	**50**	**7.018**	**<0.05**
Statins	11.0	28	15.4	45	2.211	>0.05
Antihypertensives	7.5	19	11.9	35	3.049	>0.05

Percentage and count data comparing prescription data for all those deemed 'probable suicide' and controls who had received an antidepressant prescription. Chi-square tests were calculated, with rows in bold indicating statistical significance. The 'probable suicide' group had higher rates of additional psychotropic prescriptions than the control group.

3.4.3. Prescription Records within Antidepressant Prescribed Groups

One important aspect of these results is that they demonstrate a notable rate of co-prescription, as summarised in table 3-9. This is particularly interesting for the individuals who died, as they had higher rates of all additional psychotropic prescriptions than the controls. Benzodiazepines, particularly, were co-prescribed at a significant rate, with almost 43% of the 'probable suicide' group receiving both these and an antidepressant prescription, compared to only 15% of the controls.

OST-based methadone prescriptions were recorded in 26% of the 'probable suicide' group, compared to 5% of the controls. The greater risk of death for those with both mental illnesses and drug misuse has been well-established, therefore that the vast majority of those with both an antidepressant and methadone prescription could be identified within the DRD cohort simultaneously was to be anticipated (the total was 52/65 or 80%).

Interestingly, at this level, there were no significant differences between groups in terms of statin and antihypertensive prescriptions, even though the percentages suggested a trend towards a higher prescription rate in the controls.

3.4.4. Evaluation of 'Quality' of Antidepressant Drug Prescribing

The cohort definition for this sub-section of analysis was simply the presence of at least one antidepressant prescription, over the twelve months before death, or index date. Treatment guidelines for the optimal prescription of antidepressants state that a response is typically expected within the first 4 weeks, that regular reviews are necessary and that the prescribed drug may need to be taken for at least 6 months after remission to prevent a relapse (NICE, 2022 (b)). Using the cohort prescribed at least one antidepressant in the twelve months before death or index date, I examined the prescription records and tallied the number of antidepressant prescriptions redeemed throughout the year, which represents a proxy measure for the duration of the antidepressant treatment, and in turn represents how many patients received treatment that complied with clinical guidance.

The number of antidepressant prescriptions dispensed over the course of the twelve months was a median of 8 for the 'probable suicide' group, with a range of 1-39, while the control group had a median of 5 prescriptions, with a range of 1-32.

To test for associations between increasing numbers of dispensed antidepressant prescriptions with demographic variables, a Poisson logistic regression model was calculated. This model was significant X^2 (8, N=531) = 220.385, $p<0.001$, which demonstrates that with each unit increase in the number of antidepressant prescriptions dispensed, there were significant associations with some of the tested variables. Unsurprisingly, the odds that the individual belonged to the ‘probable suicide’ group was higher with each additional antidepressant prescription over the year. Women were also associated with higher frequencies of antidepressant prescriptions. As the number of prescriptions increased, it was less likely that the individuals belonged to the 25 years old or younger group, compared to the reference group of those 26-50 years old. Lastly, each additional antidepressant was associated with belonging to the more deprived quintiles, as demonstrated by a lessening of the odds that the individual was in the less deprived quintiles (SIMD 3, 4 and 5), as quantified in table 3-10.

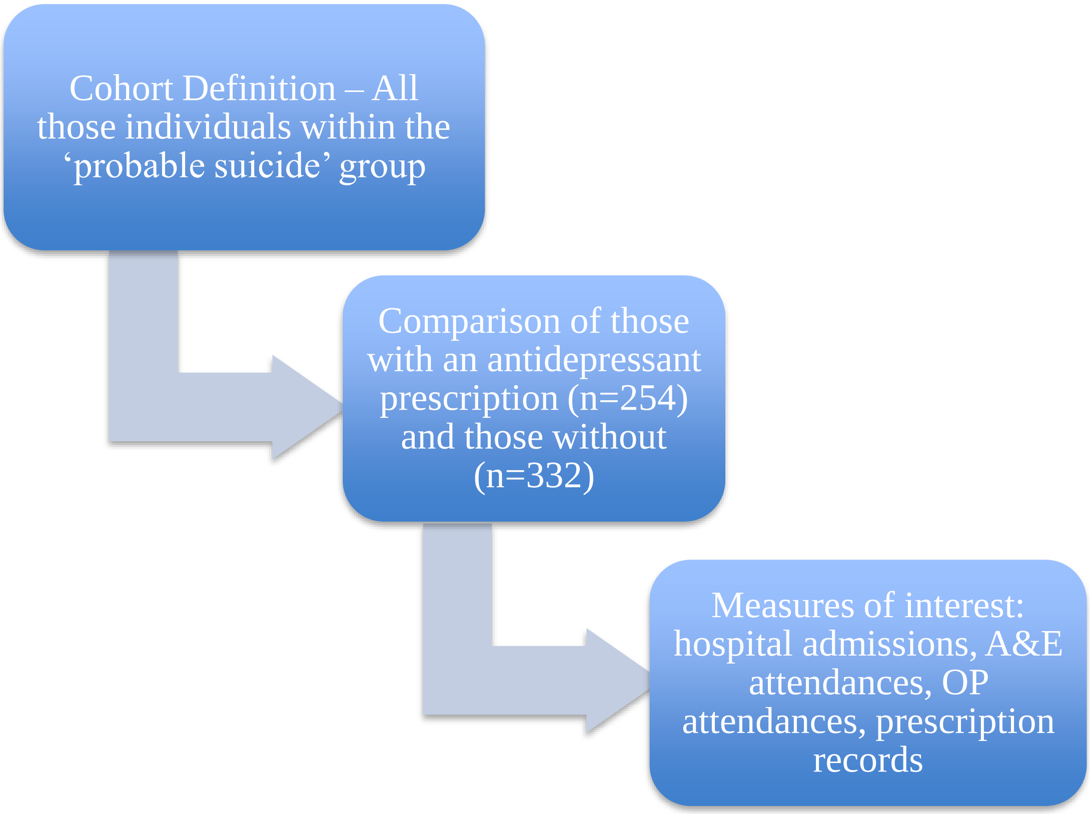
Table 3-10. Regression predicting frequencies of Antidepressant prescriptions

Variable	Exp(B)	95% CI for Exp(B)
Control Group	Reference	
‘Probable Suicide’ Group	**1.405**	**1.317-1.499**
Men	Reference	
Women	**1.208**	**1.133-1.287**
≤25 years old	**0.693**	**0.588-0.816**
26-50 years old	Reference	
≥51 years old	0.949	0.884-1.019
SIMD 1	Reference	
SIMD 2	0.930	0.859-1.006
SIMD 3	**0.764**	**0.680-0.859**
SIMD 4	**0.682**	**0.613-0.758**
SIMD 5	**0.866**	**0.773-0.971**

Odds ratios from a Poisson logistic regression model predicting prescription of an antidepressant, within the ‘probable suicide’ cohort, as the outcome. Demographic measures were used as explanatory variables and the largest sub-group was set as the reference group. Bold rows indicate statistical significance. The ‘probable suicide’ group and women were linked with higher frequencies of antidepressant prescriptions, while those under 25 years old or in less socioeconomically deprived quintiles were associated with lower frequencies of prescriptions.

3.5. Analysis of the 'Probable Suicide' Cohort

Figure 3-3. Flowchart Identifying the 'Probable Suicide' Cohort



The second sub-section of the data analysis was focused on interrogating only those in the 'probable suicide' group. Once the healthcare measures for the previous analysis had been coded, the 'probable suicide' individuals were filtered by antidepressant prescription in the twelve months before death, which resulted in relatively similar-sized cohorts, as shown in box two. Finally, similar healthcare utilisations comparisons were undertaken, using the databases previously described.

3.5.1. Introduction

Following the comparisons of healthcare utilisation across the total cohort of 'probable suicide' and control groups, and investigating those "in treatment", the final sub-section of interest was simply the 'probable suicide' group itself. One of the aims of this thesis was to investigate potential sub-groups within the category of 'probable suicide', primarily because understanding the different sub-types and needs of this population could improve our ability to design and implement targeted preventative strategies. Furthermore, the theory of gaps in the healthcare service contributing to high 'probable suicide' rates necessitates an understanding of how many of the people who die by 'probable suicide' are in contact with the healthcare service, and how these patterns of utilisation either support or contradict that argument. Both accessibility to healthcare and poverty have been linked to higher rates of 'probable suicide', therefore investigating potential differences within the 'probable suicide' cohort, on the basis of socio-economic deprivation, is likewise key to defining this sample. As such, the first set of analyses splits the 'probable suicide' group by whether they had received at least one antidepressant prescription in the twelve months before death ("in treatment" or not "in treatment"). The second set of analyses splits the individuals by high or low socio-economic deprivation status.

3.5.2. Healthcare Usage within the 'Probable Suicide' Group

Within the 'probable suicide' cohort, slightly less than half of the individuals received an antidepressant prescription in the twelve months before death (43% or 254/586 individuals). This section of the cohort attended all services at significantly higher rates than the individuals within the 'probable suicide' cohort who did not receive any antidepressant prescriptions (see Table 3-11). Unsurprisingly, the section of the cohort that received an antidepressant prescription had a considerably higher rate of psychiatric outpatient attendance than those who did not, at 63% to 20% of the groups, respectively. Mental health inpatient services were also used by a greater percentage of the individuals who had received an antidepressant prescription than those who did not (19% to 3%, respectively).

Forty two percent of those with an antidepressant prescription attended general inpatient services, compared to 21% of those without a prescription, however the rate of routine inpatient attendances was at 46% for both groups. Accident and

Emergency attendances were still considerably elevated in the group with antidepressant prescriptions (54% versus 32%), however this was the smallest difference between groups, when considering previous cohort comparisons for emergency presentations.

Non-psychiatric outpatient attendances were also significantly higher in the group of individuals who were in receipt of antidepressants, with a rate of 36% compared to 19% of the groups having at least one recorded presentation. As 61% of the group receiving antidepressants was in the most deprived quintiles (SIMD 1 and 2), compared to 46% of the group not receiving an antidepressant prescription, SIMD likely had a significant effect on healthcare access and engagement.

Table 3-11. Healthcare Utilisation, within the 'Probable Suicide' Group Only

Variable	**Antidepressant Prescribed (N=254)**		**No Antidepressant Prescribed (N=332)**		**X²**	**p value**
	%	(n)	%	(n)		
General inpatient	**42.1**	**107**	**21.1**	**70**	**30.223**	**<0.05**
Routine Attendance	45.8	49	45.7	32	0.000	>0.05
Psychiatric outpatient	**63.4**	**161**	**19.6**	**65**	**116.562**	**<0.05**
Non-psychiatric outpatient	**35.8**	**91**	**18.7**	**62**	**21.944**	**<0.05**
Mental Health Inpatient	**18.5**	**47**	**3.0**	**10**	**39.332**	**<0.05**
Accident and Emergency	**53.5**	**136**	**32.2**	**107**	**26.935**	**<0.05**

Comparison of only the individuals deemed ‘probable suicide’, split by whether they received an antidepressant prescription or not, with respect to healthcare usage across a variety of services within preceding 12m. General hospital presentations included both day-patient and elective inpatient events, therefore ‘routine attendance’ was calculated for those with at least one of these general hospital codes. Outpatient clinics were split by clinical specialty, with psychiatric codes not distinguishing between mental health or substance misuse. Chi-square tests were calculated, with rows in bold indicating statistical significance. The individuals receiving antidepressant prescriptions attended all services at higher rates than those without antidepressant prescriptions.

Table 3-12. Prescription records, within the 'Probable Suicide' Group Only

Variable	**Antidepressant Prescribed (N=254)**		**No Antidepressant Prescribed (N=332)**		**X²**	**p value**
	%	(n)	%	(n)		
Methadone	**25.6**	**65**	**9.6**	**32**	**26.511**	**<0.05**
Benzodiazepines	**42.9**	**109**	**6.3**	**21**	**111.594**	**<0.05**
Z-drugs	**31.9**	**81**	**6.6**	**22**	**63.396**	**<0.05**
Gabapentinoids	**20.1**	**51**	**3.6**	**12**	**40.655**	**<0.05**
Anticonvulsants	**26.4**	**67**	**6.9**	**23**	**41.879**	**<0.05**
Statins	**11.0**	**28**	**5.4**	**18**	**6.243**	**<0.05**
Antihypertensives	7.5	19	5.1	17	1.390	>0.05

Percentage and count data comparing prescription data for only the individuals deemed ‘probable suicide’, split by whether they had received an antidepressant prescription or not. Chi-square tests were calculated, with rows in bold indicating statistical significance. The individuals with an antidepressant prescription had higher rates of additional prescriptions.

3.5.3. Prescription Records within the 'Probable Suicide' Group

As was the case in the previous set of analyses, comparing the rates of additional prescriptions between those with or without antidepressant prescriptions in the year before death can be used to reveal a significant amount of co-prescribing within one section of the cohort. As before, benzodiazepines were the drug class most commonly co-prescribed with antidepressants, and these were significantly more prescribed for this group than those without an antidepressant prescription (43% to 6%). The other sedative drugs were also prescribed at significantly higher rates for those who received an antidepressant than those who did not, summarised in Table 3-12.

The prescription of methadone, in an OST context, was significantly more common in the group with an antidepressant prescription than those without, at 26% to 10% respectively. The group without an antidepressant prescription received very few prescriptions overall, but the modal prescription was for methadone. This would suggest that some individuals not recorded as accessing mental health treatment are in contact with other healthcare services. This group could represent those who struggle to access the healthcare required for mental illness and substance abuse comorbidity, though further research into their needs would be required.

Both statins and antihypertensives were prescribed at higher rates to those receiving antidepressants, though this was only significant considering statin prescriptions. This could suggest that these individuals were slightly older, or accessing both emergency and routine healthcare at greater rates than those generally disengaged.

3.5.4. Demographic Differences within the 'Probable Suicide' Cohort

A binary logistic regression was calculated to test for demographic associations with an antidepressant prescription in the year before death. The model was significant X^2 $(7, N=540) = 59.572$, $p<0.001$. When examining all those who died by 'probable suicide', women were much more likely to have received an antidepressant prescription than men. Those who were 25 years old or younger were significantly less likely to receive an antidepressant prescription than those 26-50 years old. Finally, compared to the most deprived quintile, those in SIMD 3 and 4 were also associated with a lower likelihood of receiving an antidepressant prescription (values listed in Table 3-13).

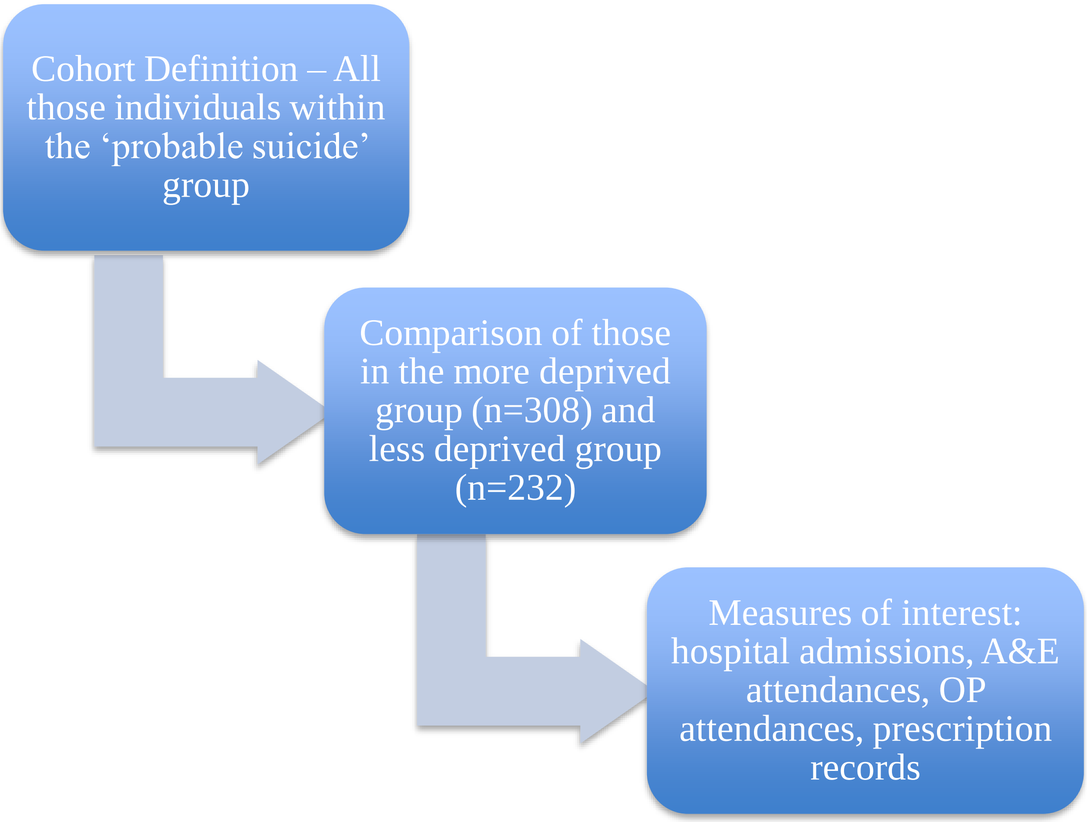
Table 3-13. Regression predicting Antidepressant Prescription in the 'Probable Suicide' Cohort

Variable	Exp(B)	95% CI for Exp(B)
Men	Reference	
Women	**3.350**	**2.201-5.099**
≤25 years old	**0.356**	**0.199-0.637**
26-50 years old	Reference	
≥51 years old	0.846	0.548-1.307
SIMD 1	Reference	
SIMD 2	0.892	0.556-1.430
SIMD 3	**0.472**	**0.251-0.887**
SIMD 4	**0.497**	**0.292-0.848**
SIMD 5	0.586	0.305-1.126

Odds ratios from a binary logistic regression model predicting prescription of an antidepressant within the ‘probable suicide’ cohort as the outcome. Demographic measures were used as explanatory variables and the largest sub-group was set as the reference group. Bold rows indicate statistical significance. Women within the ‘probable suicide’ group were more likely to have an antidepressant prescription than men, while those 25 years old or younger, or in less deprived quintiles were less likely to have an antidepressant prescription.

3.5.5. ‘Probable Suicide’ Group Analysis, focused on Socio-economic Deprivation

Figure 3-4. Flowchart Identifying the Socio-economic levels within 'Probable Suicide'



The third sub-section of the data analysis was focused on interrogating only those in the ‘probable suicide’ group. Once the healthcare measures for the previous analysis had been coded, the ‘probable suicide’ individuals were filtered by highly deprived or less deprived socioeconomic group in the twelve months before death, which resulted in relatively similar-sized cohorts, as shown in box two. Finally, similar healthcare utilisations comparisons were undertaken, using the databases previously described.

3.5.5.1. Healthcare Usage compared across Socio-economic Groups

Finally, the individuals who were deemed ‘probable suicide’ were split by relative level of socio-economic deprivation, as premature deaths are significantly more prevalent in more socio-economically deprived groups. In spite of this, there were few significant differences between groups when comparing healthcare attendance (see Table 3-14). Those in the most deprived quintiles had a higher rate of psychiatric outpatient attendance, with 50% compared to 26% of the less deprived quintiles attending. The only other difference was that the less deprived group had a much higher rate of routine general hospital attendance; suggesting an association between deprivation and more emergency attendance, concerning general inpatient attendances, at least.

3.5.5.2. Prescription Records compared across Socio-economic Groups

There were considerably more differences between socio-economic groups when examining prescription records (summarised in Table 3-15). Antidepressants were much more common in the more deprived group, compared to the less deprived group (51% versus 36%). Interestingly, while benzodiazepines and z-drug prescription rates were insignificantly different between groups, both gabapentinoids and anticonvulsants were prescribed at notably higher rates in the more deprived group, which could point towards an alternative pattern of healthcare needs than previous comparisons have revealed.

Additionally, statins and antihypertensives were prescribed at noticeably higher rates in the less deprived group, which would again corroborate the previous associations between less deprivation and an increased rate of preventative or routine healthcare.

Table 3-14. Healthcare Utilisation across Socio-economic Deprivation level

Variable	SIMD 1 and 2 (N=308)		SIMD 3, 4 and 5 (N=232)		X²	p value
	%	(n)	%	(n)		
General inpatient	32.1	99	28.4	66	0.851	>0.05
Routine Attendance	**37.4**	**37**	**57.6**	**38**	**6.519**	**<0.05**
Psychiatric outpatient	**50.0**	**154**	**26.3**	**61**	**31.036**	**<0.05**
Non-psychiatric outpatient	24.7	76	28.9	67	1.201	>0.05
Mental Health Inpatient	9.7	30	11.2	26	0.306	>0.05
Accident and Emergency	44.5	137	37.1	86	2.998	>0.05

Comparison of only those deemed ‘probable suicide’, split by socio-economic level, with respect to healthcare usage across a variety of services within preceding 12m. SIMD quintiles 1 and 2 represent high deprivation, with 3, 4 and 5 showing less deprivation. General hospital presentations included both day-patient and elective inpatient events, therefore ‘routine attendance’ was calculated for those with at least one of these general hospital codes. Outpatient clinics were split by clinical specialty, with psychiatric codes not distinguishing between mental health or substance misuse. Chi-square tests were calculated, with rows in bold indicating statistical significance. There were few differences; the more deprived group had a lower routine attendance, but a higher rate of psychiatric outpatient attendance.

Table 3-15. Prescription Records across Socio-economic Deprivation levels

Variable	SIMD 1 and 2 (N=308)		SIMD 3, 4 and 5 (N=232)		X²	p value
	%	(n)	%	(n)		
Methadone	**26.3**	**81**	**4.3**	**10**	**45.659**	**<0.05**
Antidepressants	**50.6**	**156**	**35.8**	**83**	**11.866**	**<0.05**
Benzodiazepines	25.3	78	19.4	45	2.644	>0.05
Z-drugs	17.5	54	18.1	42	0.030	>0.05
Gabapentinoids	**14.9**	**46**	**6.0**	**14**	**10.614**	**<0.05**
Anticonvulsants	**20.1**	**62**	**9.9**	**23**	**10.413**	**<0.05**
Statins	**5.2**	**16**	**12.5**	**29**	**9.244**	**<0.05**
Antihypertensives	**3.6**	**11**	**9.1**	**21**	**7.129**	**<0.05**

Percentage and count data comparing prescription data for only those deemed ‘probable suicide’, split by presence in high or low deprivation quintiles. SIMD quintiles 1 and 2 represent high deprivation, with 3, 4 and 5 representing low deprivation. Chi-square tests were calculated, with rows in bold indicating statistical significance. The more deprived group had a higher rate of psychotropic prescriptions, while the less deprived group had higher rates of statins and antihypertensives.

3.6. Multivariate Predictive Model

3.6.1. Introduction

The healthcare utilisation analysis of the 'probable suicide' group compared to the control group highlighted several key differences between groups; specifically, rates of Accident and Emergency presentations, psychiatric outpatient attendances and rates of psychotropic prescriptions frequently resulted in statistically significant differences between groups. These were generally maintained in the sub-group analyses. One of the purposes of healthcare research is to improve our understanding of a disease presentation, and the high or low-risk categories within that, to refine predictive models and increase their utility. As previously mentioned, current predictive models for 'probable suicide' usually identify being male, suicidal intent, physical health problems and having a history of self-harm as key, though non-specific, risk factors (Chan et al., 2016). The healthcare utilisation analysis presented so far has highlighted differences in service use between those who died and their matched controls, with some of these services unincluded in other predictive models. Including the variables identified in these univariate analyses may improve the power of a predictive model for 'probable suicide'.

3.6.2. Method

The full cohort of 586 'probable suicide' individuals and all 2,344 control individuals were read into the analysis, however the individuals with missing demographic analysis were excluded, leaving 540 'probable suicide' individuals and 2,319 control individuals. A binary logistic regression model was chosen, with 'probable suicide' or control cohort as the outcome variable. The additional variables that were included were chosen on the basis of significance in previously published studies and based on the analyses within this thesis. These were: demographic variables, at least one general hospital admittance, at least one psychiatric outpatient attendance, at least one Accident and Emergency presentation, at least one antidepressant prescription, at least one methadone prescription and at least one benzodiazepine prescription. These variables were chosen to capture the main differences noted, without introducing multiple variables that would overlap and lead to problems of multicollinearity – for example, including possible self-harm attendances and general Accident and Emergency presentations would have been redundant and introduced a significant assumption into the model, as the possible self-harm events are impossible to confirm with the data available.

3.6.3. Multivariate Model Results

The binary logistic regression model was significant X^2 (13, N=2859) = 711.862, $p<0.0001$, and using the Nagelkerke R^2 calculation, explained 35.5% of the variance in the data. The model, including all of the variables, classified 86.3% of the individuals correctly however, the majority of these correct classifications were in the control group. All of the variables contributed significantly to the model, with any attendance at a healthcare service or any psychotropic prescription being associated with an increased likelihood of ‘probable suicide’, compared to non-engagement as the referent categories.

Women were less likely than men to be ruled a ‘probable suicide’, however this was the least significant variable in the model, based on the Wald X^2 statistic. The most significant variable in the model was at least one psychiatric outpatient attendance, based on this statistic, and at least one psychiatric outpatient attendance had the largest odds ratio for increasing the likelihood of ‘probable suicide’ at 5.63 (odds ratios and confidence intervals summarised in table 3-16). The next most significant overall category was age group, which highlighted that those 25 years old or younger were much more likely to be ruled ‘probable suicide’ than the reference group of those 26-50 years old. The next most significant predictor, based on the Wald X^2 statistic was the receipt of at least one antidepressant prescription, followed by general hospital inpatient attendance. The next most significant variables in the model were at least one methadone prescription, an Accident and Emergency presentation, socioeconomic deprivation score, at least one benzodiazepine prescription and then gender, as mentioned. Unanticipatedly, the less deprived quintiles were associated with greater odds of belonging to the ‘probable suicide’ cohort.

The inclusion of all these factors only explained just over a third of the variance within the model, which highlights the challenge of constructing accurate predictive models for a phenomenon as complex and rare as ‘probable suicide’.

Table 3-16. Multivariate Model Predicting 'Probable Suicide'

Variable	Wald X^2 Statistic	Exp(B)	95% CI for Exp(B)
Men	**6.566**	Reference	
Women		**0.700**	**0.533-0.920**
≤25 years old		**3.897**	**2.727-5.568**
26-50 years old	**66.041**	Reference	
≥51 years old		0.849	0.654-1.104
SIMD 1	**18.884**	Reference	
SIMD 2		**1.471**	**1.071-2.020**
SIMD 3		**1.598**	**1.101-2.320**
SIMD 4		**1.874**	**1.353-2.594**
SIMD 5		**2.017**	**1.342-3.032**
No General Hospital Admittance	**25.421**	Reference	
≥1 General Hospital Admittance		**2.276**	**1.653-3.134**
No Psychiatric outpatient Attendance	**92.145**	Reference	
≥1 Psychiatric outpatient Attendance		**5.633**	**3.958-8.017**
No Accident and Emergency Presentation	**21.582**	Reference	
≥1 Accident and Emergency Presentation		**1.929**	**1.462-2.544**
No Antidepressant Prescription	**40.178**	Reference	
≥1 Antidepressant Prescription		**2.516**	**1.892-3.347**
No Methadone Prescription	**22.758**	Reference	
≥1 Methadone Prescription		**3.720**	**2.168-6.382**
No Benzodiazepine Prescription	**16.112**	Reference	
≥1 Benzodiazepine Prescription		**2.189**	**1.493-3.209**

Odds ratios from a binary logistic regression model predicting ‘probable suicide’, based on demographic and healthcare measures. The largest sub-group was set as the reference group. Wald X^2 statistic represents the unique contribution of each factor, when every other factor is kept constant, thus representing the contribution of the factor to the model. Bold rows indicate statistical significance. Women were significantly less likely to be ruled ‘probable suicide’ than men, while usage of any healthcare services significantly increased the odds of belonging to the ‘probable suicide’ cohort, especially psychiatric outpatient attendance.

3.7. Summary of 'Probable Suicide' Analysis

Of the 605 individuals initially categorised as 'probable suicide' decedents, only 586 could be validated with ICD-10 codes, though a small number of these individuals were lacking demographic data.

The comparison between the validated 'probable suicide' cohort and the matched community controls demonstrated that the 'probable suicide' cohort attended all healthcare services at higher rates. Psychiatric healthcare services showed the greatest difference in the rate of attendance, with almost 40% of the 'probable suicide' cohort attending at least once, to 4% of the control cohort. Similarly, psychotropic prescriptions were redeemed at higher rates in the 'probable suicide' cohort, with an inversion noted for routine prescriptions of antihypertensives.

Possible self-harm events were identified in a higher percentage of the 'probable suicide' cohort with Accident and Emergency presentations, and this cohort received a greater rate of psychiatric healthcare follow-up than the controls. Prescription modifications in the 21 days after the event were similar across groups.

Those with antidepressant prescriptions were isolated from both cohorts and contrasted; again, the majority of healthcare services were attended at greater rates by the 'probable suicide' cohort considered "in treatment" than the controls. The largest difference was reported in the rate of psychiatric outpatient attendance, despite all individuals receiving antidepressant prescriptions. Likewise, additional psychotropic prescriptions were redeemed at higher rates in the 'probable suicide' cohort, who were associated with a higher frequency of antidepressant prescriptions.

Focusing only on the 'probable suicide' cohort, two splits were performed; the same "in or out of treatment" concept was explored, as was a division into greater and lesser levels of socio-economic deprivation. Logically, those already "in treatment" attended all services and redeemed all further prescriptions at greater rates than the half of the 'probable suicide' cohort who did not receive an antidepressant prescription. Curiously, only psychiatric outpatient attendance was statistically distinguishable and greater in the more deprived section; though, most psychotropic prescriptions were more frequent in the group with greater deprivation. Routine statin and antihypertensive prescriptions were more common in the less deprived group comparatively.

Finally, a multivariate model was constructed to predict ‘probable suicide’ within a cohort including the community controls. Demographic variables and healthcare measures demonstrating the largest between group differences were included, however only approximately a third of the variance was explained by the model. All variables were significantly predictive, with all healthcare utilisation measures increasing the odds of being recorded a ‘probable suicide’. Unanticipatedly, the less deprived groups had slightly higher odds of belonging to the ‘probable suicide’ cohort.

4. Results of Drug-Related Death Cohort Analysis

This chapter details the results of the cohort validation within the DRD cohort, as well as the results of a variety of healthcare usage analyses. The chapter will be split into multiple sections: a comparison of the total cohort with all the matched controls, followed by a comparison of both the deceased and live individuals who had received OST prescriptions, a set of analyses looking only at the deceased and partitioned on the basis of OST prescription (as a proxy for being in treatment) and finally, an analysis of healthcare usage within the DRD group that was split on the basis of high or low deprivation. Each comparison draws out alternative control groups and lines of enquiry, each with the aim of understanding the context of healthcare usage before DRD and potential sub-groups therein.

4.1. Cohort Validation

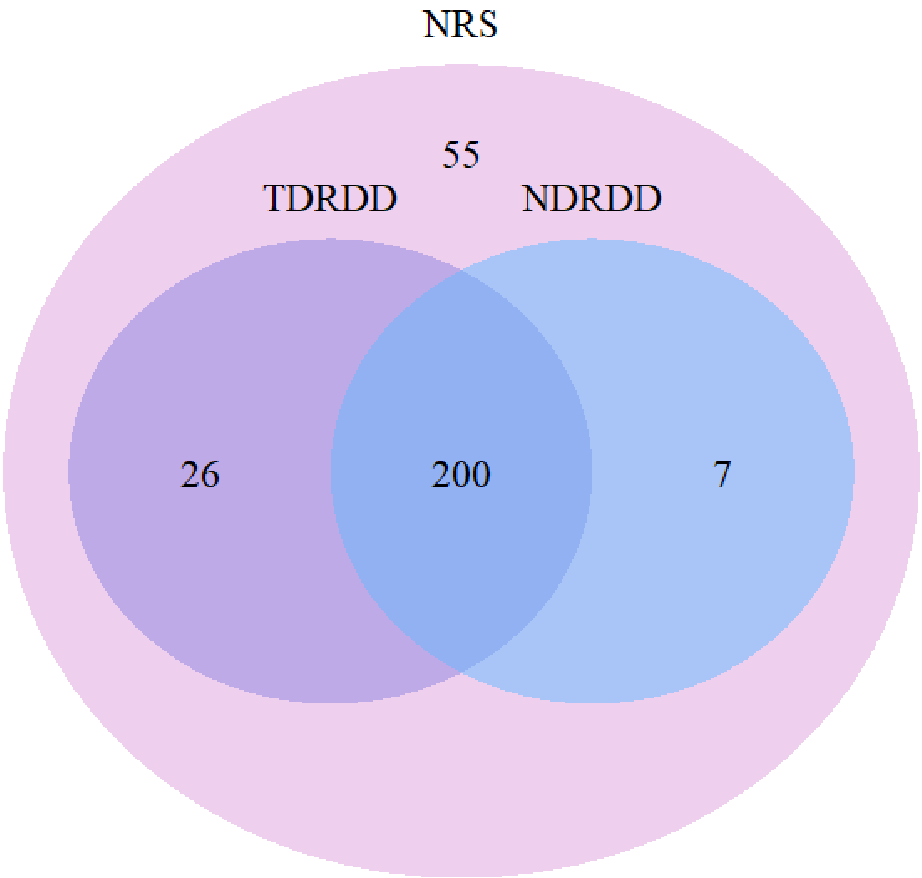
4.1.1. Identifying the Database of Origin

As discussed previously in the Methods section, defining a DRD in a standardised manner is challenging. The codes used by the NRS that form the basis of the narrow definition (with a primary focus on the presence of illicit substances present in post-mortem toxicology) seem to also form the basis of the definitions used by the NDRDD and TDRDD. The major difference between the three processes seems to be the method of data collection. Therefore, to test the hypothesis that these organisations capture the same samples, the overlap between the three different organisational processes and the statistical causes of death recorded for each individual were examined.

Initially, 311 individuals were identified from three different data feeds (NRS, NDRDD and TDRDD) as DRD and residing in Tayside during the relevant 5-year observation period. Across all three databases used to triangulate relevant individuals, there were 23 individuals that did not fulfil the ICD-10 code criteria for DRD and were, therefore, excluded. Of these 23 individuals, 6 could be found within all three databases, 10 only in the NDRDD and NRS databases and 7 in the TDRDD and NRS. The underlying cause of death code for each of these 23 individuals is included in Appendix 2. After the exclusions, the revised, validated, total was 288 DRD individuals.

Of these 288, 200 of them could be found in all three databases (69% of the cohort). Fifty-five individuals could only be found in the NRS database, using the slightly modified SIFT project ICD-10 codes with the specified T-codes. A further 26 could only be found in the TDRDD and NRS databases and finally, only 7 individuals were present in the NDRDD and NRS databases (illustrated in Figure 4-1 below).

Figure 4-1. Diagram of the overlap of DRD individuals between databases.



SIFT requested the extraction of individuals who died a drug-related death using a slightly modified version of the National Records of Scotland (NRS) narrow definition. Further individuals were isolated based on their inclusion in specialist databases: the National Drug-Related Death Database (NDRDD) and the Tayside Drug-Related Death Database (TDRDD). These databases demonstrated a significant degree of overlap, with 200 of the 288 individuals present in all three.

4.1.2. Comparing the NRS against the NDRDD and TDRDD

As before, the first step was to attempt to determine whether there were demographic associations with inclusion, or exclusion, from the specialist databases. As there were four possible levels to the outcome variable (in all three databases, in only NRS, in the NRS and NDRDD or in the NRS and TDRDD), a multinomial logistic regression analysis was conducted. The model included the demographic measures of gender, age and socio-economic deprivation (SIMD) as the explanatory factors for inclusion in the different databases. The model was significant X^2 (21, N=280) = 35.245, $p<0.05$, and had presence in all three databases as the reference category. Those between 26-50 years old were less likely to be found only in the NRS database OR 0.223 (95% CI 0.075-0.667), and also less likely to be found only in the NDRDD (and NRS) OR 0.104 (95% CI 0.016–0.668). This would suggest that the individuals within this age range are most likely to be included in all three databases and, therefore, the publications associated with these databases. As such, policy informed by these publications may not reflect the true rate of DRD in individuals outside of the 26-50 years old age range. As demonstrated in Table 4-1 below, however, the distribution of data and the number of levels within the analysis prevented certain parameter estimates from being reliably calculated. As such, while this model is statistically significant, the odds may not be valid or powerful enough for any reasonable conclusions.

As previously described, there were 4 age, gender and SIMD matched ‘controls’ for each individual, resulting in a total of 1,152 matched controls. The generation of matched comparator datasets is shown in Table 4-2, in which 71% of the DRD were male, almost 79% were aged between 26 and 50 years old and almost 51% were from the most deprived SIMD quintile.

Table 4-1. Regression predicting NDRDD and TDRDD Inclusion

Category	Variable	Exp(B)	95% CI for Exp(B)
NRS Only (n=52)			
	Men	0.924	0.453-1.885
	Women	Reference	
	≤25 years old	0.295	0.080-1.086
	26-50 years old	**0.223**	**0.075-0.667**
	≥51 years old	Reference	
	SIMD 1	0.974	0.186-5.110
	SIMD 2	0.981	0.178-5.406
	SIMD 3	0.531	0.070-4.004
	SIMD 4	5.083	0.800-32.315
	SIMD 5	Reference	
TDRDD and NRS (n=24)			
	Men	2.135	0.677-6.728
	Women	Reference	
	≤25 years old	*	
	26-50 years old	*	
	≥51 years old	Reference	
	SIMD 1	0.912	0.103-8.054
	SIMD 2	0.926	0.099-8.678
	SIMD 3	0.988	0.086-11.305
	SIMD 4	0.934	0.49-17.979
	SIMD 5	Reference	
NDRDD and NRS (n=7)			
	Men	2.484	0.277-22.276
	Women	Reference	
	≤25 years old	*	
	26-50 years old	**0.104**	**0.016-0.668**
	≥51 years old	Reference	
	SIMD 1	*	
	SIMD 2	*	
	SIMD 3	*	
	SIMD 4	*	
	SIMD 5	Reference	

Odds ratios from the multinomial logistic regression model testing for presence within specialised mortality databases. The reference category was set as presence within all three databases (i.e., the reference category contained 200 individuals). Bold rows indicate statistical significance. SIMD - Scottish Index of Multiple Deprivation with 1 = most deprived quintile and 5 least deprived quintile. * represents a sub-level for which there were too few individuals to reliably calculate an odds ratio. Individuals aged between 26-50 years old were more likely to be captured by all three processes and present in all three organisations, compared to those 51 years old or older.

Table 4-2. Demographic Data for the DRD and Control Groups

	DRD (n)	%	Control (n)	%
Men	205	71.2	820	71.2
Women	83	28.8	332	28.8
≤25 years old	41	14.2	36	3.1
26-50 years old	227	78.8	904	78.5
≥51 years old	20	6.9	212	18.4
SIMD 1	142	50.7	577	50.7
SIMD 2	79	28.2	277	24.3
SIMD 3	28	10	132	11.6
SIMD 4	20	7.1	97	8.5
SIMD 5	11	3.9	55	4.8
Total	288		1152	

Outcome of matching the DRD cohort with community controls. SIMD - Scottish Index of Multiple Deprivation (reference) with 1 = most deprived quintile and 5 least deprived quintile. 8 of the DRD individuals had no SIMD data, and 14 of the control group also were missing SIMD data.

4.2. Analysis of DRD and Matched Control Cohorts

4.2.1. Introduction

After cohort validation, the rate of healthcare utilisation and key prescriptions were extracted for each individual and analysed by group status. The aim was to contrast the rates of healthcare usage, in the twelve months before death, between the DRD cohort and the matched control group (288 individuals compared to 1152 individuals, respectively). It was important to identify and describe any differences in healthcare usage across the full cohort for both groups, both to simply test whether there were group differences, but also to have greater context for attempting to isolate sub-groups in later stages of the analysis.

4.2.2. Healthcare Usage compared across DRD and Control Groups

The DRD cohort attended all healthcare services at significantly higher rates than matched controls during the 12m sampling frame (summarised in Table 4-3). This was particularly evident for Accident and Emergency department attendances, which over half of the DRD group had, compared with 13.5% of the control cohort. Furthermore, when general hospital attendance was broken down into routine or emergency appointments, DRD individuals had a lower rate of routine appointment attendances. Overall, these data suggest higher rates of emergency healthcare in the DRD group.

Psychiatric healthcare attendances were significantly more common in the DRD group than the control group; a little under 60% of the DRD group had at least one psychiatric outpatient attendance, compared to approximately 6% of the control group. Psychiatric inpatient attendances showed a statistical difference in the same direction, with 6% of the DRD group having at least one admittance, compared to almost 1% of the control group.

Finally, non-psychiatric outpatient clinic attendance was again higher in the DRD group (at 27% and 16% comparatively), however, this was the second smallest difference in the rate of healthcare attendance between groups.

Table 4-3. Healthcare Utilisation rates across DRD and Control Cohorts

Variable	DRD (N=288)		Control (N=1152)		X²	p-value
	%	(n)	%	(n)		
General inpatient	**40.3**	**116**	**6.5**	**75**	**228.353**	**<0.05**
Routine Attendance	**44.8**	**52**	**60.0**	**45**	**4.195**	**<0.05**
Psychiatric outpatient	**58.7**	**169**	**5.9**	**68**	**466.762**	**<0.05**
Non-psychiatric outpatient	**27.4**	**79**	**15.9**	**183**	**20.633**	**<0.05**
Mental Health Inpatient	**6.3**	**18**	**0.8**	**9**	**37.452**	**<0.05**
Accident and Emergency	**52.4**	**151**	**13.5**	**156**	**207.726**	**<0.05**

Comparison of those deemed DRD with matched controls with respect to healthcare usage across a variety of services within preceding 12m. General hospital presentations included both day-patient and elective inpatient events, therefore 'routine attendance' was calculated for those with at least one of these general hospital codes. Outpatient clinics were split by clinical specialty, with psychiatric codes not distinguishing between mental health or substance misuse. Chi-square tests were calculated, with rows in bold indicating statistical significance. The DRD group attended all services at significantly higher rates than the matched control group, however the DRD group had fewer attendances coded as routine.

Table 4-4. Prescription rates across DRD and Control Cohorts

Variable	DRD (N=288)		Control (N=1152)		X²	p-value
	%	(n)	%	(n)		
Methadone	**41.0**	**118**	**2.3**	**27**	**379.651**	**<0.05**
Antidepressants	**55.2**	**159**	**14.1**	**162**	**225.177**	**<0.05**
Benzodiazepines	**26.7**	**77**	**4.5**	**52**	**139.505**	**<0.05**
Z-drugs	**20.1**	**58**	**3.3**	**38**	**105.011**	**<0.05**
Gabapentinoids	**19.8**	**57**	**2.3**	**26**	**130.421**	**<0.05**
Anticonvulsants	**24.0**	**69**	**3.6**	**42**	**133.625**	**<0.05**
Statins	2.8	8	4.7	54	2.039	>0.05
Antihypertensives	1.7	5	4.2	48		>0.05*

Percentage and count data comparing prescription records for those deemed DRD and controls. Chi-square tests were calculated, with rows in bold indicating statistical significance. * represents a low cell count, requiring Fisher's exact test rather than a Chi-square test. The DRD group received a higher rate of psychotropic treatment prescriptions, however the statistical test found no differences in the rate of preventative prescriptions.

4.2.3. Prescription Records Compared across DRD and Control Groups

There were higher rates of psychotropic drug prescribing across all categories within the DRD cohort (see Table 4-4). Although the increased rates of methadone prescribing would be expected given the key role for methadone in the management of opioid dependency, there were also elevated rates of prescribing of antidepressant, benzodiazepine, gabapentinoid and anticonvulsant drugs.

As previously noted, there was considerable overlap between the DRD cohort and the 'probable suicide' cohort of the previous chapter, with 197 individuals common to both groups. Antidepressants were prescribed at a rate of 55% within this DRD cohort, compared to only 14% of the controls. Of these 159 DRD individuals with an antidepressant prescription, 117 were also present in the 'probable suicide' cohort. Therefore, 42 of the DRD individuals receiving an antidepressant prescription received cause of death codes specific to the DRD criteria.

Although numbers of prescriptions were low, and these differences did not reach statistical significance, the opposite pattern was observed for drugs that might be considered proxy indicators of anticipatory, preventative health care – statins and antihypertensive drugs.

4.2.4. Evaluation of 'Quality' of Psychiatric Outpatient Healthcare

As described within the results of the analysis of the 'probable suicide' cohort, again the frequency of psychiatric outpatient attendance was tallied and compared; this was conceived as a proxy for regular engagement with psychiatric healthcare and whether treatment fulfilled clinical guidelines for regular check-ups.

When considering appointments made and kept, the DRD group attended a median of 4 times (range 1-58), whereas the controls attended a median of 3 times (range 1-39). A Poisson logistic regression was calculated, with the number of outpatient attendances as the outcome, using demographic variables as the possible explanatory factors. The overall model was significant X^2 (8, N=230) = 100.656, $p<0.001$, with all odds ratios in Table 4-5. For every additional psychiatric outpatient attendance, the odds ratios demonstrated an association with belonging to the DRD group, women and the least deprived quintile, compared to their respective referent groups. As the number of psychiatric outpatient attendances increased, there was a reduced association with belonging to either the second-most deprived or middle quintile of socio-economic deprivation, compared to the most deprived group, which was set as the reference. Additionally, compared to the 26–50-year-old group, those 25 years old and younger were less likely to have a high number of attendances.

Outpatient records were tagged with whether the patient attended or not, therefore the frequencies of missed psychiatric appointments were also tallied. Those who died missed a median of 3 (range 1-19) while controls missed a median of 2 (range 1-18) appointments, without notifying the clinic beforehand.

As above, the outcome of interest was frequency data, therefore the appropriate model was a Poisson logistic regression. The model was significant X^2 (8, N=183) = 66.990, $p<0.001$, and reflected many of the associations above. Those who died, women and unusually, those in the least deprived quintile were all associated with missing a greater number of outpatient appointments, relative to their reference groups (summarised in table 4-6). Only those in the second-most deprived and middle quintiles were associated with missing a smaller number of outpatient attendances, than the most deprived group.

Table 4-5. Regression predicting Psychiatric Outpatient Appointment Frequency

Variable	Exp(B)	95% CI for Exp(B)
Control	Reference	
Drug-related Death	**1.481**	**1.319-1.663**
Men	Reference	
Women	**1.125**	**1.018-1.245**
≤25 years old	**0.676**	**0.544-0.841**
26-50 years old	Reference	
≥51 years old	0.826	0.680-1.004
SIMD 1	Reference	
SIMD 2	**0.713**	**0.634-0.801**
SIMD 3	**0.785**	**0.650-0.947**
SIMD 4	0.884	0.699-1.119
SIMD 5	**1.294**	**1.019-1.643**

Odds ratios from a Poisson logistic regression model predicting increasing frequency of psychiatric outpatient attendance, within the full DRD and control cohort. Demographic measures and group status were used as explanatory variables and the largest sub-group was set as the reference group. Bold rows indicate statistical significance. Those in the DRD group, women and the least deprived quintile were all associated with a higher frequency of psychiatric outpatient attendance, while those 25 years old and younger, and those in the second-most and third-most deprived quintiles were associated with lower frequencies of attendance.

Table 4-6. Regression predicting Missed Psychiatric Outpatient Appointment Frequency

Variable	Exp(B)	95% CI for Exp(B)
Control	Reference	
Drug-related Death	**1.697**	**1.391-2.070**
Men	Reference	
Women	**1.233**	**1.055-1.441**
≤25 years old	0.783	0.576-1.064
26-50 years old	Reference	
≥51 years old	1.312	0.916-1.879
SIMD 1	Reference	
SIMD 2	**0.675**	**0.564-0.808**
SIMD 3	**0.602**	**0.428-0.848**
SIMD 4	1.115	0.739-1.684
SIMD 5	**1.636**	**1.067-2.508**

Odds ratios from a Poisson logistic regression model predicting increasing frequency of missed psychiatric outpatient attendance, within the full DRD and control cohort. Demographic measures and group status were used as explanatory variables and the largest sub-group was set as the reference group. Bold rows indicate statistical significance. The DRD group, women and those in the least deprived quintile were all associated with missing a greater frequency of psychiatric outpatient appointments, while those in the second-most and third-most quintile were associated with missing fewer appointments.

4.3. Possible Self-Harm Attendances at Accident and Emergency Services

4.3.1. Introduction

While self-harm is most commonly discussed in the context of risk factors for 'probable suicide', it is particularly relevant that a significant number of the self-harm events in the literature are overdoses (Carroll, Metcalfe and Gunnell, 2014). Unintentional overdoses are specifically associated with subsequent death by overdose (Martins et al., 2015), and the majority of the individuals within the DRD cohort overlapped with the 'probable suicide' cohort. These facts suggested it would be worthwhile to investigate similar hypotheses surrounding the prevalence of possible self-harm presentations to emergency services prior to DRD.

4.3.2. Method

The same definition was used to identify a possible self-harm event as in the 'probable suicide' cohort analysis; this included codes referring to injury/trauma/poisoning, 'psychiatry' reasons for presentation, references to self-harm or referrals to mental health services (see section 3.3.2 for further details). Again, the modal cause for a presentation to be identified as possible self-harm was a diagnosis code of injury/trauma/poisoning, with 94% or 80/85 of the DRD fulfilling this criterion and 97% or 59/61 of the control group.

The data column denoting the intent of the injury was again empty for the vast majority of presentations recorded; 88% or 459/522 of the DRD presentations had no data, and 71% or 166/234 of the control group presentations were likewise empty.

4.3.3. Rate of Attendance compared across DRD and Control Groups

Rates of Accident and Emergency presentation were significantly elevated in the DRD group compared to the controls, as established above. Of those with an Accident and Emergency presentation, 56% of the DRD group had a possible self-harm attendance, compared to 39% of the controls. A chi-square test showed this to be a statistically significant difference between groups X^2 (1, N=307) = 9.090, $p<0.05$.

To further contextualise this analysis, it is worth noting that the number of individuals in both groups with a possible self-harm presentation was very similar: 85 DRD individuals and 61 control individuals met the criteria. Of the total cohort, this represents approximately 30% and 5% respectively, which suggests that possible self-harm could be a relevant risk factor to identify a proportion of those at risk for later DRD.

4.3.4. Psychiatric Follow-up After Possible Self-harm

As in the 'probable suicide' cohort analysis (see section 3.3.2), the first possible self-harm event in the year was identified for each individual, with psychiatric follow-up initially examined for the whole year and then refined to 21 days to allow for more granular investigation. When any psychiatric healthcare follow-up was considered (inpatient or outpatient attendances, or psychotropic prescriptions), there was a very notable difference, with 54% of the DRD group receiving any type of follow-up compared with only 20% of controls. The results are summarised in Table 4-7. The sizable difference in follow-up care suggests that the healthcare service has established distinct intervention pathways, that are relatively well-targeted.

These results were then filtered by the category of psychiatric follow-up treatment received. Across both groups, the most common follow-up received was a psychotropic drug prescription (i.e., an antidepressant, antipsychotic, anticonvulsant or sedative drug), at 37% of the DRD group compared to 18% of the control group. Several of these individuals also attended a psychiatric outpatient clinic within 21 days from the possible self-harm presentation; 12 of the DRD cohort received both treatment modalities, however only 2 of the control group used both services.

Psychiatric inpatient attendance within 21 days from the event was less common than in the 'probable suicide' cohort, with only 8 of the DRD group being admitted, however 7 of these were admitted directly from Accident and Emergency services. Where the control group was concerned, 2 individuals were directly discharged to psychiatric inpatient care, and these were the only individuals with an admission within the 21-day timeframe. While the rate of psychiatric inpatient admission was not statistically significantly different, the sample sizes were small, and the significant differences within the other modalities do support a suggestion of targeted intervention pathways.

4.3.5. Psychotropic Prescription Modification

Examining treatment responsiveness after a possible self-harm event was a key aspect of the analysis, as it further interrogates the commonly stated assumption that gaps within the healthcare service are to blame for deaths soon after possible self-harm events (Vasiliadis, Ngamini-Ngui and Lesage, 2015). Changes to any of the psychotropic prescriptions (antidepressant, antipsychotic, anticonvulsant or sedative drugs), compared to the previous month were identified, with modifications noted in 18 (58.1% of those with a psychotropic prescription in 21 days) of the DRD group and 8 (72.7%) of the controls. Mindful of the small sample size, Fisher's Exact test was not significant when contrasting the percentage of individuals who had their prescriptions modified, within 21 days after a possible self-harm presentation. In both groups, over half of the individuals had their prescriptions modified, which suggests the healthcare service recognises and responds to crisis events, to a degree.

4.3.6. High Frequency Possible Self-Harm Attendance Group Analysis

Finally, a "high-risk" sub-cohort, those with 3 or more possible self-harm attendances, were identified; these were 15 DRD individuals (with a range of 3-12 attendances) and 1 control (who attended 3 times). Of these 15 DRD individuals, 10 (67%) had at least one type of follow-up in the 21 days after the first possible self-harm presentation. The one control individual did not receive any follow-up in the first 21 days after a possible self-harm presentation. Mindful of the small sample size, Fisher's Exact test was non-significant, when comparing the rate of follow-up in the DRD and control groups with high frequency possible self-harm presentations. These results point towards a sub-group of DRD with a high number of possible self-harm presentations, of whom the majority received some follow-up, however comparisons with the control group are limited by low sample size.

Table 4-7. Follow-up rates after Possible Self-harm Presentations

Variable	**DRD (N=85)**		**Controls (N=61)**		**X²**	**p value**
	%	(n)	%	(n)		
Any follow-up ≤21 days after SH:	**54.1**	**46**	**19.7**	**12**	**17.598**	**<0.05**
Psychotropic Prescription	**36.5**	**31**	**18.0**	**11**	**5.892**	**<0.05**
Psychiatric Outpatient Clinic	**29.4**	**25**	**4.9**	**3**		**<0.05***
Mental Health Inpatient	9.4	8	3.3	2		>0.05*

Comparison of possible self-harm attendances at Accident and Emergency Services, across DRD and control groups, including psychiatric follow-up in the 21 days after the presentation. Possible self-harm was defined using a variety of codes (those recording a poisoning, intentional self-harm or a psychiatric complaint, those discharged to psychiatric hospitals or those discharged with a psychiatric referral. These statistics were based solely on the first possible self-harm presentation within the year. Chi-square tests were calculated, with rows in bold indicating statistical significance. * represents a low cell count, requiring Fisher's exact test rather than a Chi-square test. The DRD group received more follow-up after a possible self-harm presentation than the control group.

4.4. Opioid Testing in Laboratory Services

4.4.1. Introduction

As described in the introduction, one of the main preventative strategies promoted to reduce DRD is the reliable provision of OST (Larney et al., 2017); one aspect of this provision is urine testing for additional opioid drugs, other than methadone or buprenorphine. This information is key for patient care, as it could indicate that the current dosage is too low for the patient's needs, resulting in continued use of potentially illicit substances. There is some debate about the efficacy of urine drug screening (Jin et al., 2020), with a call for the standardisation of the process to allow for more rigorous examination of whether it improves patient outcomes or whether the potentially stigmatising and embarrassing nature of urine testing is more harmful than beneficial. On the basis of this debate within the literature, there were several hypotheses of interest, relative to laboratory results of urine drug screens. These were:

1. To test whether the rate of patients with a drug screen ordered differed between the DRD cohort and the matched controls
2. To compare the number of tests ordered across groups, as a proxy measure for the frequency of testing
3. To calculate a mean positivity rate for additional and presumably illicit opioids, compared across DRD and control groups

4.4.2. Method

Within HIC, there was a biochemistry database, which contained information about drug screens that had been ordered by GP practices. Those testing patient's urine for methadone and other opiates were identified, extracted and then re-coded for analysis. The first outcome was simply having a test ordered, to attempt to compare the profiles of those perceived to need drug screens versus those not perceived to require at least one screening.

The frequency of tests over the year was then tallied and used to calculate a mean positivity rate. Some individuals had tests that were ruled as unsuitable, generally due to errors in the handling of the sample (e.g., the sample was noted to be in an incorrect sample tube or had a different patient's name attached). These were excluded from the calculation on the percentage of positive tests for each individual.

Additionally, for individuals who were receiving methadone prescriptions, any tests positive for methadone, but not for further opiates, were not included as positives.

4.4.3. Rate of Urine Drug Screens Ordered

As might have been predicted, the percentage of individuals with a drug screen ordered was significantly higher in the DRD group than the control group. Of the 288 DRD individuals, 118 (or 41%) were recorded as having been tested at least once for opioids in their urine, compared to 23 of the 1152 controls (2%). A chi-square test between groups demonstrated this to be statistically significant X^2 (1, N=1440) = 396.248, $p<0.001$.

The majority of these individuals were in receipt of at least one methadone OST prescription in the year before death; 75% or 88/118 of the DRD cohort and 83% or 19/23 of the controls were recorded as having received at least one OST prescription.

As an interesting note, 25% or 30/118 individuals in the DRD cohort received a methadone OST prescription, but had no urine drug screens, and 30% or 8/27 of the controls likewise received a methadone OST prescription, yet had no drug screens.

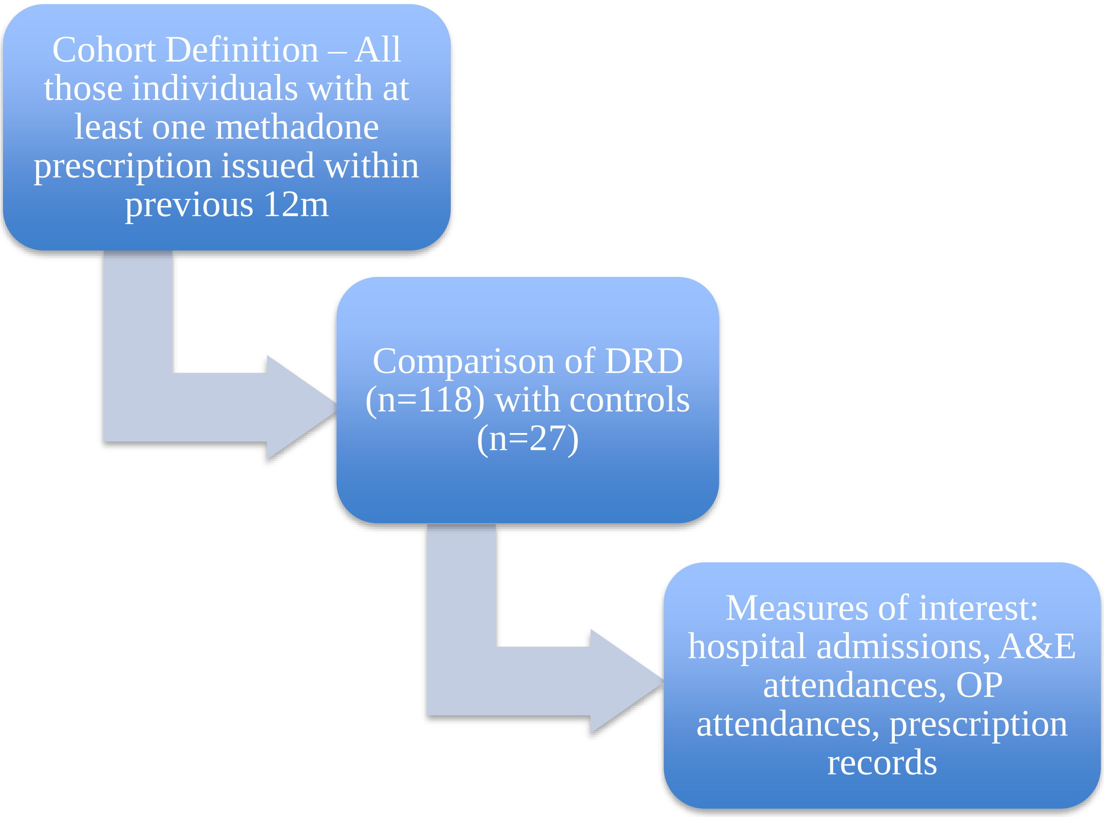
4.4.4. Mean Positivity Rate of Urine Drug Screens

After the base rate was calculated, the frequency of tests for each individual was tallied, to create a proxy measure for regular recognition by the healthcare service that the individual was at risk of supplementing their methadone dose with presumably illicit opioids. The DRD group had a median of 3 urine drug screens ordered, with a range of 1-21, while the control group had a median of 3 and a range of 1-14.

The positivity rate for each individual was calculated, bearing in mind the exclusions listed above, then a mean for each group was calculated. The mean positivity rate, across all of the individuals with drug screens ordered, was 49% in the DRD group and 38% in the control group. A Mann-Whitney U test was insignificant when comparing the mean percentage of positive tests between groups (U=1106, $p>0.05$). These results suggest that the healthcare service stratified individuals into those for whom a urine drug screen would be beneficial, but that within that category, the DRD and control individuals were more challenging to distinguish.

4.5. Analysis of those receiving Methadone OST

Figure 4-2. Flowchart Identifying the Cohort with a Methadone OST Prescription



The first sub-section of the data analysis was focused on interrogating those arguably "in treatment", therefore, receiving a methadone OST prescription over the twelve months before death, or index date for the control group. Once the healthcare measures for the previous analysis had been coded, the individuals from the full cohort were filtered by methadone prescription and group status, which resulted in a significantly smaller control cohort, as shown in box two. Finally, similar healthcare utilisations comparisons were undertaken, using the databases previously described.

4.5.1. Introduction

After comparing the healthcare utilisation of the entire cohorts of DRD and control groups, relevant sub-sections of the cohorts were extracted from the full cohort for further analysis (see Figure 4-2). The first sub-section of interest was all individuals with a methadone OST prescription in the twelve months before death. As noted in the introduction, the majority of DRD involve opioids, whether prescription or illicit type drugs; all opioid drugs are associated with the development of dependence and possible misuse, which is associated with higher odds of opioid-related death. Retrospectively investigating all the individuals arguably belonging to this "high-risk" category of being in treatment for opioid misuse could reveal significant differences in healthcare usage. Specifically, the hypotheses of this section all relate to whether there were notable differences in healthcare utilisation between those who went on to die a DRD, versus those in the 'live' control group, while all individuals received an OST prescription, within the study timeframe.

The analyses below, investigating both healthcare utilisation and prescription records, all apply to the methadone prescribed sub-section of the full cohort, amounting to 118 DRD individuals, and 27 of the control individuals. This significant difference in sample size clearly reinforces the association between opioid-misuse (as identified by being "in treatment" for this condition) and subsequent DRD.

4.5.2. Healthcare Usage within the OST Prescribed Group

Under half (41.0%) of the DRD group received at least one methadone prescription in the twelve months before death. Therefore, the DRD cohort included fewer than half who were, by convention, "in treatment" in the year prior to death. Within the Scottish health service, there are very few individuals who would be considered "in treatment", but not in receipt of OST. Of the comparator group, 2.3% were in receipt of OST within the preceding 12m. The relative number of controls was very small, which is an important caveat to bear in mind across these comparisons, summarised in table 4-8.

The DRD/OST sub-group presented to general hospital inpatient services at significantly higher rates than the control/OST sub-group (47% to 4%). As there was only one individual in the control group, a comparison of the rate of routine attendance was less reliable than in the other sample comparisons. Over half of the

DRD sub-group did present at Accident and Emergency services, compared to just under a third of the control group, which could highlight greater acute healthcare needs in those who went on to die, despite all of them being recognised as individuals requiring a prolonged healthcare intervention.

As mentioned in the Methods section, the psychiatric outpatient data did not differentiate between mental health or substance abuse appointments; as such, the very high percentages in both groups for psychiatric outpatient attendances were to be anticipated, as was the lack of statistical difference between groups in this measure.

4.5.3. Prescription Records within the OST Prescribed Group

All the individuals in this analysis already had an OST prescription, therefore one important aspect is that these results also demonstrate a notable rate of co-prescription, as summarised in Table 4-9. This is particularly concerning for the individuals who died as they had higher rates of all additional psychotropic prescriptions than the controls. Antidepressants were co-prescribed at a significant rate, with almost 65% of the DRD individuals redeeming at least one prescription over the year, and 41% of the controls. Sixty one percent of the DRD/OST cohort were prescribed a benzodiazepine, z-drug or gabapentinoid, compared to only 18.5% of the control/OST sub-group. For both sub-groups, the commonest sedative co-prescriptions were benzodiazepines, followed by gabapentinoids.

In this partition of the data, there was only one individual that received a statin prescription, and no individuals received any antihypertensive prescriptions. It is worth noting, generally in the analysis of this subset, numbers are fairly low and the majority of the 2x2 tables required Fisher's Exact test because of low cell counts for the controls, which could affect the validity of these analyses.

The association between co-prescribed methadone and either a benzodiazepine, z-drug or gabapentinoid, with the DRD group is evident from the chi-square comparison above. Association with the other demographic variables was tested for in a binary logistic regression. The outcome was co-prescription with any of the additional sedative drugs, and the model was significant X^2 (8, N=140) = 23.070, $p<0.05$, however the only significant association was belonging to the DRD group (odds ratios summarised in Table 4-10).

Table 4-8. Healthcare Utilisation across those with Methadone OST Prescriptions

Variable	DRD (N=118)		Control (N=27)		X²	p-value
	%	(n)	%	(n)		
General hospital	**46.6**	**55**	**3.7**	**1**		**<0.05***
Routine Attendance	47.3	26	100	1		>0.05*
Psychiatric outpatient	88.1	104	92.6	25	0.445	>0.05
Non-psychiatric outpatient	28.8	34	22.2	6	0.478	>0.05
Mental Health Inpatient	6.8	8	3.7	1		>0.05*
Accident and Emergency	**55.9**	**66**	**29.6**	**8**	**6.083**	**<0.05**

Including only individuals receiving a prescription for OST (methadone) a comparison of DRD with controls with respect to healthcare usage across a variety of services within preceding 12m. General hospital presentations included both day-patient and elective inpatient events, therefore 'routine attendance' was calculated for those with at least one of these general hospital codes. Outpatient clinics were split by clinical specialty, with psychiatric codes not distinguishing between mental health or substance misuse. Chi-square tests were calculated, with rows in bold indicating statistical significance. * represents a low cell count, requiring Fisher's exact test rather than a Chi-square test. The DRD group had higher general hospital attendance and Accident and Emergency presentation rates than the controls with an OST prescription, however no other differences were statistically significant.

Table 4-9. Prescription records across those with Methadone OST Prescriptions

Variable	DRD (N=118)		Control (N=27)		X²	p-value
	%	(n)	%	(n)		
Antidepressants	**64.4**	**76**	**40.7**	**11**	**5.128**	**<0.05**
Benzodiazepines	33.9	40	14.8	4		>0.05*
Z-drugs	**22.0**	**26**	**3.7**	**1**		**<0.05***
Gabapentinoids	**28.8**	**34**	**7.4**	**2**		**<0.05***
Anticonvulsants	**36.4**	**43**	**11.1**	**3**		**<0.05**
Statins	0.8	1	0.0	0		>0.05*
Antihypertensives	0.0	0	0.0	0		>0.05*

Percentage and count data comparing prescription data for DRD and controls who had received a prescription for OST. Chi-square tests were calculated, with rows in bold indicating statistical significance. * represents a low cell count, requiring Fisher's exact test rather than a Chi-square test. The DRD group had a higher rate of several psychotropic treatment prescriptions than the controls with an OST prescription.

Table 4-10. Regression predicting Methadone OST and Sedative co-prescription

Variable	Exp(B)	95% CI for Exp(B)
Control	Reference	
Drug-Related Death	**6.659**	**2.240-19.797**
Men	Reference	
Women	2.038	0.913-4.549
Under 25	0.585	0.077-4.457
26-50	Reference	
Over 51	0.205	0.020-2.141
SIMD 1	Reference	
SIMD 2	1.017	0.453-2.285
SIMD 3	0.717	0.131-3.919
SIMD 4	0.352	0.030-4.155
SIMD 5	N/A	N/A

Odds ratios from a binary logistic regression model predicting co-prescription of another sedative drug (benzodiazepine, z-drug or gabapentinoid) including only the individuals with a methadone OST prescription. Demographic measures and group status were used as explanatory variables and the largest sub-group was set as the reference group. Bold rows indicate statistical significance. Only those in the DRD were significantly associated with an increased likelihood of sedative co-prescription.

4.5.4. Evaluation of ‘Quality’ of OST Prescription

4.5.4.1. Introduction

The cohort definition for this sub-section of analysis was the presence of at least one methadone OST prescription over the twelve months before death, or index. Treatment guidelines and expectations for OST highlight that titrating the patient to the correct dosage may require several weeks, with early doses taken daily and under supervision to reduce the risk of overdose (NICE, 2022 (c)). There are also general concerns that clinical practice worldwide may not reflect optimal practice, which is that between 60-120mg per day are administered (Jin et al., 2020). As such, investigating the mean dose between the DRD and control group receiving methadone OST prescriptions was a key measure of healthcare usage, as well as an important area to examine for potential differences between the individuals who went on to die, versus those in the same high-risk group that did not.

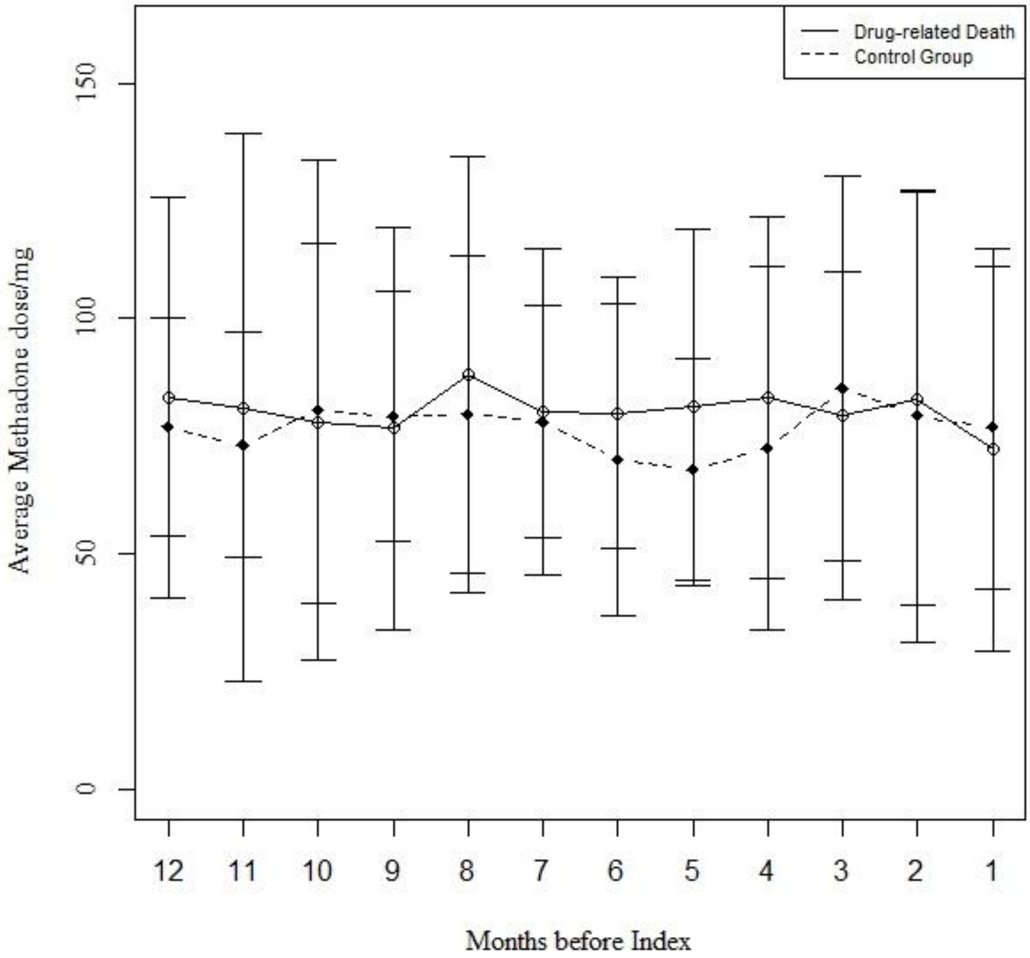
4.5.4.2. Method

Within HIC, the records for methadone OST prescriptions defaulted to the first of each month, and contained the total volume dispensed within that month. As such, the daily dose for each individual was calculated by dividing the total volume by 28, based on a traditional 28-day prescription cycle. The mean daily dose for each month was calculated for both the DRD and control groups, then analysed with an ANOVA test to allow for interactions with time and group status to be examined.

4.5.4.3. Mean Daily Dose

As shown in Figure 4-3**.**, both groups were prescribed a mean daily dose of approximately 80mg over the twelve-month observation period, without significant variation, or trend. ANOVA revealed no significant effect of group (DRD, controls), time, nor interaction [$F(11, 22) = 0.472$, $p>0.05$]. This would suggest that treatment received by both groups was similar and fulfilled clinical guidelines.

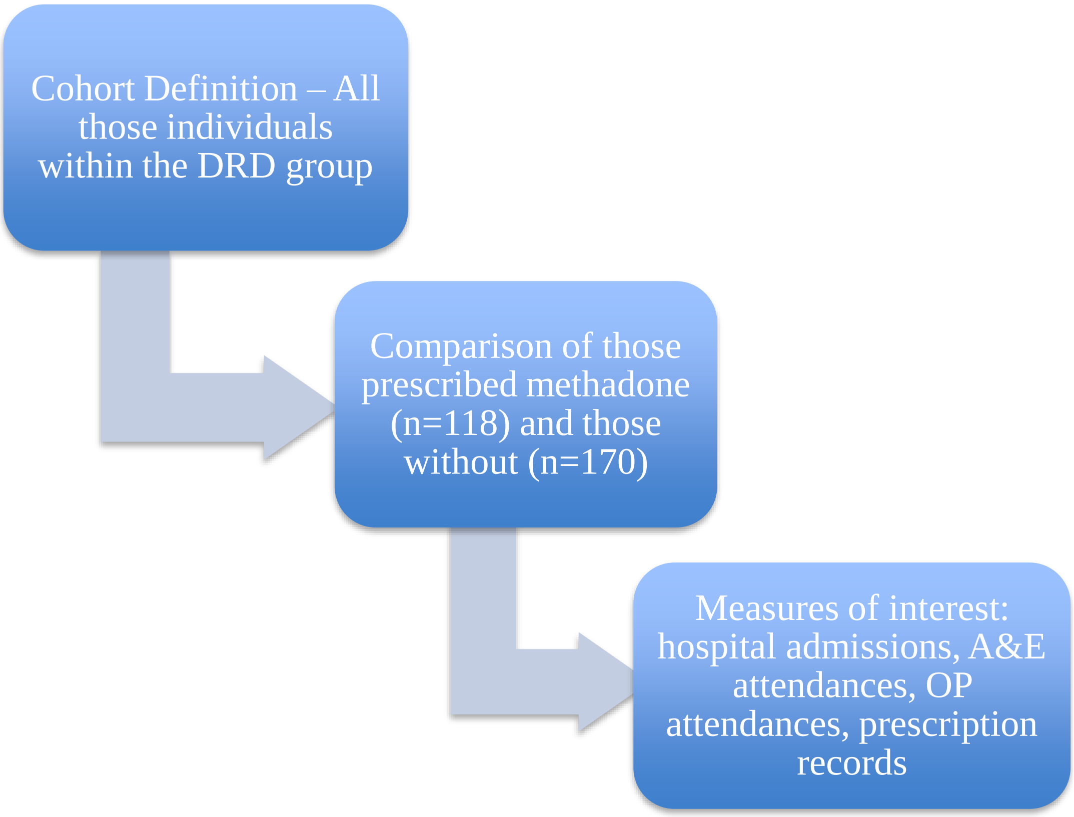
Figure 4-3. Average Daily Methadone Dose in the Year before Death



Monthly prescription volumes for methadone OST prescription records were divided by 28, then averaged by group status and 95% CI intervals were plotted. ANOVA revealed no significant differences between the DRD and control groups. Both DRD and control groups had a mean daily dose of approximately 80mg per day.

4.6. Analysis of the DRD Cohort

Figure 4-4. Flowchart Identifying the DRD Group for Analysis



The second sub-section of the data analysis was focused on interrogating only those in the DRD group. Once the healthcare measures for the previous analysis had been coded, the DRD individuals were filtered by methadone OST prescription in the twelve months before death, which resulted in relatively similar-sized cohorts, as shown in box two. Finally, similar healthcare utilisations comparisons were undertaken, using the databases previously described.

4.6.1. Introduction

Following the comparisons of healthcare utilisation across the entire DRD and control cohorts, and investigating those "in treatment", the final sub-section of interest was simply the DRD group itself. One of the aims of this thesis was to investigate potential sub-groups within the category of DRD, primarily because understanding the different sub-types and needs of this population could improve our ability to design and implement targeted preventative strategies. Furthermore, as previously described, there has been a suggestion that OST provision, in Scotland particularly, was of low accessibility and efficacy (van Amsterdam, van den Brink and Pierce, 2021), therefore an understanding of how many of the people who die from drug-related causes are engaged with relevant healthcare services, is key for corroborating or challenging that argument.

Socio-economic status has been significantly linked to general health status, and to an increased risk of substance misuse and DRD (Congdon, 2019). Therefore, investigating potential differences within the DRD cohort, on the basis of socio-economic deprivation, is likewise key to defining this sample. As such, the first set of analyses splits the DRD group by whether they had received at least one methadone OST prescription in the twelve months before death ("in treatment" or not "in treatment"). The second set of analyses splits the individuals by high or low socio-economic deprivation status.

4.6.2. Healthcare Usage within the DRD Group

Of the DRD cohort, 41% had received a methadone OST prescription in the twelvemonth before death. The previous limitation that OST prescription is linked to high levels of psychiatric outpatient attendance likely explains the significant difference between groups on that measure. That being the only difference was unanticipated, and suggests these groups may be more similar than hypothesised (summarised in Table 4-11).

4.6.3. Prescription Records with DRD Group

Antidepressant rates were notably high in both groups; that almost 50% of those not receiving an OST prescription were receiving an antidepressant prescription suggests they had been recognised by the healthcare system as in psychological distress of some kind. This further corroborates the findings established throughout this thesis, that demonstrate significant similarities between the ‘probable suicide’ and DRD cohorts.

Other sedative prescriptions were received at significantly higher rates in those prescribed methadone OST, though the difference concerning Z-drug prescription was non-significant (summarised in Table 4-12). As in other comparisons, preventative prescriptions of statins and hypertensives were low and insignificantly different.

Table 4-11. Healthcare Utilisation, within the DRD Group Only

Variable	OST / methadone Prescription (N=118)		No OST / methadone Prescription (N=170)		X²	p-value
	%	(n)	%	(n)		
General hospital	46.6	55	35.9	61	3.332	>0.05
Routine Attendance	47.3	26	42.6	26	0.253	>0.05
Psychiatric outpatient	**88.1**	**104**	**38.2**	**65**	**71.531**	**<0.05**
Non-psychiatric outpatient	28.8	34	26.5	45	0.192	>0.05
Mental Health Inpatient	6.8	8	5.9	10	0.096	>0.05
Accident and Emergency	55.9	66	50.0	85	0.983	>0.05

Percentage and count data for all DRD individuals, split by whether in receipt of a methadone prescription or not, examining healthcare usage across a variety of services. General hospital presentation included both day and inpatient cases, therefore routine attendance was calculated only for those with at least one of these general hospital presentations. Outpatient clinics were split by specialty, with psychiatric codes not distinguishing between mental health or substance misuse. Chi-square tests were calculated, with rows in bold indicating statistical significance. Only psychiatric outpatient attendance was higher in the methadone OST group.

Table 4-12. Prescription records, compared within the DRD Group Only

Variable	Methadone Prescription (N=118)		No Methadone Prescription (N=170)		X²	p-value
	%	**(n)**	**%**	**(n)**		
Antidepressants	**64.4**	**76**	**48.8**	**83**	**6.840**	**<0.05**
Benzodiazepines	**33.9**	**40**	**21.8**	**37**	**5.235**	**<0.05**
Z-drugs	22.0	26	18.8	32	0.446	>0.05
Gabapentinoids	**28.8**	**34**	**13.5**	**23**	**10.250**	**<0.05**
Anticonvulsants	**36.4**	**43**	**15.3**	**26**	**17.097**	**<0.05**
Statins	0.8	1	4.1	7		>0.05*
Antihypertensives	0.0	0	2.9	5		>0.05*

Percentage and count data for all DRD individuals, summarising prescription records, depending on whether prescribed OST (methadone) or not. Chi-square tests were calculated, with rows in bold indicating statistical significance. * represents a low cell count, requiring Fisher's exact test rather than a Chi-square test. Antidepressants and the sedative drugs, other than benzodiazepine drugs, were prescribed at a higher rate in the group with a methadone OST prescription.

4.6.4. Demographic Differences within the DRD Group

A binary logistic regression was used to predict OST prescription within the DRD group and showed significant associations with demographic factors X^2 (7, N=280) = 52.419, $p<0.05$. Interestingly, women were associated with receiving a methadone prescription compared to men. OST prescribing was also associated with greater levels of socio-economic deprivation (odds ratios summarised in Table 4-13). Those 25 years old and younger were associated with a reduced chance of receiving a methadone prescription, compared to the reference group of those 26-50 years old.

Within the DRD cohort, the rates of antidepressant prescription were higher in those prescribed OST than those not (64% vs 49%). Other than treatment status, the predictive power of demographic variables for receiving an antidepressant prescription was tested for using a binary logistic regression model that was significant X^2 (7, N=280) = 24.993, $p<0.05$. Only women were associated with receiving an antidepressant prescription. Those 25 years old and younger were associated with lower odds of receiving an antidepressant prescription, compared to those 26-50 years old. There were, however, no significant associations between SIMD quintile and receipt of an antidepressant drug prescription (shown in Table 4-14).

Table 4-13. Regression predicting Methadone Prescription, within the DRD Group

Variable	Exp(B)	95% CI for Exp(B)
Men	Reference	
Women	**2.237**	**1.212-4.130**
≤25 years old	**0.087**	**0.028-0.267**
26-50 years old	Reference	
≥51 years old	0.302	0.0911-1.007
SIMD 1	Reference	
SIMD 2	1.208	0.673-2.168
SIMD 3	0.419	0.152-1.156
SIMD 4	**0.232**	**0.063-0.864**
SIMD 5	**0.096**	**0.011-0.798**

Odds ratios from a binary logistic regression predicting at least one methadone prescription within the DRD cohort. Demographic measures were used as explanatory variables and the largest sub-group was set as the reference group. Bold rows indicate statistical significance. Women were significantly associated with methadone prescription, while those 25 years old or younger, and those in less deprived quintiles were less associated with receiving a methadone prescription.

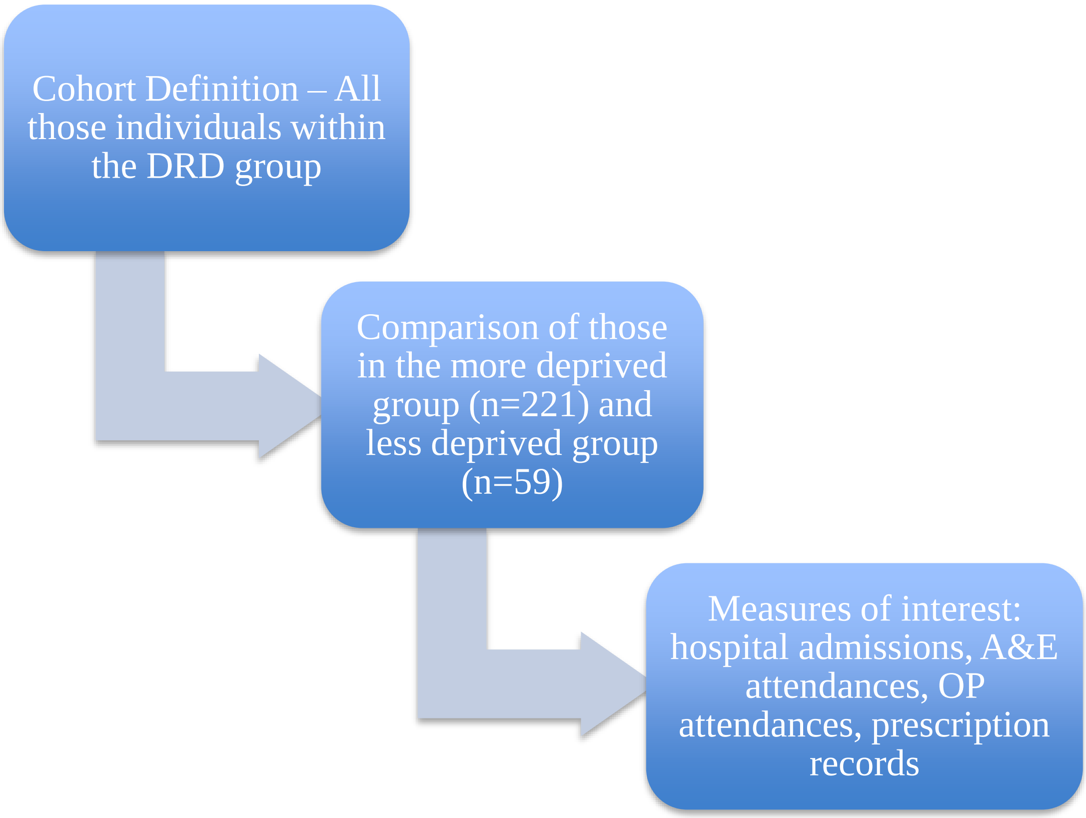
Table 4-14. Regression predicting Antidepressant Prescription, within the DRD Group

Variable	Exp(B)	95% CI for Exp(B)
Men	Reference	
Women	**3.335**	**1.809-6.145**
≤25 years old	**0.340**	**0.160-0.723**
26-50 years old	Reference	
≥51 years old	0.674	0.250-1.823
SIMD 1	Reference	
SIMD 2	0.801	0.451-1.421
SIMD 3	0.702	0.296-1.662
SIMD 4	0.786	0.294-2.104
SIMD 5	2.028	0.487-8.456

Odds ratios from a binary logistic regression predicting at least one antidepressant prescription, within the DRD cohort. Demographic measures were used as explanatory variables and the largest sub-group was set as the reference group. Bold rows indicate statistical significance. Women were associated with at least one antidepressant prescription, while those 25 years old or younger were less likely to have an antidepressant prescription than their referent categories.

4.6.5. DRD Group Analysis, focused on Socio-economic Deprivation

Figure 4-5. Flowchart Identifying the Socio-economic levels within the DRD Group



The third sub-section of the data analysis was focused on interrogating only those in the DRD group. Once the healthcare measures for the previous analysis had been coded, the DRD individuals were filtered by highly deprived or less deprived socio-economic group in the twelve months before death, which highlighted a significant level of severe deprivation within the cohort, as shown in box two. Finally, similar healthcare utilisations comparisons were undertaken, using the databases previously described.

4.6.5.1. Introduction

As premature deaths are much more prevalent in areas of socio-economic deprivation, the cohort was split into highly deprived (SIMD 1 and 2) and relatively less deprived (SIMD 3, 4 and 5). Even before comparing healthcare usage, it is important to note there were only 59 individuals out of the total of 288 (21%) in the less deprived socio-economic quintiles.

4.6.5.2. Healthcare Usage compared across Socio-economic Groups

The only significant healthcare difference was in the rate of individuals with at least one hospital inpatient attendance recorded as a routine event (see Table 4-15). Those in the less deprived quintiles had a considerably higher rate of routine attendance, again corroborating the association for a large subset of DRD with emergency healthcare usage.

4.6.5.3. Prescription Records compared across Socio-economic Groups

When comparing prescription rates between those in severe deprivation versus those in less deprived quintiles, some anticipated patterns were revealed (see Table 4-16). Methadone prescriptions were significantly higher in the most deprived group, with just under half receiving one, compared to a little over 15% of the less deprived group. Gabapentinoids and anticonvulsants were also prescribed at significantly higher rates in the more deprived socio-economic status group.

Other psychotropic drugs (i.e., antidepressant, benzodiazepine and Z-drug prescriptions) were not significantly different between deprivation levels, and nor were the preventative prescriptions of statins and antihypertensives.

Table 4-15. Healthcare Utilisation across Socio-economic Deprivation levels

Variable	**SIMD 1 and 2 (N=221)**		**SIMD 3, 4 and 5 (N=59)**		**X²**	**p value**
	%	(n)	%	(n)		
General inpatient	40.7	90	37.3	22	0.229	>0.05
Routine Attendance	**40.0**	**36**	**63.6**	**14**	**3.997**	**<0.05**
Psychiatric outpatient	61.5	136	47.5	28	3.805	>0.05
Non-psychiatric outpatient	27.1	60	32.2	19	0.587	>0.05
Mental Health Inpatient	5.9	13	8.5	5	0.520	>0.05
Accident and Emergency	52.5	116	50.8	30	0.050	>0.05

Percentage and count data for all DRD individuals, split by whether they were recorded in the high deprivation or low deprivation quintiles, examining healthcare usage across a variety of services. SIMD 1 and 2 are the quintiles representing high deprivation, with 3, 4 and 5 representing low deprivation. General hospital presentation included both day and inpatient cases, therefore routine attendance was calculated only for those with at least one of these general hospital presentations. Outpatient clinics were split by specialty, with psychiatric codes not distinguishing between mental health or substance misuse. Chi-square tests were calculated, with rows in bold indicating statistical significance. The only significant difference was that individuals in less deprived quintiles had a higher rate of routine appointments, when considering general hospital attendances.

Table 4-16. Prescription records across Socio-economic Deprivation levels

Variable	**SIMD 1 and 2 (N=221)**		**SIMD 3, 4 and 5 (N=59)**		**X²**	**p value**
	%	(n)	%	(n)		
Methadone	**47.5**	**105**	**16.9**	**10**	**17.972**	**<0.05**
Antidepressants	57.0	126	50.8	30	0.718	>0.05
Benzodiazepines	26.7	59	23.7	14	0.213	>0.05
Z-drugs	20.4	45	20.3	12	0.000	>0.05
Gabapentinoids	**22.6**	**50**	**10.2**	**6**	**4.515**	**<0.05**
Anticonvulsants	**27.6**	**61**	**11.9**	**7**	**6.272**	**<0.05**
Statins	1.8	4	6.8	4		>0.05*
Antihypertensives	0.9	2	5.1	3		>0.05*

Percentage and count data for all DRD individuals, split by whether they were recorded in the high deprivation or low deprivation quintiles, summarising prescription records. SIMD 1 and 2 are the quintiles representing high deprivation, with 3, 4 and 5 representing low deprivation. Chi-square tests were calculated, with rows in bold indicating statistical significance. * represents a low cell count, requiring Fisher's exact test rather than a Chi-square test. Methadone was prescribed at a significantly higher rate in the more deprived quintiles, as were gabapentinoids and anticonvulsants, which were the only significant differences.

4.7. Analysis of DRD Individuals Not Present in the 'Probable Suicide' Cohort

4.7.1. Introduction

Finally, a set of healthcare usage comparisons were calculated for the individuals that did not overlap with the suicide cohort. This subset arguably represents a "true" DRD population, and could therefore, present an alternative pattern to those already identified. As mentioned before, the majority of DRD are opioid-related, as such, the dividing characteristic within the cohort was whether the individual was "in treatment" or not, which was approximately half and half of the 91 individuals.

4.7.2. Healthcare Usage

Within this cohort, the only significant difference was that those who received a methadone prescription also had a higher rate of psychiatric outpatient attendance, though this is unavoidable because of the data structure. No other comparisons were significantly distinguishable (summarised in Table 4-17).

4.7.3. Prescription Records

Prescription rates within this cohort revealed few statistical differences between groups (see Table 4-18). Rates of antidepressant prescription were relatively high in both groups, and had a trend towards being more commonly prescribed in combination with methadone, however this trend did not reach statistical significance. Z-drugs and anticonvulsant prescription were redeemed by a larger percentage of individuals who were also prescribed methadone, compared to those not "in treatment", and these were the only significant observations.

Table 4-17. Healthcare Utilisation, compared across uniquely DRD individuals

Variable	Methadone Prescribed (N=44)		No Methadone Prescription (N=47)		X²	p value
	%	**(n)**	**%**	**(n)**		
General inpatient	61.4	27	51.1	24	0.979	>0.05
Routine Attendance	51.9	14	50.0	12	0.017	>0.05
Psychiatric outpatient	**88.6**	**39**	**27.7**	**13**	**34.503**	**<0.05**
Non-psychiatric outpatient	34.1	15	31.9	15	0.049	>0.05
Mental Health Inpatient	2.3	1	4.3	2		>0.05*
Accident and Emergency	61.4	27	63.8	30	0.059	>0.05

Percentage and count data for only the DRD individuals who did not overlap with the suicide cohort, split by whether they were in receipt of at least one OST (methadone) prescription, examining healthcare usage across a variety of services. General hospital presentation included both day and inpatient cases, therefore routine attendance was calculated only for those with at least one of these general hospital presentations. Outpatient clinics were split by specialty, with psychiatric codes not distinguishing between mental health or substance misuse. Chi-square tests were calculated, with rows in bold indicating statistical significance. * represents a low cell count, requiring Fisher's exact test rather than a Chi-square test. Only psychiatric outpatient attendance was significantly higher in the methadone prescribed group of DRD-only individuals.

Table 4-18. Prescription Records, compared across uniquely DRD individuals

Variable	Methadone Prescribed (N=44)		No Methadone Prescription (N=47)		X²	p value
	%	**(n)**	**%**	**(n)**		
Antidepressants	54.5	24	38.3	18	2.414	>0.05
Benzodiazepines	29.5	13	23.4	11	0.441	>0.05
Z-drugs	**27.3**	**12**	**10.6**	**5**	**4.139**	**<0.05**
Gabapentinoids	25.0	11	12.8	6	2.239	>0.05
Anticonvulsants	**34.1**	**15**	**12.8**	**6**	**5.822**	**<0.05**
Statins	2.3	1	2.1	1		>0.05*
Antihypertensives	0.0	0	0.0	0		

Percentage and count data for only the DRD individuals who did not overlap with the suicide cohort, split by whether they were in receipt of at least one OST (methadone) prescription, summarising prescription records. Chi-square tests were calculated, with rows in bold indicating statistical significance. * represents a low cell count, requiring Fisher's exact test rather than a Chi-square test. Few significant differences were noted, with only Z-drugs and gabapentinoids prescribed at higher rates for the DRD-only individuals receiving a methadone OST prescription.

4.8. Multivariate Predictive Model

4.8.1. Introduction

The healthcare utilisation analysis of the DRD group compared to the control group highlighted several key differences between groups: general hospital attendance, psychiatric outpatient attendance, methadone OST prescription and antidepressant prescriptions were regularly more common in the DRD group than in the compared control group. Predicting DRD is less common than the use of predictive modelling in other healthcare fields (Bharat et al., 2021), however there are predictive models aimed at identifying potentially fatal overdoses from hospital admissions data (Nguyen et al., 2017), or the likelihood of completing treatment (Baird, Cheng and Xia, 2022) that have been published recently. Additionally, machine learning algorithms have been used to predict all-cause mortality in the 180 days following an overdose, with moderate success; of the top 2% of individuals identified as high-risk, 20% died within 180 days, however a prohibitive total of 348 predictor variables were included (Guo et al., 2021). The cohorts that have been analysed vary widely, as do the number and type of variables included, though generally studies find overdoses to be more common for men than women, and more common in those socio-economically deprived. While the sophistication of the machine learning publication is impressive, it is important to identify models that are more feasible, less resource-intensive and focus on DRD. As such, a reduced number of healthcare attendance variables, ones that were repeatedly significant across groups, were read into a predictive model for DRD.

4.8.2. Method

The full cohort of 288 DRD individuals and all 1,152 control individuals were read into the analysis, however the individuals with any missing demographic details were excluded, leaving 280 DRD individuals and 1,138 control individuals. A binary logistic regression model was chosen, with DRD or control group as the outcome variable. The variables included were the same as those included in the 'probable suicide' cohort analysis, which were: demographic variables, at least one general hospital admittance, at least one psychiatric outpatient attendance, at least one Accident and Emergency presentation, at least one antidepressant prescription, at least one methadone prescription and at least one benzodiazepine prescription.

4.8.3. Multivariate Model Results

The binary logistic regression model was significant X^2 (13, N=1418) = 637.110, $p<0.0001$, and using the Nagelkerke R^2 calculation, explained 57.5% of the variance in the data. The model, including all of the variables, classified 88.7% of the individuals correctly however, the vast majority of these correct classifications were in the control group. Neither socio-economic level nor benzodiazepine prescription contributed to the model, however all other variables were significant. Any attendance at a healthcare service, or any of the other psychotropic prescriptions were associated with an increased likelihood DRD, compared to non-engagement as the referent categories.

The variable contributing most to the model, based on the Wald X^2 statistic was the age group, which was unanticipated. Those 25 years old or younger had the highest odds ratio for being in the DRD category, at 14.558, compared to the reference category of those 26-50 years old (see Table 4-19). The next most significant predictors were a methadone OST prescription, and then an antidepressant prescription, which correlates well with the healthcare usage analysis that has highlighted high rates of psychotropic prescribing in the DRD cohort. The next most important contributions to the model were a general hospital attendance, followed by a psychiatric outpatient attendance. Following that in significance was an Accident and Emergency presentation, then sex, which highlighted that women were less likely to be ruled a DRD than men. Neither the socio-economic level (SIMD) nor receipt of a benzodiazepine prescription contributed in a statistically significant manner to the model; this was unanticipated as SIMD is generally highly associated with DRD.

The inclusion of all of these factors did explain 58% of the variance in the data, however overwhelmingly the individuals that were successfully predicted belonged to the control group, which highlights the challenge of constructing predictive models for an outcome as complex and rare as DRD.

Table 4-19. Multivariate Model Predicting DRD

Variable	Wald X^2 Statistic	Exp(B)	95% CI for Exp(B)
Men	**9.187**	Reference	
Women		**0.501**	**0.321-0.784**
≤25 years old	**81.793**	**14.588**	**7.778-27.361**
26-50 years old		Reference	
≥51 years old		**0.456**	**0.244-0.853**
SIMD 1	4.997	Reference	
SIMD 2		1.227	0.780-1.929
SIMD 3		1.180	0.627-2.221
SIMD 4		1.902	0.949-3.813
SIMD 5		2.026	0.812-5.050
No General Hospital Admittance	**30.985**	Reference	
≥1 General Hospital Admittance		**4.099**	**2.494-6.737**
No Psychiatric outpatient Attendance	**30.666**	Reference	
≥1 Psychiatric outpatient Attendance		**4.234**	**2.541-7.056**
No Accident and Emergency Presentation	**16.199**	Reference	
≥1 Accident and Emergency Presentation		**2.426**	**1.576-3.735**
No Antidepressant Prescription	**36.477**	Reference	
≥1 Antidepressant Prescription		**3.787**	**2.458-5.834**
No Methadone Prescription	**46.086**	Reference	
≥1 Methadone Prescription		**8.866**	**4.722-16.648**
No Benzodiazepine Prescription	3.540	Reference	
≥1 Benzodiazepine Prescription		1.721	0.978-3.031

Odds ratios from a binary logistic regression model predicting DRD, based on demographic and healthcare measures. The largest sub-group was set as the reference group. Wald X^2 statistic represents the unique contribution of each factor, when every other factor is kept constant, thus representing the contribution of the factor to the model. Bold rows indicate statistical significance. Women and those 51 years old or older were significantly less likely to be a DRD, while attendance at any healthcare service and most prescriptions were associated with greater likelihood of DRD. Unusually, SIMD had no significant effect.

4.9. Summary of DRD Analysis

Of the 311 individuals initially categorised as DRD, only 288 could be validated with ICD-10 codes, though a small number of these individuals were lacking demographic data.

Comparing the validated DRD cohort and matched community controls revealed that the DRD cohort attended all healthcare services at higher rates. Psychiatric healthcare services showed the largest difference, with almost 60% of the DRD cohort attending at least once, to 6% of the control cohort. Similarly, psychotropic prescriptions were redeemed at considerably higher rates in the DRD cohort.

Possible self-harm events were identified in a higher percentage of the DRD cohort with Accident and Emergency presentations, and this cohort received an elevated rate of psychiatric healthcare follow-up. Prescription modifications in the 21 days after the event were similar across groups and insignificantly different.

A much greater percentage of the DRD group had a urine drug screen record than the controls, however the mean positivity rate for non-prescribed opioids was insignificantly different. A small number of individuals in both groups were not receiving OST, yet were scheduled for a urine drug test.

Those with methadone OST prescriptions were extracted from both cohorts and contrasted, though only the general hospital and accident and emergency services were attended at higher rates by the DRD group, with the greatest difference being general hospital attendance. Most of the additional psychotropic prescriptions were dispensed at elevated rates in the DRD group, compared to the OST control group. The mean daily dose of methadone was insignificantly different between groups.

Focusing only on the DRD cohort three splits were performed; “in or out of treatment”, division into greater and lesser levels of socio-economic deprivation, and examining the small number not also present in the ‘probable suicide’ cohort. Echoing the previous analysis, the only significant difference for was that the DRD “in treatment” had a higher rate of psychiatric outpatient attendance than those without OST prescriptions. Likewise, an OST prescription was associated with further psychotropic prescriptions. Remarkably, the only significant difference for attendance concerning deprivation levels was that the less deprived had more routine versus emergency appointments at hospital. A small number of psychotropic prescriptions were more common for the more deprivation section of the cohort. Even fewer differences were noted between the DRD-specific individuals, divided by "in or out of treatment".

Finally, a multivariate model was constructed to predict DRD. Demographic variables and healthcare measures demonstrating the largest between group differences were included, and almost two-thirds of the variance was explained. All but two variables were significantly predictive, with all healthcare utilisation measures, other than benzodiazepine, increasing the odds of being recorded a DRD. Unanticipatedly, deprivation level did not contribute to the model in a significant manner. The correct classifications were primarily of the control cohort, and highlights the challenge with constructing accurate predictive models.

5. Discussion

5.1. Introduction

This thesis has, so far, validated cohorts of both ‘probable suicide’ and DRD, considered the appropriateness of their matching to community controls and extracted a significant volume of healthcare data from routine, administrative databases. These variables have been compared across the full cohorts of ‘probable suicide’ and DRD with their matched controls, followed by analyses of specific sub-sections of the cohorts. Both the ’probable suicide’ and DRD cohorts attended healthcare services and received higher rates of psychotropic prescriptions than their matched community controls. This overarching finding had been hypothesised, based on the poorer health associated with those who die prematurely; however, data had not been previously published examining healthcare usage in one cohort, across multiple services. As such, it was key to have this real-world data concerning healthcare usage to attempt to answer the parallel hypotheses of insufficient healthcare being related to increasing numbers of ‘probable suicide’ and DRD.

Furthermore, sub-sections of the cohorts were extracted for a fine-grained analysis of potential differences between those “in treatment” for conditions highly associated with either ‘probable suicide’ or DRD; that is, depression or opioid misuse, respectively. Rates of healthcare attendance and psychotropic drug co-prescribing were still significantly higher in the cohort of individuals who died, than the control cohorts receiving the same treatment prescription. There were fewer differences between the DRD cohort in treatment and the controls in treatment, than in the ‘probable suicide’ sub-section. Additionally, within the DRD comparison, mean methadone dose throughout the year did not differ between groups. Both deceased groups attended more psychiatric outpatient clinics over the year, than the live individuals likewise “in treatment”.

The final comparisons were based on clarifying profiles within both ‘probable suicide’ and DRD. As such, these two groups were split by treatment status again. Comparing those in or out of treatment in the ‘probable suicide’ cohort showed that those receiving an antidepressant prescription were also more engaged with the other healthcare services. Interestingly, for the DRD group, treatment status seemed to have very little effect, other than higher rates of psychotropic drug prescription for the group with OST prescriptions. Other comparisons within the ‘probable suicide’ and DRD cohorts split the individuals by demographic status; those in the more deprived half had elevated rates of psychotropic prescription compared to the less deprived quintile, in the ‘probable suicide’ cohort. Unanticipatedly, the DRD cohort had very few statistical differences between the more and less deprived quintiles. The small number of individuals who were only present in the DRD cohort were extracted, and again split by whether they received methadone OST or not. Very few differences were identified, other than increased co-prescription of z-drugs and anticonvulsants.

Multivariate predictive models were calculated to identify the ‘probable suicide’ or DRD individuals, based on healthcare usage variables, compared to the matched control cohorts. As was to be anticipated from the previous results, the models demonstrated that any healthcare usage was predictive of belonging to the deceased cohorts. These models highlighted that, while the models were significant, the correct predictions of the model were primarily for the control cohorts, rather than successfully identifying the individuals who died.

5.2. Limitations of the Study

There were several limitations to the studies presented in this thesis. First, there were the inherent limitations of any retrospective, routinely collected, data-based study. All the data used within this thesis were extracted from routinely collected, public system, administrative, non-research, databases. Because these datasets were not primarily intended for research purposes (Higgins and Matthews, 2020), there were issues with data completeness and quality, which was especially notable in the possible self-harm presentation analysis, where the majority of the codes denoting the intent of the injury were missing. This introduced assumptions into the analysis and could make the findings less reliable. Additionally, the administrative nature of the databases meant that numerous factors identified within previous research as strongly associated with both 'probable suicide' and DRD were not available. This would include, for example, factors such as homelessness, benefit status, criminal justice experiences and age of first exposure to drugs or 'probable suicide' of a family or peer (Congdon., 2019, Yuodelis-Flores and Ries, 2015). A number of these variables should have been available, in that the data feeds stored within HIC included read-outs from the three relevant Local Authorities, which contained information on benefits and registered addresses, which also detail periods of homelessness. These files, however, were transferred without the required meta-data that defined the codes used, and therefore no information could be extracted from these files.

Both cohorts were relatively small; only 586 'probable suicide' and 288 DRD individuals were extracted and validated for analysis, and so it is possible that any patterns identified are specific to the Tayside area and may not generalise well. However, the demographic distributions of the cohort were similar to many of those in other healthcare studies and publications: both of these types of deaths had higher proportions of men and individuals belonging to the most deprived socio-economic groups, with the majority of them being between 26-50 years old (e.g., Chan et al., 2016, Castelpietra et al., 2017, Abrahamsson et al., 2017). As such, these results should still be generally useful for countries with similar healthcare systems and demographic distributions to Scotland.

One concern, highlighted throughout the results section and featuring also in the subsequent cluster analysis section, is that the extrapolation of any one prescription as a proxy indicator of any specific morbidity can be queried. The definition proposed to isolate those "in treatment" for both groups of deaths hinged on whether an antidepressant prescription or a methadone OST prescription had been issued, as denoted by BNF codes. This clearly is an over-simplification of the clinical reality. For example, when considering antidepressants, these are prescribed for numerous reasons other than their primary BNF indication. As such, it cannot be conclusively stated that the individuals receiving an antidepressant prescription truly represented individuals suffering from a diagnosed depression, or indeed, other mental illnesses like anxiety disorders. Furthermore, only one prescription was required to fulfil the definitions used here, despite the fact that risk of death has been reported to vary between the individuals who are regularly receiving treatment, versus those who may receive only one prescription or irregularly are engaged in healthcare services (Sordo et al., 2017, Santo et al., 2021, Castelpietra et al., 2017). The use of such proxy indicators was an unavoidable challenge with the data available for this study since there were no records of formal diagnoses or clinician's notes available. Additionally, the requirement of two or more prescriptions within a certain timeframe to classify individuals as "in treatment" was not pursued, both due to the time commitment that would have been required and to have the largest sample sizes possible for the "in treatment" comparisons.

While noted above, the lack of formal diagnoses or clinical notes is a serious limitation of its own. It necessitates the use of prescription records as proxies, yet this adjustment is ineffectual for conditions that are, or can be, treated in other ways. One key example would be individuals with personality disorders, in particular borderline personality disorder (with a potential group identified in the clustering analysis, see page 268). Individuals with these disorders are associated with significantly higher healthcare usage than individuals with other mental health conditions (Sansone, Farukhi and Wiederman, 2011) and yet have no specific psychotropic prescription recommended for their care. Patients with these diagnoses or co-morbidities would also represent further sub-groups of individuals requiring distinct treatment pathways, yet the lack of diagnostic data prevents any accurate identification of them. This also highlights another, related limitation of using only routine data, which cannot answer more complex questions like those surrounding degrees of co-morbidity, the severity of illness or the efficacy of care. These complex questions would all require highly detailed or qualitative measures that could be obtained only through supplementary, mixed-methods research. Future research could examine both the wider healthcare usage context, while inter-disciplinary researchers or clinicians could investigate these psychological aspects, thus clarifying the context and "lived experience" of the patterns identified.

These data are also several years old, therefore policies and clinical guidelines, for example around co-prescribing, have evolved. The findings around elevated co-prescribing, especially in the DRD cohort, remain potentially important, due to the highly increased risk of death they confer, and the reported rise of gabapentinoids in recent toxicology results (NRS, 2021 (a)). It is likely, for this research to be of maximum utility, that the analyses ought to be done regularly, to ensure that the healthcare patterns are closely reflective of current attendance.

The data comparison process was more complex and time-consuming than originally anticipated. Many of the community control datasets were not filtered by their index date, which meant there were healthcare records from the years 2015 and 2016 in all control databases. This resulted in the need for a significant amount of data cleaning, editing and verification before any re-coding could take place. This entailed converting data from long to wide formats, and required significant cross-checking of dates to ensure episodes for the control individuals were appropriately bounded by their index date. Furthermore, the prescription databases were large, with over 18,000 rows in the 'probable suicide' cohort database and over 180,000 in the data for the matched community controls. This meant that the number of prescriptions of interest was, of necessity, limited, due to the length of time involved in filtering and matching records. As such, I was unable to investigate prescription-based proxies for some key physical conditions, which is unfortunate, as one pattern of 'probable suicide' and DRD is linked to severe physical illness (Fegg et al., 2016, Amundsen, 2015). Future research with access to diagnostic history would improve the validity of both the "in treatment" and co-morbidity designations, and should be pursued for improved understanding of those who die and their healthcare usage patterns.

5.3. Analysis of the 'Probable Suicide' Cohort

5.3.1. Analysis of the Cohort Validation

The first step of the process was to compare and validate the statistical definitions of 'probable suicide'. While the NRS and ScotSID stated in their methods that they used the same criteria, other than ScotSID removing the deaths of individuals under the age of five, the total number of individuals included was significantly different (see page 85). The NRS dataset included 310 individuals more than the 295 individuals that were also present in ScotSID's records. Of this additional group, 285 fulfilled all ScotSID criteria, yet were missing. A binary logistic regression found several significant demographic associations; those excepted from the age group of 26-50 were more likely to be included than those within. Those in the second-least deprived socio-economic quintile, compared to the most deprived quintile, were also more likely to be included. Many of the individuals not included by ScotSID were the ones also present in the DRD category, which may explain the demographic associations, as the DRD cohort was primarily individuals between 26-50 and in the most deprived quintiles. International guidelines for the coding of deaths by acute intoxication were changed in 2011, which was partway through the sample timeframe of 2009-2014 (NRS Methodology (nrscotland.gov.uk)), however this should not have affected ScotSID's inclusion or exclusion criteria, as the codes used to define 'probable suicide' were never modified. This methodological change would simply have increased the number of 'probable suicide' individuals, as the recommendation was that deaths that previously would have received codes specific to drug-related causes would now be listed under "poisonings of undetermined intent". Therefore, these would now be included in 'probable suicide' statistics. The NRS "freeze" the databases, and therefore codes recorded, in the April of the next year (e.g., codes for 2009 would not change, irrelevant of additional data received, past April 2010). It is possible that ScotSID continued to modify their databases using further information from long-running medico-legal investigations. The two problems with this explanation are, first, that further modifications to codes are not described in the method sections of the ScotSID reports, and that it is very unlikely that so many deaths could be modified and re-coded as accidents, over five years, from one city.

Overall, these results suggest that the publications used to direct policy development in Scotland may omit a significant number of individuals, with at least 285 individuals missing from the database from only one region of Scotland. When scaled up to a national level, it is possible that the number of omitted individuals is significantly higher, thus of even greater concern. The stated aim of ScotSID is "*to provide a central repository for information on all probable suicide deaths in Scotland, in order to support epidemiology, policy-making and suicide prevention*" (ScotSID, 2021 (b)). This is evidently a valuable aim, however as the database appears to omit a large number of relevant individuals, the published reports and therefore, any policy based on these reports, may be very inaccurate and poorly reflective of the true national rate of 'probable suicide' and the demographic backgrounds of these individuals. Further validation of the definitions, methods and cohorts of ScotSID would be necessary to identify what the true explanation is, whether it is a recurrent problem and how to correct the data collection pathways to prevent this from occurring. This finding does emphasise the value and importance of my thesis, as it highlights the need to investigate past research and national databases, to ensure that they are accurate. It also implies that the number of deaths and demographic characteristics identified in my thesis are more accurate and complete than those published by ScotSID.

5.3.2. Analysis of the Total Cohort Comparison

Previous reviews of published studies have reported that individuals who die by 'probable suicide' have notable rates of healthcare engagement shortly before death (Stene-Larsen and Reneflot, 2017, Luoma, Martin and Pearson, 2002). These reports have stated that between 75-80% of individuals had presented at least once to a primary healthcare service, and between 21-42% had a "mental healthcare contact", in the year before death. These reviews summarised data from psychological autopsy studies, record reviews (generally relying on medical examiner or coronial reports) and registry studies. Focusing on the more recent and up-to-date data, half of the studies included by Stene-Larsen and Reneflot (2017) included a type of control group. These ranged from natural, accidental or sudden death control groups, 'probable suicide' cohorts not in contact with healthcare services, with only a small number using community or population-representative controls. Those with matched live controls had some significant flaws for generalisation purposes: Reutfors et al. (2010) investigated 'probable suicide' risk only during and after hospitalisation for a mental illness diagnosis, Renaud et al. (2009) considered only those between 11-18 years old, while multiple considered only older adults (e.g., Chiu et al. (2004) included those over 60 years old, Beautrais (2004) those over 55 years old, Juurlink et al. (2004) those 66 years old or older and Conwell et al. (2010) those 50 years old or older). A study from Slovenia included only 77 individuals in each group and examined only primary care records (Mesec Rodi, Roškar and Marušič, 2009). Curiously, and rather unhelpfully for a comparison of attendances rates, one study required healthcare attendance within the year of study, or the previous year, from both groups to demonstrate continued residence in the area (Morrison and Laing, 2011). Finally, Chock et al. (2015) did consider the full age range, and examined a wider variety of services than commonly found (e.g., Accident and Emergency services, that were attended by 'probable suicide' individuals at higher rates), however, there were only 86 individuals in the 'probable suicide' group. Overall, these studies demonstrate a general lack of wide-ranging, simple comparisons between the antecedent healthcare patterns of those who die of 'probable suicide', and matched, live, community controls.

In any case, the results from the reviews above indicated that the elevated rate of attendance at some of the healthcare services for the 'probable suicide' cohort were to be anticipated, especially at psychiatric outpatient and Accident and Emergency services. That the rate of healthcare attendance was significantly different across 'probable suicide' and community controls at all services, however, was unexpected. None of the studies examined included data from as many healthcare services, nor did they overwhelmingly include control groups of any kind. This emphasises the lack of clear, reliable results and comparisons, which makes it challenging to theorise effectively or identify accurately where improvements could be trialled. Furthermore, the lack of control group leads to broad suggestions that primary and secondary deficits in healthcare provision for those in crisis are to blame for 'probable suicide' deaths. This is despite 82% of individuals attending a healthcare service, which seriously challenges the concept of primary deficits, at least (Vasiliadis, Ngamini-Ngui and Lesage, 2015).

For Scotland specific data, ScotSID reports have begun to compare past healthcare usage rates with Scottish-wide population averages for the 'probable suicide' cohort. As a control group, an average population rate is a flawed choice, as it is well-established that healthcare attendance varies with gender, age and socio-economic level (Stene-Larsen and Reneflot, 2017, Luoma, Martin and Pearson, 2002), and also that 'probable suicide' is specifically distributed across these demographic patterns (Sterling and Platt, 2022, Pirkis, Nicholas and Gunnell, 2020). As such, the data used in this study demonstrates the utility of record-linkage studies in general, by matching a live control group with the 'probable suicide' cohort. As such, the reliability of the result will be increased, as the differences will be less biased by variation in gender, age or socio-economic deprivation, and their relationships with healthcare usage, than studies without this protocol.

5.3.2.1. Non-Psychiatric Healthcare

General healthcare was significantly higher in the 'probable suicide' cohort than the community controls, however the community controls who attended had a much greater proportion of individuals with a routine attendance compared to the 'probable suicide' group. This correlates well with the elevated accident and emergency department presentations in the 'probable suicide' group, as well as the higher rate of antihypertensive prescriptions present in the community controls. Taken together, these all suggest greater emergency healthcare was required by the 'probable suicide' cohort in the year before death, while those who did not go on to die were attending routine appointments and receiving preventative prescriptions. The matching between the 'probable suicide' cohort and the community controls was, however, not exact. There was a greater proportion of individuals in the 51 years old and older group in the community controls than the 'probable suicide' cohort, which could have contributed to this difference (36% to 26% respectively). Older individuals access general healthcare more regularly than younger individuals due to the greater number of physical health complaints (Cho et al., 2013, Ahmedani et al., 2014), and antihypertensives are prescribed for older patients. It is also well-established that individuals with psychiatric diagnoses present frequently to emergency services (Abar et al., 2017, Ahmedani et al., 2014). It cannot be conclusively stated that the 'probable suicide' cohort received less routine care than they ought, due to the discrepancy in age group distribution. Especially as some have reported a higher rate of depression in those receiving high-dose statins than those receiving low dose statins (Leutner et al., 2021), though this could be due to the severity of the cardiovascular conditions and the poorer prognosis implied by high dosages.

5.3.2.2. Psychiatric Healthcare

One of the key dimensions of ‘probable suicide’ prevention is held to be appropriate psychiatric healthcare. Whether the care is primary or secondary, or whether involving antidepressant prescriptions or psychosocial interventions is rarely specified. Considering a very broad definition (psychiatric inpatient and outpatient, as well as an antidepressant prescription over the year), 54% of the ‘probable suicide’ cohort experienced some form of psychiatric healthcare compared to 14% of the community controls. The most common intervention was an antidepressant prescription. Slightly under half, 43%, of the ‘probable suicide’ cohort had received at least one antidepressant prescription in the year before death, compared to 13% of the community control cohort. As noted in the introduction, the association between depression and ‘probable suicide’ is commonly emphasised, despite the fact that some studies have suggested upwards of 60% of ‘probable suicide’ decedents were ineligible for a psychiatric illness diagnosis (Milner, Sveticic and De Leo, 2012). Of course, there is undoubtedly a relationship between depression and ‘probable suicide’. Efficacious prescribing of antidepressants can and should be one of a variety of evidence-based interventions, as it has been repeatedly associated with a small reduction in ‘probable suicide’ (Zalsman et al., 2016, Cipriani et al., 2018, Gaynes et al., 2009). Despite the importance of this treatment modality, none of the healthcare attendance reviews included information on antidepressant prescribing before death by ‘probable suicide’ (Luoma, Martin and Pearson, 2002, Stene-Larsen and Reneflot, 2017). The most recent report for ScotSID notes that 52% of the individuals who died of ‘probable suicide’ in Scotland had received an antidepressant prescription in the year before death from 2011 to 2019 (ScotSID, 2021 (b)), which may suggest there is an increased rate of prescribing since the end of the data extraction for this thesis. The yearly reports, however, do not include a data on the number of individuals receiving this purportedly crucial prescription (ScotSID, 2022). This oversight seems problematic, as there can be no clear questioning of whether the rate of prescribing is efficacious, without clear data on what the rate of prescribing in an indicated population truly is.

That other psychotropic prescriptions were likewise elevated in the ‘probable suicide’ cohort is of interest, especially as anxiolytic prescriptions have not been associated with a reduction in ‘probable suicide’. Indeed, the co-prescription of antidepressant and benzodiazepine drugs has been associated with an increased risk of mortality

(Jeong et al., 2020), and benzodiazepine drugs themselves are relatively high-risk prescriptions due to their propensity towards dependence and abuse (NICE, 2022 (a)). These prescriptions will be discussed in greater length when considering the section of the analysis which included only those prescribed an antidepressant due to the high rate of co-prescribing. It is, however, worth noting that this finding would suggest that the greater healthcare needs, attributed in the literature to those who die prematurely, are being recognised and that they receive higher levels of healthcare interventions.

Psychiatric outpatient appointments being considerably more prevalent in the ‘probable suicide’ cohort than the community control cohort had been anticipated, though the magnitude of the difference was not (39% to 4%, respectively). It stands to reason that those who died of a cause related to profound psychological distress would, as a group, have a higher rate of attendance than a control group of people not necessarily indicated for that healthcare service. This is within the range given in the review by Luoma, Martin and Pearson (2002), who reported a mean of 32% with a range of 16-46% in their view of studies, however this included mental health inpatient contact rates. That rates have not materially increased since this review was compiled in 2002 is of concern, especially as there have been drives to reduce stigma and policy initiatives to encourage those struggling with suicidal ideation to speak out and access healthcare. There are also schemes encouraging average members of society to signpost loved ones towards mental health resources (Public Health Scotland, 2022). More recent studies may be required to test developments since 2014, however the lack of impact may point towards flaws in the conception of the model used to design intervention strategies. It is true that psychological studies note the effect of stigma, and that it undoubtedly mediates relationships between the individual’s perspective of themselves and reluctance to access healthcare (Chandler, 2021). It is also true that the studies which have demonstrated the greatest reductions in ‘probable suicide’ rates have been much more practicable and systemic in the interventions proposed; specifically, these were means restriction (Zalsman et al., 2016, Lim et al., 2021) and the provision of 24-hour crisis helplines (While et al., 2012).

As highlighted in the Poisson logistic regression, those who went on to die by ‘probable suicide’ also had a higher median frequency of psychiatric outpatient appointments, and were associated with an increasing frequency of appointments made and kept, as well as appointments made and missed. It is plausible that this is influenced by the higher rate of antidepressant prescriptions within the ‘probable suicide’ group, as clinical guidance is to review patient progress and potential medication side-effects relatively regularly (NICE, 2022 (b)). This could have somewhat artificially increased the rate of psychiatric outpatient appointments in the ‘probable suicide’ group. Even if that contributed to these elevated rates, it would suggest best practice guidelines were being followed and would, therefore, be an encouraging result. Other studies have also noted that an increased frequency of psychiatric follow-up appointments, after an Accident and Emergency or hospital admission, reduced the likelihood of ‘probable suicide’ in the subsequent months, compared to those not receiving additional follow-up (Vasiliadis, Ngamini-Ngui and Lesage, 2015, Brown and Green, 2014). While not examining precisely the same context as appointments in the year before death, it indicates that multiple psychiatric appointments have a protective effect, and that these associations are very likely to be cause by confounding by indication. The administrative data available in HIC precludes any analysis of the efficacy of the psychiatric interventions applied, however this is a key area for future research.

These regressions also identified a significant effect of SIMD, in that the less deprived quintiles were associated with lower frequencies of outpatient appointments; a strength of the multiple data sub-sections is demonstrated here, as it shows that the less deprived quintiles in the ‘probable suicide’ cohort had a lower rate of psychiatric outpatient attendance overall, which likely explains to this result. The reviews previously mentioned did not contain analyses of psychiatric outpatient frequency measures. Another study containing analyses on psychiatric outpatient frequency did not consider socio-economic level (Vasiliadis, Ngamini-Ngui and Lesage, 2015), nor did they report the median or range of attendance. There seemed to be a lack of published literature examining the impact of frequent psychiatric outpatient appointments, though this may be due to the lack of information in HIC that would allow for more targeted literature searches. For example, if patients were known to be undergoing CBT, the frequency of their appointments could be examined in the context of optimal CBT delivery. Without that detail, further analysis of the regression model is impossible.

One further consideration of psychiatric healthcare usage, is that mental health inpatient admissions were low, but notably and significantly more prevalent in the ‘probable suicide’ cohort. As with the psychiatric outpatient appointment rates, it was predictable that those suffering from a broadly defined psychological distress would present to psychiatric healthcare services more frequently. Where the relationship between ‘probable suicide’ and psychiatric inpatient admission is considered, the published data becomes more complex. It is known that those who die by ‘probable suicide’ have a higher rate of inpatient admission (ScotSID, 2021 (b), Musgrove et al., 2022); yet, this could simply be caused by confounding by indication. The most severely ill patients, usually considered to present the highest risk, would require, and ideally receive, the most intensive intervention available. This would be mental health inpatient admission, and therefore it could be suggestive of appropriate healthcare targeting that those who died by ‘probable suicide’, with its strong associations to psychiatric disorders, had high rates of psychiatric treatment. The added complexity comes from data that holds that a psychiatric inpatient admission itself may be somewhat traumatic, and that rates of ‘probable suicide’ on the wards themselves are an area targeted for clinical improvement, with, for example, recommendations investigating how to reduce ligature points (NCISH, 2022). Of course, a key caveat is that deaths on wards are very rare. That many deaths also happen shortly after discharge is of greater concern, and may suggest that additional after-care is necessary, both because of the pre-dating psychological distress and because of any that may relate to the loss of freedom and fear of stigma that result from inpatient admission (Musgrove et al., 2022, Owen-Smith et al., 2014). A recent meta-analysis has highlighted that the risk of ‘probable suicide’ is highest in the first week after discharge, compared to subsequent weeks and months (Chung et al., 2019), with a record-linkage study demonstrating that the risk remained elevated for the next 5 years, when contrasted against the risk for individuals with similar psychiatric diagnoses without an inpatient admission (Musgrove et al., 2022). As discussed by both publications, the prolonged, elevated risk is likely partially explained by the greater severity of illness attributed to patients for whom inpatient admission is recorded. Other explanations may centre around the patient returning to a highly chaotic environment, indeed potentially the environment that was a proximate trigger to the admission (Madsen et al., 2021, Owen-Smith et al., 2014). Early follow-up schemes are being tested (e.g., Madsen et al., 2021), however more research, both in effectively ameliorating ‘probable suicide’ risk and supporting individuals through the transition from inpatient admission to community care, is evidently required.

As a final note, the rate of a methadone OST prescribing was at 17% to 1% in the ‘probable suicide’ and community control cohorts respectively. This thesis has noted several times that the literature seems to under-represent the degree of overlap and similarity between these individuals. It is notable that of these 97 individuals receiving methadone within this ‘probable suicide’ group, only 74 were also present in the DRD cohort, indicating that 23 individuals receiving an OST prescription of methadone were ruled ‘probable suicide’ deaths only. This co-morbid group is reported to have significantly higher rates of healthcare usage, due to the severity of the ill-health associated with both of these chronic conditions (Graham et al., 2017). Certainly, this is not a large sub-group of the ‘probable suicide’ cohort, yet with the knowledge of how steeply the risk of death rises when these conditions are co-morbid with each other, and the recent calls to integrate ‘probable suicide’ prevention strategies into opioid overdose reduction initiatives (Oquendo and Volkow, 2018), it would be an oversight not to draw attention to this sub-section.

5.3.3. Analysis of the Possible Self-Harm Presentations

As highlighted in the introduction, many of the current theories and predictive models for ‘probable suicide’ emphasise the relationship between self-harm and later death. Even using a relatively wide definition for identifying possible self-harm events that were medically serious enough for an Accident and Emergency presentation, only 25% of the ‘probable suicide’ cohort fulfilled the criteria. This result illustrates the problem with the argument, present in Vasiliadis, Ngamini-Ngui and Lesage (2015), that individuals who die by ‘probable suicide’ attend Accident and Emergency services regularly, but that there are deficits in the healthcare system, related to insufficient follow-up care after a crisis. Follow-up care after presentations which suggest significant psychological distress are undoubtedly important and valuable, however these interventions would still only reach around a quarter of individuals who would be likely to go on to die by ‘probable suicide’. Research has highlighted that the majority of self-harm is not medically serious enough to result in a hospital presentation (Zortea et al., 2020), which also demonstrates the challenge (as noted in the introduction) of classifying risk factors appropriately and understanding their true prevalence.

Further questioning the concept of secondary deficits is that the total follow-up rates of psychiatric healthcare were significantly higher in the ‘probable suicide’ group, compared to the controls (48% to 12% respectively). One significant and common limitation of work investigating possible self-harm and psychiatric follow-up is that rarely are control groups used, therefore there is no real interrogation of the idea that the healthcare service is not recognising patients at risk of subsequent ‘probable suicide’ (Vasiliadis, Ngamini-Ngui and Lesage, 2015, Carr et al., 2016). This difference in follow-up care would suggest that a difference in risk is being identified and that interventions are differentially targeted between groups. Follow-up likely would have been required for the 52% of the ‘probable suicide’ cohort with a possible self-harm presentation, however it has also been recorded that patients do not remember that they were recommended follow-up, even if emergency department records state it had been (Grimholt et al., 2012). As such, experimental studies have trialled sending patient reminders or attempted active outreach to encourage follow-up attendance, with mixed results and a review concluded further research was required to identify effective, low-cost solutions (Brown and Green, 2014).

One limitation noted in the analysis was that the definition itself could create a tautology, in that those with more severe presentations may get more referrals and, based on the pattern of data, this could have artificially increased the rate of follow-up in the ‘probable suicide’ group. This is unlikely to have caused my findings, as most of the individuals fulfilled two of the criteria for the definition, and would have been included irrelevant of their record of psychiatric healthcare referral. As such the tautology within the definition should have had a minimal effect.

5.3.4. Analysis of All those with Antidepressant Prescriptions

The first sub-section of the data was to extract and compare all of the individuals who received at least one antidepressant prescription in the year before death, split by whether they went on to die a ‘probable suicide’ or not. The numbers of both cohorts were fairly similar: 254 ‘probable suicide’ individuals to 293 control individuals, yet most of the significant differences between groups remained. A key caveat, mentioned already in the limitations section above, is that without records of diagnoses, it is impossible to be certain that these antidepressant prescriptions represent treatment for an episode of depression, due to the alternative concerns like chronic pain and anxiety that can be targeted with antidepressant prescriptions. As such, comparisons with studies that relied on diagnostic codes and records could be analysing different samples than the one presented in this study, which could decrease the importance of any differences identified.

An especially notable difference between the cohorts was the rate of psychiatric outpatient attendance, which was at 63% for the 'probable suicide' group and 17% for the control group. It is worth emphasising this finding, because it would again reinforce the idea that the healthcare service is able to identify patients with different needs and target treatment combinations effectively. This is bolstered by the results of the mental health inpatient admission, which amounted to 19% to 1% for the 'probable suicide' and control groups respectively.

Additionally, rates of psychotropic co-prescription were considerably higher in the 'probable suicide' cohort with an antidepressant prescription than the control group with an antidepressant prescription; this is especially clear concerning benzodiazepines, at 43% to 15% respectively. The concern is due to the risk of benzodiazepine prescriptions in isolation (primarily, dependence and misuse), as well as the apparent increased mortality rate when prescribed in combination with antidepressants (Jeong et al., 2020). Any analysis of this kind, without psychological measures of anxiety and distress, cannot conclusively state that these prescriptions are incorrect, *per se*, because it may be that the patient presents with severe enough conditions to necessitate both prescriptions. The increased risk of mortality may suggest, however, that the safer prescribing guidelines developed since the period of the data extraction were indeed salient and needed (NICE, 2022 (a)). The true rate of comorbidity and how best to treat these patients is a key area for future research.

A tally of the number of antidepressant prescriptions redeemed was analysed in a Poisson logistic regression, which represented a proxy for the duration of treatment across the year. This model found significant associations between a higher frequency of antidepressant prescriptions and belonging to the 'probable suicide' cohort, and women, the middle-aged and the most deprived quintiles were likewise associated with higher frequencies of prescription. That the 'probable suicide' group had a higher frequency of prescription could be another example of confounding by indication, as it stands to reason that they might have a more severe profile and require more treatment than the individuals who did not go on to die. That women received more prescriptions would be anticipated, due to the regular reports that women access healthcare and receive prescriptions more readily (Castelpietra et al., 2017, Stene-Larsen and Reneflot, 2017). The middle-aged group receiving more prescriptions may be related to the recent ambiguity around how effective antidepressant prescriptions are for younger patients, as there was a concern that this age group may report higher suicidal activity (Gupta et al., 2016). This concern has not abated, and currently only fluoxetine is recommended for young patients (Miller et al., 2014). Finally, that the more socio-economically deprived groups were associated with a higher frequency of antidepressant prescriptions would correlate well with the established findings that depression is strongly associated with poverty (Cairns, Graham and Bambra, 2017, Sterling and Platt, 2022). These results would suggest that clinical guidelines for best practice in antidepressant prescribing had been followed for key groups of higher-risk patients (i.e., noting that prescriptions can take up to 4 weeks to have an effect and that prescriptions may need to be continued for several months after remission to prevent a relapse (NICE, 2022 (b)).

5.3.5. Analysis of the 'Probable Suicide' Group

Following on from these comparisons, attempts were made to classify types of healthcare use within the 'probable suicide' group, according to antidepressant prescription and socio-economic status. Both of these divisions demonstrated statistically significant differences between those "in or out of treatment" and those living in areas recorded as more or less deprived.

5.3.5.1. Division according to Antidepressant Prescription

As might be hypothesised, the section of the 'probable suicide' cohort who received an antidepressant prescription were also engaged with further healthcare services at significantly higher rates than the group without antidepressant prescriptions. This is particularly notable concerning psychiatric outpatient (63% to 20%) and mental health inpatient services (19% to 3%). Again, it is intuitive that those with antidepressant prescriptions would attend psychiatric outpatient services more than those without. Furthermore, the various studies that have attempted to describe the "no contact" group of people (mostly men) who die by 'probable suicide' show a similar pattern as in my data; those engaged with one mental health service are more likely to access further formal psychiatric healthcare and general healthcare (Hamdi et al., 2008, Tang et al., 2022). Many of these comparative reports highlight that there are associations between a recorded mental health diagnosis, previous self-harm events and family history of mental health diagnoses, and engagement with healthcare services (Hamdi et al., 2008, Tang et al., 2022, Giupponi et al., 2014). Those without any attendance, especially mental health attendance, seemed often to be men associated with financial or relational stressors that were believed to contribute significantly to the motivation for 'probable suicide' (Mallon et al., 2019, Tang et al., 2022). Unfortunately, the administrative databases used in my study did not include any information of this kind, however it is reasonable to consider that similar profiles would be present, as these studies covered several different Western countries. The logistic regression predicting antidepressant prescription within the 'probable suicide' group did demonstrate a significant odds ratio for women receiving a prescription (3.45 95% CI 2.20-5.01), and the lower odds for youth and less deprived quintiles. This likewise suggests the data corroborates well with reported demographic associations concerning those who attend at greater or lesser frequencies.

The service most attended by the group without an antidepressant prescription was the Accident and Emergency department, with 32% of the "disengaged" group presenting. Again, many studies have highlighted that emergency services may be key locations for preventative interventions like screening for suicidal ideation (Hom, Stanley and Joiner, 2015), or providing appropriate follow-up care after possible self-harm events (Brown and Green, 2014). Screening models have been trialled in emergency departments, with some reporting large increases in both screening rates and identification of patients at risk (Boudreaux et al., 2016). No studies could be found that followed patients long-term after screening in the emergency department to test the accuracy and reliability of the results, though the group mentioned above (Boudreaux et al., 2016) are continuing their research and may provide data on this question in time.

The binary logistic regression examined whether demographic variables would predict antidepressant prescription in the 'probable suicide' cohort only. As anticipated, women were more likely to receive an antidepressant prescription, which contributes to the well-known problem that women tend to have greater rates of psychiatric diagnoses and treatment, yet account for a smaller proportion of ‘probable suicide’ decedents (Castelpietra et al., 2017, Stene-Larsen and Reneflot, 2017). Men are not a homogeneous group, and therefore more research will be required to identify the reasons for which they present to healthcare services less readily. As well as certain restrictive notions of masculinity (Chandler, 2021), there are also additional factor like the suggestion that unemployment may exert a stronger effect on men’s suicidal risk than on women’s, for example (Galdas, Cheater and Marshall, 2005, Kennedy, 2001, Cairns, Graham and Bambra, 2017). These wider factors ought also to be considered and analysed to understand their impact more fully.

5.3.5.2. Division according to Socio-economic level

Unexpectedly, the cohort size when split between greater or lesser socio-economic deprivation was very similar, despite the well-established association between poverty and premature death (Pirkis, Nicholas and Gunnell, 2020, Sterling and Platt, 2022). Dundee, and therefore Tayside, are relatively deprived areas, compared with the whole of Scotland, and therefore, it is possible that the difference between SIMD 1 and SIMD 5, when narrowed down to this area, represents a smaller variation in the level of socio-economic deprivation than is present in other studies considering socio-economic deprivation.

The comparisons examining healthcare engagement within the ‘probable suicide’ group after splitting the cohort into more (SIMD 1 and 2) and less deprived (3, 4 and 5) showed very few differences in the base rate of attendance. Only psychiatric outpatient attendance and routine attendance at general hospital inpatient appointments were statistically distinguishable; those in more deprived conditions had greater rates of psychiatric outpatient care and those less deprived had a greater rate of routine healthcare, which is further corroborated by the greater prescription rates of statin and antihypertensives for the less deprived group. Health inequality has significantly increased due to policies like austerity that disproportionally affect deprived areas (Marmot et al., 2020), however it may be that the NHS being free at point-of-care makes it much more accessible to individuals in deprived circumstances, compared to countries with different healthcare systems, such as the United States.

5.3.6. Analysis of the Multivariate Model

To attempt to combine all of the significant variables discovered so far, a binary logistic regression was calculated on the total cohort, to predict 'probable suicide'. While the model was significant, and all of the variables contributed significantly to the model, still only 36% of the total variance was explained and the majority of the correct classifications were concerning the control group. As predictive models commonly report, being male and those in the 25 years old and younger age group had a higher risk of 'probable suicide' (e.g., Chan et al., 2016). Following on from the theory that healthcare in the UK is relatively accessible, it would likewise be anticipated that the poorer health associated with severe psychological distress would result in an association between healthcare usage and a greater risk of death (Musgrove et al., 2022). The only unanticipated result was that the risk of 'probable suicide' was higher in the less deprived quintiles compared to the most deprived. It is possible that this result would be caused by the matching process with the controls, which was not exact, as the control group had a smaller percentage of the least-deprived quintile than the 'probable suicide' cohort. The percentage difference is, however, minor (9.7% to 10.6%, respectively). Therefore, it is unlikely that this would be the primary explanation. It is the case that Tayside as a whole is quite deprived. As such, the variation in the relative deprivation of the quintiles could be considerably less pronounced than in other studies. Previous studies have demonstrated that both 'probable suicide' and suicidal behaviours are strongly associated with deprivation and high-area rates of unemployment, and that greater increases in unemployment lead to greater increases in 'probable suicide' rates during the economic recession of 2008 (Cairns, Graham and Bambra, 2017, Barr et al., 2012, Sterling and Platt, 2022). Further research into the precise factors that mediate the relationships between deprivation, unemployment and 'probable suicide' are key to understanding these phenomena and how they might vary across time and location.

5.3.7. Pyramid of 'Probable Suicide' Risk

To summarise the general outline so far: a variety of well-established risk factors are found in the literature, ranging from demographic to clinical variables. Predictive models and big data approaches are currently being promoted as the key tools with which prevention of 'probable suicide' will be achieved. Current models are not yet accurate enough, though the majority perspective is that further research will improve the positive predictive values and lead to improved clinical utility (Belsher et al., 2019). There are voices that challenge this perspective and suggest turning aside from predictive models, recommending that the focus be on individual patient needs or targeting sub-groups with more focused, evidence-based interventions (Large, 2018, Carter et al., 2017). Both those for and sceptical of predictive models highlight the need for an overarching theory of 'probable suicide', which would delineate the contribution of known risk factors and result in a better understanding of the individuals who die. The analytical chapters of this thesis have identified certain patterns of healthcare usage that distinguished between a 'probable suicide' cohort and matched community controls, showing that the deceased attend services at greater rates than matched, live controls. These healthcare patterns were also distinct when examining a smaller cohort containing only those individuals receiving an antidepressant prescription, and, again, differences were found within the 'probable suicide' cohort. Healthcare attendance patterns may improve our understanding of the antecedent needs of individuals who die by 'probable suicide'. These distinct patterns could aid the development of a typology, which could improve predictive models or identify groups for which targeted interventions could be designed. To illustrate the relative prevalence of these patterns, and to order them according to possible risk of 'probable suicide', a pyramidal diagram was constructed using the prevalence rate from the sample that were contained within the HIC sample studied within this thesis (shown in Figure 5-1).

The overarching concept for this diagram was that the lower section of the pyramid would depict services more widely used, thus representing lower intensities of healthcare intervention, which I extrapolated to (probably) represent lower severity of symptoms. Subsequent levels would represent less frequently used services, offering higher intensity interventions, thus identifying (likely) patients with more severe symptoms. This diagram was likewise intended to examine the potential for predictive models, by examining differences between the cohorts in the rate of mental healthcare usage in a step-wise manner from services hypothesised to be increasingly more predictive of those at greatest risk of 'probable suicide'. The cohort I had can be considered an "enriched" training cohort, as the one-to-four "case-control" matching resulted in 20% of the cohort having the outcome of interest. As such, it is an important caveat that the magnitude of the differences, and the implied utility of these usage patterns in a predictive model would likely be considerably smaller in other models that were more reflective of the true rate of ‘probable suicide’ in the general population.

As such, the first step of the pyramid was those individuals known to have received an antidepressant prescription from the GP, within the study observation window. This was calculated from community prescribing records showing that the individual had received an antidepressant prescription, but with no psychiatric outpatient attendances listed. This step showed the smallest magnitude of difference observed between the rate for the ‘probable suicide’ and the matched control cohorts, at 15.9% and 10.4% respectively. This healthcare presentation signature may reflect a group of individuals with relatively mild psychopathology who might benefit from additional targeted psycho-social support, and would generally be thought of as ‘low-risk’, even though this accounted for 15.9% of the individuals who ultimately died. As described in the introduction, there is an oversimplification in the implicit idea that any form of mental illness is a direct indicator of increased risk for ‘probable suicide’. The relative prevalence rates of mental illness and ‘probable suicide’ demonstrate that this cannot be the case, and the similar percentage of community control individuals with, for example, an antidepressant prescription likewise reveals the limitation of this assumption. Simply put, any limited degree of mental illness is probably not as helpfully predictive as implied in early studies (e.g., Barraclough et al., 1974., Cavanagh et al., 2003).

The subsequent step on the diagram, those with psychiatric outpatient attendance only, represents a similar population of individuals with at least some symptoms of mental illness, receiving relatively low-threshold mental healthcare. While the difference in prevalence between the ‘probable suicide’ cohort and the community controls is noticeable, at 11.1% to 1.5%, there are again caveats which might reduce the value of this measure in a predictive model. First, this measure would not identify the 88.9% of the ‘probable suicide’ cohort with other patterns of healthcare usage; i.e., those who had not been seen within outpatient mental health services. Second, an expression of how many people attended psychiatric outpatient clinics each year would be required to understand the relative percentage of individuals who died of ‘probable suicide’ from a service-usage perspective. As a potential group within a typology, it may suggest a group who do not benefit from the ‘treatment-as-usual’, and may provide an avenue for research to design interventions that may address their as yet unknown needs.

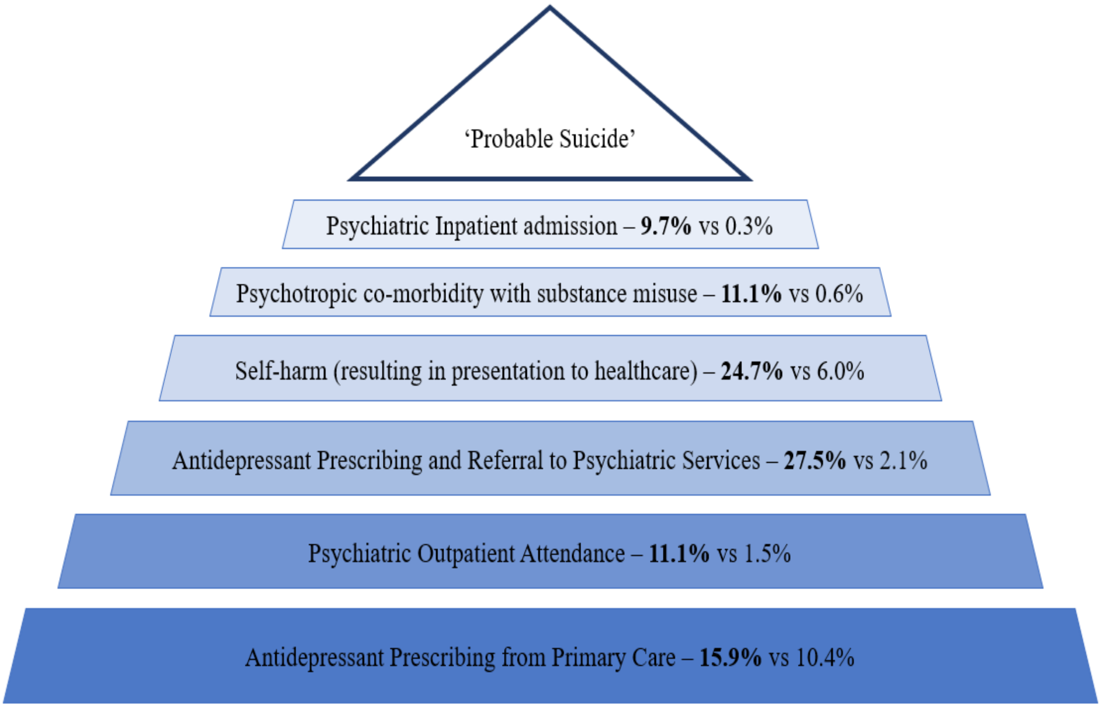
Step three of the pyramid, antidepressant prescribing combined with psychiatric outpatient attendance, was also significantly more prevalent in the ‘probable suicide’ cohort than the matched controls (27.5% to 2.1%). This would be a natural expectation, as it is clear there is some association between the severity of mental illness and later ‘probable suicide’. It usefully demonstrates an important issue in predictive modelling, as does the subsequent self-harm step, in that these healthcare attendance patterns, while theoretically indicating elevated risk, are still present in fewer than a third of the ‘probable suicide’ cohort. Furthermore, as noted above, longitudinal studies from a service-usage perspective are required to understand what the rate of ‘probable suicide’ is, within the group of individuals with this multi-modal psychiatric healthcare usage pattern.

The step considering the prevalence of a possible self-harm presentation shows that 24.7% of the ‘probable suicide’ cohort fulfilled this criterion, compared to 6.0% of the matched controls. As shown in the introduction, self-harm was also reported at between 24.2-54.5% of the total clinical population (see page 30), which corroborates concerns that current risk factors are too non-specific for use in accurate predictive models of ‘probable suicide’. Furthermore, approximately a third of these individuals received an antidepressant within 21 days of the possible self-harm presentation, with the total over the whole year likely being significantly higher. This would mean that a self-harm presentation would, in itself, likely identify individuals that were also identified by other risk factors; without a clear understanding of the individual and cumulative risk conferred by these phenomena, it would be challenging to operationalise this overlap in a simple risk model. In terms of identifying this group for targeting specific treatments, a recent review found only inconclusive evidence for long-term reduction in self-harm following Cognitive Behavioural Therapy (CBT) or Dialectical Behavioual Therapy (DBT) (Witt et al., 2021). Evidently, further research into effective interventions which demonstrate a prolonged reduction in self-harm are required.

The top two steps have the largest difference in prevalence between the ‘probable suicide’ cohort and the matched community controls. When examining psychotropic co-morbidity (prescription records of both an antidepressant and OST), 11.1% of the ‘probable suicide’ had these records, compared to only 0.6% of the community controls. Throughout this thesis, the overlap between the ‘probable suicide’ cohort and the DRD cohort has been noted, with particular emphasis on similarities in their healthcare profile (expanded on further in the subsequent clustering analysis). Individuals who are co-morbid for psychiatric illness and substance misuse are known to use healthcare services more regularly (Graham et al., 2017), and are associated with a higher risk of early death (Østergaard, Nordentoft & Hjorthøj, 2017). This represents a relatively low percentage of the individuals who went on to die, and it is worth highlighting that we do not understand mechanism that results in such an increased risk of death for co-morbid patients. Likewise with psychiatric inpatient admission, initially, the difference between the ’probable suicide’ cohort and the community controls looks significant and potentially useful, at 9.7% to 0.3%, respectively. This variable would identify (based on the sample in this thesis) at most 10% of the individuals who died by ‘probable suicide’, while the vast majority could be classified (incorrectly) as lower risk for not having this healthcare presentation. Many of the individuals with this admission would likely also be present in the lower steps of the pyramid (e.g., the self-harm presentations or antidepressant prescription steps). Likewise, without comparative data on the number of individuals with an inpatient stay each year, it would be challenging to design an intervention that could support those at-risk, without providing too much of a burden on the healthcare service (Large, 2018).

Overall, this diagram is a simplified hierarchical summary of the prevalence of healthcare patterns that could arguably represent increasing risk of ‘probable suicide’. Even the healthcare usage patterns representing theoretically the highest risk were present in approximately 10% of the ‘probable suicide’ cohort, demonstrating why accurate prediction would be numerically implausible. Prospective studies would likewise highlight how rare ‘probable suicide’ is from a clinical viewpoint at any of these services and would be a useful addition to this pyramid. Until there are theoretical models that define how psychological, demographic and clinical variables constellate, it is likely that generic predictive models will continue to be non-specific and that efficient targeting of healthcare interventions will be limited. Pursuing research that combines these risk factors into common groups may allow for an improved understanding of the differential effect of risk factors on different populations, and may allow for specific interventions to be designed and applied efficiently.

Figure 5-1. Pyramid of 'Probable Suicide' Phenomena



This pyramid illustrates a model for the relative prevalence of key phenomena for 'probable suicide', within the 'probable suicide' cohort and matched controls presented throughout the thesis. The steps of the pyramid are ordered according to a theoretical framework of increasing risk for subsequent 'probable suicide'. The first percentage, in bold, shows the percentage of individuals who died with this healthcare presentation, and the second percentage shows the value in the community control group. Due to the reported association between depression and 'probable suicide', an antidepressant prescription from the GP was used as the first step to represent a low-threshold for psychiatric healthcare, with greater intensities of intervention represented by higher levels of the pyramid. Previous literature reports that serious self-harm, co-morbidity with substance misuse (defined here as antidepressant and methadone OST prescriptions) and psychiatric inpatient admission are among the strongest predictive factors for 'probable suicide', yet these were present only in between 10-25% of the 'probable suicide' cohort. This model demonstrates why the current knowledge of risk factors is insufficient for an accurate predictive model of 'probable suicide'. Further research into the risk contributed by these healthcare attendance patterns, and how these relate to other factors for 'probable suicide' are necessary to improve the field and this brief, summarising model.

5.4. Analysis of the Drug-Related Death Cohort

5.4.1. Analysis of the Cohort Validation

The first step of the process was to compare and validate the statistical definition of a DRD. While the NRS, NDRDD and TDRDD seemed to use the same definition from a coding perspective, the processes of data capture varied slightly. The majority of the individuals identified were common to all three databases (69% or 200/288), however there was still a sizable number of individuals not present in all of the research databases. As shown in Figure 4-1, there were 7 individuals in the NDRDD only category, therefore the multinomial model was unable to calculate reliable odds ratios for inclusion across all of the levels of the model. The results suggest that those 26-50 years old were the most likely to be captured by all three databases, which may contribute to the emphasis in the literature on middle-aged men who die from drug misuse, while other types of DRD may be under-explored.

5.4.2. Analysis of the Total Cohort Comparison

There appear to be fewer studies examining the rate of healthcare usage in samples of individuals who undergo a DRD, with only one literature review identified, which was that of Lewer et al. (2020). Within this review, they demonstrated that there is sufficient evidence that those using illicit drugs rely on emergency services to a greater degree than general population averages. Furthermore, they reported that hospital admissions are likewise more common for those who use illicit drugs. A significant number of the studies included in this review included individuals identified from OST programmes, though the second-most common sample were those who injected drugs, as recruited from the community. They conclude that research is needed that investigates non-acute service and research into the quality of healthcare received. Following on from these suggestions, it is salient to note that, in this thesis, the pattern of higher healthcare for those who died a DRD was consistent across all healthcare services; both acute and outpatient services, and both psychiatric and non-psychiatric. Additionally, the DRD cohort had a higher rate of psychotropic prescription than the community controls. These results are coherent with those established in the review, though the data presented in this thesis is also unable to clearly state whether the healthcare received was appropriate and high-quality.

Considering other Scotland specific data, the NDRDD published its most recent report this year (2022) and examined deaths between 2017 and 2018, with trend data from 2009. There were more issues with data collection and completeness for this report, due to the collection occurring during the COVID-19 pandemic, which resulted in significant re-prioritisation of staff time in local health boards. Not all fields were affected, and so the report contains data on drug usage history and contact with healthcare services for the majority of DRD decedents over the 2 years of interest. There are no comparisons with external control groups, therefore the results will be discussed in the context of the DRD cohort-only analyses.

5.4.2.1. Non-Psychiatric Healthcare

As previously noted, the DRD cohort attended all services at higher rates than the community control cohorts, though as with the ‘probable suicide’ analysis, the community controls had higher rates of routine attendance in the general inpatient database. The second-largest difference between groups was the rate of Accident and Emergency presentation, which was considerably elevated in the DRD cohort compared to the controls, at 53% to 14%, respectively. Taken together, these results all suggest the same pattern of greater reliance on emergency healthcare for those who died, and more routine healthcare in the control cohort. This association is somewhat weaker than in the ‘probable suicide’ cohort, as statins and antihypertensives were not prescribed at higher rates in the control cohort; however, the DRD cohort is younger on average so the community controls would likewise be anticipated to be younger. This would likely reduce the rates of these prescriptions. On the other hand, the matching was not exact, and the difference in proportion is quite large, with only 7% of the DRD cohort belonging to the 51 years old and older category, compared to 18% of the community controls. With this degree of disparity, it is surprising that the difference in prescription rates was insignificant. As a whole, these rates add greater detail to the results noted by Lewer et al. (2020). My findings confirm the association between drug use and emergency healthcare, as well as demonstrating that the use of psychiatric and non-psychiatric outpatient clinics and psychotropic prescriptions, all unincluded by Lewer et al. (2020), are likewise elevated in the DRD cohort. Greater usage of physical healthcare services by those receiving OST prescriptions was reported by Lintzeris et al. (2016), though this study was conducted in an older cohort (those 50 years old or older). This study also reported greater usage of alcohol and benzodiazepines in older compared to younger individuals on OST. As studies and national reports have suggested that the average age of DRD decedents is increasing (e.g., Lintzeris et al., 2016, as the rationale for conducting the study and the NDRDD, 2022), these are important associations to consider. The greater number of physical and mental multi-morbidities that are naturally associated with the elderly are projected to become more common in this cohort, that is already associated with poorer health due to drug use. As such, the current design of OST services may need to be adapted to better treat older patients with a greater number of conditions and a greater risk of all-cause and drug-related mortality.

5.4.2.2. Psychiatric Healthcare

That OST was prescribed at a higher rate in the DRD group is unsurprising; recent statistics showed 89% of DRD in Scotland had an opioid (combined with other drugs) implicated in the cause of death (NRS, 2021 (a)). The rates in this study revealed that 41% of the DRD cohort, compared to only 2% of the controls, received a methadone OST prescription, within the year before death. Similarly, the NDRDD found that 41% of individuals were in receipt of OST at the time of death (2022). This value is slightly higher than the percentage would be in this thesis, as some of the individuals did not receive a methadone prescription in the month before death (a total of 30 of the 118 individuals had no prescription in that timeframe). This could have been caused by the administrative system that records prescriptions as issuing on the first of the month a data transfer was received, rather than the true prescription date (see page 81).

While van Amsterdam, van den Brink and Pierce (2021) suggested that OST in Scotland had lower accessibility and efficacy than in England and Wales, this calculation was based on different definitions between countries for identifying individuals using drugs problematically. Both countries, when using the same definition for the denominator, had a rate of 45% in treatment. This fulfils the definition of high coverage in the global review conducted by Larney et al. (2017) and is corroborated by the finding of 41% of the DRD in this thesis being in treatment; taken together, these do not support the suggestions of problematically low accessibility of OST in Scotland contributing to the high mortality rate in the country.

Individuals with problem drug use and co-morbid mental illness generally have higher rates of healthcare usage and earlier mortality than those without (Graham et al., 2017, Chen et al., 2013). As such, while the database concerning outpatient appointments did not distinguish between psychiatric outpatient and substance misuse clinics, the higher rates of mental health inpatient admissions and antidepressant prescribing in the DRD group may be considered meaningful proxy measures for elevated rates of mental health problems. Previous studies have reported even higher antidepressant co-prescription rates of 60-72% in cohorts who died a DRD and had received substance use disorder treatment (Fugelstad et al., 2021, Leece et al., 2015). The data supports an association between psychiatric healthcare (broadly defined) and DRD, however, by stratifying in multiple ways, these data show that ‘live’ controls with an OST prescription have similar rates of antidepressant prescription (41%). Further case-control studies would be required to investigate potential differences (e.g., in the severity of co-morbid mental disorders or in the nature or appropriateness of treatment) between groups and their associations with DRD. Additionally, the majority of the sample could be found within the ‘probable suicide’ cohort, and qualitative studies have found some suicidal desire attributed to the actions that resulted in non-fatal overdoses (Gicquelais et al., 2020, Connery et al., 2019). Future overdose prevention strategies will need to be aware of sub-groups that may have co-morbid psychiatric diagnoses and substance abuse, and may have elevated ‘probable suicide’ risk. The importance of including ‘probable suicide’ prevention in DRD prevention has been acknowledged (Oquendo and Volkow, 2018), but has not yet been incorporated in to governmental publications

5.4.3. Analysis of Possible Self-Harm Presentations

Possible self-harm presentations are not very commonly discussed in the context of DRD, though much research has examined non-fatal overdose events and how best to prevent them. Often these studies promote the idea of take-home naloxone (Enteen et al., 2010) or promote safe injecting rooms where healthcare personnel would be on-hand in case of emergency (Tran et al., 2021). As many of the self-harm events discussed in the literature involve self-poisoning (Carroll, Metcalfe and Gunnell, 2014), and there is a large overlap between the 'probable suicide' cohort and the DRD cohort, it seemed logical to investigate possible self-harm events in this population. Of the total cohort, 30% had presented with a possible self-harm event, compared to 5% of the community controls. A previous review suggested that a mean of 45% of drug users have experienced a non-fatal overdose at some point in their lifetime (Martins et al., 2015), though this varied significantly across country and drug type analysed by the summarised studies. The possible self-harm events identified cannot be classified as non-fatal overdoses because of a lack of specific diagnostic codes, however a study attempting to identify overdoses in emergency services using more specific ICD-10 codes (i.e., not including any with undetermined poisoning codes) concluded that there was a significant underestimate precisely because of the variety of potential codes available (Di Rico et al., 2018). Future work may refine these processes by using the specific substance poisoning codes from the Di Rico et al study, as well as more generic poisoning codes, to test whether a wider definition might identify a higher proportion of individuals, without an overwhelming number of false positives. An added challenge to refining and specifying possible illicit drug overdoses is that several of them lack unique ICD-10 codes, e.g., MDMA, ketamine and the novel psychoactive substances (Wood et al., 2019), as such, detailed data is impossible to gather until this is rectified.

Interestingly, the rate of follow-up was slightly higher in this cohort than in the 'probable suicide' cohort. Of those with a possible self-harm event, 54% of the DRD cohort received a type of psychiatric support, and 20% of the controls. Again, the significant difference in the follow-up rate would suggest that greater mortality risks are perceived in the DRD group, leading to more intensive healthcare interventions. This may be related to the known association between drug use, non-fatal overdoses and the subsequently increased risk of death from later overdoses (Martins et al., 2015). Alternatively, as many of these individuals were in receipt of an OST prescription (24/46 of the DRD individuals with a follow-up event recorded and 3/12 of the controls), it is possible that the psychiatric outpatient attendances recorded were to do with regular OST healthcare, rather than the possible self-harm event. Previous studies found significantly lower percentages of OST prescription in populations attending healthcare services with evidence of opioid misuse: e.g., 12.5% received methadone or buprenorphine over three months after an opioid use disorder diagnosis (Wakeman et al., 2020), and another showed 30% of individuals who presented at hospital after opioid overdose were prescribed OST (Larochelle et al., 2018). These studies were not framed as investigating self-harm, but they do demonstrate that care after opioid overdoses may be somewhat lacking. Future research should investigate both possible self-harm and specifically overdoses in groups of people who use drugs to refine our understanding of their prevalence rates, the type and efficacy of follow-up care and how these presentations contribute to mortality risk.

5.4.4. Analysis of the Opioid Testing in Laboratory Services

As noted, the efficacy of urine drug screening is up for debate, and authors have called for both a standardised method and additional research to investigate it fully (Jin et al., 2020, Sobel et al., 2021). Significantly more of the DRD cohort took a urine screen compared to the community controls (41% to 2%), however, similar majorities of these individuals, in both cohorts, had received an OST prescription. That more of the DRD cohort had undergone a urine test was an anticipated finding, as they are a group of individuals with implied substance misuse. Many of the aims of this thesis centred on testing the truth of the common assumptions in the field by analysing real-world data. As the rationale behind a urine drug screen is that it would reveal whether additional opioids were being consumed by the patient, it was important to analyse whether the healthcare service was correctly identifying the individuals likely to need these drug screens and whether the mean positivity rates differed between the cohorts.

The use of additional opioids with an OST prescription could indicate that the current maintenance dose is insufficient and increases the risk of overdose, therefore, it is important information for the clinician, who can then appropriately modify the treatment received (Jin et al., 2020). For this dataset, mean rate of positivity was insignificantly different between groups (49% for the DRD cohort and 38% of the controls). Mean positivity rate in a urine drug screen indicates an unexpected result (in this study) and was higher than in a recent study, however that study examined patients that were on buprenorphine (Sobel et al., 2021). Patients on buprenorphine may represent a different, and more stable population, than the general DRD-based population identified in this study. The ANOVA investigating group status and mean daily methadone dosage likewise found no statistical difference, which could suggest that those generally involved in drug misuse services have similar healthcare usage profiles. This is of interest, as it complicates the development of healthcare intervention targeting, if there are very few obvious differences in the results of healthcare tests between those who die and those who live.

5.4.5. Analysis of the OST Prescribed Cohort

One of the strengths of the sub-section analyses was that those prescribed OST could be extracted, allowing for an examination of whether there were differences in the pattern of healthcare usage between groups. Daily methadone doses of at least 80mg have been associated with higher retention in treatment, leading to greater health benefits (Degenhardt et al., 2019 (b), Jin et al., 2020). Therefore, it is encouraging that both groups received this average daily dose, over the year before death/index. A daily methadone dosage of 80mg is significantly higher than the dosages reported in earlier studies: e.g., a daily mean methadone dose of 48.3mg in Taiwan Huang and Lee (2013) and a median individual mean of 40mg in was reported in Scotland in McCowan, Kidd and Fahey (2009). Without further evidence as to patient needs and whether the dosage was sufficient for the patients who died from drug-related causes, it cannot be said that the DRD cohort ought to have received dosages that were distinct from the controls. That there was no difference in the rate of positive screens in the urine drug tests suggests that the DRD group were not using additional drugs at noticeably higher rates than the controls, and does not suggest the OST in Scotland was ineffective in this common measure of success (van Amsterdam, van den Brink, Pierce, 2021).

One key difference between the OST-treated DRD individuals and OST-treated controls was a higher rate of co-prescription of benzodiazepines, z-drugs and gabapentinoids (61% compared to 19%). Others have reported co-prescription rates of 46-71% (Abrahamsson et al., 2017) which is associated with an increase in DRD risk (McCowan, Kidd & Fahey 2009). This increased risk is thought to be due to higher doses of the additional medication potentiating respiratory depression (Macleod et al., 2019). Gabapentinoids may be prescribed for chronic pain conditions, reported at between 48-60% in opioid misuse populations across two meta-analyses reviewed by Voon, Karamouzian and Kerr, (2017), and at 53% within an earlier cohort drawn from the same regional OST population (Higgins, Smith and Matthews, 2020), therefore this rate of co-prescription could reflect complicated health needs rather than poor care (Vold et al., 2020). Recently published clinical guidance advises co-prescription only when there is no other alternative, and with monitoring for respiratory depression in the two weeks after initiation (MHRA Guidance https://cpd.mhra.gov.uk/benzodiazepines/CON234573_4). The association between DRD, co-prescribing and lower routine attendance highlighted in the data suggests implementing safer prescribing guidelines could be challenging. Furthermore, due to high rates of comorbidity, it is likely that co-prescribing cannot be completely avoided. As such, infrastructure to facilitate implementation of guidance on both safer co-prescribing and safe benzodiazepine detoxification (e.g., in the updated Clinical Guidelines on Drug Misuse and Dependence, 2017) needs to be developed.

Statin and antihypertensive prescriptions were extracted from the prescribing datasets because of the association of drug misuse with adverse cardiovascular events, which contributes to their greater risk of all-cause mortality (Santo et al., 2021), but also because of their utility as a proxy for anticipatory, or preventative healthcare. In this sample, prescription rates were very low and insignificantly different between the DRD and control cohorts. This is consistent with other studies that have shown high rates of emergency service usage and relatively lower rates of elective healthcare, which would include preventative prescriptions such as statins and antihypertensive drugs. Only one other study could be found that examined statin prescription in a cohort of individuals on OST. Interestingly, only the sub-group in treatment for diabetes mellitus as well as on OST were associated with statin prescription (Feng, Williams and Ladapo, 2020). The authors of that study suggested the greater continuity of care associated with diabetes may have led to additional preventative prescribing, but as in this sample, rates were low overall making any strong conclusion challenging. Unfortunately, the number of individuals with diabetes in the sample available to me was too small to investigate this suggestion further.

5.4.6. Analysis of DRD with and without histories of OST

5.4.6.1. Division according to OST Prescription

Focusing on all the DRD individuals meant that the analysis could investigate profiles and sub-types within the DRD cohort. It confirmed predictions of higher rates of emergency service presentation than attendance at other services, for both those in and out of treatment. A significant difference in psychiatric outpatient attendance between those with and without OST histories can be explained by the noted limitation that outpatient services code both substance misuse and mental illness attendance as psychiatric outpatient attendances. Interestingly, there were no significant differences between those with an OST prescription when compared to those without, when looking at presentations to emergency services, despite previous studies suggesting that OST reduced emergency presentations compared to untreated opioid users (Lewer et al., 2020). A vast majority of these studies, however, come from the US, using very different study designs within these different populations. For example, one was a paired analysis investigating attendance before and after the initiation of OST in a small cohort of heroin users (Skeie, Brekke, Lindbæk and Waal, 2008). Another study specifically recruited individuals injecting drugs from either a needle exchange programme or an OST programme and reported that those recruited from the OST programme attended emergency services less frequently (Stein and Anderson, 2003). People who inject drugs have been associated with higher impulsivity (Mackesy-Amiti, Boodram and Donenberg, 2020), which may be associated with higher presentation rates to emergency healthcare; it is possible that the individuals in the studies above represent groups with more severe drug use profiles, who may derive greater health improvement from OST treatment than individuals in the Tayside dataset.

Within the DRD group, higher rates of methadone prescription were associated with greater socio-economic deprivation, based on both the binary logistic model and the SIMD sample split discussed subsequently. Opioid misuse has long been associated with poverty (Congdon., 2019, van Amsterdam, van den Brink and Pierce, 2021), and approximately half of the sample belonged to the most deprived quintile. Of those who died and were in the less deprived quintiles, proportionally fewer of them were receiving OST, which suggests that treatment may vary across socio-economic group. Health inequality in the UK has widened over the past decade (Marmot et al., 2020), thus this discrepancy should be investigated for greater transparency in the relationship between health, healthcare and socio-economic status.

5.4.6.2. Division according to Socio-economic level

Finally, within the DRD-only analysis, the individuals were again split into grouped quintiles representing greater and lesser deprivation (SIMD 1 and 2, versus 3, 4 and 5). While the sample sizes themselves were very different, with 79% of the cohort in the most deprived group, there were very few healthcare differences noted. Both psychiatric outpatient attendance and methadone OST prescriptions were present at much greater rates in the more deprived group, as would be anticipated (Congdon., 2019, van Amsterdam, van den Brink and Pierce, 2021, Sterling and Platt, 2022). Gabapentinoids and anticonvulsants (which included gabapentinoid prescriptions) were also significantly elevated in the more deprived group; a significant concern as these drugs have a notable propensity for misuse and are associated with greater risks of death (Torrance et al., 2020). Indeed, have been contributing more steeply, in recent years, to DRDs in Scotland (NRS, 2021 (a)). Gabapentinoids can be prescribed for chronic pain (Torrance et al., 2020, Voon, Karamouzian and Kerr, 2017), therefore further research should investigate safer prescribing and treatment pathways to navigate these co-morbidities in the best possible way.

5.4.7. Analysis of those specifically DRD

As the majority of the DRD cohort was also present in the ‘probable suicide’ cohort, the individuals who had cause of death codes that were uniquely DRD were extracted. These individuals had cause of death codes within the F-codes and represent death from disordered drug use; this is the ruling for individuals who are known to be misusing substances. This small sub-section of 91 individuals was split by receipt of OST, however very few differences were established. Only psychiatric outpatient attendance, z-drug prescriptions and anticonvulsant prescriptions were significantly higher in the methadone OST prescribed half. These numbers were all low, but correlate with the previous findings that suggest the OST-prescribed individuals are engaged at other services at greater rates, and that they receive sedative co-prescriptions, which have been associated with an increased mortality risk (Macleod et al., 2019, Abrahamsson et al., 2017). Again, this profiling would confirm that there are different types of DRD, (loosely: one engaged and one disengaged from healthcare services), and that the same healthcare interventions will not be appropriate, nor effective, in reducing their distinct risk profiles for DRD.

5.4.8. Multivariate Model

To attempt to combine all of the significant variables discovered so far, a binary logistic regression was calculated on the total cohort to predict DRD. The model was significant, and the majority of the variables contributed significantly to the model, which explained 58% of the variance, however, the majority of the correct classifications were concerning the control group. That the variable with the biggest contribution was the age group was unanticipated, however it is likely that this was partially caused by the matching with the community controls, which was very uneven concerning age groups, with relative percentages for the 25 years old or younger age group at 14% of the DRD and 3% of the controls, and the percentage of the 51 years old and older age group at 7% and 18% respectively. As such, the contribution of this variable is likely an artefact from the distribution of the data. That SIMD did not contribute to the model was unexpected and cannot be so simply accounted for, as the SIMD matching was generally accurate. The biggest difference between the proportions of the groups present was in SIMD 2, which differed by 3.9%. As noted in the discussion for the 'probable suicide' predictive model, Dundee, and therefore Tayside implicitly, are relatively deprived areas, which may result in there being a smaller socio-economic variation, thus limiting its impact. Many studies finding significant effects of deprivation come from the United States, which does not have a healthcare service that is free at point-of-use and so healthcare use may be considerably more reduced in that context than in the UK (Sterling and Platt, 2022). That the next most important variables in the model were the psychotropic prescriptions is reassuring, as they would be hypothesised to differentiate between high-risk and low-risk individuals. It is also true that it is another instance of confounding by indication, and that it is not necessarily the prescriptions themselves that confer a greater risk of DRD, but the conditions they are designed to treat (Vold et al., 2020), which again reveals the limitations of the data available, both for this study and predictive studies based on routinely collected data alone (Bharat et al., 2021).

5.4.9. Pyramid of DRD Risk

In a similar manner to the summary of the ‘probable suicide’ analysis, a brief understanding of the risk factors for DRD will be outlined here. Various risk factors have been identified, from adverse childhood events and homelessness (Congdon, 2019), to clinical variables like opioid prescriptions or being in treatment for a substance misuse disorder. There is only a small volume of literature attempting to predict fatal overdose, and there are calls to develop routine data linkage to facilitate this field of research (Bharat et al., 2021). The studies that do attempt to predict fatal overdoses reflect the wide variety of at-risk populations, including: those receiving opioids for chronic pain (Bohnert et al., 2016), those with a history of non-fatal overdose (Guo et al., 2021) and those in substance misuse treatment (Sordo et al., 2017). Each of these groups represent specific sub-types, which may be differentially affected by similar risk factors. This must be elucidated with further research. The analytical chapters of this thesis have identified healthcare patterns which distinguished between the DRD and community controls, again, with the deceased attending at greater rates. Interestingly, few differences in healthcare usage were identified between the DRD and control individuals all in receipt of an OST prescription, other than in rates of further co-prescription. Likewise, within the DRD cohort, the differences in healthcare usage were centred on rates of psychotropic co-prescription, rather than service presentation. Further refining our understanding of antecedent healthcare usage patterns may reveal other sub-groups useful for predictive models or improved targeting of healthcare resources. To illustrate the prevalence of key types of healthcare presentation, and order them hierarchically based on likely increases in mortality risk, a diagram was constructed, using the prevalence rate from the sample contained within the HIC sample studied within the thesis (Figure 5-2).

The concept was the same as the previous pyramid; lower levels depict the usage of low-threshold care, which is more highly prevalent and denotes a smaller increase in risk compared to higher intensity interventions. As the DRD and controls were also matched in a one to four ratio, this pyramid model also functions as a limited investigation of the potential predictive value of these patterns, because it is an “enriched” cohort, with a higher rate of the outcome of interest than there would be in a testing cohort derived from the general population.

As in the ‘probable suicide’ diagram, the lowest threshold care was an antidepressant prescription from the GP. This was extrapolated in the same way, using a record of community prescribed antidepressant prescriptions, within the year before death, but with no record of psychiatric outpatient attendance. This step also had the smallest difference between the prevalence within the DRD cohort and the community control cohort, at 15.6% to 11.1%. Various studies note the impact of co-morbidity in increasing mortality risk for individuals with mental illness and substance misuse (Østergaard, Nordentoft & Hjorthøj, 2017, Macleod et al., 2019). No publications could be found which considered antidepressant prescription, in isolation, prior to a DRD, despite the existence of the self-medication hypothesis of drug use. Furthermore, the large overlap between the ‘probable suicide’ cohort and the DRD cohort, in this thesis, emphasises the importance of the relationship between these phenomena. It is possible that mental illness may be a stronger predictor of DRD than commonly considered, especially when acknowledging that problematic substance use need not only be related to illicit substances.

The subsequent step for this diagram combined antidepressant prescribing and psychiatric outpatient attendance, with a prevalence rate of 16.0% in the DRD cohort and 2.1% in the community controls. A limitation of the data for psychiatric outpatient attendances was that it did not differentiate between substance abuse or mental health appointments. To account for that limitation, this step excluded individuals with a methadone OST prescription, as they would be included in later steps. A patient requiring both an antidepressant and psychiatric outpatient attendances would reasonably be assumed to display more severe symptoms than those with only an antidepressant prescription, however as noted above, the contribution of psychological distress to DRD is somewhat under-explored in the literature. As psychological distress of some degree, here represented by a slightly higher threshold mental healthcare, contributes to the risk of DRD is an undefined manner, and is evidently a non-specific risk factor, it was placed relatively low on the pyramid. This step may also identify a group of individuals in need of other psycho-social support than ‘treatment-as-usual’. A final note is that it is regularly assumed that all individuals who die of drug-related causes ought to be receiving an OST prescription. While the majority of deaths involve an opioid (NRS, 2021 (a)), there is no proof that the individuals in this step were misusing opioids as their primary drug, and therefore other interventions, including treatments for other drugs that can be abused, for example, benzodiazepines, ought to be acknowledged and considered.

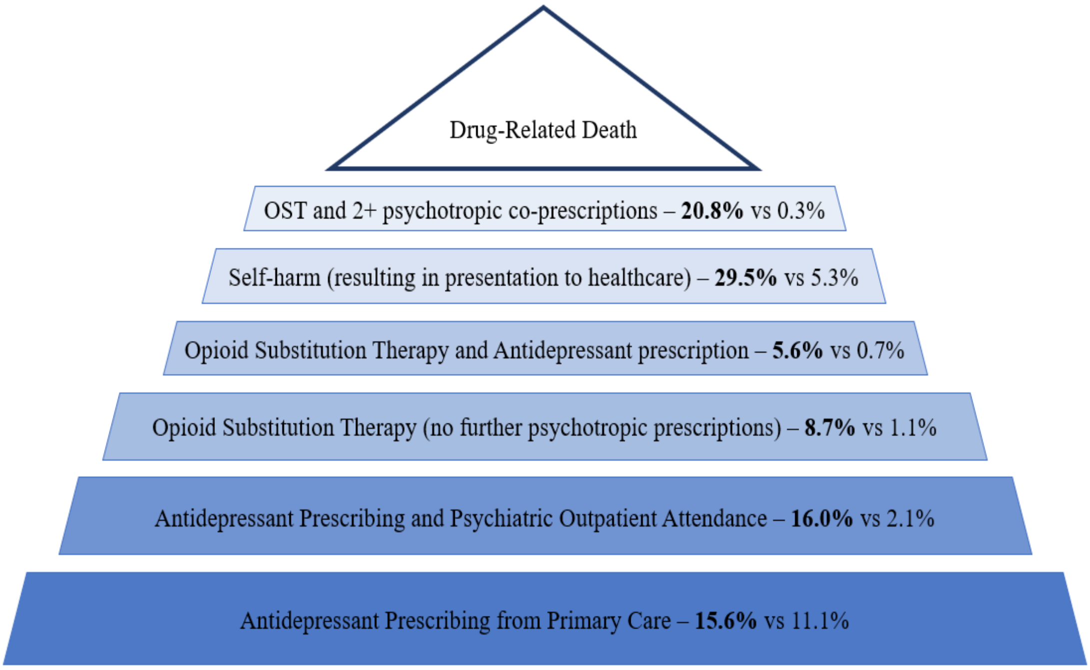
Steps three and four both contain individuals receiving a methadone OST prescription solely, or those receiving an adjunctive antidepressant, respectively and both were present in less than 10% of the DRD cohort. Within samples of individuals misusing opioids, OST is proven to reduce mortality to a degree (Santo et al., 2021, Sordo et al., 2017), however, as it is contingent on opioid misuse, and the pattern of cycling in and out of treatment is common (Degenhardt et al., 2019 (b)), those in OST still have a notably higher premature mortality rate than the general population. Indeed, for the sample from this thesis, the matched community controls contained only 27 individuals in receipt of OST out of a sample of 1,152, which evidently signals significant association between OST and DRD. It is also true that far from all patients receiving a methadone OST prescription go on to die of a drug overdose. One study examining mortality in patients starting OST in California between 2006-2010 reported that 450/32,222 or 1.4% of the individuals died of drug-related causes during the study period (Evans et al., 2015). The follow-up period was only a median of 2.6 years, however it demonstrates that studies usually focus on short follow-up periods, which are challenging to integrate into models examining long-term outcomes of a chronic, relapsing condition. Furthermore, these theoretically high-risk factors are present in less than a 10% of the population of interest, which likewise highlights the complexity of accurately establishing risk-based categories that would capture the majority of relevant individuals.

A hospital presentation that fulfilled study criteria for a possible self-harm event was the second-to-last healthcare attendance pattern included in the pyramid. This step had the largest difference between groups, with 29.5% of the DRD cohort meeting the criteria, to 5.3% of the community control cohort. The prevalence diagram in the introduction (see page 42) indicated that a history of non-fatal overdose was very common in the population of individuals using drugs at 16.6-68.0% (Martins et al., 2015). Many possible self-harm presentations are poisonings; thus, it is surprising that these terms have rarely been associated with drug overdoses, despite a growing awareness of suicidal ideation in individuals who overdose (Gicquelais et al., 2020, Connery et al., 2019). Additionally, approximately a third of these individuals received an antidepressant prescription within the 21 days for psychiatric follow-up, therefore the total of the cohort receiving an antidepressant prescription within the year is likely higher. As such, this self-harm step would likely identify individuals present in other steps of the pyramid, and there is no clear understanding of how these risk factors interact and may potentiate mortality risk. There are studies examining specifically interventions to prevent future overdoses in the emergency department. One study found that 86% of individuals discharged after an overdose had received one of three interventions; take-home naloxone, behavioural counselling or referral to outpatient addiction services (Jacka et al., 2022). This study was examining maintenance after implementation of these interventions in 2014, which demonstrates that these additional follow-up interventions require significant time and financial investment. Furthermore, this study presented no data on efficacy, which is fundamental for beneficial provision of healthcare, therefore long-term studies in this area are required.

The final step of the pyramid was an OST prescription and two or more additional psychotropic prescriptions: any two of antidepressant, benzodiazepine, z-drug, gabapentinoid or anticonvulsant drugs fulfilled the criteria. Concerningly, 20.8% of the DRD cohort had this pattern of three prescriptions, compared to 0.3% of the community controls. As guidelines recommending the avoidance of co-prescription have since been implemented (e.g., MHRA Guidance, 2015), it is likely that this percentage would be reduced in more recent data. It is undoubtedly still a key sub-group for attempting to prevent DRD, as there is a notable presence of benzodiazepine-type drugs (both prescribed and illicit) in post-mortem DRD toxicology (NDRDD, 2022). The challenge lies in ensuring appropriate prescribing practices to ameliorate patient distress, while also reducing risky co-prescriptions in this population that is known to have complex health needs (Vold et al., 2020, Higgins, Smith and Matthews, 2020). It is a noticeable percentage of the DRD cohort, however a model based on this principle would designate 79.2% of the DRD cohort as lower risk for not displaying this pattern of healthcare attendance. Evidently, this would be incorrect. Furthermore, data from a service-usage perspective would be necessary to more fully understand the prevalence of this prescription pattern and the rate of mortality in the long and short-term associated with it.

In summary, this diagram is a simplified hierarchical representation of healthcare patterns that theoretically result in increasing risk of DRD. It demonstrates that a variety of established risk patterns for DRD are present in at most a third of the cohort, which is problematic for the development of a sensitive and accurate predictive model. Additionally, it is likely that prospective studies from these services would find a low rate of DRD over any clinically useful period of follow-up, as the outcome of DRD is relatively rare. Studies like that of Guo et al. (2021) successfully predicted all-cause mortality after a hospital presentation for overdose; however, even in their sophisticated model, most of the deaths did not occur in the highest-risk group. Risk is highly time-dependent, and their model focused only on the first 180 days after a presentation, with my data covering only a year before death, though both shorter and longer periods of follow-up would be key to understand the nuances of mortality risk. Theoretical models are required that define how the psychological, demographic and clinical variables interact to increase mortality risk, and without this overarching understanding of DRD, it is likely that predictive models will be non-specific, thus limiting their clinical utility. Pursuing research that groups these risk factors into patterns and typologies may lead to an improved understanding of the various needs of patients at-risk of DRD, and lead to the development of the distinct treatment plans they may require.

Figure 5-2. Pyramid of DRD Phenomena



This pyramid illustrates a model for the relative prevalence of key phenomena for DRD, within the DRD cohort and matched controls presented throughout the thesis. The steps of the pyramid are ordered according to a theoretical framework of increasing risk for subsequent DRD. The first percentage, in bold, shows the percentage of individuals who died with this healthcare presentation, and the second percentage shows the value in the community control group. In the study cohort, antidepressant prescriptions were redeemed by a greater number of patients than methadone OST prescriptions. Thus, an antidepressant prescription from the GP represents a low-threshold for psychiatric healthcare, with greater intensities of intervention represented by higher levels of the pyramid. Previous literature demonstrates that cycling in and out of OST, as well as psychotropic co-prescriptions increase the risk of death, and that many self-harm presentations are poisoning-based and may have some degree of suicidal desire, thus they formed the upper section of the pyramid. The definition for OST in addition to 2 or more psychotropic prescriptions included antidepressant, benzodiazepine, z-drug, gabapentinoid and anticonvulsant prescriptions. The topmost level contained only 20.8% of the DRD cohort, despite being a well-established factor for increased risk of death. These factors are not strongly predictive enough, based on their limited prevalence in a DRD cohort, to identify the majority of individuals at-risk for DRD, and therefore, would do poorly to predict mortality in a prospective cohort. Further research into the risk contributed by these healthcare attendance patterns, and how these relate to other factors for DRD are necessary to improve the field and this brief, summarising model.

5.5. Summary of the Discussion

This chapter has contextualised the two previous healthcare analyses chapters. Various limitations of the analyses were noted, initially those related to the routine, administrative nature of the data collected were described. Other key caveats were the small sample sizes of both cohorts, as well as the assumptions and over-simplification that result from using a prescription as a proxy indicator of a diagnosis.

Both datasets had their cause of death codes verified against the accepted statistical definitions. Individuals were omitted from the databases used by statistical organisation, and these were found to be associated with demographic characteristics, especially socio-economic deprivation. The methods of these organisations were examined; however, no explanations could be found for these discrepancies.

Both the ‘probable suicide’ cohort and the DRD cohort attended healthcare services and received psychotropic prescriptions at significantly higher rates than their matched community controls. Previous publications have primarily considered only a ‘probable suicide’ cohort without appropriate controls, or have examined a limited number of services. This thesis is the first to demonstrate a consistent pattern of higher attendance for those who died across a wide variety of services, which questions the view that deficiencies in healthcare provision are primarily to blame for the rising number of deaths from ‘probable suicide’ or drug-related causes. Both rates of emergency healthcare and psychiatric healthcare were highly elevated in the cohorts that died, compared to the community rate, which was anticipated from the literature, as both mental illness and substance abuse are associated with poorer health generally. These results would indicate that the more intense psychiatric healthcare needs are being recognised and treated.

Possible self-harm presentations were identified in between a quarter to a third of the deceased cohorts, compared to under 10% of the community controls. These percentages are low in absolute terms, thus highlighting the concerns noted in the introduction, that these phenomena are non-specific to ‘probable suicide’ and would not regularly identify all relevant individuals. That the rates of follow-up were higher for both deceased cohorts, compared to the community controls, suggests appropriate targeting of psychiatric after-care to those that might retrospectively be defined as “high-risk”. Active outreach trials after self-harm events have only reported mixed results, and further research is likely required to implement low-cost, effective solutions.

Considering specifically the DRD cohort, the rate of unexpected positive results in drug screens from urine samples was insignificantly different between the deceased and the matched controls. Most of these individuals had prescriptions for methadone OST, and the average mean daily dose between the DRD and community controls was also insignificantly different. This may indicate that there are few differences within the sample of individuals "in treatment" for opioid misuse, who are generally reported to be a "chaotic" population and may not be particularly adherent to treatment. That the mean dosage was within the clinical range disputes the recent suggestion that OST in Scotland is ineffective and related to rising DRD. From a healthcare attendance perspective, the main difference was that the DRD in treatment received a greater number of psychotropic co-prescriptions compared to the controls. This may indicate they had more complicated health needs than the controls in treatment, as these co-prescriptions are associated with an increased risk of death, though the mechanism for this increase is unknown.

There were more differences between the 'probable suicide' cohort and the community controls in receipt of an antidepressant prescription. The 'probable suicide' cohort attended most services more than the community controls, and also received higher rates of psychotropic co-prescriptions. These differences would again indicate that higher intensity healthcare interventions were being targeted to those that theoretically represent the highest-risk group. It may likewise suggest they had more complex healthcare needs than the controls also receiving antidepressant prescriptions. Women and the socio-economically deprived were associated with a higher rate of antidepressant prescriptions, which may be associated with their higher reported rates of depression, though there are suggestions that men face more logistical barriers to receiving healthcare.

Subsequently, the deceased cohorts were split by whether the individuals were in treatment or not. As would be anticipated, those in the 'probable suicide' group receiving antidepressant prescriptions were engaged with other services at higher rates than those not receiving antidepressant prescriptions. This corroborates patterns reported elsewhere, in which factors unincluded in administrative data, like familial experience with mental illness, are associated with engagement with healthcare services. A notable percentage of the disengaged group had attended emergency services, which supports the value of research attempting to design brief interventions for use in these environments.

For the DRD cohort, the differences were again primarily related to psychotropic prescription, in which those receiving methadone also received a higher rate of additional prescriptions. This was likewise an intuitive result, though it was surprising that the OST section of the DRD cohort did not have a lower rate of emergency healthcare, as OST has been found to "stabilise" this population. Many of these findings come from the States, therefore the difference in the structure of the healthcare system may explain this difference. That there were few healthcare attendance differences may suggest that the broadly engaged and broadly disengaged groups are more similar than might be expected.

When the cohorts were split by socio-economic level, the key difference was that the less deprived half of the 'probable suicide' cohort received a greater percentage of statin and antihypertensive prescriptions. Health inequalities have grown during the period of austerity, which may mean that the less deprived group receive higher rates of preventative, routine healthcare comparatively. This was not found in the DRD cohort, however the more deprived group had greater rates of sedative co-prescriptions, again denoting the poorer health strongly associated with poverty.

Multivariate models with a variety of healthcare attendance and prescription record variables were computed to predict 'probable suicide' and DRD from their respective community cohorts. The variables for healthcare attendance all increased the association with belonging to the deceased cohorts. Unexpected results concerning socio-economic deprivation might be explained by the relatively high level of deprivation in Tayside, thus minimising the difference between the most and least deprived groups.

Lastly, pyramids ordering distinct patterns of healthcare attendance were constructed. These illustrated that the prevalence for intensive interventions like psychiatric inpatient admissions or OST with multiple psychotropic co-prescriptions are present in at most 21% of the population. This demonstrates that the patterns indicating theoretically the highest-risk of death are both non-specific and severely limited in their ability to predict the majority of either 'probable suicide' or DRD, even in an enriched sample from the community.

6. Developing Statistical Taxonomies of ‘Probable Suicide’ and DRD

As reviewed in detail earlier in this thesis, the definitions of ‘probable suicide’ and DRD are heterogeneous, changeable over time and challenging to standardise for statistical purposes and for comparative international reporting. Successful and effective healthcare interventions hinge on appropriately understanding patient needs and targeting evidence-based treatments to sub-groups, within the larger patient population. Without clear and robust taxonomies to guide the process, this type of intervention targeting is not feasible. In this section, I present a narrative review of previous attempts to classify ‘probable suicide’ and DRD, contextualising the patterns identified within the previous chapters, and introducing an exploratory clustering analysis. The aim of the exploratory analysis was to attempt to identify possible sub-groups that could point towards unique clinical presentations, which could then be targeted as samples for future clinical trials. These trials could identify specific treatments or combinations of therapies that were more suited to and efficacious for distinct groups. As such, these future interventions could be designed or applied in targeted ways, with the aim of preventing these types of deaths more effectively.

6.1. Introduction

The difficulty in predicting either ‘probable suicide’ or DRD has been discussed and demonstrated throughout this thesis. Current predictive models for ‘probable suicide’ give clinically unhelpful risk factors as significant predictors; being male for example, is clinically unhelpful, as not all male individuals seen in a psychiatric setting will be equally at-risk, nor will those with self-harm histories (Chan et al., 2016). It is also worth noting there are a growing number of calls to challenge our established concepts of ‘probable suicide’ and DRD, which emphasise the fact that current interventions have been associated with limited reductions in mortality and that other preventative interventions need to be developed (Ludwig et al., 2019, Oquendo and Volkow, 2018, Rockett et al., 2014, Fox et al., 2020, Large, 2018). These deaths are difficult to predict, with two key challenges being the lack of highly specific risk factors and the heterogeneity of the individuals who die by these means. As illustrated in the diagrams from the introduction that identified the prevalence rates of key phenomena, there is a significant “signal to noise” challenge; the prevalence of suicidal ideation is considerably higher than the rate of ‘probable suicide’. Likewise, the prevalence of non-fatal overdose, especially within groups of individuals who use drugs, is very high compared to the rate of DRD (Martins et al., 2015). This makes prediction very unlikely, simply from a mathematical perspective. Furthermore, there are no coherent taxonomies of either type of death, despite significant variation in the profiles of individuals who die from ‘probable suicide’ or DRD. A known profile across both groups would include middle-aged men from socio-economically deprived backgrounds (Chandler, 2021, Struszczyk, Galdas and Tiffin, 2019), however other profiles certainly exist. Approximately 30% of ‘probable suicide’ deaths are women, and research has highlighted an on-going increase in DRD in women (Tweed et al., 2022), though these additional profiles are rarely discussed. Certain intervention may be most effective in sub-groups of these kinds of death, and while this targeting may prevent only a small number of deaths, it may improve resource management and patient experience by ensuring patients receive the care most indicated for them. This being the case, taxonomies resulting from clustering studies could be highly beneficial for understanding distinct profiles within these types of death.

First, classifications present in the literature surrounding ‘probable suicide’ are discussed: a brief overview of certain theoretical typologies is established, then the common system of classifying deaths as violent or non-violent is examined. These are followed by a discussion of further studies, which present clusters identified through statistical means. Each of these will be appraised for what they contribute to the clarification of sub-types of ‘probable suicide’, and investigated for what they suggest in terms of areas for future research and the unanswered questions of the field. Second, studies which categorise DRD will be examined. The vast majority of literature focuses on opioid-related death, and very few of them are the traditional style of clustering research that was available for the field of suicidology. After these studies are discussed, a section highlighting any studies or clusters which investigated the overlap between ‘probable suicide’ and DRD will be discussed, especially any relating to the “deaths of despair” concept.

6.1.1. Taxonomies of ‘Probable Suicide’

6.1.1.1. Introduction

As a prelude to developing a taxonomy of ‘probable suicide’ it is worth restating the fundamental difficulty that exists in determining whether a death was intentionally caused or not. The importance of determining proving intent has itself been a major topic of research in the field of suicidology (Goodfellow, Kõlves and Leo, 2019). One particularly challenging aspect, relevant to both suicides and DRD, relates to deaths caused by self-intoxication. These are often ruled as accidental; however, it has been suggested that some, possibly many, of these deaths ought to be classed as ‘probable suicides’ due to the knowledge of the risk associated with drug use, which arguably becomes a self-harming behaviour (Rockett et al., 2014). Additionally, while over 100 countries use the tenth revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) (World Health Organization, 2019), there is no way to ensure that the various medical and legal professionals responsible for classifying causes of death would code the same death in exactly the same way (Lindqvist and Gustafsson, 2002). As such, it is likely that some of the differences reported in international reports are due to the different populations analysed, however this is an unavoidable pitfall of the topic. No inter-reliability studies could be found for post-mortem toxicological analyses and ICD-10 code assignations. Furthermore, calculating reliable concentrations of drugs post-mortem is particularly challenging, with post-mortem concentrations of drugs showing a great deal of variance, depending on the substrate analysed by the laboratory (Kennedy, 2010). There have been calls to develop international standards and accreditation schemes for toxicological laboratories, precisely to improve international comparison in this area (Wilson-Wilde, 2018).

6.1.1.2. Theoretical Taxonomies of ‘Probable Suicide’

As is frequently reported, the first academic discussion of typologies of ‘probable suicide’ was written by Emile Durkheim; a French sociologist, whose focus was on establishing the utility and validity of sociology as a science and was primarily concerned with the influence of social integration (Durkheim, 1951, Martin, LaCroix, Novak and Ghahramanlou-Holloway, 2020). His original publication on ‘probable suicide’ was in 1897, which listed four types of ‘probable suicide’, based on an interplay of social integration and moral regulation. These were: egoistic, altruistic, anomic and fatalistic. Egoistic deaths were related to low social integration and a lack of meaning in one's own life, altruistic deaths were associated with over-integration and overwhelm by a group's goals. Anomic deaths were related to a lack of social regulation, for example, in times of economic upheaval, that likewise lead to a lack of individual direction. Finally, fatalistic deaths would be defined as over-regulation from external forces, which prevent an individual from foreseeing methods of improving their own conditions; for example, prisoners in particularly oppressive institutions. While Durkheim's theory is an important starting place, and acknowledges that social forces do significantly contribute to 'probable suicide', these classifications would be both difficult to identify with any certainty and are challenging to apply in a way that could be useful clinically and preventatively.

A later psychologically-based typology was that of Edwin Shneidman, called a father of suicidology by some (Leenaars, 2010) and who published a significant volume of work examining suicide notes and constructing theories on 'probable suicide'. Shneidman firmly believed 'probable suicide' was as a result of unbearable psychological pain, leading to a development of three types of 'probable suicide'; these were egotic, dyadic or ageneratic (Shneidman, 1968). Egotic would be the result of internal conflict and pain, in which the environment and external relationships are secondary to the desire for death. Dyadic, by contrast, primarily relates to painful emotions that arise from interpersonal relationship problems, for example rejection and shame would be key motivations in this context. Ageneratic deaths seem quite distinct, in that they were conceptualised from a more sociological perspective, and primarily indicate loneliness and alienation from society at large as the key dimensions of the psychological pain. This typology highlights the interplay of the personal and social motivations commonly associated with 'probable suicide'; however, these categories are unlikely to be mutually exclusive, nor do they signpost pathways towards areas for potential interventions.

6.1.1.3. Violent or Non-violent Methods of 'Probable Suicide'

In the current day and age, the most common descriptive taxonomy for 'probable suicide' distinguishes between so-called non-violent or violent causes of death; usually poisoning versus all other types of death, respectively. Death by drowning has proven somewhat controversial; originally classified as violent (Burvill et al., 1973, Åsberg, Träskman and Thorén, 1976), however, more recently a small number of groups have conceptualised it to be passive and non-violent (Dumais et al., 2007, Brådvik, 2007, Rockett et al., 2014). A relatively recent review of the concept highlighted its importance in two key aspects: first, that the method chosen by individuals who attempt suicide and its classification of violent or non-violent can point towards high or low intent to die respectively. Second, that violent methods of either ‘probable suicide’ attempts or ‘probable suicide’ death have been analysed as proxy measures for aggression, which is linked with serotonin, therefore this taxonomy could point towards the development of biomarkers in the field of suicidology (Ludwig and Dwivedi, 2018). The association between violent methods of suicide attempts and higher intent to die was associated with an increased likelihood of repeated suicide attempts (Giner et al., 2014), which highlights a useful, potentially preventative aspect of this dichotomy. Several of the papers supported the idea that so-called violent methods of suicide attempt correlated with higher self- and other-directed aggression, however other publications did not report these differences. The mechanistic underpinning for the theory of self- and other-directed aggression relating to a violent ‘probable suicide’ method, is that aggression as a trait is associated with violence, which is in turn associated with lower concentrations of central serotonin than is the norm (Wallner and Machatschke, 2009). As such, with the serotonin theory of depression, this would suggest that violence and aggression would be significantly elevated in this population. There are several caveats to this theory; first, the association between other- and self-directed violence, represented by for example violent criminal offences and violent ‘probable suicide’ methods, has not been universally found (Stenbacka, Romelsjö and Jokinen, 2014, Webb et al., 2012). Second, the possible association between SSRI antidepressant drugs and an increased risk of self-harm and ‘probable suicide’ seems confined to adolescent patients; it also requires further validation before a strong conclusion can be reached (Gupta et al., 2016, Edinoff et al., 2021). Furthermore, the proposed action of SSRI drugs is that they increase the rate of serotonin in the synaptic cleft by inhibiting re-uptake. Their actions can take several weeks, and so it is possible that the therapeutic mechanism relies on this increase of serotonin in the synaptic cleft leading to a counteracting decrease in re-uptake transporters (Edinoff et al., 2021). As this mechanism is still an experimental hypothesis, future research will be required before the mechanistic underpinning of the serotonin theory of depression is more concretely understood.

Despite frequent publications using the classification of violent or non-violent ‘probable suicide’ methods, there had been little statistical testing of the concept itself. Recently, an Austrian proof-of-concept study pointed out that this taxonomy had come about intuitively, rather than empirically, and decided to test these dichotomous categories with a machine learning approach (Ludwig et al., 2019). Data on ‘probable suicide’ mortality was provided by Statistics Austria (the Federal Statistics Office for Austria) from 1970 to 2016, including month of death, sex, age and method of ‘probable suicide’. The five methods identified were poisoning, hanging, drowning, shooting and a miscellaneous category, which included jumping from heights. Individuals were split into 20 age groups, then split into the 5 categories for the method of ‘probable suicide’ death and analysed using the dendrogram function of Matlab. The total sample was 77,894 ‘probable suicide’ decedents, of which 72% were male, with the median age group for men being 50-54 years old and the modal ‘probable suicide’ method was hanging at 46.3% of the cohort. When the total sample was included, the clusters were poisoning, then all the other methods, with hanging and shooting as a sub-cluster within the violent methods cluster. The male-only analysis was similar, however the sub-cluster within the violent death method was hanging and drowning. The female-only analysis identified hanging and drowning as the first main cluster, then shooting, poisoning and jumping were the second cluster; within this group, shooting and poisoning formed a sub-cluster. Generally, these results did empirically support the dichotomy itself, and supported the classification of drowning as a violent method in the total cohort and male-only analysis. The authors suggested the low number of women who died by shooting, and the highly heterogenous nature of this sub-group, could be the cause of its atypical link with poisoning. Furthermore, as an acknowledged limitation of the study, the model could have been further refined if there had been access to the psychiatric history and socioeconomic status of each patient. Another important caveat is that causes of death designated as undetermined were not included in this study; this would have affected the women’s result most, as self-poisoning deaths are often classified as undetermined and women are significantly more likely to attempt ‘probable suicide’ by poisoning (Brådvik, 2007, Gray et al., 2014).

Clearly, the classification system of violent or non-violent 'probable suicide' methods has some utility; this is especially the case for the preventative aspect which considers the methods of 'probable suicide' used in an attempt to extrapolate intensities of the desire for death. This system also identifies which methods of 'probable suicide' are common and ought to be restricted to prevent 'probable suicide', especially as means restriction is well-supported as a successful preventative intervention (Lim et al., 2021). In countries where many means are already controlled (e.g., firearms laws, controlled substances, limited rooftop access), this classification system may have limited further use in furthering our understanding of the antecedent patterns of those who die by 'probable suicide'.

6.1.1.4. Statistical Classifications of 'Probable Suicide'

A recent review of the literature aimed to collate all the studies attempting to define a numerical taxonomy of 'probable suicide' (Bagley and Shahnaz, 2017). Their criteria were that the study included at least 10 descriptors, covering both socio-demographic and clinical variables, investigated in a sample size of over 50 individuals, and used a statistical method to identify potential patterns. Every study included used different variables and several used different methods, ranging from principal component analysis, two-step clustering or hierarchical clustering methods. Several of the studies discussed by Bagley and Shahnaz analysed exclusively adolescent samples, which are a small percentage both of 'probable suicide' decedents generally and within the data so far analysed for this thesis. As such, these studies will be omitted from this section and the studies with larger sample sizes, across a wider age range will be summarised here. Other studies published after their review, or not included by them, will be discussed subsequently.

The study that suggested the highest number of clusters was by Logan, Hall and Karch (2011), covering 12 US states and using data from the period 2003-2008, which was fed into a latent class analysis algorithm. The data was collected from National Violent Death Reporting System (NVDRS), which is an incident-based surveillance system that specifically collects information on violent deaths, including 'probable suicide'. It stores data on the circumstances leading up to the death as well as toxicology reports, along with other medical information. On the basis of missing data, five states were excluded from the study, which may call into question the validity of all the data included; these states were discounted on the basis of incomplete data submission to the NVDRS, which may indicate relatively low levels of interest in data sharing nationally.

From the over 28,000 ‘probable suicide’ decedents included, nine clusters were identified; three clusters detailed deaths where a psychiatric diagnosis was present with either additional crises, or alcohol problems, or neither. The following six represented clusters with a variety of life stressors: depressed mood and financial problems, alcohol problems plus life stresses, physical medical problem, recent link to crime, interpersonal problems or crisis plus alcohol at time of death, alcohol at time of death and some dependence in life. Some demographic variation was noted in that the mental health clusters had slightly higher percentages of women and deaths caused by self-poisoning compared to the other clusters, while the cluster with contributing physical health stressors had an older population on average.

While this study highlighted some interesting potential clusters, there are significant caveats which limit the generalisability and utility of the information, in addition to the concerns about data quality noted above. First, a depressed mood condition was included as a separate risk factor than diagnosed depression and there is no explanation given to warrant such similar risk factors in the methodology, though the authors note that all data came from state health departments or subcontracted entities like medical examiners. Second, any healthcare data included came from coroners or medical examiners, therefore there was no specific data on which healthcare services were attended before death. Furthermore, the modal cause of death in American studies is overwhelmingly by firearms, which is a significant contrast with the majority of international statistics. As such, these clusters are unlikely to be directly replicable, or to act as a valid classification system, outside of the US.

The second-highest number of clusters proposed from the papers in the review, was a study that identified five clusters in Toronto, Canada. Data on all individuals ruled a ‘probable suicide’ over the years 1998-2010 were extracted from the Toronto Office of the Chief Coroner (Sinyor, Schaffer and Streiner, 2014). A total of 2,886 individuals fulfilled the criteria, and variables like demographic data, a diagnosis of a mental illness, recent contact with a healthcare service and recent stressors were extracted from the coroner’s files. Only age was included as a continuous variable, while the others were converted into dichotomous formats indicating presence or absence. A two-step clustering method was used, with the most fitting number of clusters determined automatically by the statistical software (SPSS).

The five clusters were: a group that all had diagnoses of depression in their medical records and had a higher percentage of women dying from non-violent methods, a second cluster dying predominantly of violent means and with a higher rate of recent adverse events, a third cluster of mostly men with a history of substance abuse, a fourth group that was the youngest and half had a history of either bipolar disorder or schizophrenia, and finally a fifth cluster of mostly unmarried individuals that had a low proportion of mental illness diagnoses, and, interestingly, were the most likely to have left a suicide note. This fifth cluster was also the largest, while cluster 1 was the smallest. This study, while instructive, does have some limitations; the data were extracted from coroner's records and the only healthcare data included was attendance at psychiatric or emergency services in the week before death. An understanding of the clinical presentations of these clusters is paramount to their utility, yet as demonstrated by their own data, a window as short-term as one week meant that no cluster had a value of over 15% attendance and this variables featured little in the discussion of their own clusters. Furthermore, the psychiatric diagnoses and stressors were identified from interviews with next of kin, which could have been inaccurate.

Three of the studies in the review described three similar clusters in their analyses, despite using alternative clustering methods (O'Connor, Sheehy and O'Connor, 1999, Bagley, Jacobson and Rehin, 1976, Sinyor et al., 2016). O'Connor's group dichotomised all variables into binary measures, and did not include any demographic variables in the calculation of the clusters, then used a hierarchical agglomerative approach to build up the clusters by combining the individuals most similar to each other. Bagley's group again included only binary measures and used the principal component analysis method (this essentially identifies groups of variables that correlate with each other, for example, in this study, component A showed that previous suicide attempts, depression and psychiatric treatment were correlated together and affected the variance between individuals in similar ways). Sinyor's group used variables that were not limited to binary measures, and used Ward's method, which minimises the amount of variance within a cluster, and also used a hierarchical agglomerative method.

The general summary of the three clusters identified would be a mental health sub-type, a physical health sub-type and a socially challenged sub-type. Specifically, one had a high percentage of people diagnosed with a mental illness, often depression, with some individuals having additional psychiatric diagnoses. The next cluster had a lower incidence of depression, but had records of physical illnesses or disabilities. Lastly, a sizable number of people lacked notable psychiatric or physical diagnoses, resulting in little medical contact before 'probable suicide' and were more likely to live alone, occasionally with violent or criminal histories (with violence being particularly present in Bagley, Jacobson and Rehin, 1976).

Each of these studies used distinct clustering methods, and included their own specific variable lists, therefore that three similar clusters could be identified is promising for their external validity. It is worth noting only Bagley included deaths ruled as misadventure and was the only study to have a small residual group, when the 3 components were tested in a larger sample of 'probable suicide', which may be more relevant to real-world statistics, which can include deaths of undetermined intent. Sinyor's study specifically only analysed those over 80 years old, therefore the correspondence between these studies should not be overemphasised; although should further work corroborate these findings, it would suggest these clusters are appropriate for a wide age range. All of the studies had samples smaller than 200 people, therefore much larger proof-of-concept studies would be required to test these findings, however the clusters were clinically intuitive and replicable across time and different countries. O'Connor's group studied a sample from Northern Ireland, Bagley a sample in Brighton and Sinyor studied a Canadian sample, found in Toronto.

One of the more unique studies in the Bagley review was a study from Hong Kong, which aimed to investigate patterns of planning and preparedness in cases of 'probable suicide' (Chen et al., 2007). The authors note that the predictive value of the Beck Suicidal Intent Scale (SIS; Beck et al., 1974) is low and inconsistent when considering the risk of subsequent 'probable suicide' for those who have made 'probable suicide' attempts; they suggest this could be due to a potential group of "low-planned", yet still completed 'probable suicide' events. Data from psychological autopsies were used to score 'probable suicide' decedents on the SIS, by examining aspects like precautions against discovery or intervention, overt communication of intent and the degree of planning required for the method of death.

The eight objective SIS scores were read into a clustering algorithm that used Ward's method to minimise the variance within each cluster. Several other variables, including demographic information and psychiatric history were also recorded, but they were not read into the clustering algorithm. Two of the dimensions of the SIS were found not to contribute to the clustering analysis: "acting to gain help during the suicidal act" and "overt communication of intent before the act".

Two clusters were identified, which were approximately equally-sized; 71 individuals were in cluster 1, which had a higher score on the SIS scale, with 77 individuals in the lower score, and therefore presumed low-intent, second cluster. Those in the high intent group were more likely to be in financial debt or under chronic stress with fewer psychiatric diagnoses, while the low intent group were more likely to have psychiatric diagnosis and 50% of this group was receiving psychiatric treatment. There were no significant demographic differences, however those who scored a lower intent were more likely to have died by jumping from a height rather than any other method. Various economic measures have been correlated with an increased risk of 'probable suicide' (Karanikolos et al., 2013) and financial stress is recognised in other studies as a stressor, however it seemed to exert a very significant effect in this study, with 44% of cluster 1 and 19% of cluster 2 recorded as "in any formal debt arrangement". Only 148 deaths were analysed, which highlights a common problem with these studies in that the samples are usually small and may result in clusters that are unlikely to represent common groupings, especially once cultural variation is taken into effect. This is especially true in Hong Kong, as noted by the authors themselves, in which jumping from a height as a means of death is considerably more available than in other countries, which could have significantly elevated the number of 'probable suicide' decedents that were categorised as low-planned. Nonetheless, this study identifies the challenge in preventing these low-intent deaths, which would not be detected by the current risk profiles and scales in use.

Another study, published after Bagley's review, also identified two main clusters, with sub-clusters within them (Clapperton et al., 2018). This study was based in Victoria, Australia and used a regional register designed to collate information on suspected 'probable suicide' decedents, to support the required medico-legal investigations. A variety of socio-demographic and healthcare-based variables are present in this register, including evidence of mental or physical illnesses and statements from family members and friends, all of which were included in the analysis. These were all included, as the rationale of this study was to confirm or refute the findings of an earlier Australian study, which incorporated similar variables (Judd et al., 2010). A two-step clustering method was used, which combined k-means and hierarchical clustering analyses, though the method does not clarify whether the method was agglomerative or divisive. The first step split the cohort of 2,839 individuals into two clusters; the same analysis was then run again for each cluster to identify further sub-clusters.

Initially, the proposed clusters were those with, or without a mental health diagnosis, and sub-groups were established on the basis of demographics and the presence of interpersonal (death, conflict, illness) or situational stressors (work, finances, legal, substance abuse). The first mental health sub-group had the highest rate of employment and a high rate of interpersonal stressors, whereas the second sub-group had the highest proportion of retirees and treatment for physical conditions. While the first two sub-clusters had a majority of mood disorder diagnoses, the third group had a higher proportion of personality disorder and schizophrenia diagnoses, again with a high number of interpersonal and situational stressors. Lastly, the fourth sub-group had the highest proportion of women and the highest number of abuse stressors. Interestingly, the first group without a mental health diagnosis had the second highest rate of physical stressors recorded and 24% had a record of mental health treatment, while the last sub-group had 37% with a history of mental health treatment and a high rate of substance abuse. The validity of these clusters relies on the importance of psychiatric diagnoses as a risk factor for suicide, however a meta-analysis concluded that up to 66.7% of people who died by 'probable suicide' were ineligible for any diagnosis (Milner, Sveticic and De Leo, 2012). In this study, only 52% had a diagnosis therefore the system used arguably may have attributed too much significance to a psychiatric diagnosis to establish types of suicide.

6.1.2. Taxonomies of Drug-Related Deaths

6.1.2.1. Introduction

Where DRD are concerned, various demographic markers are often reported – for example, these individuals are overwhelmingly male, young adult to middle aged and white (Hickman et al., 2007, Drake et al., 2019). Especially in the United States and the United Kingdom, these factors will be clinically unhelpful, as the vast majority of the people presenting to substance misuse services will fulfil these criteria. Current evidence for the range of interventions available show efficacy in certain domains (e.g., reductions in criminality, reduction in blood-borne diseases like HCV and HIV, improved relationships with family and peers), however it is unclear how to target these interventions for maximum benefit (Bharat et al., 2021, Degenhardt et al., 2019 (b)). In spite of the recognised need to better understand the groups who use substance misuse treatment services, very few clustering studies could be identified within the literature. Firstly, theoretical taxonomies will be discussed, which were developed with no statistical underpinning, then studies relying on mathematical means to divide the samples used will be discussed.

6.1.2.2. Theoretical Taxonomies of DRD

A taxonomy of preventable overdose deaths was written in 2007, primarily to help UK government policymakers understand the profile of overdose deaths in London during 2003 (Hickman et al., 2007). Deaths were identified from coroners' records, which gave access to witness and family statements, as well as toxicology results; these deaths were cross-checked against ONS records to ensure that the ICD-10 code recorded the death as drug-related. The ONS was also investigated for any further deaths that had not been identified in the initial coroner office approach, resulting in a sample of 151 drug overdose deaths. Narratives of 61 overdoses were collected from people who had known the deceased from treatment agencies or outreach services. An expert panel of ten drug user analysts critically reviewed all of the data and constructed potential clusters, based on the demographic information from official records, as well as the stories collected.

The article concluded that there were ten types of overdose deaths: novice developing a habit or established user resuming the habit, concealed or solo user, recreational risk-taker, physical comorbidity, psychiatric comorbidity, susceptible or vulnerable user, marginalised environment user, institutionalised user, release or discharge user and dependent users with no significant event noted. There seems to be significant overlap between the theoretical types of death identified, especially between the vulnerable/susceptible user and those with psychiatric or physical comorbidities, as the definition of a vulnerable/susceptible user was one who was in danger of increasing their drug use due to emotional or physical pain. Presumably because of this theoretical overlap, the clustering method was not exclusive; individuals were present in multiple clusters, yet the authors did not discuss what types of overdoses overlapped most frequently. Additionally, the sample size was small, with only 151 overdoses identified. Overall, this study seems largely ineffective, because despite aiming to further the understanding of types of DRD in London, the clusters were not identified empirically, the sample size was small, and the clusters were non-exclusive. As such, they do not contribute much to our ability to isolate unique antecedent risk patterns that could be developed into a taxonomy of DRD for targeting preventative interventions.

Another older study similarly did not rely on statistical modelling, but separated drug deaths into 3 categories, based on discussion by the investigators (Püschel et al., 1993). These resulted in a category of deaths caused by a single drug (54.1% of the sample), the second group identified as addicted to at least 2 substances while the third category was explicitly long-term alcoholics, many of whom had recently started abusing opiates. There was a minor gender difference in that no women were present in the third category and they were slightly overrepresented in the second category. It is worth noting, however, that there were only 122 cases involved and that there was no statistical validation of the categories, thus limiting the validity and the utility of this system, as experts looking at the datasets could all highlight alternative significant groups. Additionally, the majority of drug-related deaths currently involve more than one drug (Hickman et al., 2007, NRS, 2021 (a)), therefore it is unlikely these clusters would be internationally representative or clinically useful now. This is especially relevant when considering the variation in legal classifications of drugs across countries and the fact that these classifications can change over time, which may affect both accessibility to users and attractiveness for the illicit drug market.

6.1.2.3. Statistical Taxonomies of DRD

A study in Norway used national registers to collect data from 2003-2004 then 2006-2009; this gap was to ensure equal availability of the data that noted which drugs were involved in the death (Amundsen, 2015). The definition used to extract relevant individuals was the EMCDDA “drug-induced deaths” (2022), however the codes for poisonings of undetermined intent are not included in the Norwegian Cause of Death

Registry, therefore the study does not fulfil the traditional criteria fully. Other national registers were linked with a personal identification number to extract socio-demographic data. The study used a two-step clustering approach, which calculated a similarity distance, grouped cases together and then used an agglomerative approach to join sub-groups into clusters. Included in the clustering model were: gender, age, education, disability pension, number of years with income higher than minimum pension, higher wage than minimum (curiously, based on UK wages), work-related benefits and training and social welfare benefits in last 5 years.

This paper isolated three approximately equal sized clusters: one with low education and workforce participation, one with people receiving disability pension (which also had the highest proportion of women) and the final cluster which had the highest levels of education and the highest participation in the workforce leading to the lowest amount of means-tested benefit support. The disability cluster had the highest percentage of deaths ruled as intentional poisonings and, therefore, ruled as 'probable suicides' (see section 6.1.3 for further discussion of this cluster). These socio-demographic based clusters identified more useful clusters than the taxonomy published by Hickman's group, however there was no information about antecedent healthcare usage that might lead to better targeting of preventative strategies.

Another style of clustering examined the geographical spread of DRD in Harris County, Texas, leading to an analysis of the areas' characteristics (Drake et al., 2019). Data were extracted from the medico-legal investigation system for the county, which included autopsy records and socio-demographic data for each individual. The authors discounted over 30% of the DRD available in the sample (those under 25 and those over 59), arguing that the youngest deaths were often accidental or homicidal, while older populations would be more likely to die from expected causes. This seems both inefficient and flawed, as deaths in these age groups constitute significant populations in the DRD category, and therefore ought to be investigated. Community characteristics for the regions of interest were extracted from the 2009-2013 American Community Survey, which is a census that contacts households, once every 5 years and publishes summaries of the demographic data provided. DRDs were geo-coded to their residential address, and high-risk areas were identified. These high-risk areas were mapped onto the areas described by census data, and both a single and dual kernel density was calculated. A control group of deaths by natural causes was analysed in the same way.

Only the dual kernel density was reported. The community characteristics of the first had a lower percentage minority population, but a higher percentage of people without high-school diplomas and people in poverty, compared to area 2. Interestingly, the median household income was higher and the employment rate was lower for the DRD geographical clusters than the areas identified in the natural death clusters. Income inequality was at its highest in area 1 of the DRD, which highlights a key problem of this study; by extrapolating out to community characteristics, specific data on the antecedents of the DRD group were unavailable, thus it is unclear what the truly relevant characteristics of the area are. Furthermore, the authors note that these two areas only represent 15.8% of the DRDs included in the study, which was already significantly reduced from the true number of deaths in the county. While studies of this kind have relevance for placing health interventions in areas where overdoses are common (Dworkis et al., 2018), they do not contribute a great deal to classifying key profiles of DRD for international standardisation and analysis, as they are too broad in their identification of possibly relevant characteristics.

6.1.3. Classifying the Overlap between 'Probable Suicide' and DRD

So far, the typologies discussed have implicitly treated 'probable suicide' and DRD as distinct problems, despite self-poisoning and clusters with healthcare profiles suggestive of addiction being present in the 'probable suicide' cohort analyses (Ludwig et al., 2019, Logan, Hall and Karch, 2011) and despite 'probable suicide' decedents being present in the DRD analyses (Amundsen, 2015, Drake et al., 2019). It is only recently that 'probable suicide' prevention has been explicitly stated to be necessary in opioid overdose prevention programmes (Gicquelais et al., 2020, Oquendo and Volklow, 2018). The concept of "deaths of despair" has been discussed, which includes both 'probable suicide' and DRD, as well as chronic liver disease and similar illnesses from chronic alcohol misuse (Sterling and Platt, 2022). In this section, any clusters from the previous studies which indicate an overlap will be examined.

Within the 'probable suicide' typology publications, none directly referenced the idea of a DRD; the most common acknowledgement of the overlap between 'probable suicide' and DRD was in any cluster with a higher degree of deaths from self-poisoning than alternative 'probable suicide' methods. This was noted by both

Sinyor, Schaffer and Streiner (2014) and Logan, Hall and Karch (2011), who reported clusters with a higher proportion of women, often with a history of depression and who generally died by poisoning. Clearly, these clusters do not represent traditional ideas of either DRD or the demographic groups associated with substance misuse, which may explain the lack of recognition for what these deaths could represent. Admittedly, a death ruled as specifically self-poisoning would only represent a minor section of any DRD sample, especially as the primary focus of these statistics are deaths involving illicit substances. Clarification of the medical cause of death codes would be required to investigate how many of these decedents would fulfil DRD criteria, and whether they represent a rarely acknowledged sub-type of poisoning deaths fulfilling criteria for both types of death.

Also present within the ‘probable suicide’ studies were variables indicating a history of substance abuse; the third cluster in Sinyor, Schaffer and Streiner (2014) and the third mental health diagnosis sub-cluster in Clapperton et al. (2018) reported high rates of substance abuse. Both of these clusters represent the predicted demographics of substance abuse, in that they were mostly middle-aged men, with a high rate of additional stressors (e.g., family or partner conflict). Again, without specific cause of death codes for each individual, it is impossible to state that these were overlapping DRDs, however they fulfil the anticipated profile. That very little of the discussion for either of these papers highlights the increasing rate of substance-related death globally and its relation to ‘probable suicide’ is concerning and corroborates suggestions that these phenomena ought to be explicitly linked (Oquendo and Volkow, 2018).

The only study previously described in the DRD sub-section that mentioned a unique cluster of ‘probable suicide’ decedents was in Amundsen (2015). This is particularly intriguing, as Norwegian registers do not include deaths due to poisonings of undetermined intent, therefore, the disability cluster had a higher proportion of deaths that were coded as intentional poisonings specifically. Despite this, the discussion does not elaborate on the possible links between disability, misuse of prescription drugs or illicit drugs, and the overlap between DRD and ‘probable suicide’ suggested by the study’s own data. Prescription opioid overdose is thought to be a contributing factor in the increasing rate of DRD (Seth et al., 2018), and this constitutes a significantly different population for targeted intervention, than those who die of an overdose from illicit drugs. As such, it again seems to be a large oversight not to appropriately recognise this overlap in the data and its implications for a taxonomy of DRD.

6.1.4. Summary of Clustering Literature

So far, the literature reviewed has shown that several authors worldwide have called for the development of taxonomies of both ‘probable suicide’ and DRD to further both our theoretical understanding, as well as to understand practical differences that could signpost us toward targeted interventions. The taxonomy of violent or non-violent methods of ‘probable suicide’ has been commonly reported, and has allowed for an exploration of ideas relating to aggression, impulsivity and intensity of suicidal desire. These are certainly useful concepts for clarifying the contribution of violence and impulsivity to ‘probable suicide’, however other than suggesting methods worth restricting access to, there is little immediate clinical utility. The other ‘probable suicide’ studies investigated a variety of factors commonly reported to be relevant: demographic data, mental health and physical health diagnoses, as well as inter-personal stressors. Several of these could be divided into clusters, especially ones where a mental health condition had been recognised by a healthcare provider and a group, or even groups, where there was no evidence for mental health concerns, but there was evidence for physical health conditions and/or serious personal distress (e.g., the impact of financial debt noted in Chen et al. 2007). Rarely is the overlap with DRD recognised, despite self-poisoning or undetermined poisoning events being included in the analysis. The DRD typology studies were much more limited in number, which suggests this is an area that requires further development generally. Only one study could be found that statistically examined a wide variety of DRD and attempted to construct a taxonomy of these differing presentations; one of the three clusters had a higher rate of both disability and deaths ruled as ‘probable suicide’. Again, rarely was the overlap between types of death acknowledged. These studies have regularly highlighted the salience of demographic factors, past diagnoses or healthcare presentations, methods of death and personal or situational stressors, in identifying clusters. Further work is required that incorporates these variables, while also investigating the relationship between ‘probable suicide’ and DRD.

6.2. Cluster Analysis Methods

6.2.1. Statistical Interface

The healthcare analysis of the previous chapters had been undertaken in SPSS, due to the standardised nature of the programme, the broad range of statistical tests available, and the compatibility with and license for use in the Safe Haven. Several of the clustering papers identified used software associated with R for their analysis, and the statistician support available identified resources providing R code for clustering, therefore it was chosen as the software for the clustering exploration.

R is a programming language, widely used by statisticians and data analysts across a variety of fields, primarily because of its nature as a sophisticated piece of free, open-source software. It was first released in 1995, after development by Ross Ithaka and Robert Gentleman from other early programming languages designed for statistical analysis (Giorgi, Ceraolo and Mercatelli, 2022). Since then, it has become one of the most popular pieces of software for data manipulation and analysis; this ubiquity has led to the creation of a large repository of packages, available from the Comprehensive R Archive Network (CRAN). The packages in this network have been designed and created by other R users and contain previously-written code for much more specialised analysis. Additionally, this collaborative aspect has encouraged the dissemination of resources and forums for troubleshooting errors when using R. The main method used for the clustering analysis came from one of these external resources (Filaire, 2018).

6.2.2. Clustering Algorithm

The HIC Safe Haven contains the basic R version 3.6.2 interface, however, due to the secure, cloud-based nature of the Safe Haven environment, there were initially some difficulties with downloading the required packages for the clustering analysis into R from the CRAN repository. HIC support staff supplied a modified command that downloaded packages from an internal repository associated with the virtual Safe Haven desktop, rather than the external CRAN database, which allowed successful integration of the additional packages. These were: cluster (Maechler et al., 2019), dplyr (Wickham et al., 2021), ggplot2 (Wickham, 2016), readr (Wickham and Hester, 2020), Rtsne (Krijthe, 2015) and boot (Davison and Hinkley, 1997).

The principle of any clustering algorithm is that variables are converted to a numerical scale, in which the value of the difference between the data points can be calculated. This is repeated for each variable included in the analysis, so that the total measure of distance between individuals is an average of the distance across all included variables. Data points that are close together are similar, with data points further away considered significantly different. These distances are read into the specific clustering protocol, and then a summary of each cluster can be extracted.

Based on this principle, several variables and data types from the total dataset were included to attempt to maximise the possible distance between data points and to reflect current knowledge of relevant factors. These included factors proven to be statistically different between clusters in the publications discussed above (e.g., sex, age and socio-economic status), as well as variables highlighted in the previous healthcare comparison chapters that were suggestive of sub-groups within the data (e.g., prescription rates, which represent proxies for psychiatric diagnoses, psychiatric outpatient attendance and Accident and Emergency presentations). The full list of variables included were:

- Categorical and demographic: sex, age group, socio-economic deprivation level and cause of death group ('probable suicide', DRD or both)
- Binary prescription histories: antidepressant, methadone OST and benzodiazepine
- Frequency of presentations: psychiatric outpatient clinics and accident and emergency departments

The distance metric recommended for mixed-type data is the Gower distance, available from the "cluster" package, and recommended because it is able to standardise variables of several types at once. Each variable is converted to a distance metric appropriate for whether it is numerical or categorical (Anand, 2020), and each metric standardises data distances between 0 and 1, where 0 represents identical data points and values approaching 1 indicate a large difference between data points. These distances between data points are calculated between every pair within the data, across all the variables read into the clustering algorithm. The final Gower distance for each individual is an average of all the distances, across all of the included variables. An example of a tabulated Gower distance matrix is below, in Table 6-1, and shows the output of the first stage of the analysis.

Table 6-1. Representation of a Gower distance matrix

	P1	P2	P3
P1	0	0.34	0.67
P2	0.34	0	0.05
P3	0.67	0.05	0

The table represents a Gower distance matrix. Three patients (P1, P2 and P3) have been linked to their healthcare data, which has been extracted and converted into wide-format variables. The whole dataset, containing the values for each of the healthcare measures across all the patients, has been read into the Gower formula, which has transformed the data and standardised the difference in value. The numerical value of the difference now represents the distance between the patients, based on the average difference between their healthcare usage measures. This average is used as the final Gower distance. In this example, P2 and P3 are very similar, with an average distance between them of 0.05/1, and would likely be in the same cluster. P1 and P3 are the most dissimilar, with a Gower distance of 0.67/1 and so would likely be in distinct clusters.

The final average Gower distance is read into a ‘partitioning around medoids’ algorithm. This algorithm identifies a random individual as the centre for a potential cluster, and this individual is labelled the medoid; the distances between it and the neighbouring individuals are calculated. Individuals are assigned to the medoid they are closest to, thus forming a cluster. For example, when searching for 2 clusters, 2 individuals would be randomly assigned as the medoids and all other individuals would be added to the cluster whose medoid they are closest to. This process is repeated with the random assignation of 2 different individuals as the medoids, and this process continues until the medoids with the smallest mean distances, relative to all the other observations in the clusters, have been identified. As the literature identified gave no clear indication of the appropriate number of clusters to search for, the algorithm was calculated for a range from only 2 to up to 10 clusters.

One common method to identify the most appropriate number of clusters is to calculate a measure of silhouette width. This measure compares the average distance within a cluster to the average distance between clusters, therefore it acts as a measure of cluster compactness and is used as a “goodness of fit” metric (Rousseeuw, 1987). Silhouette widths run from -1 to +1, where higher values represent a smaller distance between the observations within the cluster, compared to the observations of neighbouring clusters on average, while values approaching 0 signify little difference in the average distance within or between clusters. Negative values would suggest that observations are misclassified, as the distance between the observations within a cluster would be larger than the distance between observations of different clusters. The silhouette width calculation for the data was repeated 10,000 times using a bootstrap with replacement method, to generate 95% confidence intervals.

After examining the graphical representation of the average silhouette widths for between 2 and 10 clusters, the computation with the highest average silhouette width was extracted. The extracted summaries include inter-quartile ranges, as well as the minimum and maximum value of each numerical variable included in the analysis, while categorical variables have the total number of each category simply listed. The table for each cluster summary has been included in appendices 4, 5 and 6.

The distances thus far calculated have been in a 3-dimensional space; therefore, to visualise the clusters, the complexity of the distances had to be reduced into a 2-

dimensional structure. A recommended R code for visualising data is the t-SNE command, as it prioritises maintaining the distance between observations in the visualisation of the cluster dispersion (Gupta, 2020). As clusters are colour-coded, it also demonstrates the extent to which observations overlap with neighbouring clusters.

6.3. Results of the Clustering Analysis

6.3.1. Introduction

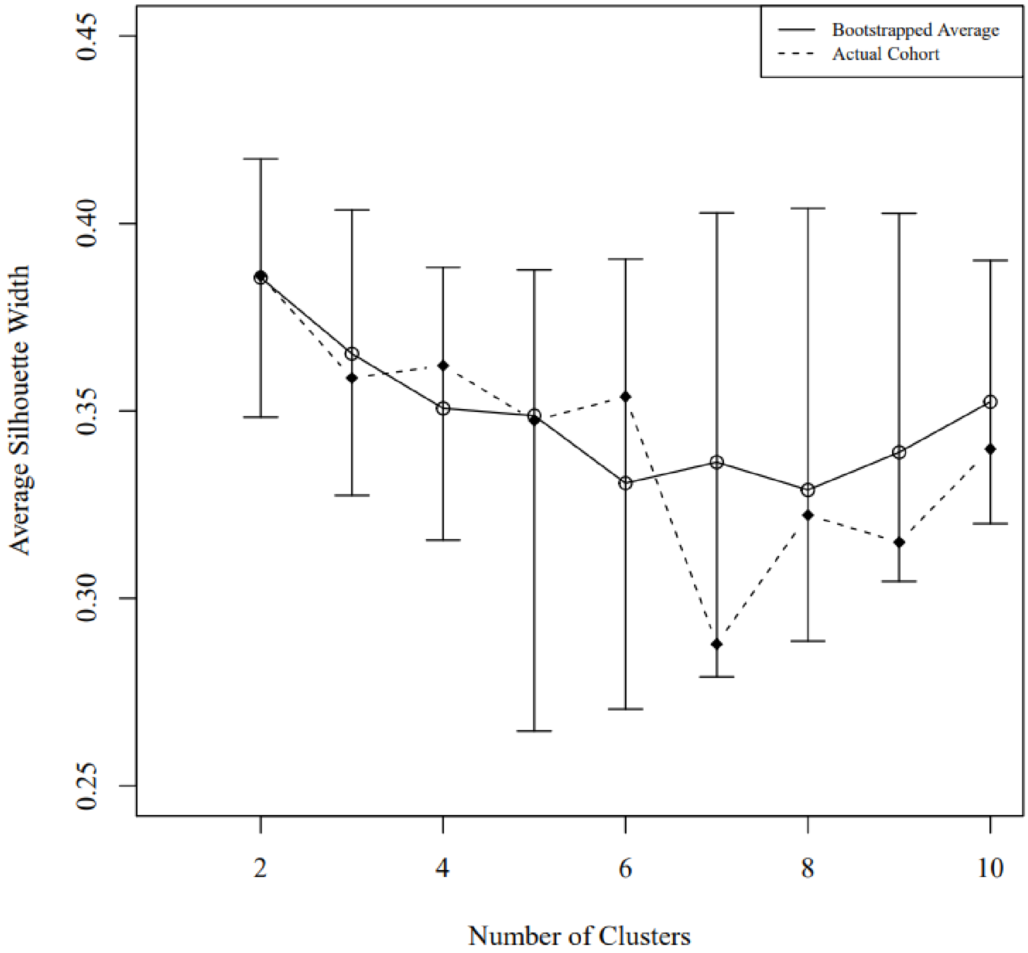
The first results presented in this chapter are the graphs extracted from R relative to the clustering using only the ‘probable suicide’ cohort. Then the clustering within only the DRD cohort follows. The final section includes both the ‘probable suicide’ and DRD individuals, on the basis that there was considerable overlap within the cohort data used for this study, as well as overlap on a theoretical basis of common risk factors (e.g., poverty, adverse childhood experiences, etc; Congdon, 2019, Sterling and Platt, 2022).

6.3.2. Clustering analysis for all those deemed ‘Probable Suicide’

6.3.2.1. Determining the Number of Clusters

This first analysis included the 586 individuals classified as ‘probable suicide’ decedents, with addresses registered in Tayside, between 2009 till 2014. The silhouette width graph below (Figure 6-1) showed that the clusters became less compact, and therefore less fitting, when the number of potential clusters increased from 2 to 8. After that point, either 9 or 10 clusters seemed to improve in appropriateness for the data. When the algorithm had to identify 2 clusters, the average silhouette width was 0.39, whereas for 10 potential clusters, the average silhouette width was 0.34. The bootstrapped average showed approximately the same fall and slight rise. As 2 clusters had the highest average silhouette width, the results were extracted. The results for 10 clusters were also extracted, on the basis that the confidence intervals were smaller than for many of the other iterations with a larger number of clusters, indicating less variation and potentially a higher repeatability of the clusters extracted.

Figure 6-1. Average Silhouette Width, including the 'Probable Suicide' Individuals



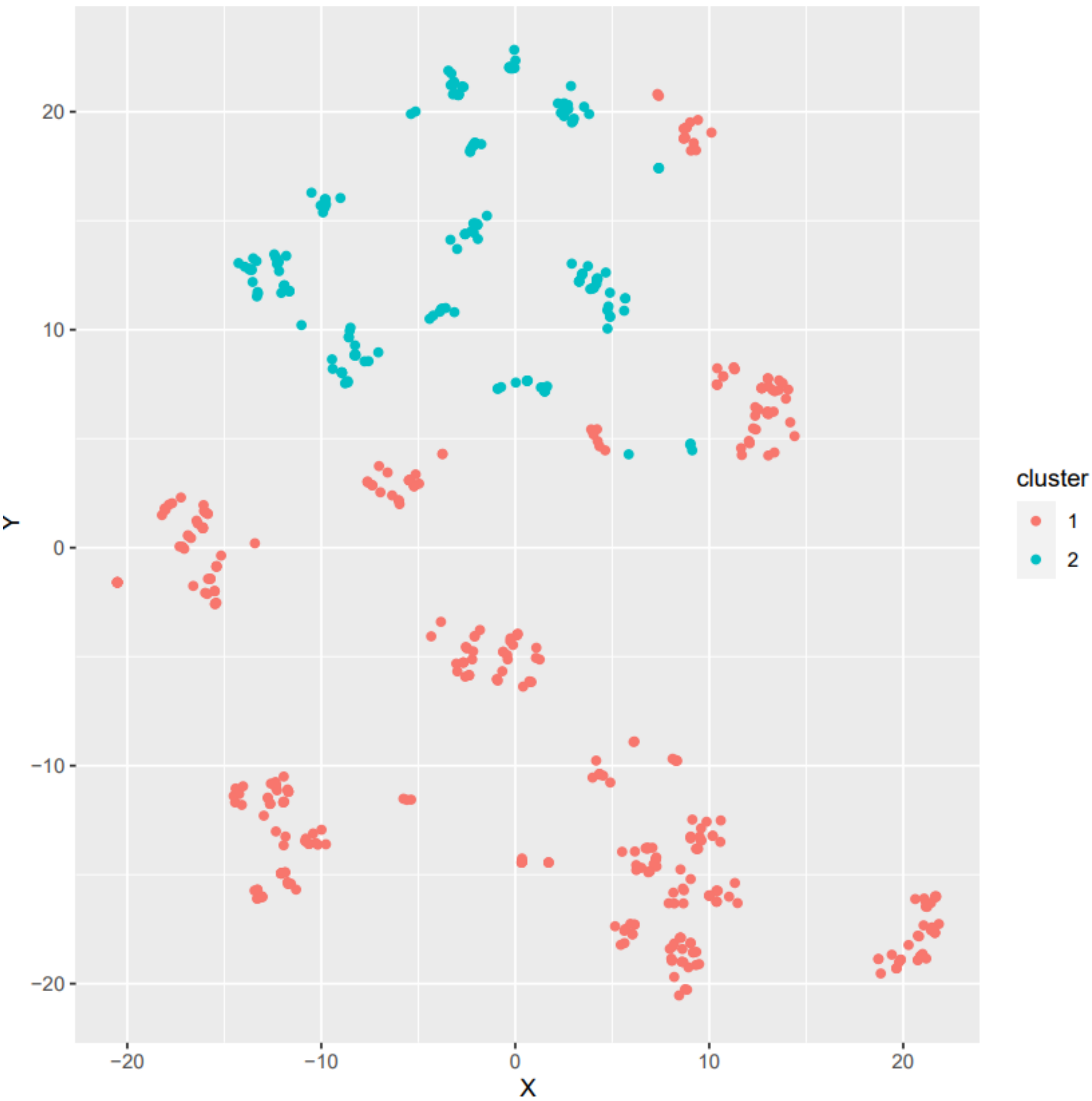
Average Silhouette Width graph across multiple clustering iterations, including only the 586 individuals in the ‘probable suicide’ cohort. Due to the unsupervised nature of the clustering algorithm, the first step involves a calculation of a “goodness of fit” measure, which is the silhouette width and runs from -1 to +1. This measure compares the average of distances between clusters and within clusters, thus quantifying the compactness of the clusters. An upper limit of ten potential clusters was chosen to ensure that clusters would have sufficient individuals to be clinically meaningful. The bars represent 95% confidence intervals. The graph suggests that two clusters fit the data best, as it has the highest average silhouette width.

6.3.2.2. Two Clusters within the ‘Probable Suicide’ Cohort

Below is Figure 6-2, which shows the 2D visualisation of the data when arranged into 2 clusters. Cluster 1 had the higher silhouette width, at 0.45 and was considerably larger with a total of 399 individuals (306 of which were men). Prescription rates and rates of healthcare attendance were very low, with a median of 0 for all healthcare measure. Specifically, the mean frequency of psychiatric outpatient attendance was 1.4, however the range reported across all of the individuals in this cluster was very large, running from 0 to 86 attendances. This group had a higher number of those whose medical cause of death codes were specific to ‘probable suicide’, rather than codes common to both ‘probable suicide’ and DRD.

Cluster 2, however, had a considerably lower silhouette width of 0.24, which suggests significant dispersion, as demonstrated in the figure below. This cluster was formed of 112 men, 73 women and 2 individuals without demographic data. Most individuals received an antidepressant prescription, with just over half receiving a benzodiazepine prescription. Mean number of psychiatric outpatient clinics attended was 5.9. These clusters seem fairly simply to represent lower and higher engagement with the healthcare service respectively. Tables a1 and a2 in appendix 4 show the outputs, as printed by R for this iteration.

Figure 6-2. Visualisation of Two Clusters, including the 'Probable Suicide' Individuals



Visualisation of two clusters, using all 586 ‘probable suicide’ death individuals. The clusters are transformed from a 3D space into a 2D space for the visualisation of the dispersion, using the t-SNE command in R, which prioritises maintaining the distance between data points, during the reduction in dimensionality. Cluster 1 is considerably larger and in red, while cluster 2 is smaller, occupies the upper middle of the plot and is in teal.

6.3.2.3. Ten Clusters within the 'Probable Suicide' Cohort

Figure 6-3 below demonstrates the dispersion of the clusters, when the algorithm attempted to identify 10 clusters within the 'probable suicide' cohort. The clusters will be described sequentially, from the cluster with the highest silhouette width (i.e., the most compact), to the cluster with the lowest silhouette width. A brief overview of the demographic data, and any identifiable differences in healthcare usage will be noted for each cluster. These clusters vary from those with very low rates of healthcare engagement (4, 10, 3 and 5), to specific combinations of key prescriptions (1, 2, 9 and 8) to clusters with high engagement with many healthcare services (7 and 6). Tables b1 to b10 in appendix 4 contain the printed readouts from R.

Extracting the silhouette width for each individual cluster showed that cluster 4 had the highest at 0.62. This cluster was 63 men, all 51 years old or older, and potentially with a lower level of deprivation than the average of the cohort (the median of the SIMD score was 3). Furthermore, these deaths were all attributable only to 'probable suicide' cause of death codes, and prescription and attendance rates were all either zero or very low.

The second-most compact cluster was cluster 10, with a silhouette score of 0.57. This cluster was 49 individuals, also all men, however there was an association with higher deprivation and all individuals were also present in the DRD cohort. Prescription and attendances rates were low, however there was a mean of 1.5 accident and emergency presentations, which was a fairly average frequency across the clusters.

Next was cluster 1, with a silhouette width score of 0.39, which was relatively small and made up of 43 men, 1 woman and 8 individuals without complete demographic information. These individuals were again associated with less deprived circumstances than the average, and were only present in the 'probable suicide' cohort. All of them received an antidepressant prescription and there was a mean of 2.25 psychiatric outpatient attendances.

Cluster 3 had a silhouette width of 0.38 and was the largest cluster, containing 132 men only. This group contained more of the 25 years old and younger individuals than any other cluster, judging from the lower quartile. All individuals were only in the 'probable suicide' cohort and again had very low prescription and attendance rates; for example, the mean psychiatric outpatient attendance was 1.02 and the mean for accident and emergency presentations was 0.47.

Cluster 7 had a silhouette width of 0.37, and was mostly women (32 to 10 men). This cluster had a very high level of deprivation—the median was SIMD 1, which is the most deprived, and no individuals were in SIMD 4 or 5, which are the least deprived quintiles—and most individuals were also present in the DRD cohort. All individuals received an antidepressant prescription, with the majority also receiving a methadone and benzodiazepine prescription. This cluster had the highest mean psychiatric outpatient attendance at 10.07.

As silhouette width scores were rounded to 2 decimal places, cluster 2 also had a score of 0.37. It contained 34 women, all of a relatively high socio-economic level, as the median SIMD score was 4, with none of the individuals in the most deprived quintile. Most of these individuals were only in the ‘probable suicide’ cohort, with most of them receiving both an antidepressant and benzodiazepine prescription. None received a methadone prescription. The mean number of psychiatric outpatient attendances was 5.53.

Next was cluster 9, which had a silhouette width of 0.27 and was mostly men (36 to 14 women). This group were all also present in the DRD cohort, however they all received an antidepressant prescription and only very few received a methadone prescription. Psychiatric outpatient attendance was quite low, with a mean of 2.1 attendances.

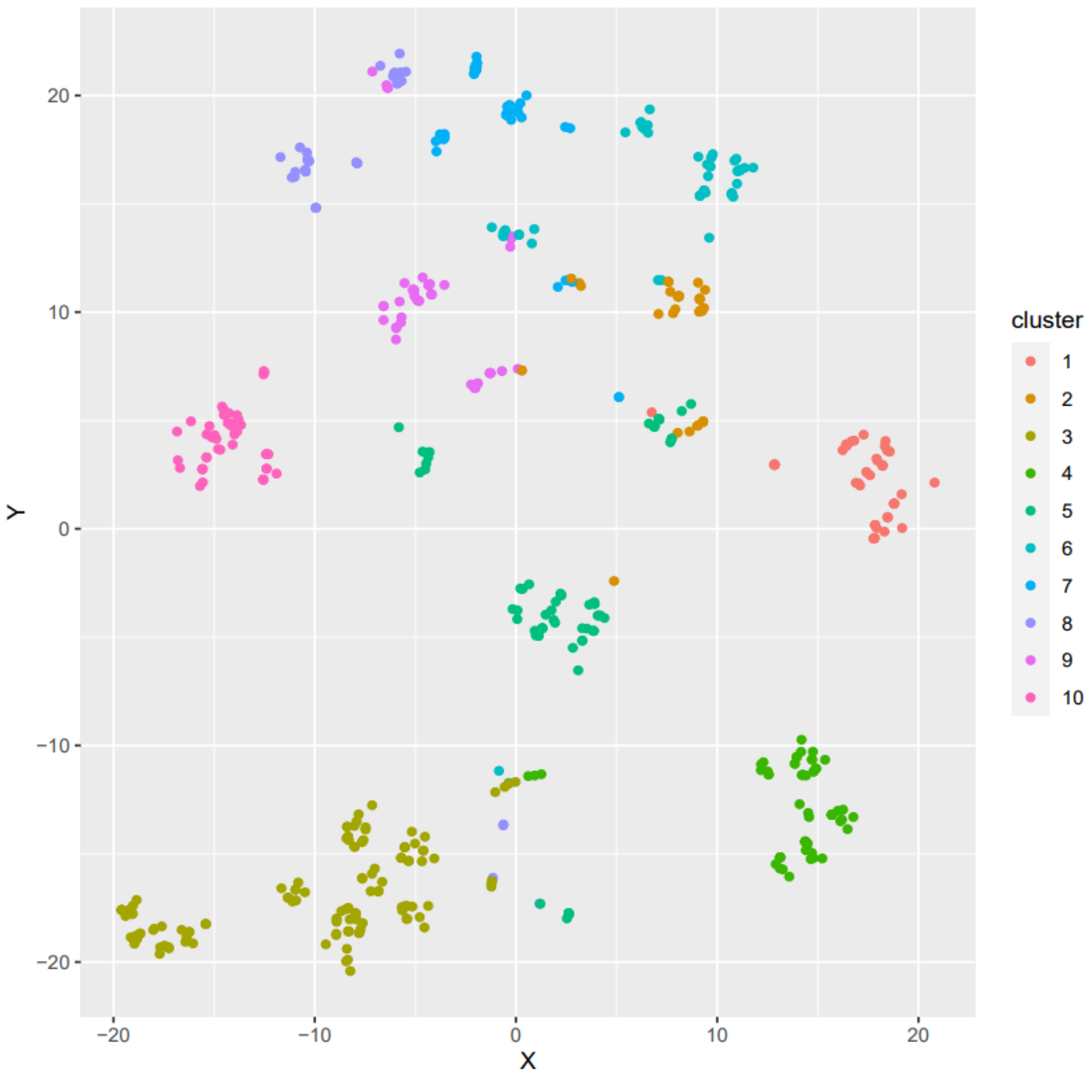
Cluster 6 had a silhouette width of 0.20, and was formed of 50 men, with 2 women and 2 individuals without demographic data. Generally, these individuals belonged only to the ‘probable suicide’ cohort, and most of the individuals had an antidepressant prescription. All individuals had a benzodiazepine prescription, which could correlate with the mean of 5.52 psychiatric outpatient attendances. This cluster had the highest mean accident and emergency presentation at 1.93.

The second-lowest silhouette width was 0.19 for cluster 8. This was 35 men, with 3 women and another 2 individuals without demographic data. There was a pattern of high deprivation, with a median SIMD score of 1 and a high number of individuals could also be found in the DRD cohort. All individuals received a methadone prescription and the mean of 6.08 psychiatric outpatient attendances was higher than that of many of the other clusters.

Cluster 5 had the lowest silhouette width of any analysis at 0.04, and the graph shows significant dispersion. The individuals assigned to this cluster were 62 women and 8 individuals lacking demographic data. Most of the individuals were only in the ‘probable suicide’ cohort, and prescription rates were very low. Mean number of psychiatric outpatient attendances was 1.29.

The average silhouette width for ten clusters within the ‘probable suicide’ cohort was 0.34, however the silhouette width of the individual clusters varied significantly, suggesting that some clusters were too dispersed to be reliable. The most compact clusters were those with very low healthcare attendance across all services, or a traditional group receiving antidepressant prescriptions and all ruled specifically as ‘probable suicide’ decedents, rather than with codes that were common to DRD definitions.

Figure 6-3. Visualisation of Ten Clusters, including the 'Probable Suicide' Individuals



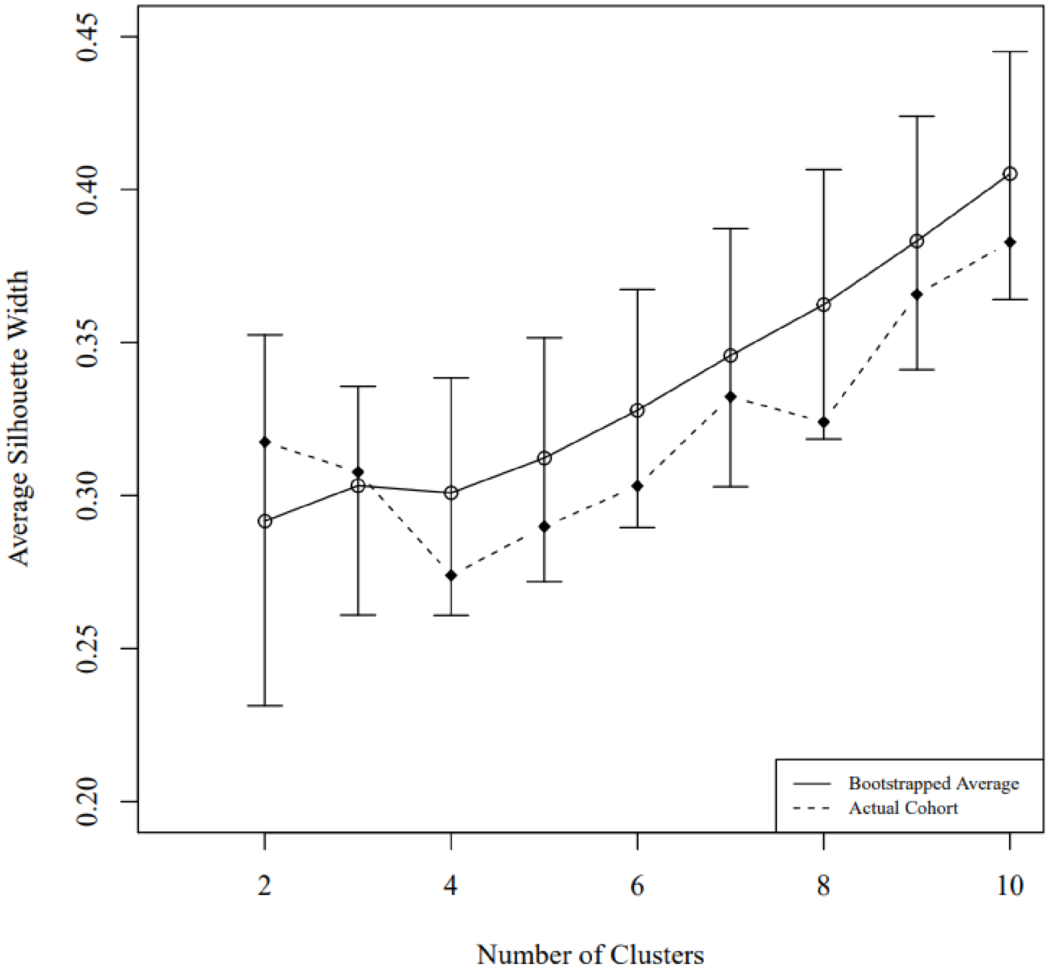
Visualisation of ten clusters, using all 586 ‘probable suicide’ individuals. The clusters are transformed from a 3D space into a 2D space for the visualisation of the dispersion, using the t-SNE command in R, which prioritises maintaining the distance between data points, during the reduction in dimensionality. Here follows a list of co-ordinates for an approximate centre of each of the clusters: Cluster 1 (18, 4), Cluster 2 (8, 10), Cluster 3 (-10, -20), Cluster 4 (15, -15), Cluster 5 (5, -5), Cluster 6 (10, 17), Cluster 7 (0, 20), Cluster 8 (-10, 15), Cluster 9 (-5, 10), Cluster 10 (-15, 5).

6.3.3. Clustering analysis for all designated as Drug-Related Deaths

6.3.3.1. Determining the Number of Clusters

Here I present the exploratory clustering analysis using the data from all of the individuals designated as DRD within the cohort, resulting in a total of 288. As Figure 6-4 shows, the trend was that the average silhouette width increased, as the algorithm attempted to identify greater numbers of clusters within the data. To best compare and contrast the results with the 'probable suicide' clustering analysis above, both the results of 2 clusters and 10 clusters were extracted. The bootstrapped average was consistently several points above that of the actual cohort, and the 95% confidence intervals show considerably less variation than in the 'probable suicide' cohort analysis, which could suggest the DRD cohort contained individuals that were more similar to each other, possibly as a result of its smaller size.

Figure 6-4. Average Silhouette Width, including only the DRD individuals



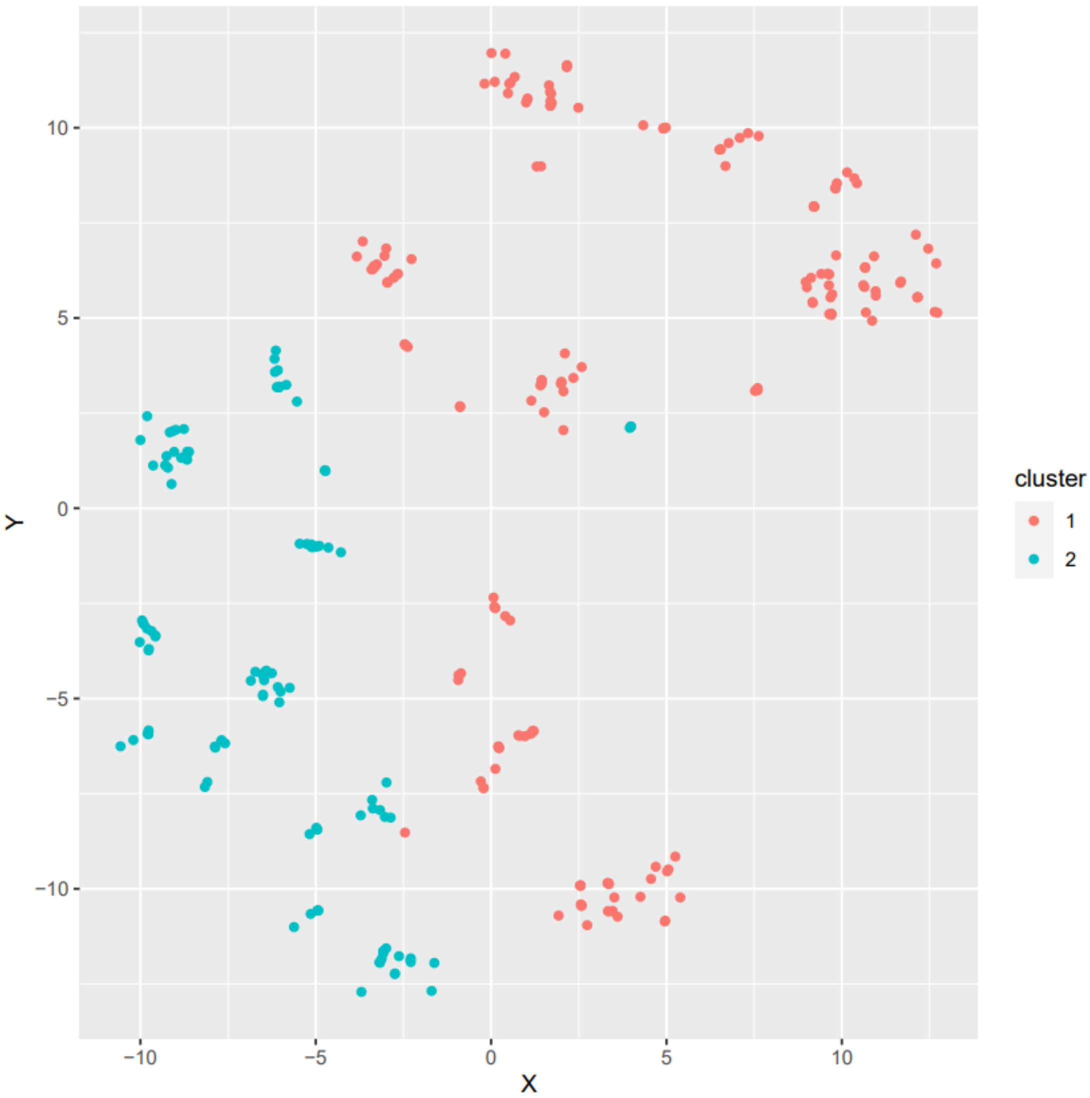
Average Silhouette Width graph across multiple clustering iterations, including only the 288 DRD individuals. Due to the unsupervised nature of the clustering algorithm, the first step involves a calculation of a "goodness of fit" measure, which is the silhouette width and runs from -1 to +1. This measure compares the average of distances between clusters and within clusters, thus quantifying the compactness of the clusters. An upper limit of ten potential clusters was chosen to ensure that clusters would have sufficient individuals to be clinically meaningful. The bars represent 95% confidence intervals.

6.3.3.2. Two Clusters within the DRD Cohort

Figure 6-5 below contains the visualisation of the attempt to identify 2 clusters within the DRD cohort. Cluster 1 had the higher silhouette width of 0.34 and was the larger cluster, with 138 men and 38 women. This cluster contained those with a lower rate of healthcare engagement; very few of the individuals received any prescriptions. The rate of healthcare attendance was low; the mean number of psychiatric outpatient attendances was 2.53, and the mean of accident and emergency presentations was 1.29. Appendix 5, tables c1 and c2 show the R printout for these clusters.

Cluster 2 was smaller, but had one clear outlier around the co-ordinates (4,2), therefore had a slightly lower silhouette width of 0.28. It contained 67 men and 45 women; however, other demographic characteristics were very similar to cluster 1. Interestingly, both clusters had similar values for the measure examining medical cause of death categories, suggesting that there was no significant difference between the number of individuals with specific DRD codes across the clusters. Most of the individuals received antidepressant, methadone and benzodiazepine prescriptions. Additionally, the mean of psychiatric outpatient attendance was 8.43, and for accident and emergency presentations it was 2.32, thus confirming the greater healthcare engagement in cluster 2.

Figure 6-5. Visualisation of Two Clusters, including only the DRD Individuals



Visualisation of two clusters, using all 288 individuals. The clusters are transformed from a 3D space into a 2D space for the visualisation of the dispersion, using the t-SNE command in R, which prioritises maintaining the distance between data points, during the reduction in dimensionality. Cluster 1 is larger and in red, while cluster 2 is smaller, occupies the lower left of the plot and is in teal.

6.3.3.3. Ten Clusters within the DRD Cohort

Figure 6-6 shows the dispersion and overlap of the results for the attempt to identify 10 clusters within the DRD cohort. As before, the clusters will be described sequentially, from the most compact to the most dispersed. The clusters show significant variations in demographic categories, and again have clusters with generally low engagement (8 and 2), a specific pattern of attendance at some of the services (1, 9, 4 and 6), and high engagement across the board of services (10, 7, 5 and 3). Tables d1 to d10 in appendix 5 contain the readouts from R.

The cluster with the highest silhouette width was cluster 1, at 0.58, which was a group of 30 men, all of whom received only antidepressant prescriptions and most of whom could also be found in the 'probable suicide' cohort.

The second-most compact cluster was cluster 8, with a silhouette width of 0.55 and was the largest cluster. As with the other clustering analyses, this largest cluster contained mostly men—51 individuals, only 3 of which were women—with very low healthcare usage. These individuals could also all be found in the 'probable suicide' cohort. Only a small number of individuals received a benzodiazepine prescription, and the mean accident and emergency presentation was 1.47.

Cluster 9 had a silhouette width of 0.50, possibly due to its small size, with 19 men and 3 women. All were also present in the 'probable suicide' cohort and there was an association with higher deprivation. Every individual received a methadone prescription, and likely correlated with that fact, mean psychiatric outpatient attendance was 5.18.

Next was cluster 4, with a silhouette width of 0.43, which also had 19 men and 3 women. These individuals were, however, only in the DRD group, and were older on average, as none of them were in the 25 years old or younger age group. All individuals received a methadone prescription and had a high rate of psychiatric outpatient attendance, at a mean of 10.73.

Cluster 10 had a silhouette width of 0.36, and was again relatively small, as it comprised of 22 women and 5 men. These were all in the 26-50 years old age group, most of them belonged to the most deprived quintile and they were present in both of the 'probable suicide' and DRD cohorts. Most individuals received all three prescriptions (antidepressants, methadone and benzodiazepines), with the highest rate of psychiatric outpatient attendance, at a mean of 12.93 appointments in the year before death.

Cluster 2 had a silhouette width of 0.35, and contained 28 men and 5 women. Most of the individuals were in the two most deprived quintiles (SIMD 1 and 2), and they were all only in the DRD cohort. Both prescription and attendances rates were very low.

Next was cluster 7, with a silhouette width of 0.30, made up of 26 men and 4 women. This cluster was formed of people only in the two most deprived quintiles, and most of these individuals could be found in both cohorts. All individuals received both antidepressant and methadone prescriptions, and attended both psychiatric outpatient attendances and accident and emergency services at higher rates than many of the other clusters (6.17 and 2.17 respectively).

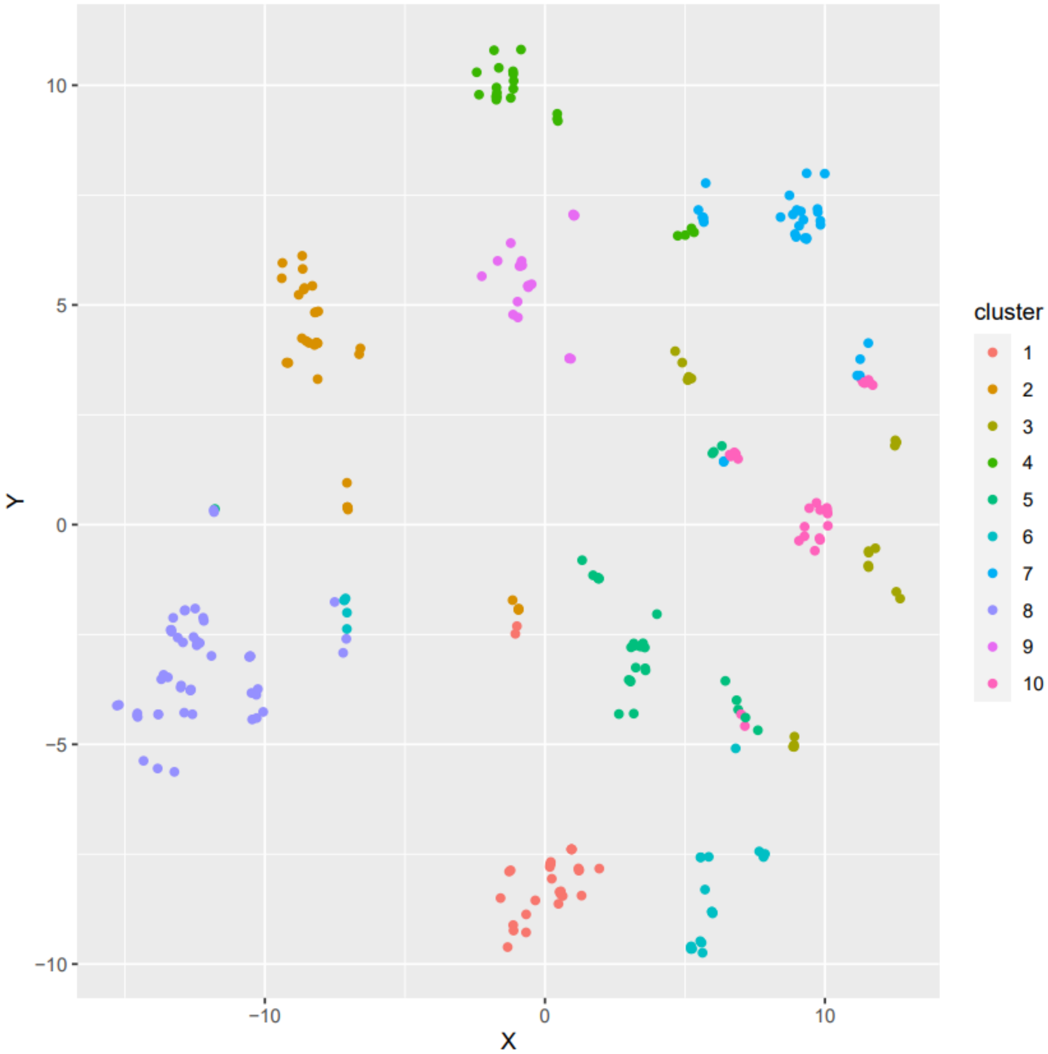
Cluster 6 had a silhouette width of 0.26, and contained only 24 women. Most of these women were in the 25 years old and younger age group, and generally were in the most deprived quintile. All individuals received an antidepressant prescription, however psychiatric outpatient attendances were very low at a mean of 1.08.

The second most dispersed cluster was cluster 5, with a silhouette width of 0.18, which was made up of 24 men and 5 women. Generally, these individuals could also be found in the ‘probable suicide’ cohort, but the demographic variables were less well differentiated than in the other clusters. The majority of these individuals received an antidepressant, and all of them received a benzodiazepine prescription, with high rates of psychiatric outpatient attendance and accident and emergency attendance—with means of 5.93 and 2.56, respectively.

The cluster with the lowest silhouette width was cluster 3, with a silhouette width of 0.17, despite being a small cluster of 14 women and 6 men. All of these individuals belonged only to the DRD cohort. This cluster was associated with high rates of all three prescriptions, and had the highest mean of accident and emergency attendance, at 3.15, of all the clusters. Mean psychiatric outpatient attendance was also high, at 9.75.

The average silhouette width for ten clusters within the DRD cohort was 0.38, and again the silhouette width varied significantly, however the lowest value was still higher than the lowest value of the ‘probable suicide’ only cohort. The most compact clusters were those with identifiable healthcare attendance patterns (e.g., all receiving either an antidepressant or a methadone prescription), or those with broadly low healthcare engagement.

Figure 6-6. Visualisation of Ten Clusters, including only DRD individuals



Visualisation of ten clusters, using all 288 DRD individuals. The clusters are transformed from a 3D space into a 2D space for the visualisation of the dispersion, using the t-SNE command in R, which prioritises maintaining the distance between data points, during the reduction in dimensionality. Here follows a list of co-ordinates for an approximate centre of each of the clusters: Cluster 1 (0, -8), Cluster 2 (-8, 5), Cluster 3 (12, -2), Cluster 4 (-2, 10), Cluster 5 (4, -3), Cluster 6 (6, -7), Cluster 7 (9, 7), Cluster 8 (-12, -3), Cluster 9 (-2, 6), Cluster 10 (10, 0).

6.4. Clustering analysis for the Combined Cohort

6.4.1. Introduction

The last clustering analysis included all of the individuals from both the ‘probable suicide’ and DRD cohort. As there was a significant overlap between the ‘probable suicide’ and DRD cohorts, totalling 197 individuals, and there are risk factors common to both types of death, an exploratory analysis was pursued to test whether there were particular patterns associated with both types of death.

6.4.2. Determining the Number of Clusters

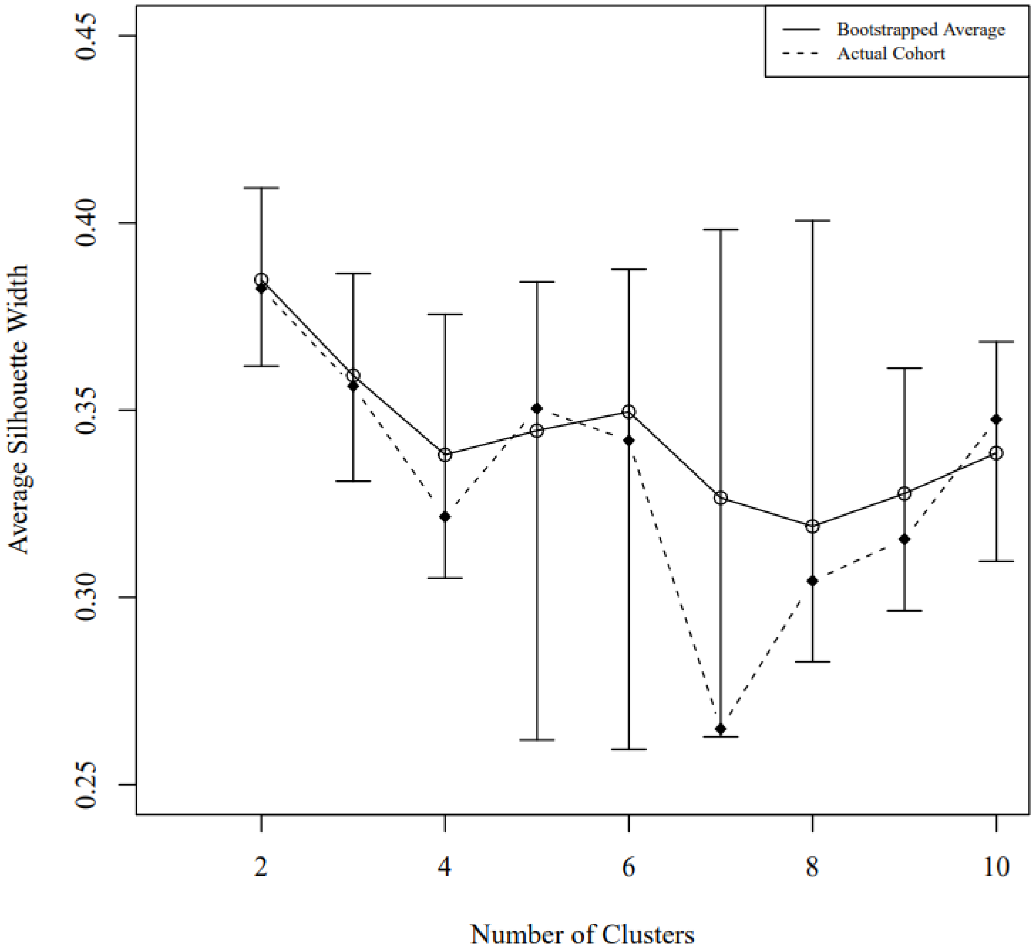
The silhouette width calculation, shown in Figure 6-7, reported values of under 0.40 for attempted identification of between 2 and 10 clusters; as such, the clusters identified are not very convincing. From this graph, the summary of two clusters and 10 clusters were extracted, for comparison with the other results. The smallest difference between the average silhouette width of the actual cohort and the bootstrapped average was when the attempted clustering had to identify only two clusters; this was to be expected as 2 clusters would represent the smallest scope for variation in clustering. The number of clusters least suited to the data, judging from the silhouette width graph, was 7.

6.4.3. Two Clusters including both cohorts

The summary of the results for two clusters showed that cluster 1 had the higher silhouette width, at 0.43 compared to 0.27 for the second cluster. As shown in Figure 6-8 below, cluster 1 was considerably larger than cluster 2, with 486 of the individuals belonging to it. The vast majority of cluster 1 were men, with very low rates of prescription and healthcare attendance, the medians for these variables were all 0—tables e1 and e2 in appendix 6 show the full output as printed by R.

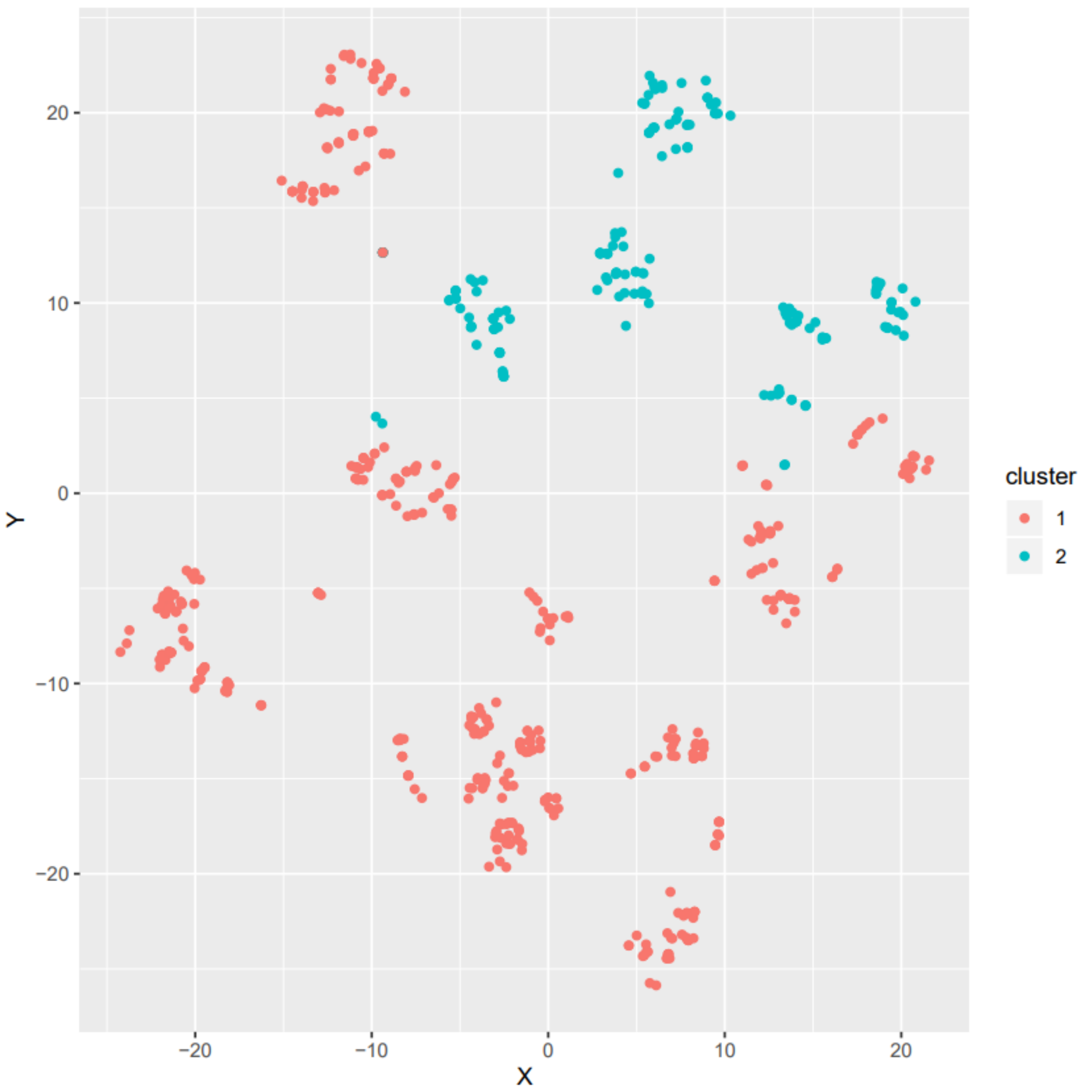
Cluster 2 was predominantly women, who were associated with antidepressant and benzodiazepine prescriptions and had a mean of 6.6 psychiatric outpatient attendances, over the year before death.

Figure 6-7. Average Silhouette Width, including the combined cohort



Average Silhouette Width graph across multiple clustering iterations, including all 677 individuals. Due to the unsupervised nature of the clustering algorithm, the first step involves a calculation of a “goodness of fit” measure, which is the silhouette width and runs from -1 to +1. This measure compares the average of distances between clusters and within clusters, thus quantifying the compactness of the clusters. An upper limit of ten potential clusters was chosen to ensure that clusters would have sufficient individuals to be clinically meaningful. The bars represent 95% confidence intervals.

Figure 6-8. Visualisation of Two Clusters, including the combined cohort



Visualisation of two clusters, using all 677 individuals. The clusters are transformed from a 3D space into a 2D space for the visualisation of the dispersion, using the t-SNE command in R, which prioritises maintaining the distance between data points, during the reduction in dimensionality. Cluster 1 is considerably larger and in red, while cluster 2 is smaller, occupies the upper right of the plot and is in teal.

6.4.4. Ten Clusters including both cohorts

Figure 6-9 demonstrates the distribution of the clusters, when all the individuals were included in the attempt to identify ten clusters. As before, the clusters will be described sequentially from highest to lowest silhouette width. A general overview of the clusters again shows a low healthcare usage group (10, 2 and 5), a group with specific healthcare engagement patterns (1, 3, 4 and 7), and a group with predominantly high healthcare usage (9, 8 and 6). Tables f1 to f10 in appendix 6 show the readouts from R.

Cluster 3 had the highest silhouette width at 0.54, and was one of the smallest clusters as it was only 35 women; all of these women had antidepressant and benzodiazepine prescriptions, additionally the median SIMD was category 4, indicating a lower level of deprivation than the majority of the cohort. Mean psychiatric attendance was 6.0 and accident and emergency presentations had a mean of 2.1.

Cluster 10 had the second highest value, with a silhouette width of 0.50, and was 74 men, who were all in the 51 years old and older category. This cluster was also associated with a slightly lower level of deprivation than the majority of the cohort (the median was SIMD 3). Prescription levels were very low. The mean of psychiatric attendance was 0.35, with accident and emergency presentations demonstrating a mean of 0.58 in this cluster, which were some of the lowest rates of attendance.

Next was cluster 1, with a silhouette width of 0.41, with 71 men and 2 individuals without demographic information. This group all received an antidepressant prescription, however no individual received either a methadone or benzodiazepine prescription. Attendance rates were quite low, with means of 1.7 for psychiatric outpatient clinics and 0.9 for accident and emergency presentations.

Cluster 9 had a silhouette width of 0.40 and contained 33 men and 3 women. The median SIMD was 1, suggesting high deprivation and the cause of death category median was 3, suggesting many of these individuals fulfilled the criteria for both ‘probable suicide’ and DRD. All individuals received both antidepressant and methadone prescriptions, with a mean of 6.3 psychiatric outpatient attendances and 1.9 accident and emergency presentations.

Cluster 4 had a silhouette width of 0.35, containing 41 men, 4 women and 3 individuals without demographic data. None of these individuals belonged to the least deprived SIMD quintile, suggesting significant deprivation in this cluster. All of the individuals had a methadone prescription. The mean number of psychiatric outpatient attendances was 7.6 and accident and emergency presentations had a mean of 1.5.

Next was cluster 2, which had a silhouette width of 0.33, and was formed of 193 men. It was the largest cluster, and as in the other clustering results, this group had some of the lowest rates of prescription and healthcare attendance—no individuals had antidepressant or methadone prescriptions—and no individuals were in the 51 years old and older age group.

Cluster 8 had a silhouette width of 0.28, and was quite small, with 30 women, 6 men and 1 individual without demographic data. This group had no individuals in SIMD 4 or 5, suggesting severe deprivation in this cluster, especially as the median was SIMD 1 (the most deprived quintile). Almost all individuals received antidepressant, benzodiazepine and methadone prescriptions. The mean number of psychiatric outpatient clinics was 12.5, with a mean of 2.0 accident and emergency presentations.

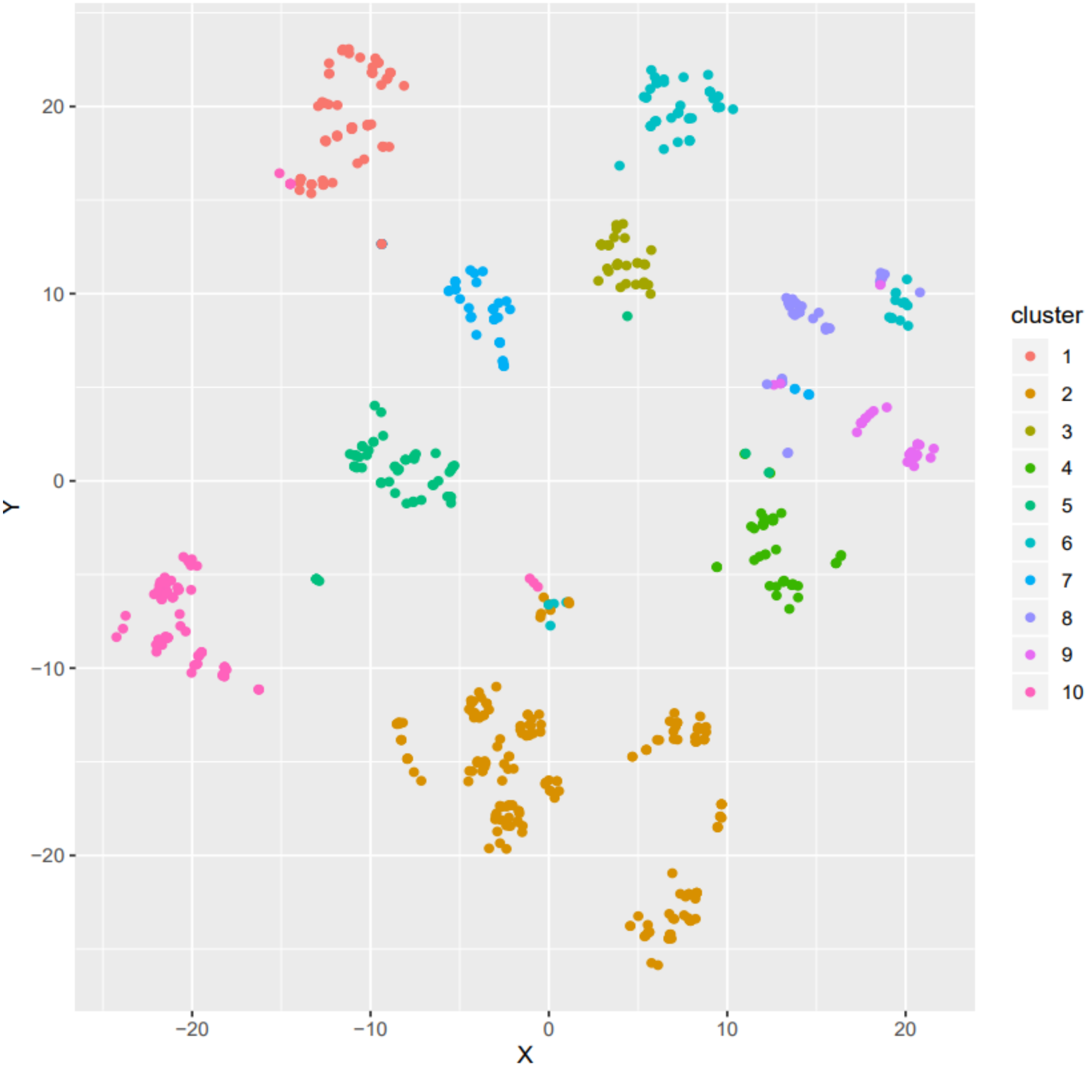
Cluster 5 had a silhouette width of 0.26, and contained 57 women, with 7 individuals without demographic data. The median SIMD was 3, which could suggest a slightly lower deprivation than average within this cluster. Very few individuals received any prescriptions, and the mean for psychiatric outpatient attendances was 0.69, with the mean for accident and emergency presentations being 0.45.

The second-most dispersed cluster was cluster 7, with a silhouette width of 0.24. It had 66 men and one individual with no demographic data. Generally, this cluster received antidepressant and benzodiazepine prescriptions, with a relatively high mean of 7.0 psychiatric outpatient attendances and 2.7 accident and emergency presentations.

The cluster with the lowest silhouette width was cluster 6 at 0.23. Cluster 6 was all men, with one individual was lacked a demographic record and another who lacked a SIMD score. Most individuals had an antidepressant prescription, and all had a benzodiazepine prescription. The mean was 6.9 psychiatric outpatient attendances, while the mean of accident and emergency attendances was higher than many other clusters at 2.7.

The average silhouette width for the combined cohort when isolating ten clusters was 0.35. The lowest silhouette width was higher than the lowest silhouettes widths for either the ‘probable suicide’ or DRD cohort alone, suggesting improved classification when all the individuals were included. The three most compact clusters represented one from each of the healthcare patterns—a high healthcare usage group, a very low usage group, and finally a group that all received antidepressant prescriptions but none received either methadone OST or benzodiazepine prescriptions.

Figure 6-9. Visualisation of Ten Clusters, including the combined cohort



Visualisation of ten clusters, using all 677 individuals. The clusters are transformed from a 3D space into a 2D space for the visualisation of the dispersion, using the t-SNE command in R, which prioritises maintaining the distance between data points, during the reduction in dimensionality. Here follows a list of co-ordinates for an approximate centre of each of the clusters: Cluster 1 (-10, 20), Cluster 2 (0, -15), Cluster 3 (5, 10), Cluster 4 (12, -5), Cluster 5 (0, -10), Cluster 6 (8, 20), Cluster 7 (-3, 10), Cluster 8 (15, 10), Cluster 9 (20, 2), Cluster 10 (-20, -7).

6.5. Discussion of Clustering Analysis

6.5.1. Summary of Findings

This section of the thesis has considered several key aspects concerning the previously published taxonomies of ‘probable suicide’ and DRD. First, there is a significant breadth of theoretical typologies of ‘probable suicide’; few of these have been empirically tested and therefore, few of these are clearly applicable or beneficial in a clinical context. Second, the literature concerning typologies of DRD is much more limited, though there have been studies aimed at improving the targeting of preventative strategies by identifying geographical areas with high-risk populations. Third, several factors could be repeatedly identified as contributing significantly to clustering analyses, especially demographic variables, like gender and age, and psychiatric healthcare histories often had distinct distributions across clusters.

Following the literature review, a clustering analysis was performed using the previously described cohorts of ‘probable suicide’ and DRD; additionally, these were combined to examine the degree of overlap and investigate the broader concept of deaths of despair. In all three cohorts, the results for the two-cluster analysis clearly identified a low healthcare engagement and high healthcare engagement group, with key demographic differences associated with healthcare usage. Each of the three cohorts was then further investigated and split into ten clusters. These clusters varied significantly in their level of overlap and dispersion; however, several interesting patterns were identified. Notably, when all of the individuals were analysed in the combined cohort, no cluster contained individuals of only one cause of death category. Additionally, parallel clusters of low engagement, those with unique patterns of attendance at certain services and those with broadly high attendance could be isolated in the ten-cluster analysis of all three cohorts.

6.5.2. Limitations of the Clustering Analysis

There are some key limitations to bear in mind when interpreting the cluster analyses. First, I was unable to include variables that have been regularly shown to be likely risk factors for both ‘probable suicide’ and DRD. Specifically, these include information on factors like histories of trauma, homelessness, employment and history of exposure to either ‘probable suicide’ or drug use in family or peers

(Congdon, 2019). Data on homelessness and employment were theoretically made available from Local Authority datasets (see Higgins and Matthews, 2020), however the meta-data file explaining the coding system and how to interpret the data was missing. Attempts were made to decipher the codes, based on similar files from Perth and Kinross Council, though the data systems were not precisely the same. To avoid introducing unverified data into the study, I chose not to include any data from the Local Authority administrative feeds.

The studies described above were specifically able to include diagnoses of mental health or substance abuse in past medical records (e.g., Clapperton et al., 2018, Sinyor et al., 2016 and Sinyor, Schaffer and Streiner, 2014). The data available in HIC did not contain histories of diagnosed conditions for any of the patients, therefore, as in the previous healthcare analysis chapters, prescriptions of interest were used as markers for relevant conditions. Antidepressant prescriptions were used as a proxy for depression, a methadone OST prescription as a proxy for opioid misuse and benzodiazepines for additional psychiatric concerns, like anxiety disorders, which could require further sedative drug prescriptions. As such, when the clusters identified in my study are compared with those who used diagnoses to code mental health sub-groups, it is impossible to be certain that the comparison is truly 'like-for-like'.

Additionally, many of the variables were in binary format: sex, 'probable suicide' or DRD type of death (in their separate analyses, though not the combined cohort), antidepressant, methadone and benzodiazepine prescription. This could have artificially constricted the data to best fit a two-cluster model, especially as it could have over-simplified the data by removing dimensions around treatment changing over time. For example, especially in OST prescribing, patients often cycle in and out of treatment, with significantly different risk profiles for death depending on their current status (Sordo et al., 2017, Santo et al., 2021). Only thirty individuals with a history of methadone did not receive a prescription in the month before their date of death. Introducing one extra layer to the methadone and antidepressant prescription variables, for example, could have simply artificially constricted the data to a three-cluster model. Furthermore, many of the previous studies used predominantly dichotomous variables and did not report that two clusters were the best fit for the data (e.g., Sinyor, Schaffer and Streiner, 2014, O'Connor, Sheehy and O'Connor, 1999, Bagley, Jacobson and Rehin, 1976). This being the case, it would suggest that the two-cluster model may be genuinely the model that categorises the data in this thesis most effectively, rather than it representing an unintended consequence of the data format.

There are no universally agreed-upon bounds when considering silhouette width, however as a general guideline, some authors report that an average value of over 0.50 is a good solution, while between 0.20 and 0.50 suggests a fair match to the data. Lower values suggest significant disparity and poor coherence of the clusters identified (Mooi and Sarstedt, 2011, Clapperton et al., 2018). This would suggest that, generally, the clustering approach used and the potential number of clusters searched for was a fair clustering solution, though not necessarily one that explained the majority of the variance, as the average silhouette width was approximately 0.35. Only four clusters had a silhouette width below 0.20, which were the final two in the 'probable suicide' cohort and the final two in the DRD cohort. Cluster 5 in the 'probable suicide' cohort analysis especially had a very low silhouette width. These results suggest that these clusters were too dispersed to represent a valid group, and may represent a collection of outliers.

Additionally, even the full combined cohort has a relatively small sample size of only 677 individuals, all gathered from one city in Scotland over the course of five years. This study likely reflects contexts and factors relevant to the time, that may have since developed (e.g., clinical recommendations on benzodiazepine prescribing, which are now advised only when there is no other alternative in the MHRA Guidance https://cpd.mhra.gov.uk/benzodiazepines/CON234573_4). These clusters would need to be tested in considerably larger samples to test their true validity and generalisability for the wider development of taxonomies of 'probable suicide', DRD and their shared healthcare profiles.

6.5.3. Interpretation of the Silhouette Width Graphs

That the silhouette width graphs of the 'probable suicide' cohort and the combined cohort were so similar was only to be predicted; the total cohort was 677, while the probable suicide cohort was 586 and, therefore, the vast majority (87%) of the combined cohort. As such, it would be hypothesised that the same number of clusters would be calculated as the most appropriate, which was two for both the 'probable suicide' and combined cohort analyses. This could suggest that constructing a basic typology of 'probable suicide', and arguably deaths of despair, is simpler than might have been anticipated. Or, as discussed, it could be an artefact of the data coding system, which is that many of the variables were in a binary format. This is unlikely, as the appropriateness of the two-cluster model presumably simply reflects an intuitive idea that those engaged with one healthcare service are more likely to be engaged with other services as they become necessary, compared to those broadly disengaged. That the average silhouette width seemed to rise at, and after, an 8-cluster solution for both the 'probable suicide' cohort and combined cohort does suggest that there are more subtle patterns of healthcare usage, which are worth investigating despite the small cluster size.

That the DRD silhouette width graph was so distinctive was unanticipated. The population of people who use drugs are often described as "chaotic", and therefore, it is arguably intuitive that there was greater variation in the profiles of people in this cause of death category. Overall, the average silhouette width was slightly lower than for the 'probable suicide' cohort and combined cohort analyses, which could also be caused by a more heterogeneous sample of individuals.

6.5.4. Interpretation of the Two-Cluster Models

In all three cohorts, cluster 1 had the higher silhouette width, which is representative of greater internal coherence and less dispersion. This cluster was also always larger than cluster two, and contained a majority of men with very low healthcare engagement rates across the board; this was especially noticeable for the key treatment drugs examined, both of which were at almost 0 (e.g., the 'probable suicide' cohort has a value of 0.19/1 for the rate of antidepressant prescription, 0.30/1 in the DRD cohort and 0.23/1 in the combined cohort). Cluster two, by comparison, was more dispersed, had fewer individuals and many more of these were women, who made up between 40-60% of this cluster. This was the high engagement group, with the rate of antidepressant prescriptions in the cluster being 0.96/1 in the 'probable suicide' cohort, 0.96/1 in the DRD cohort and 0.97/1 in the combined cohort. Cluster two also had higher rates of benzodiazepine prescription than cluster one.

To a degree, both of these clusters were predictable, as they have been well-established in the literature. For example, they reflect the first step of the clustering analysis described by Clapperton et al. (2018), which broadly identified two clusters, one with a mental health diagnosis and the other cluster without. In that study, the "mental illness" group all had a diagnosed mental illness, with the majority receiving some psychiatric healthcare in the last year. This group also had a higher percentage of women than the cluster without a mental health diagnosis. As such, that the high healthcare engagement cluster, with recognisable mental health concerns had a greater proportion of women is unsurprising; it is commonly reported that women attended healthcare services, especially psychiatric services, at higher rates than men (Hamdi et al, 2008, Cho et al, 2013, Tang et al., 2022). Psychological studies report that men are less willing to access healthcare services due to certain restrictive assumptions of masculinity (Galdas, Cheater and Marshall, 2005, Chandler, 2021). Men are not a homogenous population and there have been suggestions that logistical difficulties, like GP services being open predominantly during hours that men are at work, are partly to blame for the healthcare presentation difference (Kennedy, 2001). This argument has some merit, as the provision of 24-hour crisis care was associated with the largest fall in suicide rates, compared to other psychiatric health service modifications (While et al., 2012).

Cluster one, which was the larger cluster, containing overwhelmingly men with low healthcare usage represents the non-mental illness diagnosis group from the Clapperton et al. (2018) study. It may also be loosely correlated with the high-intent group from Chen et al. (2007), in which very low levels of psychiatric healthcare were recorded, and which was associated with significant personal distress (debt in Chen et al.'s study, and a variety of inter-personal concerns in Clapperton et al.'s study). Regular studies attempting to ameliorate the stigmatisation of mental illness or people who use drugs are published, with a view to increasing healthcare attendance that the stigma may otherwise inhibit (Stuart, 2016). These studies often implicitly suggest that healthcare services can and should be doing more to reach at-risk individuals, and suggest that healthcare service initiatives are sufficient for prevention of both 'probable suicide' and DRD. Without reliable taxonomies that improve our understanding of the variety of risk profiles commonly seen, identifying people who "ought" to be in treatment is impossible. Additionally, as emphasised repeatedly throughout this thesis, the available treatments have limited capacities to reduce either 'probable suicide' or DRD according to several meta-analyses (Fox et al., 2020, Sordo et al., 2017, Santo et al., 2021). Some of the most effective interventions to prevent these deaths have been at the wider societal level via means restriction (Zalsman et al., 2016, Lim et al., 2021). These facts all point towards the need for different interventions than those that are ‘treatment-as-usual’, especially those that acknowledge that there are many social and personal stressors that the healthcare service is not equipped to handle, for example, severe socio-economic deprivation (Chandler, 2021, Congdon, 2019, Pirkis, Nicholas and Gunnell, 2020).

6.5.5. Interpretation of the Ten-Cluster Models

In all three cohorts, there were three general types of clusters: those with low healthcare usage, those with patterns of attendance at specific services, and those with broadly high engagement at healthcare services. These parallel clusters will be grouped and discussed under these categories, to contrast any potential differences in the demographic groups and healthcare patterns of these clusters.

6.5.5.1. Interpretation of the Low Healthcare Usage Clusters

Within the ‘probable suicide’ cohort, 4 clusters had very low rates of healthcare engagement: clusters 3, 10, 5, and 4. Within the DRD cohort, only two clusters had very low rates of healthcare engagement (8 and 2). For the combined cohort, three clusters had low rates of healthcare usage, which were clusters 2, 5, and 10. This is an intuitive result based on the relative sample sizes and degree of overlap; the ‘probable suicide’ cohort was much larger than the DRD cohort, with the combined cohort being primarily the ‘probable suicide’ cohort.

The largest cluster in the ‘probable suicide’ cohort was cluster 3, which was only men, who were possible slightly younger on average than the other clusters and were very disengaged. Likewise, within the DRD cohort, the largest cluster was cluster 8, though the cluster had three women, and all of the individuals overlapped with the ‘probable suicide’ cohort. For the combined cohort, the largest cluster was cluster 2, which again was only men, none of which were in the 51 years old and older age group. None of these individuals, across any of the cohorts, received an antidepressant prescription, while benzodiazepine prescription rates were at 0.04/1. This group can be seen as analogous to the first cluster in the two-cluster model above, which was overwhelmingly composed of men with low healthcare attendance, and reflect the results of O'Connor, Sheehy and O'Connor (1999), Sinyor, Schaffer and Streiner (2014) and Clapperton et al. (2018). Possible psychological and logistical reasons have been discussed for this profile, but it is worth emphasising again that this was the largest cluster in all three cohorts. Any discussion aiming to reduce the number of these types of death that primarily focuses on optimising the provision of healthcare may continue to be less fruitful than desired, considering the lack of healthcare engagement for a large part of the cohort. These large clusters of individuals who are not engaged with the healthcare service indicate that prevention of these types of deaths cannot solely be the responsibility of the healthcare system. Wider systematic factors associated with premature death must be examined more closely to clarify their contributions and identify possible interventions (Sterling and Platt, 2022, Congdon, 2019).

A similar cluster for the 'probable suicide' and DRD cohorts could be isolated that was fairly small, suggestive of a higher-than-average number of young men belonging to the quintiles of severe deprivation and who possibly presented at Accident and Emergency services once in the year before death. These were cluster 10 in the 'probable suicide' cohort and cluster 2 in the DRD cohort. Curiously, a similar cluster could not be identified in the combined cohort ten-cluster model, despite these clusters having high silhouette widths in the analysis of the separate cohorts. High levels of deprivation are associated with poorer health, which may in turn be associated with greater use of emergency healthcare, due to more urgent healthcare needs (McCormick, Hill and Redding, 2018). These clusters likely reflect individuals reported in other studies, for example in Amundsen (2015), who reported a group of young men that belonged to a group receiving a high level of means-tested benefits.

The next set of parallel low healthcare usage clusters was an unanticipated group of only women, with a higher-than-average socio-economic level (with a mean indicating SIMD 3), and likely with a greater proportion of women in the youngest age groups. These were cluster 5 in both the 'probable suicide' cohort and combined cohort. The majority of the cause of death codes were 'probable suicide' specific. No other clustering studies seem to have identified this sub-group, as generally the clusters with a higher proportion of women were those with mental health diagnoses, rather than those without mental health records of any kind (Sinyor, Schaffer and Streiner, 2014, Clapperton et al., 2018, Logan, Hall and Karch, 2011). This may highlight the potential issue, noted by Chandler (2021), in which distress expressed by women may be more easily disregarded, due to the emphasise on how much more challenging it is for men to access healthcare. As healthcare services are necessarily limited by funding and personnel, the focus on men's mental health will have to be carefully managed to prevent similar unforeseen consequences.

Another two similar clusters were a group of older men (51 years old and older), who again had a median SIMD that indicated average socio-economic circumstances, rather than severe deprivation. This was cluster 10 in the combined cohort and cluster 4 in the 'probable suicide' cohort. These were two of the only three clusters identified in which all individuals belonged to only one age group. This older group of men may be linked with cluster 2 in Sinyor, Schaffer and Streiner, (2014), who were an older group, with low rates of mental health diagnoses, few had prior suicide attempts and the majority were married—these constitute a theoretically "low-risk" group. Clapperton et al. (2018) also identified a group of older men without a mental health diagnosis in their first sub-cluster (B1), and this group were associated with physical health stressors. Similar data for these variables were unavailable for the individuals included in this study, however a risk of 'probable suicide' has been linked with recent diagnoses of physical health concerns, for example the first 6 months of a cancer diagnosis are thought to be particularly high-risk periods (Henson et al., 2019). This could be the possible explanation for this group, though without greater data resources, this can be no more than speculation, based on other publications in the field.

6.5.5.2. Interpretation of the Unique Healthcare Pattern Clusters

All of the cohorts had four clusters that had distinctive patterns of healthcare usage, however only two of these clusters were common to all three cohorts. Within the 'probable suicide' cohort, the 4 clusters with noteworthy patterns were clusters 1, 8, 2, and 9. Within the DRD cohort, the clusters were numbers 1, 9, 6 and 4. For the combined cohort, the specific patterns were noted in clusters 1, 4, 3 and 7.

A common cluster in all three cohorts was cluster 1 in each analysis. This cluster was a group of entirely men in the combined and DRD cohort analyses, with 1 woman and 8 individuals lacking demographic data in the 'probable suicide' cohort. Everyone in this cluster received an antidepressant prescription and had, on average, 2 psychiatric outpatient attendances throughout the year. Presentation to Accident and Emergency services was also approximately 1 for each cluster. These common clusters may represent a relatively traditional group of men, known to the healthcare service to a degree; the rate of psychiatric outpatient attendances was low in terms of those receiving psychotropic prescriptions, therefore this could theoretically represent a group of men who were not entirely compliant with treatment. Adherence to treatment is notoriously low, which is problematic in different ways for the different populations. Antidepressants have a relatively gradual impact at the beginning of the treatment course; while concerning opioid misuse in particular, there is the risk of continued illicit drug misuse and potentially overdose if illicit use is not recognised by the healthcare service. As such, several studies have been developed to optimise treatment provision of both prescriptions and attempt to reduce non-adherence, especially in key contexts like antidepressant prescribing in primary care (Cameron et al., 2014, Solmi et al., 2021) or OST accessibility in prisons (Alam et al., 2019).

Reflecting the other relevant prescription examined throughout this thesis, another cluster common to all three cohorts was a group of predominantly men, with 3 or 4 women, who all received a methadone OST prescription, but rarely any other prescription. The rate of psychiatric outpatient attendances averaged between 5-8 over the year. These were cluster 8 in the ‘probable suicide’ cohort, cluster 9 in the DRD cohort and cluster 4 in the combined cohort analysis. As noted, psychiatric outpatient attendances could not be distinguished between mental health or substance misuse appointments, however it seems valid to classify this cluster as the predicted, traditional profile of men who died due to substance misuse. Substance misuse is a chronic condition, which greatly increases the risk of all-cause and specific overdose-mortality risks and this risk is only partially ameliorated by OST (Santo et al., 2021). As such, it is regularly noted that OST has only limited reductions in DRD, and that a notable percentage of those who die are in treatment; the NDRDD report (2022) found that at least 41% were in treatment at the time of death, and 58% had been in treatment since 2009. Additionally, the NDRDD note this percentage could be an underestimate due to limitations on data collection. This profile suggests that simply an OST prescription is insufficient to prevent mortality, and such patients require both optimised treatments, and, very likely, additional psycho-social support.

One similar cluster between only the ‘probable suicide’ cohort and the combined cohort was a group of 34 or 35 women respectively, who all received both an antidepressant and a benzodiazepine prescription in the year before death, while none received a methadone OST prescription. These clusters were in the less deprived quintiles, with a median of SIMD 4 across both cohorts and slightly older than the average. In the ‘probable suicide’ cohort, this was cluster 2 and it was cluster 3 in the combined cohort. This could represent the anticipated group of women with depressive disorder diagnoses, that often are recorded as non-violent self-poisoning deaths (Sinyor, Schaffer and Streiner, 2014, O’Connor, Sheehy and O’Connor, 1999). Reflecting the conclusion of the previous profile, that this group has been identified since 1999 suggests that as well as strategies to improve antidepressant prescribing and adherence (Cameron et al., 2014, Solmi et al., 2021), further psycho-social interventions are required to prevent death by ‘probable suicide’.

The clusters which showed similarities between only the DRD and combined cohorts was again a subset of women, most of whom received an antidepressant prescription and very rarely received any other prescription. These were cluster 6 in the DRD analysis and cluster 7 in the combined cohort. The cluster in the combined cohort seemed to have somewhat older individuals, who lived in slightly less deprived quintiles than the DRD-only cluster. The primary distinguishing feature between this group of women and those above seems to be that these clusters are associated with poverty and drug misuse, leading to classification as a DRD, compared to the clusters of women from less deprived quintiles, with an additional sedative prescription who were classified as ‘probable suicide’ decedents. Health inequality has widened significantly in the UK over the past decade (Marmot et al., 2020), and the data in the previous healthcare comparisons suggest that treatment may vary across socio-economic groups. Furthermore, there has been a notable increase, in Scotland, in the number of women dying from drug-related causes (Tweed et al., 2022). Further research is required to understand the precise contribution of socio-economic deprivation, health and healthcare inequality on increasing DRD, both in Scotland and worldwide.

Cluster 9 from the ‘probable suicide’ cohort analysis seems not to have a clear analogue in either the DRD or combined cohort analyses. It was a mixed group of men and women, all of whom received an antidepressant prescription, had a higher-than-average proportion of individuals in the youngest age group and attended on average 2 psychiatric outpatient appointments. All of these deaths overlapped with the DRD cohort, but did not present as a cluster in that analysis, which suggests that when combined and compared with other DRDs, these individuals could be subsumed into alternative groupings. This highlights the concern with clustering studies generally, which is that many alternative clusters can be extracted, depending on whether variables are weighted differently and what sample are included.

Finally, there was a small, unique cluster in the DRD cohort analysis, which was cluster 4. This cluster also contained individuals who all received a methadone OST prescription, however, there was a mean of 11 psychiatric outpatient attendances, which is considerably higher than the well-established methadone-prescribed cluster described above. Additionally, the cause of death codes in this sub-group were specifically DRD, which suggests this group may have been recorded under codes indicating death from substance misuse disorders, rather than a poisoning code of some kind. None of the individuals were in the least deprived quintile, which again conforms to the hypothesised connections between more severe deprivation and substance misuse (Congdon, 2019).

6.5.5.3. Interpretation of the High Healthcare Usage Clusters

Interestingly, four of the clusters identified in the DRD analysis and three in the combined cohort analysis had broadly high engagement with a variety of healthcare services, compared to only two of the ‘probable suicide’ clusters. The silhouette width graphs implied that the DRD cohort had greater internal variety, which is corroborated by the presence of clusters that do not correspond, even loosely, to clusters from the ‘probable suicide’ analysis.

The first common group to all three cohorts was a cluster with all three prescriptions present at high rates (i.e., antidepressant, methadone and benzodiazepine prescriptions were all redeemed in the year before death), and an average of 10-13 psychiatric outpatient appointments. These were cluster 7 of the ‘probable suicide’ cohort, cluster 10 of the DRD cohort and cluster 8 of the combined cohort analysis. These clusters likely contained almost the same individuals, as the cause of death codes overwhelmingly overlapped between cohorts, and all clusters had between 22-32 women and between 5-10 men. Co-morbidity of mental health concerns and substance abuse is relatively commonly reported (Abrahamsson et al., 2017), and was also reported in over half of the ‘probable suicide’ and DRD cohorts in the previous healthcare attendance sections. These co-prescriptions are associated with an increase in DRD risk (McCowan, Kidd & Fahey 2009), that is further augmented by higher doses of the additional medication, perhaps due to the potentiation of respiratory depression (Macleod et al., 2019). That this sub-group of high healthcare usage individuals was predominantly women who were receiving methadone is of particular interest, as recent literature has emphasised the increased burden of disease that women face, due to biological sensitivities to opioids, and therefore the need to adapt OST provision to account for these gender differences (Bawor et al., 2015, Hernandez-Avila, Rounsaville and Kranzler, 2004, Tweed et al., 2022). Another possibility for this group is that it could represent a group of individuals with borderline personality disorder, who are associated with high healthcare usage, which is even higher for women than men (Sansone, Farukhi and Wiederman, 2011). This cluster received a high number of prescriptions and attended services regularly, which conforms to the anticipated pattern for individuals with borderline personality disorder, however there are no psychotropic prescriptions specifically indicated for its treatment. These additional prescriptions are likely prescribed for the mental illnesses that are regularly co-morbid with this disorder, like depression, anxiety and substance misuse (Leichsenring et al., 2023). Personality disorders are relatively uncommon, difficult to diagnose and have few treatment options for their primary symptoms. As such, while HIC lacked the diagnostic data that would clarify the actual needs of these patients, further clustering studies with diagnostic data or that followed these patients over time could research these patients and their treatment outcomes more fully. If these individuals could be regularly identified, various combinations of psychotherapies and psychotropic prescriptions could be trialled and compared on their efficacy and patient acceptability. The potential for future research based on these hypotheses demonstrates the value of clustering studies that can identify distinct sub-groups, which may require specialised treatment plans.

The second common cluster to all three cohorts was a group of predominantly men who all received a benzodiazepine, very frequently also redeemed an antidepressant prescription and yet very rarely had a methadone OST prescription. This was cluster 6 in the ‘probable suicide’ analysis, cluster 5 in the DRD analysis and cluster 6 in the combined cohort. This group also had an average of approximately 6 or 7 psychiatric outpatient appointments, which suggests relatively regular engagement that would be appropriate for patients with psychotropic co-prescriptions. These were all clusters with low silhouette widths of 0.23 (in the combined cohort) or less. Due to the degree of overlap between the cohorts, and the similar healthcare patterns extracted from the clustering analysis, it is likely these clusters represent a common group of outliers. Alternatively, benzodiazepine prescriptions are commonly associated with women, therefore, it may be of interest that this atypical sub-group was primarily men with benzodiazepine and antidepressant prescriptions (Landolt et al., 2021). Further research into sedative prescriptions and how to prescribe them safely are required. This could be achieved via longitudinal studies, and if they included psychological measures, these could likewise attempt to uncover the degree to which the adverse health conditions associated with benzodiazepine prescriptions are simply confounding by indication. Mixed-methods research could also encompass database and interview-based studies, which would also have the qualitative data required to examine whether the prescriptions indicated severity of illness or dangerous prescribing practices.

The last shared cluster was only between cluster 7 in the DRD group and cluster 9 in the combined cohort. These were well-differentiated groups of mainly men, generally in the youngest age group and who all received both an antidepressant and a methadone OST prescription. Both clusters had a mean of 6 psychiatric outpatient appointments and 2 Accident and Emergency presentations. This group belonged overwhelmingly to SIMD 1, indicating severe deprivation, as well as mental illness and substance abuse co-morbidity. As has been noted many times, both mental illness and drug use are highly associated with deprivation, and these associations may have a greater impact on men than women (Barr et al., 2012, Cairns et al., 2017, Sterling and Platt, 2022). That there was a consistent profile of younger men engaged with healthcare services is promising, and it may be worthwhile for future research to investigate their pathways into healthcare service engagement and attempt to facilitate these pathways for younger men who are disengaged.

Finally, a seemingly unique cluster in the DRD cohort analysis was cluster 3, which was a very small cluster of only 20 individuals, 14 of which were women. Generally, this group received all three prescriptions, had a mean of approximately 10 psychiatric outpatient appointments and presented to Accident and Emergency services 3 times. This group seems primarily to be distinguished from other similar clusters, like DRD cluster 10, because all of the individuals had cause of death codes specific to DRD. As previously mentioned, there are suggestions that women with substance misuse problems require unique support (Tweed et al., 2022) and that healthcare services must adapt to changing contexts. Many services primarily target the demographic of younger men who inject heroin—itself a demographic that has changed over time and no longer represents the modal presentation of men to these services (Bawor et al., 2015, Hernandez-Avila, Rounsaville and Kranzler, 2004). These changing demographics emphasise the importance of understanding, and regularly updating, the profiles of individuals who die via 'probable suicide' or drug-related causes, as clarifying the antecedent profiles could signpost the patient needs for which research is required to develop more effective interventions. As these profiles would be influenced by local and national contexts, further clustering studies locally, nationally and internationally would be required to test the wider value and applicability of this method and these clusters.

6.6. Summary of the Clustering Analysis

This chapter summarised previous reports into the profiles of ‘probable suicide’ and DRD, as identified through theoretical or statistical clustering approaches. Significantly more literature could be found examining profiles within ‘probable suicide’; generally, the clusters identified were those with a history of psychiatric healthcare and those without. Sub-groups depending on demographic data, and physical illness were occasionally identified. Studies attempting to define a taxonomy of DRD were fewer in number. One key study reported 3 clusters; a higher education group, a lower education group and a group with a higher prevalence of disability pension. Few studies explicitly acknowledged the overlap between ‘probable suicide’ and DRD, despite healthcare histories of substance abuse treatment or deaths of intentional self-poisoning being reported.

Following on from the healthcare analyses contained in the previous analytical chapters, the deceased individuals were extracted from the larger cohorts. Initially, the ‘probable suicide’ and DRD cohorts were analysed separately, then a combined cohort was created and investigated. Using a clustering method designed to standardise variables of several data types, both demographic and healthcare variables were used to calculate differences between individuals. The average of these differences was used as a distance measure. An algorithm was used that randomly chose a specified number of individuals to be the centres of a cluster, and then grouped data by minimising the average distance within each cluster. This was run iteratively to create a goodness-of-fit measure running from 2 to 10 clusters.

The goodness-of-fit measure suggested that a two-cluster model was the best fit for the ‘probable suicide’ cohort and for the cohort combining both this group and the DRD cohort. These clusters broadly represented low and high healthcare engagement, with the low engagement cluster being the largest and the most compact cluster of the two. Where the DRD cohort only was analysed, the goodness-of-fit measure showed an improvement in appropriateness for the data up to the ten-cluster model, which had been set as the limit.

Ten clusters were extracted from the ‘probable suicide’ cohort and the combined cohort for the purposes of comparison with the DRD cohort, and for a fuller investigation of the value of this exploratory analysis. These ten clusters, in each cohort, could be broadly categorised into a group of clusters representing low healthcare usage, a group of clusters with attendance or prescription of a specific type of healthcare, and a third group of clusters with broadly high rates of healthcare engagement. Several of these clusters would have been predicted, based on current understanding of the healthcare profiles of those who die by ‘probable suicide’ or drug-related causes, however some of the groups could not be identified in previous literature. These may represent novel sub-groups that could be refined and incorporated to taxonomies of ‘probable suicide’, DRD and the common category known as “deaths of despair”. With further validation in larger datasets, and in cohorts from different countries, this method may improve our ability to target preventative strategies appropriately and act to prevent deaths in a more efficacious and efficient manner.

7. Conclusion

This chapter will summarise the key findings from the thesis, in relation to the aims stated in the introduction. These four aims were:

1. To interrogate the statistical definitions of ‘probable suicide’ and DRD in governmental reports
2. To compare the antecedent healthcare usage and prescription rates of a ‘probable suicide’ cohort with a matched community control cohort
    a. To divide the cohorts into relevant sub-groups for further comparison, e.g., those receiving antidepressant prescriptions and those in living in areas of high or low socio-economic deprivation
3. To compare the antecedent healthcare usage and prescription rates of a DRD cohort with a matched community control cohort
    a. To divide the cohorts into relevant sub-groups for further comparison, e.g., those receiving methadone OST prescriptions and those living in areas of high or low socio-economic deprivation
4. To consolidate and compare extracted sub-groups of ‘probable suicide’ and DRD with clusters identified from clustering or taxonomical literature

These aims were met using a variety of statistical techniques, from simple chi-square analyses to a clustering algorithm. The answers uncovered are important in the context of increasing numbers of deaths attributed to ‘probable suicide’ and DRD, both worldwide and in Scotland. Other research groups have suggested this could be due to deficits in healthcare provision, and preventative campaigns regularly promote the increased usage of mental healthcare and OST for the individuals at-risk of these types of death, respectively. There are meta-reviews of healthcare usage by those who die via ‘probable suicide’ or drug-related causes, but they have not analysed the number of services or prescriptions included in this study, made available through the use of routine, administrative data linkage. As such, the results in this thesis provide real world data, with which the assumptions of inaccessible and insufficient healthcare can begin to be interrogated.

7.1. Defining ‘Probable Suicide’ and DRD

As a key, initial piece of context, the standardised system used to code causes of death was briefly discussed. This global system allows for comparable international statistics; however, the medico-legal investigations within each country, and the data infrastructure available, will inevitably result in differences that affect the comparability of deaths categorised as ‘probable suicide’ or drug-related in each country. Additionally, there are theoretical inconsistencies in the conceptualisations of ‘probable suicide’ and DRD, both separately and as related phenomena. Deaths caused by poisonings or injuries of undetermined intent are included in ‘probable suicide’ statistics in some countries, though not universally. Defining a DRD consistently is impeded by the emphasis on considering only illicit substances. The potential overlap between ‘probable suicide’ and DRD in cases of overdose death has been under-acknowledged in the discussion of prevention strategies, though these links are beginning to be explicitly stated.

Specifically focusing on statistical publications in Scotland, serious inconsistencies were found in the ScotSID database, where over 200 individuals, all of whom appeared to fulfil criteria, were excluded. As the individuals excluded were associated with severe socio-economic deprivation, it may be that current publications informing policy under-represent the strength of the association between poverty and ‘probable suicide’. Relative to DRD, considerably fewer individuals were excluded by the organisations publishing statistical reports, however there are still important theoretical concerns respective to the inclusion only of deaths in which an illicit substance was involved, and that the list of illicit substances grows over time, resulting in shifting criteria.

As an important note, the analyses completed were only possible due to the efforts of HIC and those described by Higgins and Matthews (2020), which demonstrated the feasibility of collecting and linking data from a variety of sources. While unfortunate that the additional local authority and criminal justice datasets were unavailable, this thesis further illustrates and corroborates the merits of routine administrative data in research. As regional and national Safe Havens exist within Scotland, further research of this kind would be easily facilitated. This would improve the level of detail included in yearly statistical reports, and ensure that matched control groups could be used appropriately to quantify past-year healthcare usage.

7.2. Healthcare Analysis

The variety of comparisons that could be made both between the deceased and control cohorts, and within the ‘probable suicide’ and DRD cohorts was a significant strength of the routine data approach. Meta-analyses have highlighted a lack of appropriately chosen control groups, thus limiting the understanding of how the patterns between those who die of ‘probable suicide’ or DRD may diverge from the community pattern (Stene-Larsen and Reneflot, 2017, Lewer et al., 2020). This thesis has demonstrated that there are distinct patterns, and that, overwhelmingly, the ‘probable suicide’ and DRD cohorts attended all services (general hospital inpatient visits, psychiatric and non-psychiatric outpatient visits, mental health inpatient admissions and emergency department presentations) at considerably higher rates than the matched community controls. This is an important finding, as this pattern has been reported in psychiatric healthcare and in emergency healthcare, however not using the same cohort across a significant number of relevant services. It challenges the suggestion that it is primarily healthcare deficits which result in rising ‘probable suicide’ or DRD (Vasiliadis, Ngamini-Ngui and Lesage, 2015, van Amsterdam, van den Brink and Pierce, 2021).

Only a quarter of the ‘probable suicide’ cohort had a possible self-harm presentation to accident and emergency services. The definition constructed relied on a minor injury/poisoning/trauma category, due to the majority of the intent of injury fields being vacant. As such, it is possible that the antecedent rate of severe self-harm was higher than the rate identified in this study, however as the majority of self-harm is not severe enough to result in a hospital presentation (Zortea et al., 2020), this is an unavoidable underestimate if routine, administrative data is the only source utilised. More of the ‘probable suicide’ cohort received a type of psychiatric follow-up, in the 21 days after a presentation, compared to the control cohort, which implies a degree of successful targeting on the part of the healthcare service. As follow-up was still observed in less than half of the ‘probable suicide’ cohort, research into active outreach may be justified, though as yet, only inconclusive evidence on their efficacy has been reported (Brown and Green, 2014). Possible self-harm presentations were examined in the DRD and matched controls cohorts, and the only differences were that 30% of the DRD cohort had an attendance fulfilling the criteria, and just over half met criteria for psychiatric follow-up. Approximately half of those with follow-up were receiving OST, which may have artificially inflated psychiatric outpatient attendance closely after an emergency healthcare presentation. These results suggest that self-harm may be a more salient measure of DRD than is commonly acknowledged, which is particularly relevant to the recently demonstrated associations between suicidal ideation, both passive and active, and non-fatal overdose (Connery et al., 2019, Gicquelais et al., 2020).

The next sub-section compared all individuals with antidepressant prescriptions, split by ‘probable suicide’ or control status. Similarly, the DRD and control cohorts in OST were contrasted. This allowed for an investigation of whether there were differences between the deceased and controls, despite all being a (loosely defined) higher risk population. There were more consistent patterns that differentiated between the ‘probable suicide’ group and control cohort, than in the DRD-based comparison. For the ‘probable suicide’ cohort comparison, those who died were again associated with higher rates of healthcare usage and co-prescriptions than the controls. This is significant as it indicates that healthcare services are, to a degree, already stratifying individuals and targeting adjunctive treatment to those arguably most in need. While further research is needed to detail the treatment received and its efficacy, this is nonetheless a promising result.

Between the DRD and controls all receiving methadone OST prescriptions, the differences in healthcare usage were that those who died presented to emergency services more, and received more psychotropic co-prescriptions. Again, this would indicate that the more severe profile of illness was being recognised and targeted with a greater number of adjunctive prescriptions. The number of control individuals receiving a methadone prescription was very small, and so further research should examine whether these differences are consistent. Interestingly, the mean daily methadone dose was insignificantly different between groups, and was within the recommended clinical range of 60-120mg. Other than urine drug screens, which had similar mean positivity rates between groups, there were no data to suggest whether the dosage was efficacious or whether the DRD individuals might have required distinct doses; further research into optimising treatment and service responsiveness to patient needs would clarify the impact of OST provision on mortality risk.

A little over 40% of both the ‘probable suicide’ and DRD cohorts were in treatment for the condition most associated (in published literature) with these types of death: depression and opioid misuse. These were contrasted with the remainder of the ‘probable suicide’ and DRD cohorts to investigate sub-groups within these cohorts. As hypothesised, the individuals in the ‘probable suicide’ cohort with an antidepressant prescription were more engaged at healthcare services and received elevated rates of co-prescriptions than those without. Previous studies have suggested that individuals without recorded psychiatric illnesses, commonly men, may primarily have stressors around finances and employment (Hamdi et al., 2008, Mallon et al., 2019, Tang et al., 2022). There were no data to corroborate this, however future research using the local authority and criminal justice data could investigate these alternative stressors. Interestingly, there were few differences between the DRD in treatment and those not in methadone OST, other than elevated co-prescribing rates. That OST was not protective against emergency presentations was unexpected, as this has previously been reported (Lewer et al., 2020). This has been reported in profiles of individuals who inject drugs; thus, they may derive greater benefit from OST than those who use substances in other ways; the method of illicit drug consumption was unavailable in this sample, but may be an important avenue for refining sub-types of DRD.

Even fewer differences were noted when the deceased cohorts were split according to greater and lesser socio-economic deprivation, which was unexpected. Tayside is a relatively deprived area of Scotland; therefore, the healthcare usage may be more similar between quintiles. Additionally, many studies have been conducted in the States and the difference in healthcare cost at point-of-use will have a significant effect on healthcare usage. This may demonstrate the importance of models targeted to local areas, which could clarify the differential impact of the same risk factor.

Multivariate models predicting ‘probable suicide’ and DRD from the community cohort showed that healthcare attendance variables were associated with belonging to the deceased groups. The vast majority of the successful predictions were concerning the community control groups, illustrating that predictive models struggle to accurately identify individuals who go on to die, even in an enriched cohort. Pyramidal diagrams were constructed that likewise illustrated that the theoretically most predictive patterns (i.e., most intensive healthcare interventions) were present in relatively low levels of the deceased cohorts. This was further illustration for why predictive models, with non-specific risk factors that attempt to identify rare outcomes, may be numerically impossible when undertaken in the general population (Large, 2018).

7.3. Cluster Analysis

As summarised in the final section of the clustering analysis chapter, the literature analysis demonstrated that clustering studies using statistical methods were much more common in the field of ‘probable suicide’ compared to the DRD field. The variables included differed significantly, but generally included demographic and healthcare dimensions. Commonly identified clusters were ones with a history of psychiatric diagnosis, contrasted with those who had stressors more related to financial or relationship concerns. A recent review highlighted the need for improved taxonomies of ‘probable suicide’ (Bagley and Shahnaz, 2017), as did the key statistical clustering paper from the DRD field (Amundsen, 2015).

The analytical sub-section demonstrated that a variety of clusters could be extracted from the ‘probable suicide’, DRD and combined cohorts. Clusters from 2 to 10 were calculated in each cohort. A solution of 2 clusters fit the ‘probable suicide’ and combined cohorts best. Ten clusters suited the DRD cohort best, and so both the 2 and 10 cluster outputs were extracted from each cohort. The 2 clusters, in all 3 cohorts, were a low and high engagement group. This corroborates the patterns evident from the initial healthcare analyses chapters, that regularly demonstrated a split between those “in treatment” compared to those without, from the perspective of further healthcare usage. Furthermore, the demographic associations confirmed that the data contained patterns similar to those previously reported, in that women made up a greater proportion of the “in treatment” groups, while men formed the majority of the larger, out of treatment groups. These two profiles suggest that treatment strategies which are aimed only at improving the therapies on offer, or improving adherence to medication, will reach, at most 40% of the individuals who go on to die. Other preventative strategies, with a more universal reach will likely be key for notable reduction in both ‘probable suicide’ and DRD.

The 10-cluster analysis revealed three patterns that were broadly common to all the ‘probable suicide’, DRD and combined cohorts. These were a low healthcare engagement group, groups engaged with specific healthcare services, while the final group were highly engaged with the healthcare services. There were 4 clusters within the DRD cohort defined as high healthcare usage, compared to 3 of the combined cohort and only 2 of the ‘probable suicide’ cohort. Of specific interest were a group of women with high rates of antidepressant, OST and benzodiazepine prescriptions, as well as multiple emergency department presentations, that had cause of deaths codes fulfilling DRD criteria only. DRD in women has increased recently (Tweed et al., 2022), therefore the presence of this cluster corroborates calls for services to adapt to the changing patient demographics. These clusters could contribute to the development of taxonomies of ‘probable suicide’ and DRD, while also providing a method for services to investigate their local contexts and adapt accordingly.

7.4. Future Research

7.4.1. Avenues for further research, within the HIC sample

The cohort validation process could have created cohorts suited to a variety of sensitivity analyses. As noted in the cohort validation sections of the results chapters, a small number of individuals were included in each cohort, despite having the relevant ICD-10 codes not as the underlying cause of death. A large number of the 'probable suicide' cohort had relevant codes in the underlying cause of death category, however were missing from the ScotSID database. The majority of these individuals overlapped with the DRD cohort; thus, removing these individuals may have resulted in a greater divergence between the clustering analysis results of the 3 cohorts and may have identified distinct clusters. Additionally, 46 individuals in the 'probable suicide' cohort had missing demographic data, as did 8 of the DRD cohort. These individuals could each have been removed, and analyses re-run, to investigate the impact of their inclusion.

There were a variety of limitations, both during the data collection phase of the SIFT project and during the analytical phase. Evidently, the concerns around data completeness and the lack of data transfer from local authorities and Police Scotland prevented me from including various factors known to increase the risk of both 'probable suicide' and DRD (Higgins and Matthews, 2020). Data around homelessness and social factors like parental separation or adverse childhood events would add considerably more psychological detail to the analyses presented. These data are currently held within the Safe Haven for this sample, therefore additional attempts could be made to contact the relevant organisations to gather the necessary meta-data. Other cities, and countries, with similar data banks could likewise integrate these data analysis methods and improve the local understanding of the contributions of specific risk factors.

One particular limitation of the healthcare analysis is that primarily psychotropic prescriptions were considered. The complete bank of prescription records was a rich resource, and inclusion of key prescriptions like opioids for pain control or prescriptions indicating other physical illnesses would have allowed for further examination of important co-morbidities. If more time had been available, more of these prescriptions could have been operationalised into proxy representations of conditions related to 'probable suicide' or DRD. Of course, this would still be limited by a lack of diagnostic data, and would have introduced additional assumptions into the data.

Within the Safe Haven, there were healthcare usage records that included data on attendance at maternity services, diabetes clinics and cancer-related appointments. Each of these would have been useful contributions to further examine the difference between and within the deceased cohorts and the community controls. The limited sample size of the deceased cohorts meant that very few individuals would have attended at each service, therefore these analyses were not pursued. If the analyses were repeated in a larger sample size, these could have highlighted additional healthcare usage patterns that could be important to establish antecedent needs and opportunities for intervention.

7.4.2. Avenues for Further Research in the Wider Fields

One key aspect, highlighted throughout this thesis, is the need for clearer and more standardised definitions and terminology. That ICD-10 codes exist and have been almost universally accepted is no small feat. Yet, accurate comparisons in morbidity and mortality are hampered by the lack of overarching theories of ‘probable suicide’ or DRD, and therefore, by varied definitions between countries. Especially in the field of DRD, this is an urgent concern, as the current implicit understanding is that these deaths are related to illicit substances only; as countries diverge on continued criminalisation, decriminalisation and legalisation, this focus may no longer be viable. There have already been calls to improve the terminology used (Goodfellow, Kõlves and Leo, 2019, Rockett et al., 2014) which would improve the general field of research and hypothesis testing.

Longitudinal studies, both those based on record-linkage and smaller-scale in-depth prospective studies, would clarify the true prevalence of key risk factors for ‘probable suicide’ and DRD. These could incorporate several arms: those in treatment, who would be split at the end of the study to investigate potential differences in treatment or healthcare needs resulting in death or survival, and/or matched community controls that could likewise be analysed. The smaller-scale studies could investigate qualitatively what might trigger high and low risk periods and what types of interventions are successful in these contexts, depending on distinct patient profiles.

Urgent research is necessary to improve the ability of the field to reduce self-injurious thoughts and behaviours and prevent overdoses. That 50 years of research have elapsed without significant improvement in therapies that reduce self-harm, and that many severe episodes of self-harm are poisoning events, is of serious concern (Fox et al., 2020). There are many avenues available for research, from ecological studies examining rapid changes in suicidal ideation (Kleiman et al., 2017), to studies examining rates of antidepressant, OST and other psychotropic prescriptions at a national level and examining the impact of these treatments upon mortality rates (Degenhardt et al., 2019 (b), Larsson, 2017, Landolt et al., 2021). These avenues all contribute to our understanding of patient needs and healthcare usage, ideally improving our ability to design and implement successful interventions, though we may need to being by acknowledging how non-specific our knowledge of risk factors currently is.

Additionally, to test the long-term stability of the profiles identified in clustering analyses, longitudinal studies could run analyses at distinct points in the duration of the study. As another test of cluster stability, and whether interventions applied affect the extant clusters, it would be valuable to run a clustering algorithm within a population, apply an intervention and then apply the same clustering algorithm. This would clarify the accuracy of the suggestion that limiting access to means reduces the number of individuals who die by 'probable suicide' in a method-specific manner, as individuals have been reported not to progress to other methods (Lim et al., 2021). It could likewise identify whether seizures of illicit substances reduce DRD or whether alternative substances are procured instead.

7.5. Final Conclusions

Overall, this thesis has demonstrated the merits of routine, administrative data for furthering the understanding of antecedent healthcare usage patterns for both ‘probable suicide’ and DRD cohorts. Many comparisons were made, from different perspectives, each with their own contribution to elucidating the differences between the deceased cohorts and matched controls, as well as within the deceased cohorts. The data has demonstrated repeatedly that these individuals attend healthcare services at higher rates than the community controls, generally receive elevated rates of psychotropic co-prescription than community controls receiving the same indicated prescriptions, and that there are within-group distinctions, based on high or low engagement with other healthcare services. The clustering analysis emphasised the similarity between the ‘probable suicide’ and DRD cohorts, while identifying sub-groups that may present novel targets for additional support and alternative interventions. These results do not suggest that the healthcare service fails to identify those at-risk, but that the interventions themselves provide only small reductions in mortality. Further work will be required to standardise the terminology and definitions used in both fields, and developments and standardisations in the field of routine data transformation will be required to ensure replicability of results. Research into patient needs and profiles should continue to highlight areas for which interventions can be designed and trialled, leading to more successful preventative measures in future.

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Appendix 1 List of ICD-10 codes removed from the 'Probable Suicide' Cohort

ICD-10	Definition	Number of Cases
F10.2	Alcohol dependence	1
E10.9	Type 1 Diabetes Mellitus without complications	1
K72.9	Hepatic failure, unspecified	1
W65	Accidental drowning and submersion while in the bath-tub	1
X44	Accidental poisoning by or exposure to other and unspecified drugs, medicaments or biological substances	1
Y01	Assault by pushing from a high place	1
I25.1	Atherosclerotic heart disease of native coronary artery	3
V04.1	Pedestrian injured in collision with a heavy transport vehicle or bus	2
R99	Ill-defined and unknown cause of mortality	6
No code		2
		Total = 19/295

ICD-10 codes of the individuals removed from the 'probable suicide' cohort, all originating from ScotSID. ICD-10 codes are internationally standardised medical causes of death codes and form the basis of statistical cause of death reports.

Appendix 2 Drug-Related Death individuals who were excluded from the cohort

2a. Individuals excluded from the cohort, that were present in all 3 databases

ICD-10	Definition	Number of Cases
I38	Endocarditis, valve unspecified	1
I80.2	Phlebitis and thrombophlebitis of other deep vessels of unspecified lower extremity	1
R99	Ill-defined and unknown cause of mortality	4
		Total = 6/206

ICD-10 codes of the individuals removed from the drug-related death cohort, present in all three mortality databases. ICD-10 codes are internationally standardised medical causes of death codes and form the basis of statistical cause of death reports.

2b. Individuals excluded from the cohort, that were present in the National Records of Scotland and the National Drug-Related Death Database

ICD-10	Definition	Number of Cases
F10.2	Alcohol Dependence	4
I25.1	Atherosclerotic heart disease of the native coronary artery	1
J44.8	Other specified chronic obstructive pulmonary disease	1
R99	Ill-defined and unknown cause of mortality	4
		Total = 10/17

ICD-10 codes of the individuals removed from the drug-related death cohort, present in two data feeds: the National Records of Scotland and National Drug-Related Death Databases. ICD-10 codes are internationally standardised medical causes of death codes and form the basis of statistical cause of death reports.

2c. Individuals excluded from the cohort, that were present in the National Records of Scotland and the Tayside Drug-Related Death Database

ICD-10	Definition	Number of Cases
I25.1	Atherosclerotic heart disease of native coronary disease	1
I51.7	Cardiomegaly	1
J44.8	Other specified chronic obstructive pulmonary disease	2
Q20.3	Discordant ventriculoarterial connection	1
R99	Ill-defined and unknown cause of mortality	2
		Total = 7/33

ICD-10 codes of the individuals removed from the drug-related death cohort, present in two data feeds: the National Records of Scotland and Tayside Drug-Related Death Databases. ICD-10 codes are internationally standardised medical causes of death codes and form the basis of statistical cause of death reports.

Appendix 3 R code for the Clustering Algorithm

After data has been read in and packages installed and loaded.

```
# Standardise variables and calculate Gower distances

gower_dist <- daisy(dataframe, metric=”gower”)

# Calculate the Silhouette Width of the actual sample

sil_width <- c(NA)

for(i in 2:10){
  pam_fit <- pam(gower_dist, diss = TRUE, k = i)
  sil_width[i] <- pam_fit$silinfo$avg.width
}

plot(1:10, sil_width, xlab=”Number of Clusters”,
ylab=”Average Silhouette Width”)

lines(1:10, sil_width)

# Extract the summaries of the individual clusters

k <- 2

pam_fit <- pam(gower_dist, diss = TRUE, k)

pam_results <- dataframe %>%
  mutate(cluster = pam_fit$clustering) %>%
  group_by(cluster) %>%
  do(the_summary = summary(.))

pam_results$the_summary

# Visualise the clusters

tsne_obj <- Rtsne(gower_dist, is_distance = TRUE)

tsne_data <- tsne_obj$Y %>%
  data.frame() %>%
  setNames(c("X", "Y")) %>%
  mutate(cluster = factor(pam_fit$clustering))

ggplot(aes(x = X, y = Y), data = tsne_data) +
  geom_point(aes(color = cluster))
```

```
# Bootstrap the Silhouette Width Calculation and extract
95% CI

silf1 <- function(formula, data, indices) {
  val <- data[indices,]
  gv <- daisy(val, metric="gower")
  silw1 <- c(NA)
  (for(i in 2:10) {
    pf1 <- pam(gv, diss=TRUE, k=i)
    silw1[i] <- pf1$silinfo$avg.width
  })
  return(silw1)
}

output <- boot(data=dataframe, statistic=silf1, R=10000,
formula=pf1$silinfo$avg.width)

boot.ci(output, conf=0.95, type="all", index=2)
# Repeat above code for indexes up to 10
```

Appendix 4 R Cluster Outputs for the 'Probable Suicide' Cohort

2 clusters in the 'Probable Suicide' cohort

Table a1. Cluster 1 – Silhouette width = 0.4543018

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 306	Female 75				18
Age Group	2	2	2.129	3	1-3	18
SIMD	1	2	2.681	4	1-5	39
Type of Death	1	1	1.183	1	1-2	
Antidepressant	0	0	0.1855	0	0-1	
Methadone	0	0	0.0802	0	0-1	
Benzodiazepine	0	0	0.03509	0	0-1	
Psychiatric Outpatient Attendances	0	0	1.401	0	0-86	
Accident and Emergency Presentations	0	0	0.7243	1	0-17	

Descriptive summary of cluster 1 in 2 clusters in the 'probable suicide' cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – 'probable suicide' only, 2 – overlap with DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table a2. Cluster 2 – Silhouette width = 0.2403713

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 112	Female 73				2
Age Group	2	2	2.097	2	1-3	2
SIMD	1	2	2.194	3	1-5	7
Type of Death	1	2	1.663	2	1-2	
Antidepressant	1	1	0.9626	1	0-1	
Methadone	0	0	0.3476	1	0-1	
Benzodiazepine	0	1	0.6203	1	0-1	
Psychiatric Outpatient Attendances	0	2	5.882	8	0.62	
Accident and Emergency Presentations	0	1	1.631	2	0-17	

Descriptive summary of cluster 2 in 2 clusters in the 'probable suicide' cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – 'probable suicide' only, 2 – overlap with DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

10 Clusters in the 'Probable Suicide' Cohort

Table b1. Cluster 1 – Silhouette width = 0.3911500

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 43	Female 1				8
Age Group	2	2	2.273	3	1-3	8
SIMD	2	3	2.791	4	1-5	9
Type of Death	1	1	1	1	1	
Antidepressant	1	1	1	1	1	
Methadone	0	0	0.01923	0	0-1	
Benzodiazepine	0	0	0	0	0	
Psychiatric Outpatient Attendances	0	0	2.25	2	0-47	
Accident and Emergency Presentations	0	1	1.058	2	0-9	

Descriptive summary of cluster 1 in 10 clusters in the 'probable suicide' cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – 'probable suicide' only, 2 – overlap with DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table b2. Cluster 2 – Silhouette width = 0.3668695

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 0	Female 34				
Age Group	2	3	2.588	3	1-3	
SIMD	4	4	4	5	2-5	1
Type of Death	1	1	1.118	1	1-2	
Antidepressant	1	1	0.9706	1	0-1	
Methadone	0	0	0	0	0	
Benzodiazepine	1	1	0.7647	1	0-1	
Psychiatric Outpatient Attendances	0	1.5	5.529	5	0-62	
Accident and Emergency Presentations	0	1	1.471	1	0-15	

Descriptive summary of cluster 2 in 10 clusters in the 'probable suicide' cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – 'probable suicide' only, 2 – overlap with DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table b3. Cluster 3 – Silhouette width = 0.3760361

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 132	Female 0				
Age Group	1	2	1.727	2	1-2	
SIMD	2	3	2.802	4	1-5	11
Type of Death	1	1	1	1	1	
Antidepressant	0	0	0	0	0	
Methadone	0	0	0.0303	0	0-1	
Benzodiazepine	0	0	0.0303	0	0-1	
Psychiatric Outpatient Attendances	0	0	1.023	0	0-86	
Accident and Emergency Presentations	0	0	0.4697	1	0-5	

Descriptive summary of cluster 3 in 10 clusters in the 'probable suicide' cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – 'probable suicide' only, 2 – overlap with DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table b4. Cluster 4 – Silhouette width = 0.6186618

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 63	Female 0				
Age Group	3	3	3	3	3	
SIMD	2	3	3.1	3	1-5	3
Type of Death	1	1	1	1	1	
Antidepressant	0	0	0	0	0	
Methadone	0	0	0	0	0	
Benzodiazepine	0	0	0.04762	0	0-1	
Psychiatric Outpatient Attendances	0	0	0.3175	0	0-7	
Accident and Emergency Presentations	0	0	0.381	1	0-2	

Descriptive summary of cluster 4 in 10 clusters in the 'probable suicide' cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – 'probable suicide' only, 2 – overlap with DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table b5. Cluster 5 – Silhouette width = 0.0424792

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 0	Female 62				8
Age Group	2	2	2.129	3	1-3	8
SIMD	1	2	2.712	4	1-5	11
Type of Death	1	1	1.129	1	1-2	
Antidepressant	0	0	0.1857	0	0-1	
Methadone	0	0	0.01429	0	0-1	
Benzodiazepine	0	0	0.02857	0	0-1	
Psychiatric Outpatient Attendances	0	0	1.286	0	0-23	
Accident and Emergency Presentations	0	0	0.5857	1	0-5	

Descriptive summary of cluster 5 in 10 clusters in the 'probable suicide' cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – 'probable suicide' only, 2 – overlap with DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table b6. Cluster 6 – Silhouette width = 0.1951426

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 50	Female 2				2
Age Group	2	2	2.25	3	1-3	2
SIMD	1	2	2.353	3.5	5	3
Type of Death	1	1	1.222	1	1-2	
Antidepressant	1	1	0.9444	1	0-1	
Methadone	0	0	0.1481	0	0-1	
Benzodiazepine	1	1	1	1	1	
Psychiatric Outpatient Attendances	0	1	5.519	6.750	0-58	
Accident and Emergency Presentations	0	1	1.926	2	0-17	

Descriptive summary of cluster 6 in 10 clusters in the 'probable suicide' cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – 'probable suicide' only, 2 – overlap with DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table b7. Cluster 7 – Silhouette width = 0.3685809

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 10	Female 32				
Age Group	2	2	2.024	2	1-3	
SIMD	1	1	1.3	2	1-3	2
Type of Death	2	2	1.905	2	1-2	
Antidepressant	1	1	1	1	1	
Methadone	1	1	0.9048	1	0-1	
Benzodiazepine	0	1	0.7143	1	0-1	
Psychiatric Outpatient Attendances	3	8	10.07	14	0-33	
Accident and Emergency Presentations	0	0.5	1.524	2	0-14	

Descriptive summary of cluster 7 in 10 clusters in the 'probable suicide' cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – 'probable suicide' only, 2 – overlap with DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table b8. Cluster 8 – Silhouette width = 0.1898088

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 35	Female 3				2
Age Group	2	2	2	2	1-3	2
SIMD	1	1	1.432	2	1-4	3
Type of Death	2	2	1.875	2	1-2	
Antidepressant	0	0	0.325	1	0-1	
Methadone	1	1	1	1	1	
Benzodiazepine	0	0	0.125	0	0-1	
Psychiatric Outpatient Attendances	1	2	6.075	9.250	0-30	
Accident and Emergency Presentations	0	1	1.475	2	0-15	

Descriptive summary of cluster 8 in 10 clusters in the 'probable suicide' cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – 'probable suicide' only, 2 – overlap with DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table b9. Cluster 9 – Silhouette width = 0.2676851

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 36	Female 14				
Age Group	2	2	1.86	2	1-3	
SIMD	1	2	2.14	2	1-5	
Type of Death	2	2	2	2	2	
Antidepressant	1	1	1	1	1	
Methadone	0	0	0.1	0	0-1	
Benzodiazepine	0	0	0.06	0	0-1	
Psychiatric Outpatient Attendances	0	1	2.1	2	0-20	
Accident and Emergency Presentations	0	0	1.22	1.75	0-9	

Descriptive summary of cluster 9 in 10 clusters in the ‘probable suicide’ cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – ‘probable suicide’ only, 2 – overlap with DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table b10. Cluster 10 – Silhouette width = 0.5665325

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 49	Female 0				
Age Group	2	2	1.857	2	1-3	
SIMD	1	2	1.978	2.750	1-5	3
Type of Death	2	2	2	2	2	
Antidepressant	0	0	0	0	0	
Methadone	0	0	0	0	0	
Benzodiazepine	0	0	0.06122	0	0-1	
Psychiatric Outpatient Attendances	0	0	0.8163	1	0-13	
Accident and Emergency Presentations	0	0	1.51	1	0-17	

Descriptive summary of cluster 10 in 10 clusters in the ‘probable suicide’ cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – ‘probable suicide’ only, 2 – overlap with DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Appendix 5 R Cluster Output for the Drug-Related Death Cohort

2 Clusters in the DRD cohort

Table c1. Cluster 1 – Silhouette width = 0.3415123

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 138	Female 38				
Age Group	2	2	1.881	2	1-3	
SIMD	1	2	1.982	3	1-5	5
Type of Death	1	2	1.682	2	1-2	
Antidepressant	0	0	0.2955	1	0-1	
Methadone	0	0	0.2102	0	0-1	
Benzodiazepine	0	0	0.03409	0	0-1	
Psychiatric Outpatient Attendances	0	0	2.534	2	0-41	
Accident and Emergency Presentations	0	1	1.29	2	0-17	

Descriptive summary of cluster 1 in 2 clusters in the DRD cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – overlap with suicide. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table c2. Cluster 2 – Silhouette width = 0.2797502

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 67	Female 45				
Age Group	2	2	2	2	1-3	
SIMD	1	1	1.651	2	1-5	3
Type of Death	1	2	1.688	2	1-2	
Antidepressant	1	1	0.9554	1	0-1	
Methadone	0	1	0.7232	1	0-1	
Benzodiazepine	0	1	0.6339	1	0-1	
Psychiatric Outpatient Attendances	1	4.5	8.429	12	0-58	
Accident and Emergency Presentations	0	1	2.321	2	0-44	

Descriptive summary of cluster 2 in 2 clusters in the DRD cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – overlap with suicide. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

10 Clusters in the DRD cohort

Table d1. Cluster 1 – Silhouette width = 0.5769783

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 30	Female 0				
Age Group	2	2	1.967	2	1-3	
SIMD	1	2	2.433	3	1-5	
Type of Death	2	2	1.933	2	1-2	
Antidepressant	1	1	1	1	1	
Methadone	0	0	0	0	0	
Benzodiazepine	0	0	0	0	0	
Psychiatric Outpatient Attendances	0	0.5	1.867	2	0-20	
Accident and Emergency Presentations	0	0	0.8333	1	0-7	

Descriptive summary of cluster 1 in 10 clusters in the DRD cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – overlap with suicide. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table d2. Cluster 2 – Silhouette width = 0.3486791

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 28	Female 5				
Age Group	2	2	1.848	2	1-3	
SIMD	1	1	1.758	2	1-5	
Type of Death	1	1	1	1	1	
Antidepressant	0	0	0.1212	0	0-1	
Methadone	0	0	0	0	0	
Benzodiazepine	0	0	0.06061	0	0-1	
Psychiatric Outpatient Attendances	0	0	0.5455	0	0-9	
Accident and Emergency Presentations	0	1	0.9394	2	0-4	

Descriptive summary of cluster 2 in 10 clusters in the DRD cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – overlap with suicide. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table d3. Cluster 3 – Silhouette width = 0.1662438

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 6	Female 14				
Age Group	2	2	2.1	2	1-3	
SIMD	1	2	1.842	2	1-5	1
Type of Death	1	1	1	1	1	
Antidepressant	1	1	0.9	1	0-1	
Methadone	1	1	0.8	1	0-1	
Benzodiazepine	1	1	0.85	1	0-1	
Psychiatric Outpatient Attendances	3	4	9.75	14.75	0-33	
Accident and Emergency Presentations	0	1	3.15	3	0-20	

Descriptive summary of cluster 3 in 10 clusters in the DRD cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – overlap with suicide. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table d4. Cluster 4 – Silhouette width = 0.4252102

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 19	Female 3				
Age Group	2	2	2.045	2	2-3	
SIMD	1	2	1.905	2	1-4	1
Type of Death	1	1	1	1	1	
Antidepressant	0	0	0.1818	0	0-1	
Methadone	1	1	1	1	1	
Benzodiazepine	0	0	0	0	0	
Psychiatric Outpatient Attendances	3.25	9.50	10.73	16	0-41	
Accident and Emergency Presentations	0	1	1.818	2.750	0-11	

Descriptive summary of cluster 4 in 10 clusters in the DRD cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – overlap with suicide. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table d5. Cluster 5 – Silhouette width = 0.1782311

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 24	Female 5				
Age Group	2	2	2.034	2	1-3	
SIMD	1	2	2.207	3	1-5	
Type of Death	2	2	1.828	2	1-2	
Antidepressant	1	1	0.931	1	0-1	
Methadone	0	0	0.1034	0	0-1	
Benzodiazepine	1	1	1	1	1	
Psychiatric Outpatient Attendances	0	1	5.931	6	0-58	
Accident and Emergency Presentations	0	0	2.552	2	0-44	

Descriptive summary of cluster 5 in 10 clusters in the DRD cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – overlap with suicide. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table d6. Cluster 6 – Silhouette width = 0.2557609

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 0	Female 24				
Age Group	1	1	1.583	2	1-3	
SIMD	1	1	1.917	2	1-5	
Type of Death	2	2	1.875	2	1-2	
Antidepressant	1	1	0.7917	1	0-1	
Methadone	0	0	0	0	0	
Benzodiazepine	0	0	0.04167	0	0-1	
Psychiatric Outpatient Attendances	0	0	1.083	1	0-7	
Accident and Emergency Presentations	0	1	1.458	2	0-9	

Descriptive summary of cluster 6 in 10 clusters in the DRD cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – overlap with suicide. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table d7. Cluster 7 – Silhouette width = 0.3028156

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 26	Female 4				
Age Group	2	2	1.933	2	1-3	
SIMD	1	1	1.233	1	1-2	
Type of Death	2	2	1.8	2	1-2	
Antidepressant	1	1	1	1	1	
Methadone	1	1	1	1	1	
Benzodiazepine	0	0	0.06667	0	0-1	
Psychiatric Outpatient Attendances	1	3	6.167	8	0-29	
Accident and Emergency Presentations	0	1	2.167	2	0-15	

Descriptive summary of cluster 7 in 10 clusters in the DRD cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – overlap with suicide. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table d8. Cluster 8 – Silhouette width = 0.5455703

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 48	Female 3				
Age Group	2	2	1.843	2	1-3	
SIMD	1	2	2.042	3	1-5	3
Type of Death	2	2	2	2	2	
Antidepressant	0	0	0	0	0	
Methadone	0	0	0	0	0	
Benzodiazepine	0	0	0.03922	0	0-1	
Psychiatric Outpatient Attendances	0	0	0.7647	0	0-13	
Accident and Emergency Presentations	0	0	1.471	1	0-17	

Descriptive summary of cluster 8 in 10 clusters in the DRD cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – overlap with suicide. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table d9. Cluster 9 – Silhouette width = 0.4954653

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 19	Female 3				
Age Group	2	2	2.045	2	1-3	
SIMD	1	2	1.762	2	1-4	1
Type of Death	2	2	2	2	2	
Antidepressant	0	0	0	0	0	
Methadone	1	1	1	1	1	
Benzodiazepine	0	0	0.1364	0	0-1	
Psychiatric Outpatient Attendances	1	2	5.182	4	0-30	
Accident and Emergency Presentations	0	0.50	1.182	2	0-8	

Descriptive summary of cluster 9 in 10 clusters in the DRD cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – overlap with suicide. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table d10. Cluster 10 – Silhouette width = 0.3570043

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 5	Female 22				
Age Group	2	2	2	2	2	
SIMD	1	1	1.24	1	1-3	2
Type of Death	2	2	2	2	2	
Antidepressant	1	1	1	1	1	
Methadone	1	1	0.9259	1	0-1	
Benzodiazepine	1	1	0.7778	1	0-1	
Psychiatric Outpatient Attendances	7	9	12.93	19.50	0-33	
Accident and Emergency Presentations	0	1	1.963	2	0-14	

Descriptive summary of cluster 10 in 10 clusters in the DRD cohort, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – overlap with suicide. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Appendix 6 R Cluster Output for the Combined Cohorts

2 Clusters in Combined Cohorts

Table e1. Cluster 1 – Silhouette width = 0.4269603

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 413	Female 58				15
Age Group	2	2	2.062	2	1-3	15
SIMD	1	2	2.482	4	1-5	38
Type of Death	2	2	2.128	3	1-3	
Antidepressant	0	0	0.2263	0	0-1	
Methadone	0	0	0.1626	0	0-1	
Benzodiazepine	0	0	0.04115	0	0-1	
Psychiatric Outpatient Attendances	0	0	1.893	1	0-86	
Accident and Emergency Presentations	0	0	0.8971	1	0-17	

Descriptive summary of cluster 1 in 2 clusters using all individuals, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – 'probable suicide' only, 3 – overlap with both 'probable suicide' and DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table e2. Cluster 2 – Silhouette width = 0.2693989

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 71	Female 115				5
Age Group	2	2	2.188	2.75	1-3	5
SIMD	1	2	2.276	4	1-5	10
Type of Death	2	2	2.23	3	1-3	
Antidepressant	1	1	0.9738	1	0-1	
Methadone	0	0	0.3246	1	0-1	
Benzodiazepine	0	1	0.7016	1	0-1	
Psychiatric Outpatient Attendances	0	3	6.586	8	0-62	
Accident and Emergency Presentations	0	1	1.974	2	0-44	

Descriptive summary of cluster 2 in 2 clusters using all individuals, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – 'probable suicide' only, 3 – overlap with both 'probable suicide' and DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

10 Clusters in Combined Cohorts

Table f1. Cluster 1 – Silhouette width = 0.4127464

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 71	Female 0				2
Age Group	2	2	2.07	2	1-3	2
SIMD	1	2	2.357	3	1-5	3
Type of Death	2	2	2.288	3	1-3	
Antidepressant	1	1	1	1	1	
Methadone	0	0	0	0	0	
Benzodiazepine	0	0	0	0	0	
Psychiatric Outpatient Attendances	0	0	1.685	2	0-20	
Accident and Emergency Presentations	0	0	0.9178	1	0-9	

Descriptive summary of cluster 1 in 10 clusters using all individuals, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – 'probable suicide' only, 3 – overlap with both 'probable suicide' and DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table f2. Cluster 2 – Silhouette width = 0.3308059

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 193	Female 0				
Age Group	1	2	1.746	2	1-2	
SIMD	1	2	2.525	4	1-5	14
Type of Death	2	2	2.124	2	1-3	
Antidepressant	0	0	0	0	0	
Methadone	0	0	0	0	0	
Benzodiazepine	0	0	0.03627	0		
Psychiatric Outpatient Attendances	0	0	0.3731	0	0-13	
Accident and Emergency Presentations	0	0	0.715	1	0-17	

Descriptive summary of cluster 2 in 10 clusters using all individuals, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – 'probable suicide' only, 3 – overlap with both 'probable suicide' and DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table f3. Cluster 3 – Silhouette width = 0.5428930

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 0	Female 35				
Age Group	2	2	2.371	3	1-3	
SIMD	2	4	3.344	4.250	1-5	3
Type of Death	2	2	2.086	2	1-3	
Antidepressant	1	1	1	1	1	
Methadone	0	0	0	0	0	
Benzodiazepine	1	1	1	1	1	
Psychiatric Outpatient Attendances	1	2	6.029	6	0-62	
Accident and Emergency Presentations	0	1	2.057	2.5	0-15	

Descriptive summary of cluster 3 in 10 clusters using all individuals, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – 'probable suicide' only, 3 – overlap with both 'probable suicide' and DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table f4. Cluster 4 – Silhouette width = 0.3491233

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 41	Female 4				3
Age Group	2	2	2.044	2	1-3	3
SIMD	1	2	1.814	2	1-4	5
Type of Death	1	2	2.083	3	1-3	
Antidepressant	0	0	0	0	0	
Methadone	1	1	1	1	1	
Benzodiazepine	0	0	0.1042	0	0-1	
Psychiatric Outpatient Attendances	1	3	7.562	11.250	0-41	
Accident and Emergency Presentations	0	1	1.458	2	0-11	

Descriptive summary of cluster 4 in 10 clusters using all individuals, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – 'probable suicide' only, 3 – overlap with both 'probable suicide' and DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table f5. Cluster 5 – Silhouette width = 0.2609895

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 0	Female 57				7
Age Group	1	2	2.035	3	1-3	7
SIMD	1	3	2.759	4	1-5	10
Type of Death	2	2	2.062	2	1-3	
Antidepressant	0	0	0	0	0	
Methadone	0	0	0.03125	0	0-1	
Benzodiazepine	0	0	0.04688	0	0-1	
Psychiatric Outpatient Attendances	0	0	0.6875	0	0-16	
Accident and Emergency Presentations	0	0	0.4531	0.25	0-4	

Descriptive summary of cluster 5 in 10 clusters using all individuals, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – 'probable suicide' only, 3 – overlap with both 'probable suicide' and DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table f6. Cluster 6 – Silhouette width = 0.2275577

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 66	Female 0				1
Age Group	2	2	2.197	2	1-3	1
SIMD	1	2	2.338	3	1-5	2
Type of Death	2	2	2.075	2	1-3	
Antidepressant	1	1	0.9254	1	0-1	
Methadone	0	0	0.194	0	0-1	
Benzodiazepine	1	1	1	1	1	
Psychiatric Outpatient Attendances	0	1	6.985	8	0-86	
Accident and Emergency Presentations	0	1	2.746	2	0-44	

Descriptive summary of cluster 6 in 10 clusters using all individuals, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – 'probable suicide' only, 3 – overlap with both 'probable suicide' and DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table f7. Cluster 7 – Silhouette width = 0.2412228

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 0	Female 44				6
Age Group	2	2	2.136	3	1-3	6
SIMD	1	2	2.182	3.250	1-5	6
Type of Death	2	2	2.18	3	1-3	
Antidepressant	1	1	1	1	1	
Methadone	0	0	0.1	0	0-1	
Benzodiazepine	0	0	0	0	0	
Psychiatric Outpatient Attendances	0	1	3.64	3	0-47	
Accident and Emergency Presentations	0	1	1.32	2	0-9	

Descriptive summary of cluster 7 in 10 clusters using all individuals, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – 'probable suicide' only, 3 – overlap with both 'probable suicide' and DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table f8. Cluster 8 – Silhouette width = 0.2762102

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 6	Female 30				1
Age Group	2	2	2.028	2	1-3	1
SIMD	1	1	1.343	2	1-3	2
Type of Death	2	3	2.541	3	1-3	
Antidepressant	1	1	0.9459	1	0-1	
Methadone	1	1	1	1	1	
Benzodiazepine	1	1	0.8108	1	0-1	
Psychiatric Outpatient Attendances	4	9	12.54	18	0-33	
Accident and Emergency Presentations	0	0	2	2	0-19	

Descriptive summary of cluster 8 in 10 clusters using all individuals, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – 'probable suicide' only, 3 – overlap with both 'probable suicide' and DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table f9. Cluster 9 – Silhouette width = 0.3975315

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 33	Female 3				
Age Group	2	2	1.917	2	1-2	
SIMD	1	1	1.528	2	1-5	
Type of Death	1	3	2.417	3	1-3	
Antidepressant	1	1	1	1	1	
Methadone	1	1	1	1	1	
Benzodiazepine	0	0	0.1111	0	0-1	
Psychiatric Outpatient Attendances	1	3	6.25	8.25	0-29	
Accident and Emergency Presentations	0	1	1.944	2	0-15	

Descriptive summary of cluster 9 in 10 clusters using all individuals, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – 'probable suicide' only, 3 – overlap with both 'probable suicide' and DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.

Table f10. Cluster 10 – Silhouette width = 0.4998489

	Quartile 1	Median	Mean	Quartile 3	Range	N/A
Sex	Male 74	Female 0				
Age Group	3	3	3	3	3	
SIMD	2	3	3.141	4	1-5	3
Type of Death	2	2	2.014	2	1-3	
Antidepressant	0	0	0.06757	0	0-1	
Methadone	0	0	0	0	0	
Benzodiazepine	0	0	0.04054	0	0-1	
Psychiatric Outpatient Attendances	0	0	0.3514	0	0-7	
Accident and Emergency Presentations	0	0	0.5811	1	0-9	

Descriptive summary of cluster 10 in 10 clusters using all individuals, as printed by R. Age group signifies 1 – those 25 years old or younger, 2 – 26-50 years old, and 3 – those 51 years old or older. SIMD is categorised from 1 (highest deprivation) to 5 (lowest deprivation). Type of death represents 1 – DRD only, 2 – 'probable suicide' only, 3 – overlap with both 'probable suicide' and DRD. Antidepressant, methadone and benzodiazepine prescriptions were categorised as ever (1) or never (0). A small number of individuals lacked some demographic data, hence the missing values in sex, age and SIMD.